Rapid Organocatalytic Formation of Carbon Monoxide: Application towards Carbonylative Cross Couplings

Ben Zoller,[a] Josef Zapp,[b] and Peter H. Huy*[a]
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1 Method Development

1.1 Optimization of Carbonylative Amide Synthesis (Scheme 2 A-D)

Based on the procedure of the group of Skrydstrup, in which SilaCOgen 2 was applied as CO surrogate,[1] the reaction conditions were optimized for the preparation of amide 10a with ex situ formation of CO from formic acid (Table S1). Under otherwise identical conditions SilaCOgen could be replaced through formic acid as CO source (entry 1).

Table S1. Optimization of reaction conditions of the synthesis of amide 10a.

| entry | deviations from scheme | solvent | conv. (1) [%] | y. 10a(2) [%] | lab journal no. |
|-------|------------------------|---------|---------------|---------------|----------------|
| 1a    | 2.0 equiv 9a, Pd(dba)2, 10 mol% PPh3, 4 equiv NEt3, [8a] = 0.15 M | dioxane | ≥98 | 81 | BZ066 |
| 2     | 2.0 equiv 9a, Pd(dba)2, 10 mol% PPh3, 4 equiv NEt3 | toluene | " | 84 | BZ061 |
| 3     | 2.0 equiv 9a, 10 mol% PPh3, 4 equiv NEt3 | dioxane | " | 83 | BZ060 |
| 4     | / | toluene | " | 81 | BZ182 |
| 5     | DMF instead of FPyr | " | " | 76 | BZ080 |
| 6     | 20 mol% DMF instead of 10 mol% FPyr | " | " | 85b | PH4246 |
| 7     | / | EtOAc | " | 77 | BZ063 |
| 8     | 1.5 equiv NEt3 | toluene | 60 | 48 | BZ076 |
| 9     | 60 °C, 2.0 equiv 12a | " | 58 | 29 | BZ067 |
| 10    | no CO formation | / | ≤2 | / | B074 |

According to general protocol 1 (chapter 0 on page 25) 1-iodo-4-methoxybenzene (117 mg, 0.50 mmol, 1.0 equiv) and butylamine (0.75-1.0 mmol, 1.5-2 equiv) were transformed into amide 10a by means of Pd(dba)2 or Pd(OAc)2 (10 μmol, 2 mol%), PPh3 (30-50 μmol, 6-10 mol%), NEt3 (0.75-2.0 mmol, 1.5-4 equiv) in the solvent (0.15-1 M) through heating to 80 °C for 15-22 h. Yields were determined with the aid of dibenzyl ether as internal NMR standard. Thereby, CO was formed from formic acid (0.75 mmol, 1.5 equiv), FPyr (10 mol%) and TCT (57 mol%) in the given solvent (2 M with respect to 6). a. [6] = 0.25 M. b. Isolated yield after chromatography using 1.00 mmol of para-iodoanisol.

(1) The conversion was determined from the ratio of the singlets of 10a at 3.83 ppm and of 8a at 3.77 ppm (3H) in the 1H-NMR spectra of the crude materials.
(2) The yield was determined from the 1H-NMR spectra of the crude products with the aid of dibenzylether as internal standard (s, 4H at 4.56 ppm) under reference to the above-mentioned singlets.
In order to neutralize HCl released in the CO chamber, the amount of NEt$_3$ was increased from 2 to 4 equiv in comparison to the literature.

The concentration of the yield-limiting starting material 8a could be raised from 0.15 to 1 M, which is advantageous in terms of scalability (and sustainability, see entry 2). Simultaneously, the solvent dioxane was replaced by less toxic toluene. In addition, Pd(dba)$_2$ could be exchanged by simpler Pd(OAc)$_2$ (entry 3). Finally, the amount of PPh$_3$ and NEt$_3$ were reduced from 10 to 6 mol% and 4 to 3 equiv, respectively (entry 4).

FPyr can also be substituted by plain DMF (entry 5). 20 mol% of DMF were required to match the efficiency of 10 mol% FPyr (entry 6). Instead of toluene even more environmentally friendly EtOAc can be engaged as solvent (entry 7). Importantly, 1.5 equiv of NEt$_3$ are not sufficient, because the amide 10a was formed in only 48% yield (entry 8). Furthermore, at 60 °C a low conversion of the starting iodoarene 8a was attained (entry 9). Notably, without reaction of formic acid and TCT in the presence of FPyr no product 10a was generated at all (entry 10).

In the following, the scope of solvents for both, CO and amide 10a production, was examined more closely based on the conditions in entry 4 in Table S1 (Table S2). Engagement of dioxane for both processes resulted in amide 10a in 89-91% isolated yield (entries 1+2, two independent experiments). Carbon monoxide preparation in MeCN furnished product 10a in the same yield (entry 3). Beside MeCN and dioxane also THF is a suitable solvent, the usage of which delivered 10a in 84-85% yield (entries 5+6).

Table S2. Solvent screening for the synthesis of amide 10a.

| entry | Solvent CO chamber | Solvent Coupling chamber | yield 10a [%] | Lab journal no. |
|-------|--------------------|--------------------------|---------------|----------------|
| 1     | dioxane            | dioxane                  | 91            | PH4082         |
| 2     | "                  | "                        | 89            | PH4056         |
| 3     | MeCN               | "                        | 89            | PH4064         |
| 4     | THF                | "                        | 85            | PH4059         |
| 5     | THF                | THF                      | 84            | PH4065         |
| 6$^a$ | DMF@rt             | dioxane                  | 84            | PH4078         |
| 7     | "                  | DMF                      | 60            | PH4060         |
| 8     | toluene            | dioxane                  | 81            | PH4073         |

10a was synthesized according to general procedure 1 (chapter 0 on page 25) from 8a (1.00 mmol, 1.0 equiv). Yields refer to isolated material after chromatographic purification. a. CO formation conducted at RT, no FPyr used.
Interestingly, application of MeCN as solvent in the cross coupling chamber resulted in low conversion of 8a and pronounced side-product formation (not shown). CO can be even prepared at room temperature, when DMF is harnessed as solvent and catalyst (entry 6). However, DMF is not an appropriate solvent for the cross coupling, which furnished 10a in a diminished yield of 60% (entry 7). The lowest yield with 81% was accomplished in the case of toluene as solvent for CO formation (entry 8). This is not surprising, because CO generation is slowest in toluene (see chapter 2, page 8).
1.2 Comparison with other Methods for the Activation of Carboxylic Acids (Scheme 4)

In order to compare the current method for the ex situ CO formation with established activation approaches for carboxylic acids applied to formic acid, a set of comparison experiments was conducted as compiled in Table S3.

Table S3. Comparison of the current with other methods for the activation of carboxylic acids.

| entry | reagent (mol%) | base (equiv) | amount of NEt₃ (equiv) | yield [%] | Lab journal no. |
|-------|----------------|--------------|------------------------|-----------|-----------------|
| 1*    | This work      | /            | /                      | 81*       | BZ080           |
| 2*    | This work: w/o purging with N₂ | / | 81 | BZ182 |
| 3     | TCT (57)       | /            | 3.0                    | 17        | 42              | BZ188 |
| 4     | "              | "            | "                     | 21        | 35              | BZ313 |
| 5*    | NMM (1.8)      | /            | 3.0                    | 11        | 62              | BZ190 |
| 6     | "              | "            | "                     | 11        | 56              | BZ193 |
| 7     | "              | "            | "                     | 23        | 51              | BZ314 |
| 8     | SOCl₂ (170)    | /            | 3.0                    | 80        | 6               | BZ194 |
| 9b    | "              | /            | "                     | 56        | 5               | BZ197 |
| 10b   | "              | /            | 4.5                    | 83        | 8               | BZ201 |
| 11b   | "              | /            | 6.0                    | 81        | 8               | BZ228 |
| 12    | (COCl)₂ (170)  | /            | 3.0                    | 48        | 18              | BZ195 |
| 13b   | "              | /            | "                     | 52        | 22              | BZ198 |
| 14b   | "              | /            | 4.5                    | 16        | 48              | BZ202 |
| 15    | "              | /            | "                     | 14        | 54              | BZ222 |
| 16b   | "              | /            | 6.0                    | 2         | 44              | BZ227 |
| 17bc  | (COCl)₂ (85)   | /            | "                     | 11        | 48              | BZ230 |
| 18    | Ac₂O (300)     | /            | 1.5                    | 32        | 42              | BZ191 |
| 19    | "              | /            | 4.5                    | 5         | 37              | BZ229 |

*With 10 mol% FPyr. According to general procedure 6 (see chapter 3.2.7 on page 46) 4-idoanisoisole (0.50 mmol, 1.0 equiv) was coupled with butylamine (1.5 equiv), whereas CO was formed from formic acid. a. Isolated yield after chromatography. b. Reagent injected through septum. c. With 0.75 equiv formic acid.

(3) The yield was determined from the ¹H-NMR spectra of the crude product with the aid of dibenzylether as internal standard (s, 4H at 4.56 ppm) under reference to the singlet of 10a at 3.83 ppm and of 8a at 3.77 ppm (3H), respectively.
The transformation of 1-iodo-4-methoxybenzene and n-butylamine into amide 10a in the presence of 1.5 equiv of CO was chosen as benchmark reaction. Under the optimized conditions product 10a was isolated after chromatographic purification in 81% yield (entry 1). Albeit carboxylic acids usually do not react with TCT even at a temperature of 80 °C,[2] CO incooperation afforded amide 10a in moderate yields of 35-42% in the absence of FPyr (entries 3+4). Thereby, two independent experiments were run under identical conditions in order to verify reproducibility.

Carboxylic acids have been activated by means of TCT and NMM to afford amides, for instance.[3] Analogous reaction with formic acid allowed for the preparation of amide 10a in moderate yields (entries 6+7), also when FPyr was applied (entry 5). In fact, thionyl chloride is the most common reagent for the conversion of carboxylic acids into acid chlorides. However, reaction of formic acid with SOCl₂ turned out to be rather inefficient for the ex situ formation of CO (entries 8-11). Independently, on the amount of NEt₃ in the coupling chamber, amide 10a was generated in rather low yields between 6 and 8%.

Oxalyl chloride is another very typical reagent for the preparation of carboxylic acid chlorides. Nevertheless, attempted CO formation applying (COCl)₂ gave rise of the target compound in moderate yields up to 54% at best (entries 12-16). Thereby, lower yields were effected by the utilization of only 3 equiv NEt₃ (entries 12+13), while an enhanced outcome was observed using 4.5-6 equiv NEt₃ (entries 14-16). Since chlorination of carboxylic acids with oxalyl chloride already results in the generation of 1 equiv of CO, in principal the double amount of CO is released in the experiments in entry 11-15. Interestingly, also substoichiometric amounts of formic acid and (COCl)₂ enable the synthesis of amide 10a in a moderate yield of 48% (entry 17). Since both, thionyl and oxalyl chloride are much more reactive than TCT there is a chance that CO escapes the gas reactor before the latter one is sealed with a screw cap (entries 8+12+15). However, even when the reaction apparatus is sealed and subsequently the afore-mentioned acid chlorides are added with the aid of a syringe through the septum, yields did not improve (entries 9-11, 13+14, 16+17).

Finally, formation of the mixed anhydride of formic and acetic acid was considered as potential source of CO (entries 18-19).[4] In agreement with the literature formic acid activation was accomplished in the absence of a solvent. Nevertheless, yields for amide 10a remained with 37-42% in two identical experiments moderate.
1.3 Carbon Monoxide Incorporation

In order to examine the amount of CO incorporated into the product, experiments with formic acid as yield-limiting starting material were carried out in the synthesis of amide 10a as model reaction (Table S4). Under standard conditions, which included CO preparation and cross coupling in dioxane at 80 °C, the amide 10a was obtained in 73% yield (entry 1). Notable, when 1.5 equiv of formic acid are employed as in the present work, 67% conversion are sufficient to deliver 1 equiv of CO.

Table S4. Formic acid as yield-limiting component in the production of amide 10a.

| entry | Solvent | FPyr [mol%] | T [°C] | yield 10a [%](4) | Lab journal no. |
|-------|---------|-------------|--------|-----------------|----------------|
| 1     | dioxane | 10          | 80     | 73              | PH4091         |
| 2     | “       | 20          | “      | 78              | PH4096         |
| 3     | “       | “           | 100    | 88              | PH4102         |
| 4     | MeCN    | “           | 80     | 74              | PH4109         |
| 5a,b  | DMF@rt  | “           | “      | 81              | PH4112         |
| 6a,c  | “       | “           | “      | 84/79d          | PH4118         |

10a was synthesized as given in general procedure 1 (chapter 0 on page 25) from formic acid (1.00 mmol, 1.0 equiv). Yields were determined by means of Bn₂O as internal NMR-standard. a. CO formation conducted at room temperature. b. The stock solution of formic acid in DMF was added into the CO chamber, which was closed with a screw cap afterwards. c. The HCO₂H solution in DMF was added through the septum of the screw cap into the CO chamber. d. Isolated yield after chromatographic purification.

An increase of the FPyr loading to 20 mol% enhanced the level of CO build-in with a yield of 10a of 78% (entry 2). An elevated reaction temperature of 100 instead of 80 °C gave rise of the secondary amide 10a in 88% yield (entry 3). CO formation in MeCN afforded product 10a in 74% yield (entry 4). Higher levels of CO assembly were accomplished, when DMF was applied as solvent for the CO production at room temperature (entries 5+6). After injection of the stock solution of HCO₂H in DMF into the CO chamber through the septum, the amide 10a

(4) The yield was determined from the ¹H-NMR spectra of the crude materials by means of dibenzylether as internal standard (s, 4H at 4.56 ppm) under reference to the singlet of 10a at 3.83 ppm (3H).
was formed in 84% yield (79% isolated yield, entry 6). Since unidentified side-products in small amounts were observed in all experiments, levels of CO incorporation might be higher than the yields of 10a.
2 Gas Volumetry (Figure 1)

2.1 Analysis of Gas Volumetry

The gas volume was monitored against the time by means of an in-house build gas volumeter, of which a detailed experimental setup and procedure can be found in chapter 3.2.8 on page 47. According to the ideal gas equation the gas amount $n_{\text{gas}}$ was approximated based on the measured volume $V$, the temperature $T$ and the atmospheric pressure $p$ as follows:

$$n_{\text{gas}} = \frac{p \cdot V}{R \cdot T}$$

(1)

with the gas constant $R = 8.314462 \, \text{J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$

Taking into account the balanced reaction equation, HCl is formed in stoichiometric amounts:

$3 \text{H}_2\text{CO}_2\text{H} + 3 \text{Cl} = 3 \text{CO} + 3 \text{HCl}$

With $g = \text{gaseous}$, solv. $= \text{solvated}$, $s = \text{solid}$

Therefore, the gas generated consists not only of CO but also of HCl, which both also dissolve in the liquid phase. In addition, at elevated reaction temperatures, the solvent evaporates contributing to the gas volume. Thus, the gas phase consists of CO, HCl and the applied solvent:

$$n_{\text{gas}} = n(\text{CO}, g) + n(\text{HCl}, g) + n(\text{solvent}, g)$$

(2)

For the reason of comparability, in all measurements the gas generation was monitored at the reaction temperature $T$ for 60 min in the same intervals. Afterwards, the heating bath was removed and the gas volume was followed for additional 30 min to estimate the total amount of carbon monoxide formed. As an example, the molar amount of gas $n_{\text{gas}}$ released in the reaction of formic acid with TCT in the presence of 10 mol% of FPyr in MeCN at 70 °C is displayed in Figure S1 (green data points). Thereby, $n_{\text{gas}}$ was calculated according to equation (1) relying on the measured gas volume $V_{\text{gas}}$. To determine the solvent amount in the vapour phase, which is given as $n(\text{solvent}, g)$ in equation (2), a second measurement was carried out, in which the same solution of formic acid and FPyr was heated to 70 °C in the absence of TCT (blue data points).
Figure S1. Gas formation in MeCN at 70 °C (based on data in Table S9 on page 143 and Table S24, page 175).

Also in the absence of TCT a rapid gas formation was observed, in which a plateau is observed early at 5.5 min. Moreover, after cooling down from 70 °C to ambient temperature, the vapour volume is reduced, but some solvent remained in the gas phase. As the generation of gas is similar in the case of heating MeCN to 70 °C (grey points in Figure S1), no carbon monoxide is formed without using TCT. The slightly lower amount of evaporated solvent can be attributed to an elevation of the boiling point (ebullioscopy), when formic acid and FPyr are dissolved in MeCN.

Interestingly, the amount of solvent in the gas phase \( n(\text{solvent}) \) is basically not influenced by the solvent volume applied, at least in a range of 300-1000 \( \mu \text{L} \) (see Figure S42, page 177). This may be rationalized by the only slight change of the overall volume of the gas phase in the reaction apparatus. Therefore, the vapour monitoring with and without TCT do not have to be performed using the same solvent volume.

To clearly visualize the gas production, the ratio between \( n(\text{gas}) \) and the initial amount of formic acid \( n_0(\text{HCO}_2\text{H}) = 0.292 \text{ mmol} \) in %, which is denoted as gas yield, is plotted against the time in Figure S2 according to:

\[
\text{gas yield} = \frac{n(\text{gas})}{n_0(\text{HCO}_2\text{H})} = \frac{n(\text{gas})}{0.292 \text{ mmol}} \times 100\%
\]  

(3)
If CO would be released as exclusive gaseous component, ≤100% gas yield should be reached. However, the amount of gas formed after 60 min of heating and after cooling down to room temperature are 162% and 116%, respectively. This higher values verify that evaporated solvent and HCl also contribute to the vapour phase volume (compare equation (2)).

![Figure S2. Gas yield applied against reaction time.](image)

The separate monitoring of the gas formation in the absence of TCT allows to estimate the amount of evaporated solvent \(n(\text{solvent}, g)\). In Figure S3 the difference \(\Delta n(\text{gas})\) between the evolution of gas in the presence of TCT \(n(\text{gas})\) and absence \(n(\text{solvent}, g)\) as determined by equation (5) are shown, which is referred to as gas yield under consideration of evaporated solvent.

\[
\frac{\Delta n(\text{gas})}{n_0(\text{HCO}_2\text{H})} = \frac{n(\text{gas}) - n(\text{solvent}, g)}{n_0(\text{HCO}_2\text{H})} \times 100\% \tag{5}
\]

This results in a correction of the maximum gas amount at 70 °C and ambient temperature to 127% and 108%, respectively.
Figure S3. Difference of gas formation in the presence and absence of TCT and determination of the initial rate of gas generation (only filled data points are considered).

Taking equation (2) into account, $\Delta n(gas)$ is equal to the amount of CO $n(CO, g)$ and HCl $n(HCl, g)$ in the gas phase.

$$\Delta n(gas) = n(gas) - n(solvent, g) = n(CO, g) + n(HCl, g)$$  \hspace{1cm} (6)

The total amount of CO and HCl formed are equal according to the balanced reaction equation.

$$n(CO, total) = n(HCl, total)$$  \hspace{1cm} (7)

However, both, CO and HCl are distributed between the vapour and liquid phase:

$$n(CO, total) = n(CO, g) + n(CO, solv.)$$  \hspace{1cm} (8)

$$n(HCl, total) = n(HCl, g) + n(HCl, solv.)$$  \hspace{1cm} (9)

Therefore, the amount of both in the vapour phase may not be equal:

$$n(CO, g) \neq n(HCl, g)$$  \hspace{1cm} (10)
Since the solubility of CO in solvents such as MeCN is low, its amount in the vapour phase corresponds approximately to the overall amount of CO generated. This simplifies equation (8) to:

\[ \rightarrow n(CO, g) = n(CO, total) - n(CO, solv.) \approx n(CO, total) \]  \hspace{1cm} (11)

At room temperature a virtually complete dissolution of HCl in the liquid phase is expected, which allows to simplify equation (6) with (11) to:

\[ \text{at } rt \text{ and low conversions:} \]

\[ \Delta n(gas) \approx n(CO, g) \approx n(CO, total) \quad \text{with } n(HCl, g) \approx 0 \]  \hspace{1cm} (11)

Hence, the gas yield \( \Delta n(gas)/n_0(HCO_2H) \) after cooling down to room temperature at 90 min allows an estimation of the amount of CO generated. In the present example in Figure S3 the gas yield >100\%, namely 108\%, might be reasoned through (1) deviations from the behaviour of ideal gases and (2) a higher amount of gaseous solvent \( n(\text{solvent}) \), because the overall volume of the gas phase is increased due to CO.

Additionally, in the beginning of the transformation of methanoic acid the amount of HCl in the vapour phase is low, hydrogen chloride is mostly dissolved in the liquid phase and \( n(HCl, g) \) can be neglected. Therefore, equation (11) is also applicable to low conversions of methanoic acid. According to the stoichiometric reaction equation (see above), for each molecule formic acid consumed one molecule of CO arises. Thus, the gas yield \( \Delta n(gas)/n_0(HCO_2H) \) is equal to the conversion of formic acid at low levels of conversion:

\[ \text{at low conversions:} \]

\[ \text{conv.}(HCO_2H) = \frac{n_0(HCO_2H) - n(HCO_2H)}{n_0(HCO_2H)} = \frac{n(CO, total)}{n_0(HCO_2H)} \approx \frac{\Delta n(gas)}{n_0(HCO_2H)} \]  \hspace{1cm} (12)

The initial rate of CO formation can be estimated by a linear regression taking data points up to 20\% gas yield = conversion into account (Figure S3). In most measurements, the evolution of gas in the very beginning was faster in the absence of TCT, which might be explained by a lower boiling point of the reaction mixture and an endothermic dissolution enthalpy of TCT.\(^6\)

As a result, the gas yield taking evaporated solvent into account can be \( \leq 0\% \) at the outset, which is why these data points are omitted in the determination of the regression line. The points actually used for the calculation of the regression line in Figure S3 are filled, while those neglected are hollow. In the current experiment the initial rate is 5.7\%/min or 0.057•min\(^{-1}\).
Beside the initial rate and the gas yield after cool down, the reaction duration $t_{2/3}$, after which a gas yield $\Delta n_{\text{gas}}/n_0(\text{HCO}_2\text{H}) > 67\%$ had been accomplished, was selected as third feature to compare different reaction conditions. According to equation (12), at this time approximately 67% conversion of formic acid are reached. Since in the carbonylative cross couplings herein 1.5 equiv of formic acid were utilized mostly, 67% conversion correspond to the formation of 1.0 equiv of CO. In the present example, 67% gas yield were achieved after 17 min.

The lower the boiling point of the tested solvent was, the stronger is the difference of the gas amount between the measurement with and without TCT in the beginning. As an example the gas development using EtOAc showed a significantly elongated incubation period (Figure S4). The gas yield $\Delta n_{\text{CO}}/n_0(\text{HCO}_2\text{H})$ is negative until 6.5 min (Figure S5). Nevertheless, the initial rate can still be estimated roughly neglecting these negative data points.

**Figure S4.** Observation of the gas evolution in EtOAc employing 10 mol% of FPyr (green) and without TCT (blue, data obtained from Table S14 and Table S15).
**Figure S5.** Development of gas in EtOAc taking evaporated solvent into account (for data see Table S14).

When a volumeter with a metric instead of volumetric scale is used, the gas volume can be easily calculated as stated in equation (9) based on the height of the water level \( h(\text{gas}) \) and the diameter \( d \) or the radius \( r \) of the glass tube of the volumeter. Indeed, some of the current measurements were performed using a volumeter with a metric scale. For the reason of simplicity the calculated and rounded volumes \( V(\text{gas}) \) are stated in chapter 3.4 (page 141).

\[
V(\text{gas}) = h(\text{gas}) \cdot \pi r^2 = h(\text{gas}) \cdot \pi \left(\frac{d}{2}\right)^2
\]  

(13)

Theoretically, the HCl formed could dissolve in the water of the U-shaped volumeter (see chapter 3.2.8 on page 47 for technical details), which would mitigate the volume of the gas phase. However, albeit several volumetric measurements were carried out without changing the water in the voltmeter, we never experienced a change of the pH. This rules out a dissolution of HCl in the water of the volumeter in significant amounts.
2.2 Gas Formation in DMF at Room Temperature

Figure S6 shows the gas formation with formic acid using DMF as solvent and catalyst at room temperature. The green data points represent a measurement with an excess of TCT (41 mol% = 1.23 equiv) over HCO₂H (1 equiv), while the yellow data points stem from an experiment with TCT (33.3 mol%) as the limiting starting material and an excess of formic acid (2 equiv).

The solubility of HCl in organic solvents such as dioxane and EtOAc is ≥4 and >1 mol/L, respectively. DMF is a polar solvent and good hydrogen bond acceptor and, therefore, a similar or higher solubility of HCl >1 mol/L can be anticipated. Therefore, in both experiments HCl should dissolve completely in DMF and does virtually not contribute to the gas phase (final concentration [HCl] = 1 mol/L, n(HCl) ≈ 0 mmol). In addition, the molar amount of evaporated DMF is roughly zero, because of the high boiling point of DMF (153 °C). Hence, equation (2) and (12) can be simplified as follows:

$$n(gas) = n(CO, g) + n(HCl, g) + n(solvent, g) \approx n(CO, total)$$  \hspace{1cm} (2)

$$\text{conv.}(HCO_2H) = \frac{n(CO, total)}{n_0(HCO_2H)} \approx \frac{n(gas)}{n_0(HCO_2H)}$$  \hspace{1cm} (8)

Since the amount of gas n(gas) is equal to n(CO, total), the conversion of formic acid corresponds to the gas yield n(gas)/n₀(HCO₂H). Indeed, in the instance of an excess of TCT already after 4.5 min 67% (= t₂/₃) conversion were accomplished. After 90 min 98% gas yield were achieved, which means that formic acid had almost been completely consumed.
When TCT was employed as limiting starting material (33 mol%), 80% gas yield was obtained after 90 min, which supports 80% conversion of TCT. Since at 67% conversion two chlorine atoms on the triazine scaffold have been substituted, in the present experiment also the final third Cl atom was replaced partially. A $t_{1/2}$ time of 14 min verifies a slower generation of CO in comparison to the first experiment with an excess of TCT. Figure S7 shows the determination of the initial rates, which are 30 and 18%/min in the case of an excess of TCT and formic acid, respectively. In conclusion, an excess of formic acid does not accelerate the formation of CO.

![Figure S7. Initial rates of gas formation. For underlying data see Table S7 and Table S8 starting at page 141.](image)

### 2.3 Solvent Screening

In order to keep the amount of evaporated solvent $n$(solvent) as low as possible (compare equation (2)), a low reaction temperature $T$ allows more accurate results. Orientation experiments for the CO formation using MeCN and THF indicated 70 °C as best reaction temperature for the solvent screening with 10 mol% of FPyr (Scheme S1). Based on our previous experience in the FPyr catalyzed chlorination of carboxylic acids engaging TCT, six different solvents were selected for gas volumetric measurement. In Figure S8 gas kinetics for the afore-mentioned solvents considering the amount of solvent in the gas phase are compiled. The visual comparison immediately suggests the following ranking:
To further verify this assessment, (1) initial rates (i. r.) and relative initial rates in reference to the measurement in toluene, in which the CO evolution was slowest, (2) $t_{2/3}$ time and (3) the gas yield under consideration of the evaporated solvent after cooling down to ambient temperature were compared (Table S5).

Surprisingly, the initial rate for CO formation in DMF at room temperature (see previous chapter) was four times faster than in MeCN, which turned out as optimal solvent when 10 mol% of FPyr were used (entries 1+2). While in DMF 67% conversion of formic acid were reached after 4.5 min, in MeCN 14-17 min of heating to 70 °C were necessary for the same result. This vast difference is explained by the dual role of DMF as solvent and catalyst in a high excess. In fact, the rate of CO formation strongly depends on the solvent applied. Based on the initial rate, carbon monoxide generation is 14-17 times faster in MeCN than in toluene (entries 2+7).
In 2-MeTHF and toluene 60 min of heating to 70 °C were not sufficient to result in a gas yield of 67% ($t_{2/3} > 60$ min, entries 6+7). Overall, initial rates, $t_{2/3}$ and the gas yields at the end of the cool down phase confirmed the above mentioned solvent ranking. The repetition of the gas kinetic in MeCN verified a reasonable reproducibility, wherefore two values are given for each parameter in Table S5 (see also Figure S12). Figure S9 concludes the results graphically. Already in our previous method for the activation of carboxylic acids by means of TCT,[2] MeCN and THF were identified as optimal solvents, while toluene and 2-MeTHF lead to significantly depleted yields. Both, EtOAc and dioxane were suitable but less sufficient than MeCN and THF. Since usage of less appropriate solvents such as toluene effected a lower levels of gas formation, reactions were carried out with 1000 µmol HCO$_2$H. In the instance of the well-suitable solvents MeCN and THF a scale down to 300 µmol was necessary in order to not exceed the capacity of the volumeter.

Table S5. Comparison of solvents.

| Entry | Solvent  | bp. [°C] | i. r. [%/min] | relative i. r. | $t_{2/3}$ [min] | n(gas)/n$_0$(HCO$_2$H) [%] |
|-------|----------|----------|---------------|----------------|-----------------|-----------------------------|
| 1     | DMF, rt  | 153      | 29.9          | 75             | 4.5             | 98                          |
| 2     | MeCN     | 82       | 5.7/6.7       | 14/17          | 17/16           | 108/109                     |
| 3     | THF      | 66       | 4.4           | 11             | 22              | 92                          |
| 4     | EtOAc    | 77       | 3.4           | 8.5            | 35              | 85                          |
| 5     | dioxane  | 101      | 1.3           | 3.3            | 55              | 65                          |
| 6     | 2-MeTHF  | 79       | 1.2           | 3.0            | >60             | 47                          |
| 7     | toluene  | 110      | 0.4           | 1.0            | >60             | 16                          |

i.r. = initial rate
Figure S9. Summary results of solvent screening.
2.4 Variation of Catalyst Loading

Next, the FPyr amount was varied using MeCN as solvent in order to study the effect of the catalyst loading on the CO formation (Figure S1). Indeed, the rate of gas generation increases significantly, when the amount of FPyr is raised from 5 to 10 and 20 to 30 mol% (green data points). With both, 20 and 30 mol% FPyr, maximum gas yields of 168% at 70 °C and 123% after cooling down to ambient temperature were accomplished. Thus, full consumption of formic acid is accomplished in these cases. Interestingly, with 10 mol% DMF (yellow points) the gas evolution is weaker than with 5 mol% FPyr.

![Figure S10](image-url). Gas formation with different loadings of FPyr and DMF in MeCN at 70 °C (data available in chapter 3.4.3, page 173).

Importantly, the level of gas formation was the same, when either TCT (blue points) or FPyr (red points) were omitted. This proves that CO and HCl are only formed in the presence of FPyr (or DMF). In both measurements the maximum gas evolution (32-34%) was reached after 5.5 min.

In Figure S11 the gas yields $\Delta n(\text{gas})/n_0(\text{HCO}_2\text{H})$ under consideration of the amount of solvent $n(\text{solute})$ are displayed, whereas in Table S6 (relative) initial rates, gas yields $\Delta n(\text{HCO}_2\text{H})/n_0(\text{HCO}_2\text{H})$ and $t_{2/3}$ are summarized. The initial rate for CO generation in DMF at room temperature is still twice as high as in MeCN at 70 °C using 30 mol% of FPyr (entries...
Gas generation applying 5 mol% of FPyr shows a slightly higher initial rate (3.4 compared to 2.9%/min), a higher gas yield (89 instead of 82%) and a lower $t_{2/3}$ duration (28 instead of 40 min) than with 10 mol% DMF. Therefore, DMF is a less efficient catalyst than FPyr, which we have also observed in previous formamide catalyzed substitutions methods.[2,8]

**Figure S11.** Gas formation with different loadings of FPyr and DMF in MeCN at 70 °C under consideration of the volume of MeCN in the gas phase (data available in chapter 3.4.3, page 173).

**Table S6.** Initial rates and gas yield at room temperature and $t_{2/3}$ for different catalyst loadings.

| Entry | Catalyst | i. r. [%/min] | relative i. r. | n(gas)/n(HCO$_2$H) [%] | $t_{2/3}$ [min] |
|-------|----------|---------------|----------------|------------------------|-----------------|
| 1     | DMF, rt  | 29.9          | 8.8            | 98                     | 4.5             |
| 2     | 30 mol% FPyr | 12.6          | 3.7            | 117                    | 7               |
| 3     | 20 mol% FPyr | 9.7/10.6     | 2.8/3.1        | 117/115                | 9/10            |
| 4     | 10 mol% FPyr | 5.7/6.7      | 1.7/2.0        | 108/109                | 17/16           |
| 5     | 10 mol% FPyr* | 3.3           | 1.0            | 76                     | 40              |
| 6     | 5 mol% FPyr  | 3.4           | 1.0            | 89                     | 28              |
| 7     | 10 mol% DMF | 2.9           | 0.9            | 82                     | 40              |

* [HCO$_2$]$_0$ = 0.3 mol/L.

Two independent sets of gas volumetric measurements using 20 mol% (blue points) and 10 mol% (green points) of FPyr prove a reasonable reproducibility (Figure S12). A decrease of the concentration of formic acid from 1 to 0.3 mol/L effected a significantly mitigated rate of
gas formation (compare entries 4+5 in Table S6). Hence, CO generations should be carried out with high HCO$_2$H concentrations.

**Figure S12.** Development of gas from formic acid using 20 mol% and 10 mol% FPyr (two independent measurements each, blue and green points), respectively, to probe levels of reproducibility and with a substrate concentration [HCO$_2$H] of 0.3 mol/L (yellow data points).
3 Experimental Part

3.1 General Conditions

Unless otherwise stated all $^1$H-, $^{19}$F- and $^{13}$C-NMR spectra, the latter of which were recorded broadband proton decoupled, were recorded at room temperature in CDCl$_3$ on Bruker instruments (Avance II 400 or Avance I 500). Chemical shifts ($\delta$) are reported in parts per million (ppm) from tetramethylsilane (TMS) using the residual solvent resonance ($^{13}$C-NMR) or TMS ($^1$H-NMR) as the internal standard (CDCl$_3$: 7.26 ppm for $^1$H NMR, 77.00 ppm for $^{13}$C NMR). Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). High resolution mass spectra were recorded either on a MAT 95Q spectrometer (CI) of Finnigan or on a Bruker Solarix 7 Tesla MALDI/ESI/APPI FTICR imaging spectrometer (ESI). Optical rotations were determined on a Perkin Elmer polarimeter 341. Melting points (uncorrected) were determined on a MEL-TEMP II machine of Laboratory Devices Inc.

Analytical TLC was carried out using precoated silica gel plates (Fluka TLC plates silica gel 60 F$_{254}$ on PET-foils). TLC plates were visualized under UV irradiation (254 nm) or with KMnO$_4$- (3 g KMnO$_4$ and 20 g K$_2$CO$_3$ in 300 mL water) and Ce(SO$_4$)$_2$/PMA (= phosphomolybdic acid, 10 g Ce(SO$_4$)$_2$·4 H$_2$O, 25 g PMA, 80 mL 95% H$_2$SO$_4$, 920 mL water) stain solutions. Flash column chromatographic purifications were performed with technical grade silica gel M 60 from Macherey-Nagel (40-63 $\mu$m, 60 A).

Gas chromatography (GC) was conducted on a GC-2010 from Shimadzu with a CP-Chirasil-DX CB column (length 25 m, diameter 0.25 mm, 0.25 $\mu$m layer thickness) from Agilent Technologies and a FS Supreme-5 MS column (length 25 m, diameter 0.25 mm, 0.25 $\mu$m layer thickness) from EMR, respectively, and nitrogen as carrier gas. Compounds were either detected by an FID (Chirasil-DX CB column) or a GCMS-QP2010 Plus mass detector from Shimadzu (Supreme 5 MS column). High pressure liquid chromatography (HPLC) was conducted on a D-7000 machine from Merck-Hitachi with a Chiracel OD-H column of Daicel Industries (length 250 mm, diameter 4.6 mm). Visualisation was realized by a diode array UV detector (wavelength 190-300 nm)

Chemicals were purchased from Sigma-Aldrich, Acros, TCI chemicals, Carbolution and Alfa Aesar and used without further purification. $^{13}$C-enriched formic acid was obtained from Sigma-Aldrich (CAS [1633-56-3], isotopic purity 99 atom% $^{13}$C, delivered in an ampulla), and stored under nitrogen in a Schlenk-tube. Petrolether (= PE, bp. 40-60 °C, technical grade) was distilled prior usage; all other solvents were utilized without further purification. Dry solvents were purchased from Acros.
3.2 General Procedures

Caution, TCT, a fine-powdered, dusty solid with a typical chlorine like smell, is (inter alia) very toxic by inhalation. Therefore, it should be only handled in a well ventilated fume hood. Outside a fume hood we strongly recommend to handle TCT only in closed vessels such as dram vials with a screw cap or one-necked flasks with a stopper.

Due to HCl and CO evolution, both of which are highly toxic and corrosive, pressure is developed during the carbonylative cross coupling. Therefore, the reaction apparatus can burst. Consequently, all carbonylative cross coupling must be performed in a well ventilated fume hood and under suitable protection (e.g. through a burst shield). The reaction vessels may only be opened carefully after cooling down to ambient temperature remaining in the fume hood.

Commercial N-formylpyrrolidine (FPyr) can be conveniently prepared from formic acid, Ac₂O and pyrrolidine on a 2 mol scale using standard laboratory glassware ≤1 L.[8] Carbonylative cross couplings were conducted in COware gas reactors from SyTracks with a total volume of 20 mL, which are commercial available at Sigma-Aldrich (Order-No. STW1-1EA, Figure S13). Thereby, CO was formed in one reaction chamber, the cross coupling was conducted in the other. The gas reactors were heated to 80 °C in a drying cabinet overnight before usage. In the manuscript the CO Chamber is denoted as Chamber 1 and the Coupling Chamber as Chamber 2.

Figure S13. Ex situ generation of CO in COware gas reactors with two separate reaction chambers.
Due to residual Pd traces isolated products may be black or intensively brown coloured. These impurities can be removed by stirring a solution of the respective coupling product in an appropriate solvent with charcoal (30-50 wt%) for several hours. An exemplary procedure can be found in chapter 3.2.3 (page 37).

### 3.2.1 General Procedure 1: Synthesis of Amides (Scheme 2 A-D)

The procedure was adapted from reference [9] using SilaCOgen 2 as yield-limiting CO source and applying Pd(OAc)$_2$ instead of Pd(dba)$_2$.

**CO Chamber** One chamber of the COware gas reactor is charged successively with Pd(OAc)$_2$ (4.4 mg, 20 μmol, 2 mol%), PPh$_3$ (15.7-21.0 mg, 60-80 μmol, 6-8 mol%), the respective aryl iodide 8 (1.0 mmol, 1.0 equiv), the amine 9 (1.5 mmol, 1.5 equiv) and a stir bar. After the CO chamber has been charged with TCT (see below), dry dioxane or reagent-grade toluene (1.0 mL, 1 M) and NEt$_3$ (420 μL, 3.0 mmol, 3.0 equiv) are introduced and the chamber is sealed with a screw cap with septum. In general, yields and conversions are higher, when dioxane is used as a solvent instead of toluene.

**Coupling Chamber** With FPy: The second reaction chamber is loaded in a well-ventilated fume hood with TCT (107 mg, 1.50 mmol, 1.5 equiv) and a 2.0 M/0.13 M stock solution of formic acid/FPyr in the solvent (750 μmol, 1.5 mmol/100 μmol, 1.5 equiv/10 mol%; 2 M with respect to formic acid) is added in a single portion after the introduction of dioxane/toluene and NEt$_3$ into the CO chamber (see above). Next, the chamber is closed with a screw cap with septum and the reaction device is placed in an oil bath, which has been preheated to 80 °C, and stirred for 8-20 h (600 rpm). Especially in the case of dioxane, initially a clear solution is obtained in the CO chamber and a gas formation occurred (Figure S14 A). After 10-15 min a colourless solid starts to precipitate (probably cyanuric acid, Figure S14 A) and after stirring overnight a pale yellow suspension is formed (Figure S14 C). In the coupling chamber in the

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(5) For instance, prepared from 152 μmol/186 mg formic acid, 26.2 μL/27.2 mg FPy in 2 mL solvent.

(6) When toluene is used as a solvent, formic acid (57.2 μL, 69.7 mg, 1.5 mmol, 1.5 equiv) is added neat after TCT, because it is of low solubility in toluene. Subsequently, a 0.13 M solution of FPy in the toluene is added.

(7) The reaction apparatus can be purged for 10-30 s with N$_2$ before it is closed with the screw cap. However, in multiple experiments this has no positive effect on the yield of the product 10, when 8 mol% of PPh$_3$ are used.
beginning a clear yellow to red solution is obtained ((Figure S14 A+B), whereas heating overnight results typically in a black suspension (Figure S14 C, most likely Pd-black). In addition, a fog formation (HNEt₃Cl) can be seen in the gas phase (Figure S14 B). After cooling down to room temperature the excess pressure was carefully realised. Alternatively, the CO chamber can be loaded with formic acid (57.2 μL, 69.7 mg, 1.5 mmol, 1.5 equiv), FPyr (9.8 μL, 10.2 mg, 100 μmol, 10 mol%) and the solvent (0.75 mL, 2 M with respect to formic acid). Finally, TCT (57 mol%) is added in a single portion and the reaction chamber is closed with a screw cap with septum.

In DMF: The CO chamber is charged in a well-ventilated fume hood with TCT (57 mol%). Immediately after loading with THF and NEt₃ of the coupling chamber (see above), a 2.0 M stock solution of formic acid in dry DMF (0.75 mL, 1.5 mmol, 1.5 equiv) is added quickly in a single portion into the CO chamber, which is closed directly afterwards with a screw cap with septum. Next, only the coupling chamber is placed in an oil bath, which has been preheated to 80 °C (Figure S15 A), and the reaction mixtures are stirred overnight (600 rpm). At the outset a clear solution is obtained in the CO chamber and a lively gas evolution can be observed. After 10 min a colourless solid starts to precipitate and past stirring overnight a colourless to yellow suspension is formed. For the appearance of the reaction mixture in the coupling chamber see above.

**Aqueous Work up:** The reaction mixture in the coupling chamber is diluted with EtOAc (2 mL) and aqueous 2 N HCl solution (2 mL) and taken up with a 20 mL syringe. The chamber is rinsed with further EtOAc/2 N HCl solution (2 x 2 mL/1 mL) and EtOAc (2 mL) and the phases are separated with the aid of the syringe. Next, the aqueous phase is washed with brine (1 x 4 mL), dried over MgSO₄, concentrated under reduced pressure and dried at

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(8) E.g. 152 μL/186 mg HCO₂H in 2 mL DMF.
(9) To avoid loss of carbon monoxide the CO chamber can be first closed with the screw cap and secondly the stock solution of formic acid is added through the septum. However, the above-described procedure allows to reuse the same septum for multiple times. When the reaction vessel is closed with the screw cap after addition of the stock solution of formic acid in DMF, the reaction apparatus cannot be purged with nitrogen due to the very fast CO generation.
(10) Typically, some black precipitate (most probably elemental Pd) remains. However, this does not hamper the phase separation and we never encountered blockage of the needle of the 20 mL syringe used instead of an extraction funnel. Nevertheless, the black solid can be removed by a filtration through a sintered funnel with a layer of celite (5-10 mm) by suction prior to the phase separation.
(11) The acidic work up allows to remove NEt₃ and an excess of the amine 9. In the case of basic aryl iodides of type 8 (e.g. pyridines) 2 N NaOH solution in water must be used instead!
the rotary evaporator at 20 mbar for 5 min, which typically affords the crude material as a black oil.

Occasionally, the reaction mixture is not subjected to an aqueous work, but adsorbed on silica gel to be loaded onto the silica gel column. Therefore, the heterogeneous reaction mixture is transferred with CH₂Cl₂ (ca. 10 mL) to a 50 mL flask, silica gel is added (mass ratio theoretical yield/SiO₂ 1:5-1:9)¹² all volatile components are removed in vacuo and the residue is dried at the rotary evaporator at 5 mbar for 5 min.

**Determination Yield with Internal Standard** To the crude material after aqueous work up is added an exactly weighed amount of a feasible internal NMR-standard (30-60 mg dibenzylether), the mixture is dissolved in CDCl₃ (500 µL) and 50 µL of this solution are diluted with further CDCl₃ (500 µL) and subjected to ¹H-NMR spectroscopy.

**Chromatographic Purification** Due to low solubility in the eluent, the crude materials are mostly adsorbed on silica gel through dissolution in CH₂Cl₂ (ca. 10 mL), addition on silica gel (ratio weight crude material/SiO₂ 1:2-1:5) and the solvent is removed under reduced pressure. The fine-powdered residue is loaded onto the surface of a silica gel column (relation of weight theoretical yield or crude product/SiO₂ 1:30-1:100). Elution with EtOAc/PE or EtOAc/nHex mixtures, respectively, concentration with CH₂Cl₂ at the rotary evaporator to remove residual EtOAc and drying at the rotary evaporator at 20 mbar for 15 min then affords the desired amide 10. Occasionally, the products 10 have to be dried in high vacuum to remove residual solvent traces. Polar amides such as 10a with very low solubilities in PE and nHex are best chromatographed using EtOAc/CH₂Cl₂ mixtures as mobile phase. In this instance, the crude material is dissolved in the eluent (0.5 mL) to be loaded onto the silica gel column. Thereby, in the beginning a coloured impurity is usually eluated (Figure S15 B+C).

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¹² The minimum amount of SiO₂ was applied, which allowed to obtain a fine-powdered, non-sticky powder after concentration under reduced pressure.
Figure S14. CO formation and cross coupling in dioxane at 80 °C. A Reaction start, clear solutions can be observed in both chambers, while in the CO chamber a gas evolution is visible. B After 10 min reaction time a colourless solid precipitates in the CO chamber. C Past stirring overnight a black suspension is obtained in the coupling chamber.
Figure S15. A Reaction setup for CO formation in DMF at room temperature and cross coupling at 80 °C. B Column chromatographic purification, whereby in the beginning coloured impurities are eluated (red arrow). C Collected fractions after chromatography (fractions 11-23 contain product 10a).
3.2.2 Representative Graphical Procedure for the Preparation of Amides

In the following, an experiment for the synthesis of amide 10a is described (PH4082) according to general procedure I (chapter 0 on page 25).

1.\text{A} For the preparation of the 2.0 M formic acid/0.13 M FPyr stock solution a balance is tared to zero with a 2 mL volumetric flask.

1.\text{B} With the aid of a 200 \( \mu \)L Eppendorf pipette formic acid is weighed (152 \( \mu \)L, 188.1 mg, 4.0 mmol).

2.\text{A} The balance is tared again.

2.\text{B} FPyr (26.2 \( \mu \)L, 26.9 mg, 0.27 mmol) is weighed in the flask.

3. Next, the flask is filled with dry dioxane (ca. 2 mL) in order to obtain a 2.0 M/0.13 M solution of formic acid and FPyr in dioxane (not shown).
4.A The SyTracks gas reactor is placed in a 50 mL beaker and tared.

4.B Pd(OAc)$_2$ (4.6 mg, 20 µmol, 2 mol%) is added to the coupling chamber.
5.A The balance is tared with a weighing boat (or paper).
5.B PPh₃ (21.3 mg, 80 μmol, 8 mol%) is added.

6.A The balance is tared.
6.B PPh₃ is added into the coupling chamber. The mass difference (20.7 mg) is noted.

7.A The balance is tared with a new weighing boat, 4-iodoanisole (8a) is added (234.6 mg, 1.00 mmol, 1.0 equiv).
7.B The balance is tared, then 4-iodoanisole is added to the coupling chamber. The mass difference of 233.6 mg (= 234 mg) is noted in the lab journal.
The balance is tared to zero with the gas reactor and *n*-butylamine (**9a**, 150 µL, 109.1 mg, 1.5 mmol, 1.5 equiv) is added by means of an Eppendorf pipette. Then, a stir bar is added to the *coupling chamber*, which is closed with a screw cap with septum afterwards (thus, no TCT can be accidentally added in the next step).

**8.B** The balance is tared to zero with a closed 4 mL glass vial containing an excess of TCT.
The following steps are performed in a well ventilated fume-hood.

9.A Both, the vial with TCT and the gas reactor are relocated into a well-ventilated fume hood. In the following, the CO chamber is charged with TCT, the glass vial with TCT is closed and the amount of TCT taken out is controlled on the balance outside of the fume hood.

9.B This process is repeated until the correct weight is reached. Care has to be taken that no TCT is spilled during this process. Next, a stir bar is added to the CO chamber.

10.A The coupling chamber is opened and dioxane (1.0 mL, 1 M) is added with the aid of a 1 mL syringe.

10.B Subsequently, NEt₃ (420 µL, 3.0 mmol, 3.0 equiv) is added by means of a 1 mL syringe and the chamber is closed tightly with the screw cap.
11.A The reaction apparatus is placed above an oil bath, which had been preheated to 80 °C.
11.B The stock solution of 2.0 M formic acid and 0.13 M FPyr (750 μL, 1.5 mmol HCO₂H/100 μmol FPyr, 1.5 equiv/10 mol%), which has been prepared in step 1-3, is added in a single portion into the CO chamber with the aid of a 1 mL syringe.
Finally, the oil bath is raised and stirring is started (600 rpm). The reaction mixtures are heated for 14 h to 80 °C.

Pictures of the reaction mixtures and the chromatographic purification are available in Figure S14 and Figure S15 B+C on page 28-29. Work up delivered the crude title amide 10a as a dark red oil (291 mg, 140%), of which 1H-NMR confirmed full conversion of 4-iodoanisole (8a). Ultimately, column chromate-graphic purification on silica gel (23.8 g, ratio of masses crude 10a/SiO2 82:1) with EtOAc/CH2Cl2 15:85 yielded amide 10a as an orange oil (187.9 mg, 0.91 mmol, 91%), which solidified at ambient temperature.
3.2.3 Representative 10 mmol Scale Procedure

In the following the 10 mmol scale synthesis of \( N \)-benzyl 4-chlorobenzamide (10j, PH4286) is described.

The following equipment is required to set up the reaction (Figure S16):

- 400 mL gas reactor from SyTracks (order no. STW6)
- 2 x 200 mL beakers to place the gas reactor
- 2 magnetic stir bars
- 3 x weighing funnel or papers
- 2 x large spatulas
- 3 x small spatulas
- 1 x funnel
- 10 mL flask + PE stopper
- 1 x 10 mL syringe
- 2 x 5 mL syringes
- 3 x 1 mL syringes
- 6 x needles

![Figure S16. Equipment to start the reaction.](image-url)
The coupling chamber was charged with Pd(OAc)$_2$ (45 mg, 200 μmol, 2 mol%), PPh$_3$ (209 mg, 800 μmol, 8 mol%) and 1-chloro-4-iodobenzene (2.39 g, 10.0 mmol, 1.0 equiv) with the aid of the weighing funnels. In order to charge the CO chamber with TCT, a 10 mL flask with a PE stopper was tared on a balance to zero. In a well-ventilated fume hood the flask was loaded with TCT (1.07 g, 5.7 mmol, 57 mol%), whereby the weight was checked on the balance outside the fume hood. The gas reactor was placed in well ventilated fume hood and TCT was added via a funnel into the CO chamber (Figure S17 A).

![Figure S17. Addition of TCT to the CO chamber.](image)

Next, the funnel was rinsed with dry dioxane (5.0 mL, 2 M). Thereby, the tip of the funnel has to be turned away from the coupling chamber in the right in Figure S17 B (see red arrow). Otherwise, dioxane would also get into the coupling chamber. Subsequently, the funnel was removed and formic acid (570 μL, 15.0 mmol, 1.5 equiv) was added to the CO chamber. Then, dry toluene (10.0 mL, 1 M),$^{(13)}$ NEt$_3$ (4.2 mL, 30.0 mmol, 3.0 equiv) and benzylamine (1.64 mL, 15.0 mmol, 1.5 equiv, measured with a 1 mL syringe) were added to the coupling chamber, which was closed with a screw cap with septum afterwards. Eventually, FPyr (100 μL, 1.0 mmol, 10 mol%) was introduced into the CO chamber. After closing the CO chamber with a screw cap with septum the gas reactor was placed in an oil bath, which had been preheated to 80 °C.

After stirring (400 rpm) for 24 h at 80 °C, the oil bath was removed and the reaction mixtures were allowed to cool down under stirring for further 15 min at ambient temperature. The CO

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(13) For this particular examples better yields of 10a and high levels of conversion of aryl iodide 8j were accomplished in toluene instead of dioxane.
chamber was opened carefully to release an excess of gas pressure. After stirring for 5 min EtOAc (10 mL) and 2 N HCl solution in water (10 mL) were added to the coupling chamber. Next, the CO chamber was emptied with the aid of a glass pipette and the content of the coupling chamber was poured into a 100 mL extraction funnel. The preceding emptying of the CO chamber avoided mixing during the content of the coupling chamber was poured into the extraction funnel. Subsequently, the coupling chamber was rinsed with EtOAc/2 N HCl solution (2 x 10 mL/10 mL) and the phases were separated. The aqueous phase was extracted with EtOAc (1 x 15 mL) and the combined organic phases were washed with brine (1 x 30 mL), dried over MgSO₄, concentrated under reduced pressure and dried for 5 min at 5 mbar at the rotary evaporator. ¹H-NMR of the crude material (3.19 g, 130%, brown solid) revealed a conversion of 8j of approximately 89%. The conversion was determined based on the ratios of the multiplet of 8j at 7.73-7.71 ppm and the multiplet of 10j at 7.09-7.07 ppm (both 2 H). Comparison of the ¹H-NMR spectrum of the crude product with those of 10j and 8j indicated that several side-products had formed. Therefore, the actual conversion might be higher.

Figure S18. ¹H-NMR of the crude material.

Then, the crude material was dissolved in a minimum amount of CH₂Cl₂ (ca. 50 mL) under careful heating with a heatgun, silica gel (8.0 g, mass relation crude product/SiO₂ 1:2.5) was added, the solvent was removed in vacuo and the residue was dried at the rotary evaporator at
5 mbar for 5 min.\(^{(14)}\) Next, column chromatography purification on silica gel (106 g, mass ratio crude 10j/SiO\(_2\) 1:33) using EtOAc/CH\(_2\)Cl\(_2\) 6:94\(^{(15)}\) as eluent and drying at the rotary evaporator at 5 mbar for 20 min afforded the title compound as a brownish solid in 75% yield (1.866 g, 7.54 mmol) and a purity of ≥95% according to \(^1\)H-NMR.

To remove coloured impurities, the amide 10j was dissolved in the minimum amount of CH\(_2\)Cl\(_2\) (60 mL) under heating with a heat gun, charcoal (510 mg, ca. 30 wt%) was added and the resulting suspension was stirred (600 rpm) for 1 h. Afterwards, filtration over a sintered Hirsch funnel with a ca. 2 cm layer of celite, rinsing with further CH\(_2\)Cl\(_2\) (2 x 10 mL), concentration and drying at 5 mbar at the rotary evaporator for 15 min of the combined filtrates delivered the title amide as a pale yellow solid (1.803 g, 7.28 mmol, 73%, 98% mass recovery).

Analytical data for 10j can be found in chapter 3.3.1.11 (page 83).

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\(^{(14)}\) Due to the low solubility of 10j in organic solvents, the crude material cannot be applied as solution onto silica gel column.

\(^{(15)}\) Use of EtOAc/nHex 30:70 as eluent, in which the product 10j showed an \(r\) value of 0.35, resulted in the very sluggish elution of amide 10j. In addition, the isolated product contained impurities. Most likely, the low solubility of 10j in EtOAc/nHex-mixtures causes pronounced diffusion during chromatographic purification.
3.2.4 General Procedure 2: Synthesis of Esters (Scheme 2 E-F)

The cross coupling protocol was adapted from reference [10], wherein 1 atm of CO was applied.

**CO Chamber** The first reaction chamber is charged with Pd(OAc)$_2$ (2.2-4.4 mg, 10-20 µmol, 2 mol%), Xantphos (11.6-23.1 mg, 20-40 µmol, 4 mol%), the aryl bromide 11 (0.50-1.0 mmol, 1.0 equiv), reagent-grade MeOH (200-400 µL, 5.0-10.0 mmol, 10 equiv) and reagent-grade NEt$_3$ (1.0-2.0 mL, 0.5 M).

**CO Chamber** The CO chamber was equipped as described in general procedure 1 (chapter 0, page 25) with TCT (55-107 mg, 0.29-0.57 mmol, 57 mol%) and a stock solution of FPyr (10 mol%) in reagent-grade THF (0.38-0.75 mL, 2 M). Eventually, the reaction apparatus is purged with nitrogen for approximately 10 s without stirring to avoid CO formation and is immediately closed with the second screw cap. Then, the gas reactor is placed in an oil bath, which has been preheated to 80 °C, and stirring at 600 rpm is continued at 80 °C overnight (16-19 h). Commonly, in the cross coupling chamber a clear solution forms in the beginning, whereas upon stirring overnight a black solid precipitated (most likely elemental Pd).

**Work Up** After cooling down to room temperature the reaction mixture is diluted with EtOAc (5 mL), filtered over a sintered funnel (porosity level 3) and with a layer of celite (ca. 5-10 mm) by suction. The reaction chamber and the celite layer are rinsed with additional EtOAc (3 x 5 mL), the collected filtrates are concentrated under reduced pressure and dried at the rotary evaporator for 5 min at 20 mbar.

**Determination Yield with Internal Standard** and **Chromatographic Purification** are conducted as described general protocol 1 (chapter 0, page 25).
3.2.5 General Procedure 3: Synthesis of Alkynones (Scheme 3)

The cross coupling protocol was adapted from reference [11], in which 1 atm of CO was utilized.

**Coupling Chamber** The coupling chamber is loaded with CuI (0-5 mol%), Pd(PPh₃)₂Cl₂ (35.1 mg, 50 μmol, 5 mol%), the respective aryl iodide 8 (1.00 mmol, 1.0 equiv), alkyne 14 (1.5 mmol, 1.5 equiv) and a stir bar. After the CO chamber has been loaded with TCT and a stir bar (see below), reagent-grade THF (3.3 mL, 0.3 M) and NEt₃ (490 μL, 3.5 mmol, 3.5 equiv in the case of 1.5 equiv HCO₂H or 630 μL, 4.5 mmol, 4.5 equiv when 2.5 equiv HCO₂H are utilized) are added to the coupling chamber and the chamber is sealed with a screw cap with septum. To minimize direct Sonogashira coupling yielding 18, the solution of HCO₂H is introduced to the CO chamber immediately afterwards (Figure S20 A).

In particular, with electron deficient aryl iodides 8 and aromatic alkynes 14 increased amounts of aryl alkynes 18 without incorporation of CO are formed. Low amounts of CuI or even no CuI are critical to accomplish reasonable chemoselectivities 15/18. Omission of CuI results also in longer reaction durations of up to 2 d to reach full consumption of 8. In addition, a higher amount of carbon monoxide improves the ratio 15/18 in favour of ynone 15. Due to electrostatic repulsion weighing of an exact amount of CuI into the COware gas reactor is non-trivial. This is why the amount of CuI varies in the experiments herein between 2 and 4 mol%.

In the case of coupling of electron-poor iodoarenes 8 with alkynes 14 that bear protons in the 3 and 4-position, isomerization to dienones of type 19 was observed (up to 20 mol% with respect to 15). Especially, long reaction durations as in the absence of CuI increased the amount of these side-products.

**CO Chamber** In DMF: The CO chamber is charged with TCT (107 mg, 0.57 mmol, 57 mol% or 179 mg, 0.95 mmol, 95 mol% when 2.5 equiv formic acid are used). Immediately after loading with THF and NEt₃ of the coupling chamber (see above), a 2.0 M stock solution of

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(16) Low substrate concentrations effected enable improved chemoselectivities in terms of carbonylation and direct Sonogashira coupling.
formic acid in dry DMF (0.75 mL, 1.5 mmol, 1.5 equiv or 1.25 mL, 2.5 mmol, 2.5 equiv)\textsuperscript{(17)} is added swiftly in a single portion into the CO chamber, which is closed directly afterwards with a screw cap with septum.\textsuperscript{(18)} Next, the reaction mixtures are stirred at room temperature (600 rpm) overnight (16-24 h). Typically, in the CO chamber a clear solution is forming and a lovely gas evolution can be observed (Figure S19). After approximately 10 min a solid starts to precipitate (Figure S20 B). In the coupling chamber a dark red solution is obtained in the beginning, whereas after stirring overnight a black suspension is formed (Figure S20 C).

**With FPy**: The CO chamber is charged in a well-ventilated fume hood with TCT (107 mg, 0.57 mmol, 57 mol\%). After introduction of THF and NE\textsubscript{3} to the coupling chamber (see above), a 2.0 M/0.13 M solution of HCO\textsubscript{2}H/FPyr in THF (0.75 mL, 1.5 mmol HCO\textsubscript{2}H/100 \(\mu\)mol FPy, 1.5 equiv HCO\textsubscript{2}H/10 mol\% FPy)\textsuperscript{(19)} is added to the CO chamber, which is next sealed with a screw cap with septum. Then, the CO chamber is placed under stirring (600 rpm) in an oil bath for 15 min, which has been preheated to 80 °C, to accelerate CO formation and the reaction apparatus is stirred at 600 rpm at room temperature overnight (20-22 h).

**Work Up** After cooling down to room temperature (if necessary) the coupling chamber is opened carefully in a well ventilated fume hood under stirring. In particular, in the case of 2.5 equiv CO, a strong gas evolution can be observed. In the following, EtOAc (1 mL) and 2 N HCl solution (aq., 1 mL) are added to the coupling chamber, of which the content is taken up with a 20 mL syringe. The reaction chamber is successively rinsed with EtOAc/2 N HCl solution (2 x 2 mL/2 mL) and EtOAc (1 x 3 mL), the phases are separated,\textsuperscript{(20)} the organic phase is washed with brine (1 x 4 mL) and dried over MgSO\textsubscript{4}. After concentration and drying at 20 mbar for 5 min at the rotary evaporator typically the crude material is obtained as a black oil.

**Chromatographic Purification** is performed as described in general protocol 1 (chapter 0, page 25). Crude ynones 15 with electron-deficient aryl residues are best not adsorbed on silica gel in order to charge the silica gel column. Instead, dissolution/dilution in a 1:1 mixture of EtOAc and the respective eluent (0.5 mL) is recommended.

In general, we experienced in the cases lower and sometimes poorly reproducible yields with electron-poor ynones of type 15, which are potent Michael acceptors. As previously

\textsuperscript{(17)} E.g. 152 \(\mu\)L/186 mg HCO\textsubscript{2}H in 2 mL DMF.

\textsuperscript{(18)} To avoid loss of carbon monoxide the CO chamber can be first closed with the screw cap and secondly the stock solution of formic acid is added through the septum. However, the above-described procedure allows to reuse the same septum for multiple times.

\textsuperscript{(19)} For example, 152 \(\mu\)L/186 mg HCO\textsubscript{2}H and 26.1 \(\mu\)L/27.2 mg FPy in 2 mL reagent-grade THF.

\textsuperscript{(20)} During this process all solids dissolve, a dark red (but clear) organic phase and a pale yellow organic phase are formed. Work up with diluted HCl-solution allows to remove NE\textsubscript{3}. 

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observed in the case of alkyl chlorides,[8] alkylation of the silica gel is a likely explanation for this outcome.

**Figure S19.** Reaction start CO formation in DMF at room temperature (with 2.5 equiv formic acid and 3.3 mL THF). TCT dissolved very quickly in DMF and a vital gas formation can be seen in the CO chamber. Upon stirring is started, all solids dissolve in THF in the coupling chamber.

**Figure S20.** CO formation in DMF (with 1.5 equiv formic acid and 2.0 mL THF). A The chambers are charged rapidly successively with NEt₃ (right) and a stock solution of formic acid in DMF (left). B Reaction after 10 min, whereat a solid begins to precipitate in the CO chamber. C Reaction mixtures after stirring overnight.
3.2.6 General Procedure 4: Synthesis of β-Nitroketones (Scheme 2 G)

The cross coupling protocol was adapted from reference [12], wherein COgen 1 (2.5 equiv) was applied.

**Coupling Chamber** The first chamber is charged with aryl iodide 8 (0.40 mmol, 1.0 equiv), Pd(OAc)$_2$ (4.5 mg, 20 μmol, 5 mol%), Xantphos (11.6 mg, 20 μmol, 5 mol%) and dry MgCl$_2$ (46 mg, 0.48 mmol, 1.2 equiv). After preparation of the CO chamber, dry MeNO$_2$ (commercial from Sigma-Aldrich, 4 mL, 0.1 M) and reagent-grade NEt$_3$ (360 μL, 2.6 mmol, 6.5 equiv) are added to the coupling chamber, which is subsequently sealed with a screw cap.

**CO Chamber** The CO chamber was loaded with formic acid (38.1 μL, 46.0 mg, 1.00 mmol, 2.5 equiv), FPyr (3.9 μL, 4.1 mg, 40 μmol, 10 mol%) and dry THF (0.5 ml, 2 M with respect to formic acid). After MeNO$_2$ and NEt$_3$ have been introduced to the coupling chamber, TCT (70.0 mg, 0.38 mmol, 95 mol%) is added to the CO chamber, which is subsequently flushed with nitrogen for circa 10 s without stirring and sealed with a screw cap. Then, the gas reactor is placed in an oil bath, which has been preheated to 60 °C, and stirred at 600 rpm at 60 °C overnight (16-18 h).

**Work Up** The reaction mixture in the coupling chamber is transferred with CH$_2$Cl$_2$ (5 mL) to a 25 mL flask, 10 vol% of aqueous HOAc solution (3 mL) are added and the mixture is stirred for 1 h at room temperature. Next, the phases were separated, the organic phase was extracted with CH$_2$Cl$_2$ (1 x 3 mL), dried over Na$_2$SO$_4$ and concentrated under reduced pressure.

**Determination Yield with Internal Standard** and **Chromatographic Purification** are performed as described general protocol 1 (chapter 0, page 25).

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(21) Prior to reaction, MgCl$_2$ is dried in high vacuum under heating in a sand bath to 200 °C for approximately 8 h.
3.2.7 General Procedure 5: Synthesis of Amides based on Alternative Methods for CO Formation (Scheme 4)

**Coupling Chamber** The coupling chamber is charged with Pd(OAc)$_2$ (2.2 mg, 10 µmol, 2 mol%), PPh$_3$ (7.9 mg, 30 µmol, 6 mol%), 4-iodoanisole (117 mg, 0.50 mmol, 1.0 equiv), n-butylamine (74.2 µL, 54.9 mg, 0.75 mmol, 1.5 equiv) and the respective amount of NEt$_3$ (105-420 µL, 1.5-6.0 mmol, 1.5-6.0 equiv). After the CO chamber has been loaded with all components except of the reagent, dry toluene (0.50 mL, 1 M) is given into the coupling chamber and the chamber is closed with a screw cap.

**CO Chamber** Using TCT as reagent: The CO chamber is loaded with formic acid (28.6 µL, 34.9 mg, 0.75 mmol, 1.5 equiv), NMM as base (101 µL, 0.90 mmol, 1.80 equiv), FPyr (0/4.9 µL, 0/5.1 mg, 0/5 µmol, 0/10 mol%) and dry toluene (0.38 mL, 2 M with regard to formic acid). Finally, TCT (52.5 mg, 0.29 mmol, 57 mol%) is added in a single portion without stirring, the CO chamber is either sealed with a screw cap immediately after or before addition of the reagent. In the latter case, the reagent is added through the septum with the aid of a Hamilton syringe. Then, the reaction apparatus is placed in an oil bath, which has been preheated to 80 °C and stirred for 18 h at the very same temperature.

Using acid chlorides as reagent: The CO chamber is equipped with formic acid (28.6 µL, 34.9 mg, 0.75 mmol, 1.5 equiv) and dry toluene (0.38 mL, 2 M with regard to formic acid). Finally, the reagent, either oxalyl chloride (74 µL, 0.85 mmol, 1.7 equiv) or thionyl chloride (62 µL, 0.85 mmol, 1.7 equiv), is added without stirring. Thereby, the CO chamber is either sealed with a screw cap with septum immediately after or before addition of the reagent. In the latter case, the reagent is added through the septum with the aid of a Hamilton syringe. Then, the reaction apparatus is placed in an oil bath, which has been preheated to 80 °C, and stirred for 18 h.

Using Ac$_2$O as reagent: The CO chamber is charged with formic acid (28.6 µL, 34.9 mg, 0.75 mmol, 1.5 equiv) and acetic acid anhydride was added as reagent (142 µL, 1.5 mmol, 1.5 equiv). In the following, the CO chamber is closed with a screw cap, the reaction apparatus is placed in an oil bath preheated to 80 °C and stirred for 18 h.
After cooling down to room temperature, the reaction mixture in the coupling chamber is taken up with EtOAc (6 mL) and aqueous 1 N NaOH-solution (4 mL) with the aid of a 20 mL syringe. The phases are separated, the organic phase is extracted with more EtOAc (2 x 3 mL), the combined phases are washed with brine (1 x 6 mL), dried over MgSO₄, concentrated under reduced pressure and dried for 5 min at 5 mbar at the rotary evaporator.

Determination Yield with Internal Standard are conducted as described in general protocol 1 (chapter 0, page 25).

3.2.8 General Procedure 6: CO Formation for Gas Volumetric Measurements

In terms of apparative setup the gas volumetric measurements were performed as described in reference [1] of the group of Skrydstrup.

\[
\begin{align*}
\text{H}_2\text{O} & \xrightarrow{\text{TCT (27-54 mol%) or DMF (1 M), rt}} \text{CO} + \text{HCl} \\
(0.6-1.4 \text{ equiv}) & \text{FPyr (0-30 mol%) or solvent (0.6-1.4 M), T} \\
\end{align*}
\]

The experimental set-up for the gas volumetric measurements is displayed in Figure S21. The CO formation is carried out in a 10 mL Schlenk tube, which is sealed with a well-greased glass stopper. The Schlenk tube is connected via a rubber tube with an in-house build U-shaped gas volumeter. The volumeter is constructed from two 25 mL burettes (left) and a straight glass tube (right), which are joint by a U-shaped glass tube. While the straight glass tube is terminated by a NS 14 ground joint, which allows connection to the Schlenk tube, the burette part is open to the environment.
Figure S21. Experimental set-up for gas volumetric measurements consisting of an in-house build gas volumeter and a 10 mL Schlenk tube, which are connected by a tube. The water level is marked with blue arrows.

At the outset, a 10 mL Schlenk tube is marked at a height of 15 mm (see Figure S22 B). Next, the Schlenk tube is charged with TCT (99% purity, 40-41 mol%) in a well-ventilated fume-hood as described in Figure S22. A stir bar is added and the reaction vessel is connected to the Volumeter above an oil bath, which has been preheated to the reaction temperature $T$ (see Figure S23 A).
Figure S22. A A balance with a 4 mL glass vial with a screw cap containing an excess of TCT is tared to zero. B In a well ventilated fume hood a 10 mL Schlenk tube, which is placed into a 100 mL Erlenmeyer beaker, is charged with TCT by means of a spatula (red arrow indicates marking at 15 mm height). C The amount of TCT added to the Schlenk tube is controlled on the balance. This process is repeated until the intended amount of TCT has been accomplished. D Reaction setup for CO formation in DMF at room temperature.

In the following, a stock solution of formic acid (99% purity, 1 M) and FPyr (97% purity, 0-0.3 M) in the reaction solvent (1 M) is prepared in a 2 mL volumetric flask as shown in steps 1-3 in the representative graphical procedure in chapter 3.2.2 on page 30. It is important to choose the amount of formic acid properly in order not to exceed the capacity of the volumeter.
Figure S23. A Reaction start with Schlenk tube charged with TCT, water levels are marked with blue arrow. B Schlenk flask is immersed into the oil bath down to the blue marking at 1.5 cm (red arrow). The thermosensor (in the background) should be installed closely to the Schlenk tube.

Since formic acid is poorly soluble in toluene, formic acid is added neat after charging of the Schlenk tube with TCT. The following steps have to be conducted swiftly. The formic acid (0.3-1 mmol, 1.0 equiv) and FPyr (0-30 mol%) stock solution (300-1000 μL) are added into to the Schlenk tube by means of a 1 mL syringe in one portion. Immediately after the Schlenk tube is closed with a well-greased glass stopper, which is fixed with a metal clamp. Now the level of the water in the gas volumeter is noted as starting point. In the following, stirring is initiated (400 rpm) and the oil bath is raised until the level of the oil and the marking on the Schlenk tube are in accordance (Figure S23 B). At this point the time measurement is started. A constant immersion depth of the Schlenk tube into the oil bath is important for the reproducibility of the measurements.

The gas volume is monitored for 60 min at the reaction temperature T, after which the oil bath is lowered, stirring is interrupted and the monitoring is continued for 30 min (see Figure S24 B). For all measurements data points are collected with the same time distances as
described for the representative experiment in chapter 3.4, page 141). In addition, the ambient temperature and pressure (manometer of a membrane pump) were noted.

In the case of DMF as solvent a septum was used instead of a glass stopper (measurement at room temperature, see Figure S22 D). The formic acid stock solution in DMF is added through the septum into the Schlenk tube to avoid loss of CO.

Figure S24. A Gas volumeter with difference in water levels marked blue red arrows. B Cool down phase, red line at Schlenk flask indicated 1.5 cm height.

To probe the gas tightness of the experimental setup, occasionally the apparatus was left overnight after the final measurement. The following day, the volume had only marginally changed ≤0.2 mL, which verifies the virtual impermeability towards gases.
3.3 Experimental Procedures and Analytical Data

3.3.1 Synthesis of Amides 10 (Scheme 2 B-D)

3.3.1.1 Synthesis of \( N-n \)-Butyl 4-methoxybenzamide (10a)

![Diagram of synthesis process]

| entry | Solvent | CO chamber | Solvent | Coupling chamber | t [h] | yield 10a [%] | Lab journal no. |
|-------|---------|------------|---------|-----------------|------|--------------|----------------|
| 1     | dioxane |            | dioxane |                 | 14   | 91           | PH4082         |
| 2     | "       |            | "       |                 | 16   | 89           | PH4056         |
| 3     | MeCN    |            | "       |                 | 16   | 89           | PH4064         |
| 4     | THF     |            | "       |                 | 13   | 85           | PH4059         |
| 5     | THF     |            | THF     |                 | 16   | 84           | PH4065         |
| 6     | DMF@rt  | dioxane    | dioxane |                 | 8    | 84           | PH4078         |
| 7     | "       |            | DMF     |                 | 13   | 60           | PH4060         |
| 8     | toluene |            | dioxane |                 | 17   | 81           | PH4073         |
| 9     | "       | toluene    |         |                 | 19   | 81\(^c\)     | BZ182          |
| 10\(^d\) | "       | "          |         |                 | 19   | 89           | BZ181          |
| 11\(^e\) | DMF@rt  | dioxane    |         |                 | 14   | 84\(^c\)/79  | PH4118         |
| 12\(^f\) | dioxane |            |         |                 |      |              | PH4246         |
| 13\(^g\) | toluene | toluene    |         |                 | 17   | ≤3\(^c\)     | BZ229          |

a. Yield refer to isolated material after chromatographic purification. b. CO formation conducted at RT, no FPyr used. c. Yield determined with Bn\(_2\)O as internal NMR standard. d. Reaction conducted at 100 °C with 4-bromoanisole instead of 4-iodoanisole. e. Carried out with 1.0 equiv HCO\(_2\)H, 40 mol% TCT and 1.2 equiv 4-iodoanisole. F. With 20 mol% DMF instead of 10 mol% FPyr g. Reaction was performed in a 4 mL glass vial containing all reaction components.

CO formation and cross coupling in dioxane guaranteed preparation of the title amide in reproducible yields of 89-91% (entries 1+2). For the experiment in entry 1 a graphical procedure is given in chapter 3.2.2 on page 30. Carbon monoxide synthesis in MeCN delivered 10a in essentially the same yield of 89% (entry 3). However, cross coupling in MeCN resulted in incomplete conversion and poorer chemoselectivity (not shown). When CO generation was performed in THF, amide 10a could be isolated in 84-85% yield (entries 4+5). Thereby, carbonylative amination could also be carried out in THF instead of dioxane (entry 5).

Importantly, the production of CO can also be conducted in DMF as solvent (and catalyst) at room temperature, which delivered the amide 10a in a yield of 84% (entry 6). However, CO formation and carbonylative coupling in DMF gave rise of 10a in a diminished yield of 60% (entry 7). Formic acid could be even transformed in CO in toluene, which provided the title amide in a yield of 81%.
amide in 81% yield regardless, if dioxane or toluene was utilized as solvent in the cross coupling proves (entries 8-9). In conclusion, for the carbonylative amination, dioxane and THF are the best solvents, whereas toluene also allows for sufficient results. In contrast, MeCN and DMF are non-viable. In entries 1-9 full consumption of 4-iodoanisole was accomplished.

Significantly, coupling with 4-bromoanisole at an elevated temperature of 100 °C furnished amide 10a in a good yield of 89% (entry 10). Finally, CO formation using formic acid as yield-limiting compound (1.0 equiv) gave rise of amide 10a in 84% yield, as determined by means of an internal NMR standard and in 79% isolated yield (entry 11). When the CO production and cross coupling are conducted in the very same reaction vessel, almost on amide 10a is obtained (entry 12).

**Entry 1, PH4082:** A graphical procedure is available in chapter 3.2.2 on page 30 for this experiment. According to general protocol 1 (chapter 0, page 25) the coupling chamber was charged with Pd(OAc)$_2$ (4.4 mg, 20 µmol, 2 mol%), PPh$_3$ (21.0 mg, 80 µmol, 8 mol%), 4-iodoanisole (234 mg, 1.00 mmol, 1.0 equiv), n-butylamine (150 µL, 110 mg, 1.5 mmol, 1.5 equiv), NEt$_3$ (420 µL, 304 mg, 3.0 mmol, 3.0 equiv) and dry dioxane (1.0 mL, 1 M). Into the CO chamber were added TCT (107 mg, 0.57 mmol, 57 mol%) and finally a 2.0 M HCO$_2$H/0.13 M FPyr stock solution in dry dioxane (750 µL, 1.5 mmol, 1.5 equiv of HCO$_2$H/100 µmol, 10 mol% of FPyr). At the outset, in the CO chamber was obtained a clear solution.

After heating to 80 °C for 14 h, work up delivered the crude title compound as a dark red oil (291 mg, 140%), of which $^1$H-NMR confirmed full conversion of 4-iodoanisole (8a). Ultimately, column chromatographic purification on silica gel (23.8 g, ratio of masses crude 10a/SiO$_2$ 82:1) with EtOAc/CH$_2$Cl$_2$ 15:85 yielded amide 10a as an orange oil (187.9 mg, 0.91 mmol, 91%), which solidified at ambient temperature.

**Entry 2, PH4056:** This experiment was conducted as described in entry 1 with the minor deviation, that the reaction mixtures were stirred for 16 h at 80 °C. $^1$H-NMR of the crude material (266 mg, 129%, black oil) indicated complete conversion of 4-iodoanisole. Ultimately, purification with the aid of column chromatography on silica gel (22.4 g, mass relation crude product/SiO$_2$ 1:83) using EtOAc/CH$_2$Cl$_2$ 15:85 gave rise of the title amide 10a as a yellow oil (184.7 mg, 0.89 mmol, 89%), which turned into a yellow solid upon storage at ambient temperature.

**Entry 3, PH4064:** Following general procedure 1 (chapter 0, page 25) the title amide was synthesized from 4-iodoanisole (1.00 mmol, 1.0 equiv) and n-butylamine (1.5 equiv) using Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%) and NEt$_3$ (3.0 equiv) in dioxane (1 M). Thereby, CO formation was carried out with TCT (57 mol%) and a 2.0 M HCO$_2$H/0.13 M FPyr stock solution.
in dry MeCN (750 µL, 1.5 equiv formic acid/10 mol% FPyr). Past 16 h of heating to 80 °C, aqueous work up furnished the crude product as a black oil (311 mg, 150%). ¹H-NMR revealed complete consumption of 4-iodoanisole. Next, chromatographic purification on silica gel (22.4 g, weight of crude material with respect to SiO₂ 1:72) as stationary phase and EtOAc/CH₂Cl₂ 15:85 afforded product 10a as yellow oil (183.9 mg, 0.89 mmol, 89%), which solidified at ambient temperature.

**Entry 4, PH4059:** In accordance with standard operating procedure (chapter 0, page 25) the product 10a was obtained by combination of Pd(OAc)₂ (2 mol%), PPh₃ (8 mol%), 4-iodoanisole (1.00 mmol, 1.0 equiv), nBuNH₂ (1.5 equiv), dry dioxane (1 M) and NEt₃ (3.0 equiv) upon heating to 80 °C for 13 h. Thereby, carbon monoxide was formed with the aid of a 2.0 M HCO₂H/0.13 M FPyr solution in reagent-grade THF (750 µL, 1.5 equiv formic acid/10 mol% FPyr) and TCT (57 mol%). Then, the crude material (276 mg, 133%, black oil, ≥98% conversion of 4-iodoanisole) was subjected to column chromatographic purification on silica gel (21.8 g, mass ratio crude 10a/silica gel 1:79), which yielded product 10a as a yellow solid (175.8 mg, 0.85 mmol, 85%).

**Entry 5, PH4065:** Preparation of the title compound as delineated in general procedure 1 (chapter 0, page 25) was conducted with 4-iodoanisole (1.00 mmol, 1.0 equiv), nBuNH₂ (1.5 equiv), Pd(OAc)₂ (2 mol%), PPh₃ (8 mol%) and NEt₃ (3.0 equiv) in reagent-grade THF (1.0 mL, 1 M) under stirring at 80 °C for 16 h. CO was obtained by mixing TCT (57 mol%) with a 2.0 M formic acid/0.13 M FPyr stock solution in reagent-grade THF (750 µL, 1.5 equiv HCO₂H/10 mol% FPyr). Column chromatographic purification of the crude material (278 mg, 134%, black oil, full conversion of 8a as judged by ¹H-NMR) engaging silica gel (26.6 g, relation of weights crude product/SiO₂ 1:74) and EtOAc/CH₂Cl₂ 15:85 finally furnished amide 10a as a pale yellow solid (174.6 mg, 0.84 mmol, 84%).

**Entry 6, PH4078:** The synthesis of 10a was performed as given in general protocol 1 (chapter 0, page 25) using Pd(OAc)₂ (2 mol%), PPh₃ (8 mol%), 4-iodoanisole (1.00 mmol, 1.0 equiv), n-butylamine (1.5 equiv), NEt₃ (3.0 equiv) in dry dioxane (1 M) at 80 °C under stirring for 8 h. Carbon monoxide was produced from TCT (57 mol%) and a 2.0 M HCO₂H solution in dry DMF (750 µL, 1.5 equiv formic acid) under stirring for 8 h at room temperature. Eventually, chromatographic purification of the crude product (294 mg, 142%, dark red oil, full consumption of 4-iodoanisole according to ¹H-NMR) on silica gel (23.5 g, mass ratio crude 10a/SiO₂ 1:81) with EtOAc/CH₂Cl₂ delivered amide 10a as a yellow solid in 84% yield (174.1 mg, 0.84 mmol, 84%).

**Entry 7, PH4060:** The production of amide 10a was carried out as described in entry 6, with the deviation that in the coupling chamber was also used dry DMF (1 M) as solvent and a reaction duration of 13 h. Aqueous work up provided the crude material as a black oil (245 mg, 118%), of which ¹H-NMR unravelled ≥98% conversion of 4-iodoanisole. In the end, purification
by means of column chromatography on silica gel (22.5 g, ratio weight crude product with regard to SiO$_2$ 1.92) employing a 15:85 mixture of EtOAc/CH$_2$Cl$_2$ as eluent resulted in the isolation of amide 10a as a yellow solid (124.0 mg, 0.60 mmol, 60%).

**Entry 8, PH4073:** In agreement with general protocol 1 (chapter 0, page 25) the coupling chamber was charged successively with Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%), 4-iodoanisole (1.00 mmol, 1.0 equiv), nBuNH$_2$ (1.5 equiv), dry dioxane (1 M) and NEt$_3$ (3.0 equiv). Into the CO chamber were introduced TCT (57 mmol), formic acid (57.2 μL, 69.7 mg, 1.5 mmol, 1.5 equiv) and a 0.13 M stock solution of FPyr in reagent-grade toluene (750 μL, 100 μmol, 10 mol%).\(^{(22)}\) The reaction apparatus was heated to 80 °C for 17 h. Finally, column chromatographic purification of the crude material (291 mg, 141%, black oil), of which $^1$H-NMR confirmed full conversion of 4-iodoanisole, using silica gel (21.4 g, ratio crude 10a/SiO$_2$ 1:74) and EtOAc/CH$_2$Cl$_2$ 15:85 gave rise of amide 10a (167.6 mg, 0.81 mmol, 81%) as a black solid.

**Entry 9, BZ182:** In alignment to general procedure 1 (chapter 0, page 25) the title amide was accessed using Pd(OAc)$_2$ (2 mol%), PPh$_3$ (15.7 mg, 60 μmol, 6 mol%), 4-iodoanisole (1.00 mmol, 1.0 equiv), nBuNH$_2$ (1.5 equiv) and NEt$_3$ (3.0 equiv) in reagent-grade toluene (1.0 mL, 1 M). Thereby, the CO chamber was charged successively with formic acid (1.5 equiv), FPyr (9.8 μL, 10.2 mg, 100 μmol, 10 mol%) and reagent-grade toluene (0.75 mL, 2 M). After stirring for 19 h at 80 °C work up delivered the crude product, of which $^1$H-NMR with dibenzylether (32.0 mg) confirmed full conversion of 4-iodoanisole and the amide 10a in a yield of 81%.

**Entry 10, BZ181:** In alignment to general procedure 1 (chapter 0, page 25) the reaction chamber was charged with 4-bromoanisole (187 mg, 1.00 mmol, 1.0 equiv), Pd(OAc)$_2$ (4.4 mg, 20 μmol), PPh$_3$ (15.7 mg, 60 μmol, 6 mol%), n-butylamine (150 μL, 110 mg, 1.5 mmol, 1.5 equiv) NEt$_3$ (420 μL, 305 mg, 3.0 mmol, 3.0 equiv) and toluene (1.0 mL, 1 M). Into the CO chamber were added formic acid (57 μL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 μL, 10.2 mg, 100 μmol, 10 mol%), toluene (0.75 mL, 2 M) and finally TCT (107 mg, 0.57 mmol, 57 mol%). The reaction apparatus was purged with nitrogen, closed with a screw cap and stirred for 19 h at 100 °C. Finally, adsorption on silica gel (1.5 g, relation weight theoretical yield/SiO$_2$ 1:7) of the crude reaction mixture and chromatographic purification on silica gel (20.8 g, ratio weight theoretical yield/SiO$_2$ 1:99) employing EtOAc/PE 65:35 gave the title compound as a pale yellow solid in 89% yield (184.8 mg, 0.89 mmol).

**Entry 11, PH4118:** In orientation to general protocol 1(chapter 0, page 25) the coupling chamber was charged with Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%), 4-iodoanisole (281 mg, 1.2 mmol, 1.2 equiv), dry dioxane (1 M) and NEt$_3$ (3.0 equiv) and was closed with a screw cap with septum. The CO chamber was loaded with TCT (75 mg, 0.40 mmol, 40 mol%) and was

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\(^{(22)}\) Formic acid is of poor solubility in toluene and can therefore not be added a stock solution in this solvent.
sealed with a screw cap with septum. Then, a 2.0 M solution of HCO$_2$H in dry DMF (500 µL, 1.00 mmol, **1.0 equiv**) was added into the CO chamber through the septum. In the following the cross coupling chamber was heated to 80 °C for 17 h, while the reaction mixture in the CO chamber was stirred at room temperature. $^1$H-NMR of the crude product (327 mg, 158%, black oil) with dibenzylether (51.8 mg) showed the title amide in a yield of 84% alongside with 35% of unreacted 4-idoanisole. Eventually, purification with the aid of column chromatography on silica gel (26.3 g, mass relation crude material/SiO$_2$ 1:80) with EtOAc 15:85 afforded amide **10a** as a black solid in 79% yield (164.4 mg, 0.79 mmol, 79%).

**Entry 12, PH4246:** In accordance to general procedure 1 (chapter 0, page 25) the title compound was prepared from 4-idoanisole (1.00 mmol, 1.0 equiv) and $n$-butylamine (1.5 equiv) using Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%) and NEt$_3$ (3.0 equiv) in dioxane under heating to 80 °C for 18 h. CO was produced from TCT (57 mol%) with a 2.0 M and 0.27 M, respectively, stock solution of formic acid (1.5 equiv) and DMF (20 mol%) in dioxane. $^1$H-NMR of the crude material (287 mg, 139%, black oil) after aqueous work up confirmed full consumption of the starting aryl iodide. Finally, purification with the aid of column chromatography on silica gel (23.7 g, mass relation crude material/SiO$_2$ 1:82) using EtOAc/CH$_2$Cl$_2$ 15:85 afforded the product **10a** as a black oil in 85% yield (175.5 mg, 0.85 mmol).

**Entry 13, BZ226:** In alignment to general protocol 1 (chapter 0, page 25) a 4 mL glass vial with a stir bar was charged with Pd(OAc)$_2$ (2 mol%), PPh$_3$ (6 mol%). 4-idoanisole (500 µmol, 1.0 equiv), butylamine (1.5 equiv), NEt$_3$ (3.0 equiv), formic acid (1.5 equiv), FPyr (10 mol%), and dry toluene (1 M). Then, TCT was added (57 mol%), the vial was closed with a screw cap with septum and heated in an alumina carousel to 80 °C for 17 h. After aqueous work up, $^1$H-NMR with dibenzylether as internal standard revealed amide **10a** only in minor traces ≤3%.

$\text{M} \ (C_{12}H_{17}NO_2) = 207.27 \ \text{g/mol}; \ \text{mp.} \ 50-54 \ ^\circ\text{C}, \ \text{Lit-mp.:} \ 48-50 \ ^\circ\text{C};^{[13]}$

$\text{r}_1 \ (\text{SiO}_2, \ \text{EtOAc}/\text{CH}_2\text{Cl}_2 \ 15:85) = 0.34; \ ^1\text{H-NMR} \ (400 \ \text{MHz, CDCl}_3) \ \delta \ [\text{ppm}] = 7.75-7.73 \ (m, 2H, 3-H), 6.91-6.88 \ (m, 2H, 4-H), 6.29 \ (\text{br. s, 1H, NH}, 3.83 \ (\text{s, 3H, 6-H}), 3.45-3.40 \ (m, 2H, 1'-H), 1.62-1.54 \ (m, 2H, 2'-H), 1.44-1.35 \ (m, 2H, 3'-H), 0.94 \ (t, 3J_{H:3} = 7.3 \ \text{Hz, 3H, 4'-H}); \ ^{13}\text{C-NMR} \ (100 \ \text{MHz, CDCl}_3) \ \delta \ [\text{ppm}] = 167.18 \ (C-1), 162.08 \ (C-5), 128.73 \ (C-3), 127.24 \ (C-2), 113.74 \ (C-4), 55.46 \ (C-6), 39.84 \ (C-1'), 31.90 \ (C-2'), 20.26 \ (C-3'), 13.88 \ (C-4'); \ \text{GC-MS} \ (\text{Cl}, \ 70 \ \text{eV}) \ m/z \ [\%] = 248 \ (3, [M+Allyl]^+), 236 \ (20, [M+Et]^+), 222 \ (5, [M+Me]^+), 208 \ (100, [M+H]^+), 207 \ (20, [M]^+), 206 \ (5, [M-H]^+), 165 \ (11), 151 \ (6, [4-MeO(C_6H_4)CONH_2]^+), 135 \ (40, [M-NHMe]^+), 109 \ (6) 92 \ (2, [BnH]^+), 77 \ (2, [Ph]^+).$

The NMR data is in match with the literature.$^{[13]}$
**H-NMR spectrum of N-n-butyl 4-methoxybenzamide (400 MHz, CDCl₃).**

**C-NMR spectrum of N-n-butyl 4-methoxybenzamide (100 MHz, CDCl₃).**
3.3.1.2 Synthesis of N-(2-morpholin-4-ylethyl) 4-chlorobenzamide (Moclobemide, 10b)

BZ139: In agreement with general protocol 1 (chapter 0, page 25) the title compound was synthesized from 4-chloro-1-iodobenzene (239 mg, 1.00 mmol, 1.0 equiv) and 4-(2-aminoethyl)morpholine (197 µL, 195 mg, 1.5 mmol, 1.5 equiv) with Pd(OAc)$_2$ (2.2 mg, 20 µmol, 2 mol%), PPh$_3$ (15.7 mg, 60 µmol, 6 mol%) and NEt$_3$ (420 µL, 305 mg, 3.0 mmol, 3.0 equiv) in toluene (1.0 mL, 1 M) under heating to 80 °C for 23 h. CO was generated from formic acid (57 µL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 µL, 10.2 mg, 100 µmol, 10 mol%) and TCT (107 mg, 0.58 mmol, 57 mol%) in toluene (0.75 mL, 2 M in terms of formic acid). In the following, the reaction mixture was concentrated to dryness with silica gel (2.4 g, mass relation theoretical yield/SiO$_2$ 1:9), the residue was subjected to column chromatographic purification on silica gel (19.4 g, ratio of weight theoretical yield/SiO$_2$ 1:73) under gradient elution MeOH/EtOAc/NEt$_3$ 4:96:0 (100 mL $\rightarrow$ 4:92:2, which yielded the title compound as a pale yellow solid (217 mg, 0.81 mmol, 81%).

M (C$_{13}$H$_{17}$ClN$_2$O$_2$) = 268.74 g/mol; mp. 135-137 °C (lit.-mp. 135-137 °C).[14] R$_f$ (SiO$_2$, MeOH/EtOAc 5:95) = 0.16; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ [ppm] = 7.73-7.70 (m, 2H, 3'-H), 7.42-7.40 (m, 2H, 4'-H), 6.79 (s, 1H, NH) 3.73 (t, $^3$J$_{4',3'}$ = 4.4 Hz, 4H, 4'-H), 3.54 (t, $^3$J$_{q',q}$ = 5.6 Hz, 2H, 1'-H), 2.60 (t, $^3$J$_{2',1'}$ = 5.8 Hz, 2H, 2'-H), 2.50 (t, $^3$J$_{3',4'}$ = 4.4 Hz, 4H, 3'-H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ [ppm] = 166.27 (C-1), 137.54 (C-5), 132.90 (C-2), 128.74 (C-4), 128.29 (C-3), 66.91 (C-4'), 56.75 (C-2'), 53.26 (C-3'), 36.04 (C-1'); GC-MS (Cl, 70 eV) m/z [u] (%) =
271 (6, [M\(^{37}\text{Cl}\)]\(^+\)), 269 (14, [M\(^{35}\text{Cl}\)]\(^+\)), 210 (2), 184 (11, [M\(^{37}\text{Cl}\)-N(CH\(_2\text{CH}_2\text{O})]+)), 182 (14, [M\(^{35}\text{Cl}\)-N(CH\(_2\text{CH}_2\text{O})]+)), 170 (15), 157 (18), 156 (63, [4-Cl(C\(_6\text{H}_4\text{C(OH)NH})]+)), 141 (20, [4-\(^{37}\text{Cl}(C\(_6\text{H}_4\text{CO})]+)), 139 (51, [4-\(^{35}\text{Cl}(C\(_6\text{H}_4\text{CO})]+)), 138 (71), 116 (44), 100 (34, [O(CH\(_2\text{CH}_2\text{NCH}_2\text{2})\]+), 88 (100, [O(CH\(_2\text{CH}_2\text{NH}_2\text{2})]+), 86 (62, [O(CH\(_2\text{CH}_2\text{CH}_2\text{CH})\text{NH}]\)+), 72 (31), 70 (35), 58 (36).

The NMR data is in match with the literature.\(^2\)

\(^1\text{H-NMR spectrum of Moclobemide (400 MHz, CDCl}_3\).}
\(^{13}\text{C}\)-NMR spectrum of \textit{Moclobemide} (100 MHz, CDCl\(_3\)).

Mass spectrum of \textit{Moclobemide} (Cl, 70 eV).
3.3.1.3 Synthesis of 1-\(^{13}\)C-N-(2-morpholin-4-ylethyl) 4-chlorobenzamide (Moclobemide, \(^{13}\)C-10b)

BZ154: According to general protocol 1 (chapter 0, page 25) the coupling chamber was charged with 4-chloro-1-iodobenzene (239 mg, 1.00 mmol, 1.0 equiv), 4-(2-aminomethyl)morpholine (197 µL, 195 mg, 1.5 mmol, 1.5 equiv), Pd(OAc)_2 (2.2 mg, 20 µmol, 2 mol%), PPh_3 (15.7 mg, 60 µmol, 6 mol%), NEt_3 (420 µL, 305 mg, 3.0 mmol, 3.0 equiv) and toluene (1.0 mL, 1 M). The CO chamber was loaded with \(^{13}\)C-enriched formic acid (99 atom% \(^{13}\)C, 57 µL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 µL, 10.2 mg, 100 µmol, 10 mol%), toluene (0.75 mL, 2 M in terms of formic acid) and TCT (107 mg, 0.58 mmol, 57 mol%). The reaction apparatus was flushed with nitrogen and heated for 17 h to 80 °C. Next, the reaction mixture was adsorbed on SiO\(_2\) (1.7 g, ratio of mass theoretical yield/silica gel 1:6) and the title compound was obtained after column chromatographic purification harnessing SiO\(_2\) (18.9 g, ratio of weight theoretical yield/SiO\(_2\) 1:70) under gradient elution MeOH/EtOAc/NEt\(_3\) 4:96:0 (100 mL) → 4:92:2 as a pale yellow solid (217 mg, 0.81 mmol, 81%).

\( M \) (C\(_{12}\)\(^{13}\)CH\(_1\)Cl\(_2\)N\(_2\)O\(_2\)) = 269.73 g/mol; mp. 135-137 °C (i); \( r_i \) (SiO\(_2\), MeOH/EtOAc 5:95) = 0.16; 
\(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) [ppm] = 7.73-7.70 (m, 2H, 3-H), 7.42-7.40 (m, 2H, 4-H), 6.80 (s, 1H, NH) 3.73 (\( \psi \)-t, \( ^3\)J\(_{\psi,3} = 4.6\) Hz, 4H, 4′-H), 3.54 (\( \psi \)-q, \( ^3\)J = 5.6 Hz, 2H, 1′-H), 3.56-3.51 (m, 2H, 2′-H), 2.60 (t, \( ^3\)J\(_{H,4} = 6.1\) Hz, 2′-H), 2.50 (t, \( ^3\)J\(_{H,4} = 4.3\) Hz, 4H, 3′-H); 
\(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \( \delta \) [ppm] = 166.26 (C-1), 137.54 (C-5), 132.89 (d, \( ^1\)J\(_{C,1} = 65\) Hz, C-2), 128.74 (d, \( ^3\)J\(_{C,1} = 4\) Hz, C-4), 128.29 (d, \( ^2\)J\(_{C,3} = 3\) Hz, C-3), 66.91 (C-4′), 56.75 (C-2′), 53.25 (C-3′), 36.03 (C-1′); 
GC-MS (Cl, 70 eV) m/z [u] (%) = 272 (4, \([M^{37}\text{Cl}]^+\)), 270 (14, \([M^{35}\text{Cl}]^+\)), 211 (6), 185 (13, \([M^{37}\text{Cl}]-\text{N(CH}_2\text{CH}_2\text{)}\_2\text{O}]^+\)), 183 (15, \([M^{35}\text{Cl}]-\text{N(CH}_2\text{CH}_2\text{)}\_2\text{O}]^+\)), 171 (16), 157 (60, \([4-\text{Cl(C}_{6}\text{H}_4\text{)}^{13}\text{C(OH)}\text{NH}_2\text{]}^+\)), 142 (31, \([4-^{37}\text{Cl(C}_{6}\text{H}_4\text{)}^{13}\text{CO}]^+\)), 140 (46, \([4-^{35}\text{Cl(C}_{6}\text{H}_4\text{)}^{13}\text{CO}]^+\)), 139 (63), 116 (39), 100 (28, \([O(\text{CH}_2\text{CH}_2\text{)}\_2\text{NCH}_2\text{]}^+\)), 88 (100, \([O(\text{CH}_2\text{CH}_2\text{)}\text{NH}]^+\)), 86 (57, \([O(\text{CH}_2\text{CH}_2)(\text{CH}_2\text{CH})\text{NH}]^+\)), 72 (31), 70 (31), 61 (28).

The NMR data is in match with the Moclobemide sample not enriched in \(^{13}\)C (see above).
$^1$H-NMR spectrum of N-(quinol-$8^-$yl) 2-methylbenzamide (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of N-(quinol-$8^-$yl) 2-methylbenzamide (100 MHz, CDCl$_3$).
**3.3.1.4 Synthesis of N,N-Diethyl 3-methylbenzamide (DEET, 10c)**

**BZ183:** As delineated in general protocol 1 (chapter 0, page 25) the title compound was prepared from 3-iodotoluene (218 mg, 1.00 mmol, 1.0 equiv) and diethylamine (155 µL, 110 mg, 1.50 mmol, 1.5 equiv) under heating to 80 °C for 18 h with Pd(OAc)$_2$ (2.2 mg, 20 µmol, 2 mol%), PPh$_3$ (15.7 mg, 60 µmol, 6 mol%), and NEt$_3$ (420 µL, 305 mg, 3.0 mmol, 3.0 equiv) in toluene (1.0 mL, 1 M). Carbon monoxide was produced from formic acid (57 µL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 µL, 10.2 mg, 100 µmol, 1.0 mol%) and TCT (107 mg, 0.58 mmol, 57 mol%) in toluene (0.75 mL, 2 M with respect to formic acid). In the end, adsorption of the reaction mixture on silica gel (1.3 g, relation of masses theoretical yield/SiO$_2$ 1:7), column chromatographic purification on silica gel (19.3 g, weight ratio theoretical yield/SiO$_2$ 1: 100) with EtOAc/PE 25:75 and drying at the rotary evaporator at 5 mbar for 5 min furnished the insecticide DEET as a brownish oil (169.5 mg, 0.89 mmol, 89%).

$M\ (C_{12}H_{17}NO) = 191.27$ g/mol; $r_1\ (SiO_2, \text{EtOAc/PE} \ 20:80) = 0.24$; $^1\text{H-NMR} \ (500 \text{MHz, CDCl}_3) \ \delta \ [ppm] = 7.26 \ (\psi-t, J = 7.3 \text{ Hz, 1H, 6-H}), 7.20-7.18 \ (m, 2H, 3-H, 5-H), 7.15-7.13 \ (m, 1H, 7-H), 3.54 \ (\text{br. s, 2H, 1′-H}_a), 3.25 \ (\text{br. br. s, 2H, 1′-H}_b), 2.36 \ (s, 3H, 8-H), 1.24-1.10 \ (m, 6H, H-2′);$  

$^{13}\text{C-NMR} \ (125 \text{MHz, CDCl}_3) \ \delta \ [ppm] = 171.43 \ (C-1), 138.13 \ (C-2), 137.16 \ (C-4), 129.69 \ (C-5), 128.14 \ (C-6), 126.83 \ (C-3), 123.06 \ (C-7), 43.18 \ (C_b-1′), 39.08 \ (C_a-1′), 21.29 \ (C-8), 14.13 \ (C_b-2′), 12.81 \ (C_a-2′);$  

$\text{GC-MS} \ (\text{CI, 70 eV}) \ m/z \ [u] \ [%] = 232 \ (2, [M+allyl]^+), 220 \ (25, [M+Et]^+), 219 \ (20, [M]^+), 218 \ (8, [M+Me]^+), 217 \ (8, [M+MeH]^+), 191 \ (1, [M]^+), 189 \ (1, [M-H]^+)$.

Mass spectrum of 1-(phenylacetyl) pyrrolidine (CI, 70 eV).
206 (5, [M+Me]⁺), 192 (100, [M+H]⁺), 190 (47, [M-H]⁺), 119 (25, [M-NEt₂]⁺), 100 (4, [Et₂NCO]⁺), 91 (5, [Bn]⁺), 65 (2, [Cp]⁺).

The NMR data is in match with the literature.²

¹H-NMR spectrum of N,N-diethyl 3-methylbenzamide (400 MHz, CDCl₃).
$^{13}$C-NMR spectrum of $N,N$-diethyl 3-methylbenzamide (100 MHz, CDCl$_3$).

Mass spectrum of $N,N$-diethyl 3-methylbenzamide (Cl, 70 eV).
3.3.1.5 Synthesis of N-2-Phenylethyl 3-(tert-butyloxycarbonyl) benzamide (10d)

BZ147: As described in general protocol 1 (chapter 0, page 25) the title compound was prepared from tert-butyl 3-iodobenzoate (302 mg, 0.92 mmol under consideration of 11 mol% residual Boc₂O, 1.0 equiv, for synthesis see chapter 3.3.5.1 on page 134) and 2-phenylethyl amine (189 μL, 181 mg, 1.50 mmol, 1.50 equiv) using Pd(OAc)₂ (2.2 mg, 20 μmol, 2 mol%), PPh₃ (15.7 mg, 60 μmol, 6 mol%) and NEt₃ (420 μL, 305 mg, 3.0 mmol, 3.0 equiv) in toluene (1.0 mL, 1 M). CO was generated from formic acid (57 μL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 μL, 10.2 mg, 100 μmol, 10 mol%) and TCT (107 mg, 0.58 mmol, 57 mol%) in toluene (0.75 mL, 2 M with respect to formic acid). After purging with nitrogen, the reaction apparatus was heated in an oil bath for 17 h at 80 °C. Aqueous work up gave the crude amide 10d (362 mg, 120%) as a yellow oil, of which ¹H-NMR verified full conversion of tert-butyl 3-iodobenzoate. In addition, 10 mol% of tert-butyl 3-(2-oxo-2-(phenethylamino)acetyl) benzoate in regard to the title compound were detected. Eventually, the crude material was adsorbed on silica gel (1.8 g, relation of masses crude product/SiO₂ 1:5), purified with the aid of column chromatography on silica gel (19.3 g, weight ratio crude title compound/SiO₂ 1:53) with EtOAc/PE 20:80 as eluent system, which facilitated isolation of amide 10d as brownish oil in 73% yield (219 mg, 0.67 mmol). Moreover, tert-butyl 3-(2-oxo-2-(phenethylamino)acetyl) benzoate was obtained as side-product (33.6 mg, 0.10 mmol, 11%).

N-2-Phenylethyl 3-(tert-butyloxycarbonyl) benzamide (10d)

M (C₂₀H₂₃NO₃) = 325.41 g/mol; n (SiO₂, EtOAc/PE 20:80) = 0.26; ¹H-NMR (400 MHz, CDCl₃) δ [ppm] = 8.24 (ψ-t, ¹J = 1.5 Hz, 1H, 3-H), 8.11-8.08 (m, 1H, 5-H), 7.92 (m, 1H, 7-H), 7.47 (ψ-t, ¹J = 7.7 Hz, 1H, 6-H), 7.35-7.31 (m, 2H, 5´-H). 7.26-7.23 (m, 3H, 4´-H, 6´-H), 6.33 (s, 1 H, NH), 3.75-3.70 (m, 2H, 1´-H), 2.94 (t, ²J₂,₁ = 7.0 Hz, 2H, 2´-H), 1.60 (s, 9H, 10-H);¹³C-NMR (100 MHz, CDCl₃) δ [ppm] = 166.73 (C-1), 164.96 (C-8), 138.75 (C-3´), 134.71 (C-2 or C-4), 132.30 (C-2 or C-4), 132.22 (C-5), 131.11 (C-7), 128.76 (C-4´), 128.70 (C-5´), 128.64 (C-6), 127.28 (C-3), 126.60 (C-6´), 81.66 (C-9), 41.26 (C-1´), 35.63 (C-2´), 28.12 (C-10); HR-MS (Cl, [C₂₀H₂₃NO₃⁺] calc. 326.1756 u found 326.1751 u.

tert-butyl 3-(2-oxo-2-(phenethylamino)acetyl) benzoate

M (C₂₁H₂₅NO₄) = 353.42 g/mol; ¹H-NMR (400 MHz, CDCl₃) δ [ppm] = 8.84 (s, 1H, 4-H), 8.49 (d, ³J₈,₇ = 7.8 Hz, 1H, 8-H), 8.23 (d, ³J₆,₇ = 7.7 Hz, 1H, 6-H), 7.53 (ψ-t, ²J = 7.8 Hz, 1H, 6-H), 7.35-7.31 (m, 2H, 5´-H), 7.27-7.23 (m, 3H, 4´-H, 6´-H), 7.19 (br. s, 1H, NH), 3.67 (ψ-q, ³J = 6.7 Hz, 2H,
1\textsuperscript{H}-NMR spectrum of \textit{N}-2-phenylethyl 3-(tert-butyloxy carbonyl) benzamide (400 MHz, CDCl\textsubscript{3}).

\textsuperscript{13}C-NMR (100 MHz, CDCl\textsubscript{3}) \(\delta_{\text{ppm}}\) = 187.08 (C-2), 164.71 (C-9), 161.36 (C-1), 138.19 (C-3'), 134.90 (C-6 or C-8), 134.85 (C-6 or C-8), 133.38 (C-3 or C-5), 132.50 (C-3 or C-5), 131.85 (C-4), 128.73 (C-4' or C-5'), 128.70 (C-4' or C-5'), 128.47 (C-7), 126.72 (C-6'), 81.76 (C-10), 40.61 (C-1'), 35.39 (C-2'), 28.11 (C-11).
$^{13}$C-NMR spectrum of $N$-2-phenylethyl 3-(tert-butyloxycarbonyl) benzamide (100 MHz, CDCl$_3$).

$^1$H-NMR spectrum of $N$-2-phenylethyl 3-(tert-butyloxycarbonyl) benzamide (400 MHz, CDCl$_3$).
13C-NMR spectrum of N-2-phenylethyl 3-(tert-butyloxy carbonyl) benzamide (100 MHz, CDCl3).

3.3.1.6 Synthesis of N-(3,5-Bis(trifluoromethyl)phenyl) 4-chlorobenzamide (10e)

BZ126: According to general protocol 1 (chapter 0, page 25) 4-chloro-1-iodobenene (239 mg, 1.00 mmol, 1.0 equiv) and 3,5-bis(trifluoromethyl) aniline (235 µL, 344 mg, 1.5 mmol, 1.5 equiv) were allowed to react at 80 °C for 17 h in the presence of Pd(OAc)2 (2.2 mg, 20 µmol, 2 mol%), PPh3 (15.7 mg, 60 µmol, 6 mol%) and NEt3 (420 µL, 305 mg, 3.0 mmol, 3.0 equiv) in toluene (1.0 mL, 1 M). Thereby, carbon monoxide was formed from formic acid (57 µL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 µL, 10.2 mg, 100 µmol, 10 mol%), TCT (107 mg, 0.58 mmol, 57 mol%) and toluene (0.75 mL, 2 M in regard to formic acid). Adsorption of the title compound on silica gel (1.8 g, ratio masses theoretical yield/SiO2 1:5) and purified with the aid of column chromatography on silica gel (19.6 g, relation of weight theoretical yield/SiO2 1:53) engaging EtOAc/PE 5:95 as mobile phase to afford the title compound as a bright brownish solid (259 mg, 0.70 mmol, 70%).

M (C15H8ClF6NO) = 367.68 g/mol; mp. 163-164 °C; r1 (SiO2, EtOAc/PE 5:95) = 0.29; 1H-NMR (400 MHz, CDCl3) δ [ppm] = 8.33 (br. s, 1H, NH), 8.14 (s, 2H, 2'-H), 7.81-7.79 (m, 2H, 3-H), 7.64 (s, 1H, 4'-H), 7.45-7.43 (m, 2H, 4-H); 13C-NMR (100 MHz, CDCl3) δ [ppm] = 165.30 (C-1),
139.09 (C-5 or C-1'), 139.06 (C-5 or C-1'), 132.47 (q, $^2J_{CF} = 34$ Hz, C-3'), 131.95 (C-2), 129.24 (C-4), 128.50 (C-3), 122.95 (q, $^1J_{CF} = 273$ Hz, C-5'), 120.07 (q, $^4J_{CF} = 4$ Hz, C-2'), 118.06 (sept, $J = 5$ Hz, C-4'); $^{19}$F-NMR (380 MHz, CDCl$_3$) δ [ppm] = -63.12; HR-MS (CI, [C$_{15}$H$_9$NO$_{35}$ClF$_6$]$^+$) calc. 368.0277 u found 368.0272 u.

$^1$H-NMR spectrum of N-(3,5-bis(trifluoromethyl)phenyl) 4-chlorobenzamide (400 MHz, CDCl$_3$).
\[^{13}\text{C}-\text{NMR}\] spectrum of \(N\)-(3,5-bis(trifluoromethyl)phenyl) 4-chlorobenzamide \(100\ \text{MHz, CDCl}_3\).

\[^{19}\text{F}-\text{NMR}\] spectrum of \(N\)-(3,5-bis(trifluoromethyl)phenyl) 4-chlorobenzamide \(380\ \text{MHz, CDCl}_3\).
3.3.1.7 Synthesis of \(N-(2\text{-}(1\text{H}-\text{Indole}-3\text{-yl})\text{ethyl})\) 4-cyanobenzamide (10f)

In the case of the title compound an aqueous work did not improve the yield in comparison to adsorption of the reaction mixture on silica gel and subsequent column chromatographic purification.

![Chemical structure](image)

**BZ122**: As delineated in general protocol 1 (chapter 0, page 25) the title amide was produced from 4-iodobenzonitrile (228.5 mg, 1.00 mmol, 1.0 equiv) and tryptamine (240 mg, 1.50 mmol, 1.50 equiv) using Pd(OAc)\(_2\) (2.2 mg, 20 \(\mu\)mol, 2 mol%), PPh\(_3\) (15.7 mg, 60 \(\mu\)mol, 6 mol%) and NEt\(_3\) (420 \(\mu\)L, 305 mg, 3.0 mmol, 3.0 equiv) in toluene (1.0 mL). For CO formation formic acid (57 \(\mu\)L, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 \(\mu\)L, 10.2 mg, 100 \(\mu\)mol, 10 mol%), toluene (0.5 mL, 2 M in regard to 4-iodobenzonitrile) and TCT (107 mg, 0.58 mmol, 57 mol%) were utilized. After 17 h of heating to 80 °C the reaction mixture was concentrated with silica gel (1.6 g, mass relation theoretical yield with respect to SiO\(_2\) 1:6), the residue was subjected to column chromatographic purification on silica gel (18.0 g, ratio weight theoretical yield/SiO\(_2\) 1:62) engaging EtOAc/PE 50:50 provided the title amide as reddish solid in a yield of 70% (203 mg, 0.70 mmol, 70%).

**BZ120**: The title compound was synthesized as described in the previous procedure. In deviation from the previous operating procedure an aqueous work up was performed as follows. Next, aqueous work up yielded the crude material (401 mg, 139%). At last, the crude material was dissolved in MeOH (ca. 10 mL), concentrated with SiO\(_2\) (2.0 g, mass ratio crude material to SiO\(_2\) 1:5) and the residue was purified with the aid of column chromatography using silica gel (16.5 g, ratio masses crude product in regard to SiO\(_2\) 1:41) with EtOAc/PE 55:45, which gave rise of the title compound as a reddish solid in a yield of 68% (198 mg, 0.68 mmol).

\[\text{M} (C_{18}H_{15}N_3O) = 289.34 \text{ g/mol g/mol; mp.} 167-169 \degree \text{C; } r_i \text{ (SiO}_2, \text{ EtOAc/PE 40:60) = 0.18;}\]

**\(^1H\)-NMR** (400 MHz, DMSO-d\(_6\), \(\delta [ppm]\) = 10.82 (br. s, indole-NH), 8.87 (t, \(3J_{NH,1'} = 5.5 \text{ Hz, amide NH}), 8.01-7.99 (m, 2H, 3-H) 7.97-7.94 (m, 2H, 4-H), 7.58 (d, \(3J_{NH,2'} = 7.8 \text{ Hz, 1H, 9'-H), 7.35 \text{ (d, } 3J_{5,5'} = 8.1 \text{ Hz, 1H, 6'-H}), 7.19 \text{ (d, } 3J_{6,9} = 1.9 \text{ Hz, 1H, 4'-H), 7.07 \text{ (} \psi-t, 3J = 7.6 \text{ Hz 1H, 7'-H), 6.98 (} \psi-t, 3J = 7.2 \text{ Hz, 1H, 8'-H), 3.57 \text{ (td, } 3J_{1,2'} = 6.9 \text{ Hz, 3J}_{1',NH} = 6.5 \text{ Hz, 2H, 1'-H), 2.97 (t, } 3J_{2',3'} = 7.4 \text{ Hz, 2H, 2-H); } ^{13}C\)-NMR** (100 MHz, DMSO-d\(_6\), \(\delta [ppm]\) = 164.72 (C-1), 138.65 (C-2), 136.24 (C-5'), 132.40 (C-4), 128.00 (C-3), 127.25 (C-10'), 122.68 (C-4'), 120.93 (C-7'), 118.37 (C-6), 118.24 (C-9', C-8'), 113.46 (C-5), 111.73 (C-3'), 111.39 (C-6'), 40.41 (C-1'), 25.00 (C-2').
$^1$H-NMR spectrum of $N$-(2-(1H-indole-3-yl)ethyl) 4-cyanobenzamide (400 MHz, DMSO-d$_6$).

$^{13}$C-NMR spectrum of $N$-(2-(1H-indole-3-yl)ethyl) 4-cyanobenzamide (400 MHz, DMSO-d$_6$).
3.3.1.8 Synthesis of (S)-N-(1-Hydroxy-3-methylbutan-2-yl) 4-nitrobenzamide (10g)

**BZ123:** As described in general operating procedure 1 (chapter 0, page 25) 1-ido-4-nitro-benzene (249 mg, 1.00 mmol, 1.0 equiv) was combined in the cross coupling chamber with Pd(OAc)$_2$ (2.2 mg, 20 µmol, 2 mol%), PPh$_3$ (15.7 mg, 60 µmol, 6 mol%), (S)-valinol (16.6 µL, 155 mg, 1.5 mmol, 1.5 equiv), NEt$_3$ (420 µL, 305 mg, 3.0 mmol, 3.0 equiv) and toluene (1.0 mL, 1 M). The second reaction chamber was charged with formic acid (57 µL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 µL, 10.2 mg, 100 µmol, 10 mol%), toluene (0.75 mL, 2 M) and eventually TCT (107 mg, 0.58 mmol, 57 mol%). The whole apparatus was purged with nitrogen and stirred at 80 ° for 20 h. Lastly, adsorption on silica gel (1.8 g, ratio of masses of theoretical yield/SiO$_2$ 1:7) of the reaction mixture, purification by means of column chromatography on silica gel (17.1 g, proportion amount theoretical yield/SiO$_2$ 1:68) employing EtOAc/PE 60:40 afforded the title amide as a brownish solid (188 mg, 0.75 mmol, 75%).

**M** ($C_{12}H_{16}N_2O_4$) = 252.27 g/mol; **mp.** 95-97 °C; **r$_f$** (SiO$_2$, EtOAc/PE 60:40) = 0.24; **$^1$H-NMR** (400 MHz, CDCl$_3$) δ [ppm] = 8.23-8.21 (m, 2H, 4-H), 7.94-7.91 (m, 2H, 3-H), 6.71 (d, $^3$J$_{NH,2}$ = 8.6 Hz, NH), 3.99-3.93 (m, 1H, 2´-H), 3.81 (br. s, 2H, 1´-H), 2.91 (br. s, 1H, OH), 2.07-1.98 (m, 1H, 3´-H), 1.04-1.00 (m, 6H, 4); **$^{13}$C-NMR** (100 MHz, CDCl$_3$) δ [ppm] = 166.34 (C-1), 149.61 (C-2), 140.34 (C-5), 128.32 (C-3), 123.84 (C-4), 63.20 (C-1´), 57.72 (C-2´), 29.34 (C-3´), 19.66 (C-a-4´), 19.21 (C-b-4´); **GC-MS** (Cl, 70 eV) m/z [u] (%) = 275 (2, [M-H$_2$O+Allyl]$^+$), 263 (10, [M-H$_2$O+Et]$^+$), 249 (4, [M-H$_2$O+Me]$^+$), 235 (100, [M-H$_2$O+H]$^+$), 191 (37), 175 (9), 163 (6), 117 (7); **$[^{10}$D$]_D$** (c = 1.075 g/100 mL, CHCl$_3$) = -40.7; **HR-MS** (Cl, [C$_{12}$H$_{17}$N$_2$O$_4$]$^+$) calc. 253.1188 u found 253.1190 u.
$^1$H-NMR spectrum of (S)-N-(1-hydroxy-3-methylbutan-2-yl) 4-nitrobenzamide (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of (S)-N-(1-hydroxy-3-methylbutan-2-yl) 4-nitrobenzamide (100 MHz, CDCl$_3$).
Mass spectrum of (S)-N-(1-hydroxy-3-methylbutan-2-yl) 4-nitrobenzamide (CI, 70 eV).

3.3.1.9 Synthesis of N-Butyl 4-Methylbenzamide (10h)

**BZ093:** The title compound was prepared as given in general protocol 1 (chapter 0, page 25) using Pd(OAc)$_2$ (4.4 mg, 20 μmol, 2 mol%), PPh$_3$ (15.7 mg, 60 μmol, 6 mol%), 4-iodotoluene (218 mg, 1.00 mmol, 1.00 equiv), n-butylamine (150 μL, 110 mg, 1.5 mmol, 1.5 equiv), and NEt$_3$ (420 μL, 305 mg, 3.0 mmol, 3.0 equiv) and toluene (1.0 mL, 1 M) in the coupling chamber. The CO chamber was equipped with formic acid (57 μL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 μL, 10.2 mg, 100 μmol, 10 mol%), toluene (0.75 mL, 2 M) and finally TCT (107 mg, 0.58 mmol, 57 mol%). Past purging with N$_2$, the reaction mixture was stirred for 14.5 h at 80 °C. In the end, the reaction mixture was adsorbed onto silica gel (1.5 g, mass ratio theoretical yield/SiO$_2$ 1:8) and subjected to column chromatography on silica gel (14.5 g, relation weight theoretical yield/SiO$_2$ 1:76) applying EtOAc/PE 15:85, which furnished the title amide as a brownish solid (165 mg, 0.86 mmol, 86%).

M (C$_{12}$H$_{17}$NO) = 191.27 g/mol; mp. 53-55 °C (lit.-mp. 52-54 °C);$^{[15]}$ r$_1$ (SiO$_2$, EtOAc/PE 15:85) = 0.25; $^1$H-NMR (400 MHz, CDCl$_3$) δ [ppm] = 7.67-7.64 (m, 2H, 3-H), 7.23-7.21 (m, 2H, 4-H), 6.12 (br. s, 1H, NH), 3.47-3.42 (m, 2H, 1´-H), 2.39 (s, 3H, 6-H), 1.59 (m, 2H, 2´-H), 1.41 (m, 2H, 3´-H), 0.95 (t, $^3$J$_{4,3}$ = 7.3 Hz, 3H, 4-H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ [ppm] = 167.51 (C-1), 141.59 (C-5), 132.01 (C-2), 129.06 (C-4), 126.86 (C-3), 39.75 (C-1´), 31.77 (C-2´), 21.40 (C-6), 20.17 (C-3´), 13.79 (C-4´); GC-MS (CI, 70 eV) m/z [u] (%): 232 (3, [M+allyl]$^+$). 220 (22,
[M+Et]^+), 192 (100, [M+H]^+), 149 (7), 136 (2, [4-Me(C₆H₄)C(OH)NH₂]^+), 119 (21, [4-Me(C₆H₄)CO]^+), 100 (5), 91 (2, [Bn]^+).

The NMR data is in agreement with the literature.[15]

^1H-NMR spectrum of N-butyl 4-methylbenzamide (400 MHz, CDCl₃).
$^{13}$C-NMR spectrum of $N$-butyl 4-methylbenzamide (100 MHz, CDCl$_3$).

Peak 1: R.Time: 13.876(Sum: 3564)
Mass Peaks: 142

Mass spectrum of $N$-butyl 4-methylbenzamide (Cl, 70 eV).
3.3.1.10 Synthesis of \(N1-((1R,2S)-1\text{-Hydroxy}-1\text{-phenylpropan-2-yl})-N1\text{-methyl-N3-(2-}(\text{thiophen-2-yl})\text{ethyl) isophthalamide} \ (10i)\)

The product \(10i\) was isolated in a moderate yield of 59%, since dehalogenation of the starting aryl iodide to yield \(N2\text{-}(\text{thiophen-2-yl})\text{ethyl benzamide}\) was observed.

**BZ143:** As described in general protocol 1 (chapter 0, page 25) in the coupling chamber were combined with Pd(OAc)\(_2\) (2.2 mg, 20 \(\mu\)mol, 2 mol%), PPh\(_3\) (15.7 mg, 60 \(\mu\)mol, 6 mol%), 3-Iod-\(N2\text{-}(\text{thiophen-2-yl})\text{ethyl benzamide}\) (356 mg, 1.00 mmol, 1.0 equiv, for synthesis see chapter 3.3.5.2, on page 136), (\,-\)-ephrine (198 mg, 1.20 mmol, 1.2 equiv), NEt\(_3\) (420 \(\mu\)L, 305 mg, 3.0 mmol, 3.0 equiv) and toluene (1.0 mL, 1 M). The CO chamber was charged with formic acid (57 \(\mu\)L, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 \(\mu\)L, 10.2 mg, 100 \(\mu\)mol, 10 mol%), toluene (0.75 mL, 2 M) and at last TCT (107 mg, 0.58 mmol, 57 mol%). The reaction apparatus was subsequently flushed with nitrogen and heated to 80 °C for 16 h. After aqueous work up, the crude material was obtained as a brownish oil (550 mg, 131%), of which \(\text{\textsuperscript{1}H-NMR}\) showed a complete consumption of 3-iodo-\(N2\text{-}(\text{thiophen-2-yl})\text{ethyl benzamide} and 8% mol% of \(N2\text{-}(\text{thiophen-2-yl})\text{ethyl benzamide}\) in regard to the title compound. In the end, adsorption of the crude material on silica gel (1.65 g, mass relation crude product/SiO\(_2\) 1:3) and column chromatographic purification on silica gel (18.5 g SiO\(_2\), ratio of masses crude material/SiO\(_2\) 1:34) harnessing EtOAc/PE 75:25 as mobile phase allowed for the isolation of the title compound as bright brownish solid (250 mg, 0.59 mmol, 59%). Alongside, \(N2\text{-}(\text{thiophen-2-yl})\text{ethyl benzamide}\) was isolated as brownish oil in 35% yield (79.9 mg, 0.35 mmol) in circa 80% purity as approximated by the underlying \(\text{\textsuperscript{1}H-NMR}\) spectrum.

\(N1-((1R,2S)-1\text{-Hydroxy}-1\text{-phenylpropan-2-yl})-N1\text{-methyl-N3-(2-}(\text{thiophen-2-yl})\text{ethyl) isophthalamide} \ (10i)\)

NMR at room temperature in CDCl\(_3\) showed two isomers in a ratio of 61:39. Since high temperature NMR at 373 K in DMSO-\(d_6\) only showed one species, these isomers must be rotamers. Therefore, the rotameric ratios \(r\) are stated for the room temperature measurement. Arbitrarily, the rotamer, of which the first separate multiplet could be identified screening the \(\text{\textsuperscript{1}H-NMR}\) spectrum from low to high field, was denoted as rotamer 1 rot1.
M (C_{23}H_{28}N_{2}O_{3}S) = 422.54 g/mol; mp. 84-86 °C; r
(SiO₂, EtOAc/PE 75:25) = 0.29; ¹H-NMR (400 MHz, CDCl₃, δ [ppm] = 7.76-7.69 (m, 1H, 5-H), 7.63-7.13 (m, 8H, ArH), 6.99-6.94 (m, 2H, 13-H, 14-H), 6.85 (d, ²J_{13,14} = 4.0 Hz, 1H, 12-H), 6.57-6.53 (br. s, 1H, NH), 4.91 (br. s, 1H, 3'-Hrotr1, ²'-Hrotr1), 4.02 (s, 1H, OHrotr1, δ = 59.41 rotr1/rotr2), 3.83-3.80 (m, 1H, 2'-Hrotr2, δ = 40.60 rotr2/rotr1), 3.67-3.66 (m, 2H, 9-H), 3.11 (t, ³J_{0,9} = 6.7 Hz, 2H, 10-H), 2.99 (s, 3H, 8'-Hrotr2), δ = 36.64 rotr2/rotr1), 2.93 (br. s, 1H, OHrotr2, δ = 41.59 rotr2/rotr1), 2.67 (s, 1.8H, 8'-Hrotr1, δ = 64.36 rotr1/rotr2), 1.35 (d, ³J_{1,2'} = 6.8 Hz, 2H, 1'-H); ¹³C-NMR (100 MHz, CDCl₃) δ [ppm] = 171.83 (C-8), 166.88 (C-1), 141.90 (C-4'), 141.30 (C-11), 137.00 (CAr), 134.93 (CAr), 132.21 (CAr), 132.1 (CAr), 129.62 (CAr), 128.45 (CAr), 127.85 (CAr), 127.26 (CAr), 126.58 (CAr), 126.27 (CAr), 125.57 (CAr), 125.27 (CAr), 124.14 (CAr), 76.5 (Crot1-3', rot1), 75.69 (Crot3-'), 59.95 (Crot3-2'), 57.89 (Crot1-2'), 41.56 (C-6), 35.39 (Crot1-8'), 29.91 (C-10), 28.59 (Crot2-8'), 14.63 (Crot2-1'), 12.5 (Crot1-1'); ¹H-NMR (500 MHz, DMSO-d₆, 373 K) δ [ppm] = 8.31 (br. s, 1H, NH), 7.84-7.82 (m, 1H, 7-H or 5-H), 7.55-7.52 (m, 1H, 3-H), 7.41 (υ-t, ³J = 7.7 Hz, 1H, 6-H), 7.29-7.23 (m, 6H, 14-H, 5'-H, 6'-H, 7'-H), 7.05 (d, ²J_{6,10} = 7.6 Hz, 1H, 1-H or 5-H), 6.95 (dd, ³J = 5.0 Hz, 3.8 Hz, 1H, 13-H), 6.92-6.91 (m, 1H, 12-H), 5.22 (d, ³J_{3,2'} = 5.2 Hz, 1H, OH), 4.72 (br. s, 1H, 3'-H), 3.59-3.55 (m, 2H, 9-H), 3.12 (t, ³J_{1,9} = 7.0 Hz, 2H, 10-H), 2.99 (s, 1H, 2'-H), 2.83 (br. s, 3H, 8'-H), 1.30 (d, ³J_{1,2'} = 6.8 Hz, 3H, 3'-H); ¹³C-NMR (100 MHz, DMSO-d₆, 373 K) δ [ppm] = 169.44 (C-1), 165.33 (C-8), 142.87 (C-4'), 141.20 (C-11), 136.99 (C-2 or C-4), 134.41 (C-2 or C-4), 128.03 (C-5 or C-3), 127.54 (C-6), 127.26 (C-6'), 126.93 (C-5 or C-3), 126.54 (C-7), 126.31 (C-13), 125.81 (C-5'), 124.54 (C-3), 124.45 (C-12), 123.21 (C-14), 74.23 (C-3'), 40.56 (C-9), 28.76 (C-10), 12.57 (C-1'); [α]D²⁰ (c = 1.01 g/100 mL, CHCl₃) = -31.6; HR-MS (Cl, [C_{23}H_{28}N_{2}O_{3}S]⁺) calc. 423.1742 u found 423.1741 u.

**N-2-(thiophen-2-yl)ethyl benzamide**

M (C_{13}H_{13}NOS) = 231.31 g/mol; ¹H-NMR (400 MHz, CDCl₃) δ [ppm] = 7.73-7.71 (m, 2H, 3-H), 7.50-7.46 (m, 1H, 5-H), 7.42-7.39 (m, 2H, 4-H), 7.16 (dd, ³J_{6,5} = 5.1 Hz, 4', 4' = 1.2 Hz, 1H, 6'-H), 6.96 (dd, ³J_{5,6} = 5.1 Hz, ³J_{5,4} = 3.4 Hz, 1H, 5'-H), 6.88-6.86 (m, 1H, 4'-H), 6.40 (br. s, 1H, NH), 3.74-3.70 (m, 2H, 1'-H), 3.17-3.15 (m, 2H, 2'-H); ¹³C-NMR (100 MHz, CDCl₃) δ [ppm] = 167.55 (C-1'-7), 141.23 (C-3'), 134.67 (C-2'), 131.44 (C-5), 128.53, (C-4), 127.10 (C-5'), 126.82, (C-3), 125.44 (C-4'), 124.01, (C-6'), 41.28 (C-1'), 29.85 (C-2').

The NMR data is in agreement with reported data.¹⁶

(¹⁶) Neither C-2' nor C-8' could be detected in the ¹³C-, HSQC- or HMBC-NMR-spectra.
$^1$H-NMR spectrum of $N_1-((1R,2S)-1$-hydroxy-$1$-phenylpropan-$2$-yl)-$N_1$-methyl-$N_3$-(2-(thiophen-$2$-yl)ethyl) isophthalamide (400 MHz, CDCl$_3$).
$^{13}$C-NMR spectrum of $N_1$-((1R,2S)-1-hydroxy-1-phenylpropan-2-yl)-$N_1$-methyl-$N_3$-(2-(thiophen-2-yl)ethyl) isophthalamide (100 MHz, CDCl$_3$).

$^1$H-NMR spectrum of $N_1$-((1R,2S)-1-hydroxy-1-phenylpropan-2-yl)-$N_1$-methyl-$N_3$-(2-(thiophen-2-yl)ethyl) isophthalamide (500 MHz, 373 K, DMSO-d$_6$).
**13C-NMR spectrum of N1-((1R,2S)-1-hydroxy-1-phenylpropan-2-yl)-N1-methyl-N3-(2-(thiophen-2-yl)ethyl) isophthalamide (500 MHz, 373 K, DMSO-d$_6$).**

### 3.3.1.1 Synthesis of N-Benzyl 4-chlorobenzamide (10j)

| entry | conditions | Conv.$^a$ | Yield 10j |
|-------|------------|-----------|-----------|
| 1     | CO chamber: TCT (57 mol%), FPy (10 mol%), dioxane (2 M), **24 h 80 °C**
       | Coupling chamber: 8j (1.0 equiv), H$_2$NBn (1.5 equiv), Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%), NEt$_3$ (3.0 equiv), toluene (1 M), **24 h 80 °C**
       | 89 | 75 (1.9 g) |
| 2     | CO chamber: TCT (57 mol%), FPy (10 mol%), **dioxane (2 M), 17.5 h 80 °C**
       | Coupling chamber: 8j (1.0 equiv), H$_2$NBn (1.5 equiv), Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%), NEt$_3$ (3.0 equiv), toluene (1 M), **17.5 h 80 °C**
       | 81 | 70 (1.7 g) |
| 3     | CO chamber: TCT (57 mol%), FPy (10 mol%), **toluene (2 M), 18 h 80 °C**
       | Coupling chamber: 8j (1.0 equiv), H$_2$NBn (1.5 equiv), Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%), NEt$_3$ (3.0 equiv), toluene (1 M), **18 h 80 °C**
       | 88 | 69 (1.7 g) |
| 4     | CO chamber: TCT (57 mol%), FPy (10 mol%), **dioxane (2 M), 16.5 h 80 °C**
       | Coupling chamber: 8j (1.0 equiv), H$_2$NBn (1.5 equiv), Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%), NEt$_3$ (3.0 equiv), dioxane (1 M), **16.5 h 80 °C**
       | 74 | 68 (1.7 g) |
| 5     | CO chamber: TCT (57 mol%), FPy (10 mol%), dioxane (2 M), **24 h 80 °C**
       | Coupling chamber: 8j (1.0 equiv), H$_2$NBn (1.5 equiv), Pd(OAc)$_2$ (2 mol%), PPh$_3$ (8 mol%), NEt$_3$ (3.0 equiv), toluene (1 M), **24 h 80 °C**
       | 82 | 70 (0.17 g) |

8j = 4-chloro-1-iodobenzene. Isolated yield after chromatographic purification if not otherwise mentioned. a. The conversion was estimated as described in chapter 3.2.3 (page 37). b. Yield determined by $^1$H-NMR with mesitylene as internal standard.
The title compound was isolated in 75% on a 10 mmol scale after heating to 80 °C for 24 h (entry 1). A shortened reaction time of 17.5 h resulted in a mitigated yield of 70% (entry 2). Use of toluene for CO formation instead of dioxane caused a slightly diminished yield of 69% (entry 3). Since the conversion of 8j in this case is with 88% compared to 81% higher than in the previous case, pronounced formation of side-products must have occurred. When both CO formation and cross coupling were carried out in dioxane, the amide 10j was isolated in a lower yield of 68%. Finally, a 1 mmol scale reaction afforded the title amide in 70% isolated yield.

Entry 1, PH4286: This experiment has been described in chapter 3.2.3 (page 37).

Entry 2, PH4278: The amide 10j was synthesized from aryl iodide 8j (10.0 mmol, 1.0 equiv) and BnNH₂ (1.5 equiv) employing Pd(OAc)₂ (2 mol%), PPh₃ (8 mol%) and NEt₃ (3.0 equiv) in toluene (1 M) under stirring at 80 °C for 17.5 h following the procedure in entry 1. Thereby, CO was generated from formic acid (1.5 equiv) and TCT (57 mol%) with FPyr (10 mol%) in dioxane (2 M). Work up as described in entry 2 delivered the crude material as a brown solid (2.97 g, 120%), of which ¹H-NMR showed circa 81% consumption of 8j. Adsorption on silica gel (7.0 g, mass ratio crude 10j/SiO₂ 1:2.3) and purification with the aid of column chromatography harnessing SiO₂ (120.0 g, relation of weight crude 10j with respect to SiO₂ 1:40) and EtOAc/CH₂Cl₂ 5:95 → 6:94 gave the amide 10j as a brownish solid in 70% yield (1.709 g, 69.6 mmol).

Entry 3, PH4285: In accordance with the procedure in entry 1, Pd(OAc)₂ (2 mol%), PPh₃ (8 mol%), iodo arene 8j (10.0 mmol, 1.0 equiv), toluene (1 M), NEt₃ (3.0 equiv) and BnNH₂ (1.5 equiv) were combined and heated to 80 °C for 18 h. In doing so, CO was released using TCT (57 mol%), formic acid (1.5 equiv), toluene (2 M) and FPyr (10 mol%). Aqueous work up as stated in entry 2 furnished the crude coupling product as a black solid (2.93 g, 119%), of which ¹H-NMR indicated 88% conversion of 8j. Eventually, adsorption on silica (6.1 g, mass ratio crude material with regard to SiO₂ 1:2.1) and column chromatographic purification on silica gel (123 g, ratio crude 10j/SiO₂ 1:42) using EtOAc/CH₂Cl₂ 6:94 afforded the benzamide 10j as a brownish solid (1.689 g, 6.87 mmol, 69%).

Entry 4, PH4273: Based on the protocol given in entry 1, iodide 8j (10.0 mmol, 1.0 equiv) was allowed to react with benzyl amine (1.5 equiv) in the presence of Pd(OAc)₂ (2 mol%), PPh₃ (8 mol%) and NEt₃ (3 equiv) in dioxane (1 M) at 80 °C for 16.5 h. Thereby, CO was developed employing TCT (57 mol%), formic acid (1.5 equiv) and FPyr (10 mol%) in dioxane (2 M). Past aqueous work up as delineated in entry 3 furnished the crude title compound as a brown solid (3.13 g, 128%), of which ¹H-NMR indicated 74% conversion of 8j. In the end, adsorption on silica gel (8.9 g, relation weights crude 10j/SiO₂ 1:2.9) and purification with the aid of column
chromatography using silica (121 g, mass relation crude product/SiO$_2$ 1:39) and EtOAc/CH$_2$Cl$_2$ 3:97→4:96→5:95 delivered amide 10j as a brown solid in 68% yield (1.664 g, 6.77 mmol).

**Entry 5, PH4295:** According to general procedure 1 (chapter 0 on page 25) iodo arene 8j (239 mg, 1.00 mmol, 1.0 equiv) was reacted with benzyl amine (160 μL, 1.50 mmol, 1.5 equiv) in the presence of Pd(OAc)$_2$ (4.4 mg, 20 μmol, 2 mol%), PPh$_3$ (21.0 mg, 80 μmol, 8 mol%) and NEt$_3$ (420 μL, 3.00 mmol, 3.0 equiv) in toluene (1.0 mL, 1 M) at 80 °C for 22 h). Thereby, CO was formed from 1.5 equiv of HCO$_2$H in dioxane. Aqueous work up yielded the crude title amide as a red solid (303 g, 123%), of which $^1$H-NMR revealed approximately 82% conversion. According to mesitylene as NMR standard, the title amide 10j was formed in 68% yield alongside with 15% of the starting material. Finally, adsorption on silica gel (0.88 g, mass ratio crude material/SiO$_2$ 1:2.9) and subsequent column chromatographic purification engaging SiO$_2$ (23.2 g, ratio weight SiO$_2$/crude 10j 77:1) with EtOAc/CH$_2$Cl$_2$ 6:94 as eluent mixture gave amide 10j as a brown solid in 70% yield (172.9 mg, 0.704 mmol).

M (C$_{14}$H$_{11}$NOCl) = 245.71 g/mol; mp. 161-163 °C, (lit-mp. 162 °C)[17] r$_f$ (SiO$_2$, EtOAc/CH$_2$Cl$_2$ 6:94) = 0.52; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ [ppm] = 7.73-7.71 (m, 2H, 3-H), 7.40-7.36 (m, 2H, 4-H), 7.36-7.27 (m, 5H, 3´-H, 4´-H, 5´-H), 6.51 (br. s, 1H, NH), 4.61 (d, $^3$J$_{NH}$ = 5.7 Hz); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ [ppm] = 166.29 (C-1), 137.90 (C-2´), 137.74 (C-5), 132.67 (C-2), 128.78 (C-4, C-4´), 128.39 (C-3), 127.87 (C-3´), 127.67 (C-5´), 44.17 (C-1´).

The NMR data is in match with the literature.[17]
\(^1\)H-NMR spectrum of \(N\)-benzyl 4-chlorobenzamide (400 MHz, CDCl\(_3\)).

\(^{13}\)C-NMR spectrum of \(N\)-benzyl 4-chlorobenzamide (100 MHz, CDCl\(_3\)).
3.3.2 Synthesis of Esters (Scheme 2 E+F)

3.3.2.1 Synthesis of Methyl 4-(2-(1,3-Dioxan-2-yl)ethoxy) benzoate (12a)

BZ180: 2-(2-(4-bromophenoxy)ethyl)-1,3-dioxane (295 mg, 1.03 mmol, 1.0 equiv, for synthesis see chapter 3.3.5.3, page 138) was transformed into the title compound as described in general protocol 2 (chapter 3.2.4, page 41) through heating to 60 °C for 16 h with Pd(OAc)$_2$ (2.2 mg, 20 μmol, 2 mol%), Xantphos (23.1 mg, 40 μmol, 4 mol%), MeOH (410 μL, 10.0 mmol, 10 equiv) and NEt$_3$ (2 mL, 0.5 M). Thereby, carbon monoxide was obtained from formic acid (57 μL, 70 mg, 1.5 mmol, 1.5 equiv) and TCT (107 mg, 0.58 mmol, 57 mol%) with FPyr (9.6 μL, 10.2 mg, 100 μmol, 10 mol%) in THF (0.75 mL, 2 M). Work up furnished the crude material as a brownish oil (366 mg, 133%), of which $^1$H-NMR verified full conversion of the starting aryl bromide. At last, concentration with SiO$_2$ (1.6 g, ratio weight crude 12a/SiO$_2$ 1:4) and column chromatographic purification on silica gel (20.8 g, relation masses crude product/SiO$_2$ 1:57) with EtOAc/PE 20:80 as mobile phase resulted in the acetale 12a as a pale yellow oil (223 mg, 0.84 mmol, 81%).

$^1$H-NMR (400 MHz, CDCl$_3$) δ [ppm] = 7.99-7.97 (m, 2H, 3-H), 6.93-6.90 (m, 2H, 4-H), 4.78 (t, $^3$J$_{HH}$ = 5.2 Hz, 1H, 8-H), 4.15-4.09 (m, 4H, 6-H, 9-H$_a$), 3.88 (s, 3H, 1´-H), 3.82-3.75 (m, 2H, 9-H$_b$), 2.15-2.03 (m, 3H, 7-H, 10-H$_a$), 1.38-1.34 (m, 1H, 10-H$_b$); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ [ppm] = 166.85 (C-1), 162.66 (C-5), 131.50 (C-3), 122.44 (C-2), 114.06 (C-4), 99.26 (C-8), 66.87 (C-9), 63.45 (C-6), 51.79 (C-1´), 34.87 (C-7), 25.72 (C-10); HR-MS (CI, [C$_{14}$H$_{18}$O$_5$]$^+$) calc. 266.1154 u found 266.1156 u.
$^1$H-NMR spectrum of $N$-(quinol-8-yl) 2-methylbenzamide (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of $N$-(quinol-8-yl) 2-methylbenzamide (100 MHz, CDCl$_3$).
3.3.2.2 Synthesis of Methyl 4-(dimethoxymethyl) benzoate (12b)

**BZ209:** According to general protocol 2 (chapter 3.2.4, page 41) 1-bromo-4-(dimethoxymethyl)benzene (225 mg, 0.97 mmol, 1.0 equiv) was reacted at 80 °C for 19 h with MeOH (410 µL, 10.0 mmol, 10 equiv) in the presence of Pd(OAc)$_2$ (2.2 mg, 20 µmol, 2 mol%) and Xantphos (23.1 mg, 40 µmol, 4 mol%) in NEt$_3$ (2 mL, 0.5 M). In the process, CO was produced from formic acid (57 µL, 70 mg, 1.5 mmol, 1.5 equiv) and TCT (107 mg, 0.58 mmol, 57 mol%) in the presence of FPyr (9.6 µL, 10.2 mg, 100 µmol, 10 mol%) in THF (0.75 mL, 2 M). Subsequently, work up delivered the crude title compound as a yellow oil (237 mg, 113%), of which $^1$H-NMR attested full consumption of the starting material. No aldehyde H-atom could be detected. Afterwards, the crude product was adsorbed on silica gel (1.1 g, mass ratio crude 12b/SiO$_2$ 1:5) and the residue was subjected to column chromatographic purification on silica gel (19.5 g, relation weight crude product/SiO$_2$ 1:81) with EtOAc/PE 4:96, which allowed for the isolation of the title compound as a colourless oil in 83% (169 mg, 0.80 mmol) yield.

M (C$_{11}$H$_{14}$O$_4$) = 210.23 g/mol; r$_r$ (SiO$_2$, EtOAc/PE 4:96) = 0.18; $^1$H-NMR (400 MHz, CDCl$_3$) δ [ppm] = 8.06-8.03 (m, 2H, 3-H), 7.54-7.52 (m, 2H, 4-H), 5.44 (s, 1H, 6-H), 3.92 (s, 3H, 1-’H), 3.33 (s, 6H, 7-H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ [ppm] = 166.82 (C-1), 142.88 (C-5), 130.16 (C-2), 129.48 (C-3), 126.76 (C-4), 102.30 (C-6), 52.61 (C-7), 52.08 (C-1’); GC-MS (Cl, 70 eV) m/z [u] (%) = = 239 (10, [M+Et]$^+$), 225 (3, [M+Me]$^+$), 211 (95, [M+H]$^+$), 195 (15, [M-Me]$^+$), 179 (100, [M-OMe]$^+$), 165 (50), 133 (3), 105 (2), 75 (35, [CH(OMe)$_2$]$^+$); HR-MS (Cl, [C$_{10}$H$_{11}$O$_3$]$^+$, ) calc. 179.0708 u found 179.0712 u.

The NMR data is in agreement with reported data.$^{[18]}$
H-NMR spectrum of methyl 4-(dimethoxymethyl) benzoate (400 MHz, CDCl₃).

^1^H-NMR spectrum of methyl 4-(dimethoxymethyl) benzoate (400 MHz, CDCl₃).

^13^C-NMR spectrum of methyl 4-(dimethoxymethyl) benzoate (100 MHz, CDCl₃).
Mass spectrum of methyl 4-(dimethoxymethyl) benzoate (Cl, 70 eV).

3.3.2.3 Synthesis of Methyl 4-acetylbenzoate (12c)

BZ174: As stated in general procedure 2 (chapter 3.2.4, page 41) the title compound was produced from 4-bromoacetophenone (199 mg, 1.00 mmol, 1.0 equiv) under heating for 17 h to 80 °C using Pd(OAc)$_2$ (2.2 mg, 20 μmol, 2 mol%), Xantphos (23.1 mg, 0.58 μmol, 57 mol%), MeOH (410 μL, 10.0 mmol, 10 equiv) and NEt$_3$ (2 mL, 0.5 M). CO was generated from formic acid (57 μL, 70 mg, 1.5 mmol, 1.5 equiv) and TCT (107 mg, 0.58 mmol, 57 mol%) in the presence of FPyr (9.6 μL, 10.2 mg, 100 μmol, 10 mol%) in THF (0.75 mL, 2 M). Work up yielded the crude ester 12c as a yellow solid (219 mg, 123%), of which $^1$H-NMR indicated full conversion. Adsorption on silica gel (1.1 g, weight ratio crude material/SiO$_2$ 1:5) and subsequent chromatographic purification on silica gel (17.0 g, relation masses crude 12c in regard to SiO$_2$ 1:78) harnessing EtOAc/PE 10:90 as eluent system finally facilitated the isolation of ester 12c as colourless solid in 81% yield (144 mg, 0.81 mmol).

M (C$_{10}$H$_{10}$O$_3$) = 178.19 g/mol; mp. 95-96 °C, (lit-mp. 95 °C);$^{[19]}$ r$_t$ (SiO$_2$, EtOAc/PE 10:90) = 0.26; $^1$H-NMR (400 MHz, CDCl$_3$) δ [ppm] = 8.14-8.11 (m, 2H, 3-H), 8.02-8.00 (m, 2H, 4-H), 3.95 (s, 3H, 1’-H), 2.65 (s, 3H, 7-H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ [ppm] = 197.48 (C-6), 166.16 (C-1), 140.17 (C-5), 133.84 (C-2), 129.77 (C-3), 128.16 (C-4), 52.41 (C-1’), 26.82 (C-7); GC-MS (Cl, 70 eV) m/z [u] (%) = 219 (1, [M+Allyl]$^+$), 207 (5, [M+Et]$^+$), 193 (7, [M+Me]$^+$), 179 (100, [M+H]$^+$), 178 (5, [M]$^+$), 163 (25, [M-OME]$^+$), 147 (10, [M-OMe]$^+$), 137 (2), 135 (3, [M-Ac]$^+$), 119 (2, [H$_3$CCO(C$_6$H$_4$)]$^+$), 91 (3, [Bn]$^+$).
The NMR data is in match with the literature.[19]

$^1$H-NMR spectrum of methyl 4-acetylbenzoate (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of methyl 4-acetylbenzoate (100 MHz, CDCl$_3$).
**3.3.2.4 Synthesis of Methyl 2-(acetylamido) benzoate (12d)**

**BZ175:** In accordance with general protocol 2 (chapter 3.2.4, page 41) the coupling chamber was charged with \(N\)-2-bromophenyl acetamide (214 mg, 1.00 mmol, 1.0 equiv), \(\text{Pd(OAc)}_2\) (2.2 mg, 20 \(\mu\)mol, 2 mol%), \(\text{Xantphos}\) (23.1 mg, 40 \(\mu\)mol, 4 mol%), \(\text{MeOH}\) (410 \(\mu\)L, 10.0 mmol, 10 equiv) and \(\text{NEt}_3\) (2 mL, 0.5 M). The CO chamber was loaded with formic acid (57 \(\mu\)L, 70 mg, 1.5 mmol, 1.5 equiv), \(\text{FPyr}\) (9.6 \(\mu\)L, 10.2 mg, 100 \(\mu\)mol, 10 mol%), \(\text{THF}\) (0.75 mL, 2 M in reference to formic acid) and at last TCT (107 mg, 0.58 mmol, 57 mol%). Heating for 17 h to 80 °C and subsequent work up gave rise of the crude material as a yellow solid (290 mg, 150%, ≥98% conv. as determined by \(^1\text{H-NMR}\)).

Concentration with silica gel (1.5 g, relation of masses of crude product in regard to \(\text{SiO}_2\) 1:5) and chromatographic purification with the aid of column chromatography on silica gel (19.5 g, relation of weight crude \(12\text{d}/\text{SiO}_2\) 1:67) with \(\text{EtOAc/PE}\) 15:85 in the end furnished the title ester as a colourless solid (177 mg, 0.92 mmol, 92%).

\[
\text{M (C}_{10}\text{H}_{11}\text{NO}_3) = 193.20 \text{ g/mol; mp. 98-99 °C (mp.-lit: 99-100 °C);}^{[20]} \text{ r} (\text{SiO}_2, \text{EtOAc/PE} 15:85) = 0.28; \text{ }^1\text{H-NMR} (400 MHz, \text{CDCl}_3) \delta [ppm] = 11.05 (br. s, 1H, NH), 8.70 (d, \text{ }^3\text{J}_{6,5} = 8.4 \text{ Hz, 1H, 4-H}), 8.02 (dd, \text{ }^3\text{J}_{6,7} = 8.0 \text{ Hz, }^4\text{J}_{7,5} = 1.6 \text{ Hz, 1H, 7-H}), 7.56-7.51 (m, 1H, 5-H), 7.09-7.05 (m, 1H, 6-H), 3.92 (s, 3H, 1'-H), 2.24 (s, 3H, 9-H); \text{ }^{13}\text{C-NMR} (100 MHz, \text{CDCl}_3) \delta [ppm] = 169.00 (C-8), 168.71 (C-1), 141.54 (C-3), 134.62 (C-5), 130.72 (C-7), 122.34 (C-6), 120.25 (C-4), 114.70 (C-2), 52.26 (C-1'), 25.44 (C-9); \text{ GC-MS (Cl, 70 eV) m/z [u] (%) = 234 (1, [M+Allyl]^+)},
\]
222 (4, [M+Et]^+), 194 (25, [M+H]^+), 193 (45, [M]^+), 176 (20), 162 (100, [M-OMe]^+), 152 (45, [2-H$_2$N(C$_6$H$_4$)CO$_2$Me]+H$^+$), 151 (40, [2-H$_2$N(C$_6$H$_4$)CO$_2$Me]$^+$), 120 (20, [2-H$_2$N(C$_6$H$_4$)CO]$^+$), 119 (35), 92 (6, [BnH]^+), 77 (1, [Ph]^+), 65 (2, [Cp]^+).

The NMR data is in match with the literature.[20]

$^1$H-NMR spectrum of methyl 2-(acetylamido) benzoate (400 MHz, CDCl$_3$).
C-NMR spectrum of methyl 2-(acetylamido) benzoate (100 MHz, CDCl₃).

Mass spectrum of methyl 2-(acetylamido) benzoate (Cl, 70 eV).
3.3.2.5 Synthesis of Methyl 2-pyridinyl carboxylate (12e)

**BZ179:** Following general protocol 2 (chapter 3.2.4, page 41) the ester 12e was synthesized originating from 2-bromopyridine (96 µL, 158 mg, 1.00 mmol, 1.0 equiv) applying Pd(OAc)$_2$ (2.2 mg, 20 µmol, 2 mol%), Xantphos (23.1 mg, 40 µmol, 4 mol%), MeOH (410 µL, 10.0 mmol, 10 equiv) and NEt$_3$ (2 mL, 0.5 M). Carbon monoxide was formed from formic acid (57 µL, 70 mg, 1.5 mmol, 1.5 equiv) and TCT (107 mg, 0.58 mmol, 57 mol%) in the presence of FPyr (9.6 µL, 10.2 mg, 100 µmol, 10 mol%) in THF (0.75 mL, 2 M). After 16 h of stirring at 80 °C, work up furnished the crude pyridine derivative 12e as brownish oil (181 mg, 132%), of which $^1$H-NMR verified full conversion. Eventually, adsorption on silica gel (1.1 g, relation masses crude title compound/SiO$_2$ 1:6), subsequent purification by means of column chromatography on silica gel (18.2 g, ratio weight crude material with respect to SiO$_2$ 1:101) utilizing EtOAc/PE 55:45 and drying at the rotary evaporator for 20 min at 50 mbar enabled the isolation of ester 12e as a yellow oil (110.3 mg, 0.80 mmol, 80%).

**BZ200:** The title compound was prepared as described in the previous experiment with the deviation that 2-chloropyridine (113.5 mg, 1.00 mmol, 1.0 equiv) was engaged as starting material (reaction time 16 h). After work up and drying at 100 mbar for 5 min at the rotary evaporator $^1$H-NMR of the crude product (222 mg, 162%) revealed a conversion of 81% and an 9 mol% 2,2´-bipyridine with respect to ester 12e. Chromatographic purification with the aid of column chromatography on silica gel (19.5 g, ratio crude product/SiO$_2$ 1:88) using EtOAc/PE 55:45 furnished the title ester after drying at the rotary evaporator for 20 min at 50 mbar as yellow oil (109 mg). Taking 36 mol% residual CH$_2$Cl$_2$ in regard to the volatile ester 12e into account, compound 12e was obtained in a yield of 65% (0.65 mmol). In order to load the crude material onto the silica gel column, it was adsorbed on SiO$_2$ (0.95 g, mass ratio 1:4).

$^1$H-NMR (400 MHz, CDCl$_3$) δ [ppm] = 8.77-8.75 (m, 1H, 6-H), 8.15 (d, $^3$J$_{3,4}$ = 7.8 Hz, 1H, 3-H), 7.86 (ψ-td, $^3$J = 7.7 Hz, $^4$J$_{4,5}$ = 1.7 Hz, 1H, 4-H), 7.50 (ddd, $^3$J = 7.6, 4.7, $^4$J$_{5,3}$ = 1.1 Hz 1H, 5-H), 3.97 (s, 3H, 1´-H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ [ppm] = 165.60 (C-1), 149.70 (C-6), 147.81 (C-2), 136.96 (C-4), 126.88 (C-5), 125.03 (C-3), 52.79 (C-1´); GC-MS (Cl, 70 eV) m/z [u] (%) = 178 (3, [M+Allyl]$^+$), 166 (10, [M+Et]$^+$), 152 (8, [M+Me]$^+$), 138 (100, [M+H]$^+$), 106 (50, [M-OMe]$^+$), 79 (30, [pyridine]$^+$), 78 (16, [pyridinium]$^+$).

The NMR data is in match with the literature.$^{[21]}$
H-NMR spectrum of methyl 3-pyridinyl carboxylate (400 MHz, CDCl₃).

C-NMR spectrum of methyl 2-pyridinyl carboxylate (100 MHz, CDCl₃).
Mass spectrum of methyl 2-pyridinyl carboxylate (CI, 70 eV).

### 3.3.2.6 Synthesis of Methyl 4-methoxybenzoate (12f)

The synthesis of ester 12f afforded a reaction temperature of 80 °C, since heating to 60 °C overnight effected a conversion of only 27%.

**BZ172:** As described in general protocol 2 (chapter 3.2.4, page 41) the ester 12f was accessed from 4-bromoanisole (120 µL, 187 mg, 1.0 mmol, 1.0 equiv) using Pd(OAc)$_2$ (2.2 mg, 20 µmol, 2 mol%), Xantphos (23.1 mg, 40 µmol, 4 mol%), MeOH (410 µL, 10.0 mmol, 10 equiv) and NEt$_3$ (2 mL, 0.5 M). CO was synthesized from formic acid (57 µL, 70 mg, 1.5 mmol, 1.5 equiv), FPyr (9.6 µL, 10.2 mg, 100 µmol, 10 mol%), THF (0.75 mL, 2 M with respect to HCO$_2$H) and TCT (107 mg, 0.58 mmol, 57 mol%). After heating to 80 °C for 19 h and work up the crude material was obtained as a yellow solid (209 mg, 126%). $^1$H-NMR confirmed ≥98% conversion of the bromoarene. Eventually, adsorption on silica gel (1.2 g, mass ratio crude product/SiO$_2$ 1:6) and column chromatographic purification on silica gel (16.0 g, relation of masses crude 12f/SiO$_2$ 1:76) with EOAc/PE 4:96 delivered the title compound as a colourless solid (127.5 mg, 0.77 mmol, 77%).

**BZ203:** This experiment was conducted as the previous with the deviation that the reaction mixture was heated to 60 °C 18 h. $^1$H-NMR of the crude material with dibenzylether as internal standard (22.4 mg) revealed the title compound in only 11% yield besides remaining starting material (73%, 27% conversion).
M (C₉H₁₀O₃) = 166.18 g/mol; mp. 47-49 °C (lit.-mp. 48-52 °C);[^22] r₁ (SiO₂, EtOAc/PE 4:96) = 0.26; ^1H-NMR (400 MHz, CDCl₃) δ [ppm] = 7.99 (m, 2H, 3-H), 6.91 (m, 2H, 4-H), 3.88 (s, 3H, 1'-H), 3.85 (s, 3H, 6-H).; ^13C-NMR (100 MHz, CDCl₃) δ [ppm] = 166.83 (C-1), 163.29 (C-5), 131.55 (C-3), 122.57 (C-2), 113.56, (C-4), 55.37 (C-6), 51.81 (C-1); GC-MS (Cl, 70 eV) m/z [u] (%) = 195 (6, [M+Et]+), 181 (3, [M+Me]+), 167 (100, [M+H]+), 166 (30, [M]+), 135 (35, [M-OMe]+), 123 (14), 107 (2, [M-CO₂Me]+), 92 (3, [BnH]+), 77 (3, [Ph]+), 59 (4, [CO₂Me]+).

The NMR data is in agreement with reported values.[^22]

[^1H-NMR spectrum of methyl 4-methoxybenzoate (400 MHz, CDCl₃).]
$^{13}$C-NMR spectrum of methyl 4-methoxybenzoate (100 MHz, CDCl$_3$).

Mass spectrum of methyl 4-methoxybenzoate (Cl, 70 eV).
3.3.3 Synthesis of β-Nitroketones (Scheme 2 G)

3.3.3.1 Synthesis of 1-(4-Methoxyphenyl)-2-nitroethan-1-one (13a)

BZ199: According to general protocol 4 (chapter 3.2.6 on page 45) the title compound was synthesized from 4-iodoanisole (93.6 mg, 0.40 mmol, 1.0 equiv) through heating to 60 °C for 17.5 h. ¹H-NMR of the crude product (164 mg, 210 mol%, orange solid) indicated a conversion of 95% and showed 23 mol% 4-methoxybenzoic acid in regard to the title compound. Purification by means of column chromatography on silica gel (17.7 g, mass ratio crude material/SiO₂ 1:108) with EtOAc/PE 20:80 and 0.1 vol% HOAc afforded the title ketone as a pale yellow solid (53.6 mg, 0.27 mmol, 69%). In order to charge the silica gel column, the crude title compound was dissolved in CH₂Cl₂ (10 mL), SiO₂ was introduced (0.92 g, relation weight crude product/SiO₂ 1:6) and the mixture was concentrated to dryness. In addition, 4-methoxybenzoic acid, was isolated as by-product (10.7 mg, 0.07 mmol, 17%).

**1-(4-Methoxyphenyl)-2-nitroethan-1-one**

**M** (C₉H₉NO₄) = 195.17 g/mol; rᵢ (SiO₂, EtOAc/PE 20:80) = 0.15; ¹H-NMR (400 MHz, CDCl₃); δ [ppm] = 7.87-7.85 (m, 2H, 3-H), 7.01-6.99 (d, 2H, 4-H), 5.84 (s, 2H, 1'-H), 3.91 (s, 3H, 6-H);¹³C-NMR (100 MHz, CDCl₃) δ [ppm] = 183.94 (C-1), 165.00 (C-5), 130.72 (C-3), 126.39 (C-2), 114.53 (C-4), 81.03 (C-1’), 55.69 (C-6);
The NMR data is in agreement with the literature.[¹²]

**4-Methoxybenzoic acid**

**M** (C₈H₈NO₃) = 152.15 g/mol; rᵢ (SiO₂, EtOAc/PE 20:80) = 0.23; ¹H-NMR (400 MHz, CDCl₃) δ [ppm] = 8.08-8.06 (m, 2H, 3-H), 6.96-6.94 (m, 2H, 4-H), 3.88 (s, 3H, 6-H);¹³C-NMR (100 MHz, CDCl₃) δ [ppm] = 171.46 (C-1), 164.04 (C-5) 132.35 (C-3), 121.62 (C-2), 113.74 (C-4), 55.48 (C-7).
$^1$H-NMR spectrum of 1-(4-methoxyphenyl)-2-nitroethan-1-one (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of 1-(4-methoxyphenyl)-2-nitroethan-1-one (100 MHz, CDCl$_3$).
3.3.4 Synthesis of Ynones (Scheme 3)

3.3.4.1 Synthesis of 1-(4-Methoxyphenyl)-2-nonyl-1-one (15a)

| entry | conditions | Yield 15a [%] |
|-------|------------|---------------|
| 1     | CO chamber: HCO₂H (1.5 equiv), TCT (57 mol%), DMF (2 M), 25 h rt/ Coupling chamber: Cul (4 mol%), Pd(PPh₃)₂Cl₂ (5 mol%), 8a (1.0 equiv), 1-octyne (1.5 equiv), NEt₃ (3.5 equiv), THF (0.5 M), 25 h rt | 79 |
| 2     | CO chamber: HCO₂H (1.5 equiv), TCT (57 mol%), DMF (2 M), 48 h rt/ Coupling chamber: Cul (4 mol%), Pd(PPh₃)₂Cl₂ (5 mol%), 8a (1.0 equiv), 1-octyne (1.5 equiv), NEt₃ (3.5 equiv), THF (0.3 M), 48 h rt | 89 |
| 3     | 80 °C/Coupling chamber: Cul (2 mol%), Pd(PPh₃)₂Cl₂ (5 mol%), 8a (1.0 equiv), 1-octyne (1.5 equiv), NEt₃ (3.5 equiv), THF (0.3 M), 48 h rt | 76 |

All yields refer to isolated material after chromatographic purification. 8a = 4-iodoanisole.

After a reaction duration of 1 d, which effected a conversion of 8a of 93%, the title ynone was isolated in 79% yield (entry 1). An increase of the reaction time to 2 d resulted in full consumption (entry 2). In the very same experiment a lower concentration (0.5→0.3 M) also allowed for an enhanced chemoselectivity with respect to CO incooperation versus direct Sonogashira coupling, which provided ketone 15a in a yield of 89%. Finally, also catalytic CO formation at 80 °C enabled the preparation of coupling product 15a in 76% yield (entry 3).

**Entry 1, PH4106:** Following general protocol 3 (chapter 3.2.5 on page 42) the title ynone was prepared from 4-iodoanisole (8a, 234 mg, 1.00 mmol, 1.0 equiv) and 1-octyne (14a, 220 µL, 165 mg, 1.50 mmol, 1.5 equiv) engaging Cul (6.9 mg, 36 µmol, 4 mol%) and Pd(PPh₃)₂Cl₂ (5 mol%) in THF (2.0 mL, 0.5 M) under stirring for 25 h at room temperature. Thereby, CO was generated from 1.5 equiv HCO₂H in DMF at room temperature. Aqueous work up provided the crude ketone 15a as a black oil (347 mg, 142%), whereby ¹H-NMR attested 93% conversion of 4-iodoanisole and a ratio of 15a with regard to 1-(4-methoxyphenyl)-1-octyne of 90:10. Eventually, purification with the aid of column chromatography on silica gel (27.8 g, mass relation crude material/SiO₂ 1:79) using EtOAc/nHex 8:92 as eluent furnished the product 15a as an orange oil (192.0 mg, 0.79 mmol, 79%). To load the crude material onto the silica gel column, it was adsorbed on silica gel (1.26 g, relation weight crude 15a/SiO₂ 1:79).

**Entry 2, PH4115:** In accordance with general protocol 3 (chapter 3.2.5 on page 42) the title compound was produced from 4-iodoanisole (8a, 1.00 mmol, 1.0 equiv) and 1-octyne (14a, 1.5 equiv) applying Cul (8.0 mg, 42 µmol, 4 mol%) and Pd(PPh₃)₂Cl₂ (5 mol%) in THF (3.3 mL,
0.3 M) under stirring for 48 h at room temperature. Thereby, CO formation was performed utilizing 1.5 equiv of formic acid in DMF at ambient temperature. Work up yielded the crude product (355 mg, 135%, black oil), of which ¹H-NMR proved full consumption of 4-iodoanisole and a ratio of 15a with respect to 1-(4-methoxyphenyl)oct-1-yne of 95:5. Finally, chromatographic purification using silica gel (27.2 g, mass ratio crude material/SiO₂ 1:78) with EtOAc/PE 8:92 gave rise of the title ynone as a red oil (218.0 mg, 0.89 mmol, 89%). In order to load the silica gel column, the crude material was adsorbed on silica gel (0.82 g, ratio of weight crude material/SiO₂ 1:2.3).

**Entry 3, BZ133:** In accordance with general protocol 3 (chapter 3.2.5 on page 42) the title compound was synthesized from 4-iodoanisole (8a, 1.00 mmol, 1.0 equiv) and 1-octyne (14a, 1.5 equiv) under stirring for 22 h at room temperature. In doing so, CO was produced from 1.5 equiv HCO₂H in the presence of FPyr (10 mol%) in THF at 80 °C. Work up delivered the crude material as a brown oil (330 mg, 135%), of which ¹H-NMR confirmed 96% conversion and showed 15a in relation to 1-(4-methoxyphenyl)-1-octyne of 92:8. In the end, chromatographic purification using silica gel (17.3 g, mass relation crude material/SiO₂ 1:52) with EtOAc/PE 3:97 yielded the title ynone as an orange oil (186.0 mg, 0.76 mmol, 76%). In order to load the silica gel column, the crude product was adsorbed on silica gel (1.35 g, ratio of weight crude material/SiO₂ 1:4).

![Chemical structure](attachment:chemical_structure.png)

**M** (C₁₈H₂₀O₂) = 244.33 g/mol; **rₗ (SiO₂, EtOAc/nHex) = 0.28 (8:92); **¹H-NMR** (400 MHz, CDCl₃) δ [ppm] = 8.12-8.10 (m, 2H, 3-H), 6.95-6.93 (m, 2H, 4-H), 3.88 (s, 3H, 6-H), 2.48 (t, 3J₃,₄ = 7.2 Hz, 2H, 3´-H), 1.70-1.63 (m, 2H, 4´-H), 1.51-1.44 (m, 2H, 5´-H), 1.36-1.29 (m, 4H, 6´-H, 7´-H), 0.90 (t, 3J₆,₇ = 6.9 Hz, 3H, 8´-H); **¹³C-NMR** (100 MHz, CDCl₃) δ [ppm] = 176.93 (C-1), 164.22 (C-5), 131.86 (C-3), 130.33 (C-2), 113.67 (C-4), 95.93 (C-2´), 79.61 (C-1´), 55.50 (C-6), 31.19 (C-6´ or C-7´), 28.60 (C-5´), 27.79 (C-4´), 22.44 (C-6´ or C-7´), 19.15 (C-3´), 13.97 (C-8´); **GC-MS** (CI, 70 eV) m/z [u] (%) =273 (21, [M+Et]⁺), 259 (8, [M+Me]⁺), 245 (100, [M+H]⁺), 244 (23, [M]⁺), 227 (12), 215 (6, [M-ET]⁺), 201 (3, [M-Pr]⁺), 187 (17, [M-Bu]⁺) 137 (21), 135 (52, [4-MeO(C₆H₄)CO]⁺); The NMR data is in match with the literature.[23]
$^1$H-NMR spectrum of 1-(4-methoxyphenyl)non-2-yn-1-one (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of 1-(4-methoxyphenyl)non-2-yn-1-one (100 MHz, CDCl$_3$).
Mass spectrum of 1-(4-methoxyphenyl)non-2-yn-1-one (Cl, 70 eV).

3.3.4.2 Synthesis of 1-(3-Methylphenyl)-2-nonyn-1-one (15b)

CO generation in DMF afforded the title ketone in 85% yield (PH4111), while carbon monoxide preparation using 10 mol% FPyr at 80 °C in THF gave rise of product 15b in 71% yield (BZ160).

**PH4111**: As described in general protocol 3 (chapter 3.2.5 on page 42) the title compound was produced from 3-iodotoluene (219 mg, 1.00 mmol, 1.0 equiv) and 1-octyne (220 µL, 165 mg 1.50 mmol, 1.5 equiv) using CuI (3.8 mg, 20 µmol, 2 mol%) and Pd(PPh₃)₂Cl₂ (5 mol%) in THF (2.0 mL, 0.5 M) through stirring for 25 h at room temperature. Work up gave rise of the crude material as a black oil (320 mg, 140%), of which ¹H-NMR testified full consumption of meta-iodotoluene and ynone 15b and 1-(3-methylphenyl)-1-octyne in a ratio of 93:7. Ultimately, purification using column chromatography on silica gel (27.7 g, mass relation crude 15b/SiO₂ 1:86) with EtOAc/nHex 3:97 yielded the ketone 15b as an orange oil (193.9 mg, 0.85 mmol, 85%). In order to charge the silica gel column, the crude coupling product was adsorbed on silica gel (0.87 g, ratio weight crude product/SiO₂ 1:2.7).

**BZ160**: As described in general protocol 3 (chapter 3.2.5 on page 42) the title compound was synthesized from 3-iodotoluene (219 mg, 1.00 mmol, 1.0 equiv) and 1-octyne (220 µL 1.50 mmol, 1.5 equiv) through stirring for 20 h at room temperature. CO production was carried
out in THF with 1.5 equiv methanoic acid at 80 °C using FPyr (10 mol%). Work up gave rise of the crude material as a black oil (264 mg, 116%), of which ¹H-NMR attested full consumption of meta-iodotoluene and a chemoselectivity of 83:17 15b/1-(3-methylphenyl)-1-octyne. After all, purification with the aid of column chromatography on silica gel (17.7 g, relation of masses crude product/SiO₂ 1:67) with EtOAc/PE 2:98 allowed to isolate the title compound as a yellow oil (163 mg, 0.71 mmol, 71%). In order to charge the silica gel column, the crude material was adsorbed on SiO₂ (1.25 g, weight crude product/SiO₂ 1:5).

M (C₁₆H₂₀O) = 228.33 g/mol; r₁ (SiO₂, EtOAc/nHex 3:97) = 0.29; ¹H-NMR (400 MHz, CDCl₃) δ [ppm] = 7.96-7.94 (m, 2H, 3-H, 7-H), 7.41-7.40 (m, 1H, 5-H), 7.38-7.34 (m, 1H, 6-H), 2.50 (t, J₃,₄ = 7.1 Hz, 2H, 3’-H), 2.42 (s, 3H, 8-H), 1.71-1.64 (m, 2H, 4’-H), 1.51-1.45 (m, 2H, 5’-H), 1.36-1.29 (m, 6’-H, 7’-H), 0.91 (m, 3H, 8’-H); ¹³C-NMR (100 MHz, CDCl₃) δ [ppm] = 178.42 (C-1), 138.27 (C-2), 136.95 (C-4), 134.65 (C-5), 129.80 (C-3), 128.33 (C-6), 126.96 (C-7), 96.63 (C-2’), 79.77 (C-1’), 31.20 (C-6’ or C-7’), 28.61 (C-5’), 27.75 (C-4’), 22.47 (C-6’ or C-7’), 21.23 (C-8), 19.19 (C-3’), 13.98 (C-8’); GC-MS (Cl, 70 eV) m/z [u] (%) = 257 (15, [M+Et]+), 243 (8, [M+Me]+), 229 (100, [M+H]+), 228 (15, [M]+), 213 (10, [M-Me]+), 200 (12, [M-C₃H₂]+), 185 (12, [M-Pr]+), 171 (12, [M-Bu]+), 137 (14, [M-(3-Me(C₆H₄))]+), 119 (55, [3-Me(C₆H₄)CO]+), 105 (4, [PhC≡O]+), 91 (6, [Bn]+).

The NMR data is in match with the literature.[24]
$^1$H-NMR spectrum of 1-(3-methylphenyl)non-2-yn-1-one (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of 1-(3-methylphenyl)non-2-yn-1-one (100 MHz, CDCl$_3$).
3.3.4.3  Synthesis of 1-(2-Thiophenyl)-2-nonyn-1-one (15c)

PH4135: As described general protocol 3 (chapter 3.2.5 on page 42) the title ynone was produced from 2-iodothiophene (111 μL, 210 mg, 1.00 mmol, 1.0 equiv) and 1-octyne (220 μL, 165 mg, 1.00 mmol, 1.0 equiv) with CuI (5.0 mg, 26 μmol, 3 mol%) and Pd(PPh3)2Cl2 (5 mol%) in THF (3.3 mL, 0.3 M) under stirring for 13 h at ambient temperature. In the process, CO synthesis was performed with 1.5 equiv formic acid in DMF at room temperature. Work up gave the crude material as a black oil (315 mg, 143%), whereby 1H-NMR verified full conversion and a ratio of the title compound with regard to 2-thiophenyl-1-octyne of 89:11. Afterwards, purification with the aid of chromatography on SiO2 (27.6 g, mass relation crude material/silica gel 1:86) utilizing EtOAc/nHex (8:92) afforded the ketone 15c as a red oil in 87% yield (190.6 mg, 0.87 mmol). In order to charge the silica gel column, the crude material was adsorbed on SiO2 (0.84 g, relation of masses crude product/silica gel 1:2.4).

M (C13H16OS) = 220.33 g/mol; r (SiO2, EtOAc/nHex 8:92) = 0.36; 1H-NMR (400 MHz, CDCl3) δ [ppm] = 7.89 (dd, 3J5,4 = 3.8 Hz, 4J5,3 = 1.2 Hz, 3-H), 7.68 (dd, 3J5,4 = 4.9 Hz, 4J5,3 = 1.2 Hz, 5-H), 7.14 (dd, 3J4,5 = 4.9 Hz, 3J4,3 = 3.9 Hz, 4-H), 2.47 (t, 3J5,4 = 7.0 Hz, 2H, 3´-H), 1.70-1.62 (m, 2H, 4´-H), 1.51-1.43 (m, 2H, 5´-H), 1.36-1.31 (m, 4H, 6´-H, 7´-H), 0.92-0.89 (m, 3H, 8´-H); 13C-NMR (100 MHz, CDCl3) δ [ppm] = 170.02 (C-1), 145.04 (C-2), 134.79/134.76 (C-3, C-5), 109
128.13 (C-4), 95.39 (C-2'), 79.29 (C-1'), 31.18 (C-6'), 28.56 (C-5'), 27.69 (C-4'), 22.45 (C-7'), 19.09 (C-3'), 13.98 (C-8'); GC-MS (CI, 70 eV) m/z [u] (%) = 249 (2, [M+Et]+), 235 (3, [M+Me]+), 221 (100, [M+H]+), 203 (15), 192 (24), 187 (24), 177 (8, [M-Pr]+), 163 (12, [M-Bu]+), 150 (9), 137 (13, [nHexCCCO]+), 111 (67, [2-thiophenylCO]+), 97 (7), 81 (7, [hexadienyl]+), 79 (8), 67 (16, [pentadienyl]+), 55 (9, [butadienyl]+).

The NMR data matches literature data.[25]

$^1$H-NMR spectrum of 1-(2-thiophenyl)-2-nonyln-1-one (400 MHz, CDCl$_3$).
$^{13}$C-NMR spectrum of 1-(2-thiophenyl)-2-nonyl-1-one (100 MHz, CDCl$_3$).

Mass spectrum of 1-(2-thiophenyl)-2-nonyl-1-one (CI, 70 eV).
3.3.4.4 Synthesis of 1-(2-Methylphenyl)-2-nonyne-1-one (15d)

PH4143: According to general protocol 3 (chapter 3.2.5 on page 42) the title compound was synthesized using CuI (10.2 mg, 54 μmol, 5 mol%), Pd(PPh₃)₂Cl₂ (70 mg, 100 μmol, 10 mol%), ortho-iodotoluene (127 μL, 218 mg, 1.00 mmol, 1.0 equiv), 1-octyne (220 μL, 165 mg, 1.5 mmol, 1.5 equiv), NEt₃ (630 μL, 4.5 mmol, 4.5 equiv) in THF (reagent-grade, 3.3 mL, 0.3 M) under stirring at room temperature for 5 d.(24) In doing so, CO was produced from 2.5 equiv formic acid in DMF at ambient temperature. Finally, the crude material (386 mg, 169%, black oil), of which ¹H-NMR verified full consumption of ortho-iodotoluene, was subjected to chromatographic purification on silica gel (28.1 g, mass ratio crude product/SiO₂ 1:72) with EtOAc/nHex 3:97, which furnished the title ynone as an orange oil in 73% yield (165.8 mg, 0.73 mmol). In order to charge the silica gel column, the crude product was adsorbed on silica gel (0.89 g, relation of masses of crude product/SiO₂ 1:2.5).

M (C₁₄H₂₃O) = 228.34 g/mol; r₁ (SiO₂, EtOAc/nHex 3:97) = 0.30; ¹H-NMR (400 MHz, CDCl₃) δ [ppm] = 8.20 (dd, 3J₇,6 = 7.8 Hz, 4J₁,₂ = 1.2 Hz, 1H, 7-H), 7.42 (d, 3J₄,₅ = 7.6 Hz, 1H, 8-H), 7.23 (d, 3J₃,₄ = 7.2 Hz, 2H, 4´-H), 1.69-1.61 (m, 2H, 4´-H), 1.50-1.43 (m, 2H, 5´-H), 1.37-1.30 (m, 4H, 6´-H, 7´-H), 0.92-0.89 (m, 3H, H-8); ¹³C-NMR (100 MHz, CDCl₃) δ [ppm] = 179.98 (C-1), 140.26 (C-3), 135.77 (C-2), 133.15 (C-7), 132.56 (C-5), 131.99 (C-4), 125.67 (C-6), 95.45 (C-2´), 81.19 (C-1´), 31.20 (C-6´ or C-7´), 28.61 (C-5´), 27.75 (C-4´), 22.46 (C-6´ or C-7´), 21.86 (C-8), 19.15 (C-3´), 13.98 (C-8´); GC-MS (CI, 70 eV) m/z [u] (%) = 257 (2, [M+Et]+), 243 (2, [M+Me]+), 229 (100, [M+H]+), 199 (12, [M-Et]+), 185 (7, [M-Pr]+), 171 (69, [M-Bu]+), 157 (41), 145 (27), 137 (26, [nHexCCCO]+), 132 (46), 119 (58, [2-(H₂C)(C₆H₄)CO]+), 105 (5, [PhCO]+), 91 (18, [2-(H₂C)(C₆H₄)₂]+), 81 (7, [hexadienyl]+), 67 (19, [pentadienyl]+), 55 (10, [butenyl]+); HR-MS (CI, [C₁₀H₁₂O]+) calc. 229.1587 u found: 229.1590 u.

The NMR data is a fair agreement with literature data of 1-(2-methylphenyl)-2-heptyn-1-one.(26)

(24) Reaction of ortho-iodotoluene and 1-octyne in the presence of CuI (2 mol%), Pd(PPh₃)₂Cl₂ (5 mol%) and NEt₃ (3.5 equiv) for 24 h at ambient temperature resulted in 30% conversion only (of ortho-iodotoluene). Thereby, CO was generated from 1.5 equiv formic acid in DMF at room temperature.
$^1$H-NMR spectrum of 1-(2-methylphenyl)non-2-yn-1-one (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of 1-(2-methylphenyl)non-2-yn-1-one (100 MHz, CDCl$_3$).
Mass spectrum of 1-(2-methylphenyl)non-2-yn-1-one (Cl, 70 eV).
3.3.4.5 Synthesis of 1-(3-Pyridinyl)-2-nonyn-1-one (15e)

Coupling in the absence of Cul allowed for the synthesis of ynone 15e in an enhanced yield of 68% (PH4177) instead of 64% (PH4144).

**PH4177:** Following general protocol 3 (chapter 3.2.5 on page 42) the title ynone was synthesized from 3-iodopyridine (205 mg, 1.00 mmol, 1.0 equiv) and 1-octyne (220 µL, 165 mg, 1.5 mmol, 1.5 equiv) utilizing Pd(PPh₃)₂Cl₂ (35.1 mg, 50 µmol, 5 mol%) **without Cul** in THF (3.3 mL, 0.3 M) under stirring for 48 h (25) at room temperature. The CO preparation was conducted with 2.5 equiv HCO₂H in DMF at ambient temperature. Since the title compound contains a basic pyridine moiety in the work was used 2 N NaOH solution in water instead of 2 N HCl. ¹H-NMR of the crude material indicated full consumption of 3-iodopyridine, a ratio of 15e with respect to 1-pyridin-3-yl-1-octyne of ≥20 mol% of (2E,4E)-1-pyridin-3-yl-2,4-nonadien-1-one in reference to 15e. Finally, chromatographic purification by means of column chromatography on silica gel (28.3 g, mass crude material/SiO₂ 1:91) using EtOAc/nHex 30:70 as mobile phase afforded ketone 15e as a red oil in 68% yield (146.7 mg, 0.681 mmol).

Thereby, the crude product was dissolved in EtOAc (0.25 mL) and the eluent (0.25 mL) in order to be applied onto the silica gel column. Some late fraction containing the target compound and (2E,4E)-1-pyridin-3-yl-2,4-nonadien-1-one were discarded.

**PH4144:** In accordance with general protocol 3 (chapter 3.2.5 on page 42) the title compound was prepared from 3-iodopyridine (1.00 mmol, 1.0 equiv) and 1-octyne (1.5 equiv) **utilizing Cul** (3.8 mg, 20 µmol, 2 mol%), Pd(PPh₃)₂Cl₂ (5 mol%) in THF (3.3 mL, 0.3 M) under stirring for 18 h at room temperature. Therein, CO was formed from 2.5 equiv formic acid in DMF at ambient temperature. ¹H-NMR of the crude material (297 mg, black oil) after basic work up attested full conversion of iodopyridine and displayed a relation of 93:7 of the title ketone with respect to 1-(3-pyridinyl)-1-octyne. In the end, purification by means of column chromatography on silica gel (30.1 g, ratio SiO₂/crude material of 100:1) with EtOAc/nHex 30:70 facilitated the isolation of the title compound as a red oil in 64% yield (137.4 mg, 0.64 mmol). In order to charge the silica gel column, the crude title ketone was adsorbed on silica gel (0.74 g, mass relation crude product with respect to SiO₂ 1:2.5).

Repetition of this experiment showed a poor reproducibility, since the title compound was isolated in only 46% yield. This was reasoned by the adsorption on silica gel before the column chromatographic purification.

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(25) 19 h of reaction duration only allowed to convert 75% of 3-iodopyridine in the absence of Cul (PH4172).
**M** (C_{14}H_{17}NO) = 215.30 g/mol; r_{f} (SiO_{2}, EtOAc/nHex 30:70) = 0.33; **^{1}H-NMR** (400 MHz, CDCl_{3})

\[ \delta [\text{ppm}] = 9.35 \text{ (br. s, 1H, 3-H)}, 8.82 \text{ (br. s, 1H, 5-H)}, 8.37-8.35 \text{ (m 1H, 7-H)}, 7.44 \text{ (dd, } ^{3}J = 7.9, 4.8 \text{ Hz 1H, 6-H)}, 2.53 \text{ (t, } ^{3}J_{3',4'} = 7.1 \text{ Hz, 2H, 4'}-\text{H}), 1.73-1.66 \text{ (m, 2H, 4'}-\text{H}), 1.52-1.45 \text{ (m, 2H, 5'}-\text{H)}, 1.37-1.31 \text{ (m, 4H, 6'}-\text{H, 7'}-\text{H}), 0.93-0.89 \text{ (m, 3H, 8'}-\text{H});

**^{13}C-NMR** (100 MHz, CDCl_{3})

\[ \delta [\text{ppm}] = 176.55 \text{ (C-1)}, 153.96 \text{ (C-5)}, 151.39 \text{ (C-3)}, 136.10 \text{ (C-7)}, 132.16 \text{ (C-2)}, 123.36 \text{ (C-6)}, 98.62 \text{ (C-2')}, 79.10 \text{ (C-1')}, 31.13 \text{ (C-6' or C-7')}, 28.58 \text{ (C-5')}, 27.63 \text{ (C-4')}, 22.40 \text{ (C-6' or C-7')}, 19.19 \text{ (C-3')}, 13.94 \text{ (C-8')};

**GC-MS** (Cl, 70 eV) m/z [u] (%) = 244 (12, [M+Et]^+), 230 (8, [M+Me]^+), 216 (100, [M+H]^+), 200 (4, [M-Me]^+), 186 (31, [M-Et]^+), 172 (11, [M-Pr]^+), 158 (21, [M-Bu]^+), 137 (6), 130 (5), 106 (50, [pyridinylCO]^+), 93 (29), 79 (17, [pyridine]^+), 78 (11, [pyridinyl]^+), 67 (13), 55 (5);

**HR-MS** (Cl, [C_{14}H_{18}NO]^+)

calc. 216.1383 u found: 216.1397 u.

The NMR data is in a fair agreement with literature data of 1-(3-pyridinyl)-2-heptyn-1-one.\(^{[27]}\)

\[ ^{1}H\text{-NMR spectrum of 1-(3-pyridinyl)-2-nonyl-1-one (400 MHz, CDCl}_{3}. \]
C-NMR spectrum of 1-(3-pyridinyl)-2-nonyl-1-one (100 MHz, CDCl$_3$).

Mass spectrum of 1-(3-pyridinyl)-2-nonyl-1-one (Cl, 70 eV).
3.3.4.6 Synthesis of 1-(4-Cyanophenyl)-2-nonyn-1-one (15f)

| entry | conditions | 15f/18f<sup>a</sup> | Yield<sup>b</sup> 15f/18f [%] |
|--------|------------|---------------------|-----------------|
| 1      | CO chamber: HCO<sub>2</sub>H (2.5 equiv), TCT (95 mol%), DMF (2 M), 23 h rt | ≥98:2 | 69/n.d. |
|        | Coupling chamber: Pd(PPh<sub>3</sub>)Cl<sub>2</sub> (5 mol%), 8f (1.0 equiv), 1-octyne (1.5 equiv), NEt<sub>3</sub> (4.5 equiv), THF (0.3 M), 23 h rt | | |
| 2      | CO chamber: HCO<sub>2</sub>H (2.5 equiv), TCT (95 mol%), DMF (2 M), 20 h rt | 55:45 | 41/n.d. |
|        | Coupling chamber: CuI (4 mol%), Pd(PPh<sub>3</sub>)Cl<sub>2</sub> (5 mol%), 8f (1.0 equiv), 1-octyne (1.5 equiv), NEt<sub>3</sub> (4.5 equiv), THF (0.3 M), 20 h rt | | |
| 3      | CO chamber: CuI (2.5 mol%), Pd(PPh<sub>3</sub>)Cl<sub>2</sub> (5 mol%), 8f (1.0 equiv), 1-octyne (1.5 equiv), NEt<sub>3</sub> (3.5 equiv), THF (0.3 M), 20 h rt | 43:57 | 31/40 |

<sup>a</sup> Determined from the <sup>1</sup>H-NMR of the crude material. <sup>b</sup> Isolated yield after chromatographic purification. 8f = 4-iodobenzonitrile

Target ketone 15f was isolated in 69% yield after synthesis without CuI (entry 1). In the presence of CuI significant amounts of 1-(4-cyanophenyl)-1-octyne (18f) were formed, which caused largely depleted yields of 15f of 31-41% (entries 2+3). In addition, higher amounts of CO shift the chemoselectivity 15f/18f in favour for ketone 15f (entries 2+3). Notably, in the experiment in entries 2 and 3 the crude product was adsorbed on silica gel in order to be applied onto the silica gel column, whereas in entry 1 the crude title compound was diluted with the eluent. All other Sonogashira coupling products of type 18 in this section were assigned in analogy to compound 18f to determine chemoselectivities based on the integral ratios of the triplets of 3´-H in the <sup>1</sup>H-NMR spectra of the crude materials.

Entry 1, PH4170: In accordance with general procedure 3 (chapter 3.2.5 on page 42) the title ynone was produced without CuI from 4-iodobenzonitrile (229 mg, 1.00 mmol, 1.0 equiv) and 1-octyne (220 µL, 165 mg, 1.5 equiv) using Pd(PPh<sub>3</sub>)Cl<sub>2</sub> (5 mol%) in THF (3.3 mL, 0.3 M) under stirring for 23 h at room temperature, whereby CO was formed from 2.5 equiv HCO<sub>2</sub>H in DMF. Aqueous work up yielded the crude ketone 15f as a dark red oil (336 mg, 140%), of which <sup>1</sup>H-NMR confirmed full conversion and a ratio 15f/18f of ≥98:2. Ultimately, column chromatographic purification employing silica gel (28.2 g, mass ratio crude product/SiO<sub>2</sub> 1:83) with EtOAc/nHex 8:92 as eluent mixture afforded the title alkyne 15f as a red oil in 69% yield (163.9 mg, 0.685 mmol). <sup>1</sup>H-NMR indicated 3 mol% of dienone 19f with respect to ynone 15f. In order to charge the silica gel column, the crude material was not adsorbed on silica gel but diluted with EtOAc (0.25 mL) and the eluent (0.25 mL).
Entry 2, PH4141: In agreement with general protocol 3 (chapter 3.2.5 on page 42) the ynone 15f was synthesized from 4-iodonitrile (1.00 mmol, 1.0 equiv) and 1-octyne (1.5 equiv) using Cul (7.6 mg, 40 μmol, 4 mol%) and Pd(PPh₃)₂Cl₂ in THF (0.3 M) under stirring at ambient temperature. Thereby, CO formation was conducted with 2.5 equiv formic acid in DMF at room temperature. After stirring for 20 h work up yielded the crude ynone 15f as a black oil (329 mg, 138%). ¹H-NMR confirmed full conversion of 4-iodobenzonitrile and a chemoselectivity of 55:45 15f/18f. Eventually, purification with the aid of column chromatography on silica gel (43 g, mass relation crude 15f/SiO₂ 1:133) with EtOAc/nHex 8:92 as eluent system gave rise of the title carbonyl compound as a red oil in 41% yield (97.3 mg, 0.467 mmol). In doing so, the crude product was adsorbed on silica gel (0.79 g, ratio weight 15f/silica gel 1:2.4) and loaded onto the chromatography column.

Entry 3, PH4129: According to general protocol 3 (chapter 3.2.5 on page 42) the ketone 15f was prepared from 4-iodobenzonitrile (1.00 mmol, 1.0 equiv) and 1-octyne (1.5 equiv) employing Cul (4.7 mg, 25 μmol, 2.5 mol%) and Pd(PPh₃)₂Cl₂ (5 mol%) in THF (3.3 mL, 0.3 M) under stirring for 24 h at room temperature. Carbon monoxide was liberated in DMF exploiting 1.5 equiv HCO₂H at ambient temperature. After work up the crude material (331 mg, 137%) was obtained as a black oil, of which ¹H-NMR proved full conversion of 4-iodobenzonitrile and showed the products 15f/18f in a ratio of 43:57. Finally, column chromatographic purification on silica gel (26.8 g, ratio mass crude product/SiO₂ 1:81) with EtOAc/nHex 5:95 (250 mL) → 10:90 resulted in the isolation of the title ketone as a red oil (74.9 mg, 0.31 mmol, 31%) alongside with alkyn 18f as a yellow oil (85.3 mg, 0.40 mmol, 40%). To load the crude material onto the silica gel column, the crude material was adsorbed on silica gel (0.93 g, relation weight crude product/SiO₂ 1:2.8).

1-(4-cyanophenyl)-2-nonyl-1-on (15f)

M (C₁₆H₁₇NO) = 239.32 g/mol; r₁ (SiO₂, EtOAc/nHex) = 0.35 (10:90), 0.33 (8:92); ¹H-NMR (400 MHz, CDCl₃) δ [ppm] = 8.23-8.21 (m, 2H, 3-H), 7.80-7.78 (m, 2H, 4-H), 2.53 (t, 2H, 3j₃,₄ = 7.1 Hz, 3'-H), 1.73-1.65 (m, 2H, 4'-H), 1.52-1.44 (m, 2H, 5'-H), 1.37-1.32 (m, 4H, 6'-H, 7'-H), 0.93-0.89 (m, 3H, 8'-H); ¹³C-NMR (100 MHz, CDCl₃) δ [ppm] = 176.30 (C-1), 139.65 (C-6), 132.31 (C-4), 129.73 (C-3), 117.85 (C-2), 116.90 (C-5), 99.11 (C-2'), 79.25 (C-1'), 31.13 (C-6'), 28.60 (C-5'), 27.62 (C-4'), 22.42 (C-7'), 19.24 (C-3'), 13.95 (C-8'); GC-MS (Cl, 70 eV) m/z [u] (%) = 268 (6, [M+Et⁺]) 254 (24, [M+Me⁺]), 240 (100, [M+H⁺]), 224 (4, [M-Me⁺]), 210 (9, [M-Et⁺]), 196 (5, [M-Pr⁺]), 182 (12, [M-Bu⁺]), 171 (7), 130 (38, [4-NC(C₆H₄)CO⁺]), 109 (6, [nHexCC⁺]), 67 (14, [pentadienyl⁺]), 55 (6, [butenyl⁺]).

The NMR data is in agreement with the literature.[²⁸]

(2E,4E)-1-(4-Cyanophenyl)-2,4-nonadien-1-on (19f)
Characterized as minor component of mixture with ketone 19f with a ratio of 34:66. Only well separated signals have been listed.

\( M \) (C\(_{16}\)H\(_{27}\)NO) = 239.32 g/mol; \( r_t \) (SiO\(_2\), EtOAc/nHex) = 0.28 (8:92); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) [ppm] = 8.01-7.99 (m 2H, 3-H), 7.46-7.39 (m, 1H, 2´-H), 6.82 (d, \( ^3J_{1,2} \) = 15.0 Hz, 1H, 1´-H), 6.37-6.34 (m, 1H, 3´-H), 6.32-6.29 (m, 1H, 4´-H); 13C-NMR (100 MHz, CDCl\(_3\), extracted from HMQC and HMBC-NMR) \( \delta \) [ppm] = 189.24 (C-1), 148.24 (C-4´), 146.96 (C-2´), 128.78 (C-3´), 128.42 (C-3), 122.43 (C-1´), 32.78 (C-5´).

The NMR data is in fair match with those of \((2E,4E)\)-1-(4-Cyanophenyl)-2,4-hexadien-1-on.\(^{[29]}\)

All other dienones of type 19 in this chapter were assigned in analogy.

1-(4-Cyanophenyl)-1-octyne (18f)

\( M \) (C\(_{15}\)H\(_{17}\)N) = 211.31 g/mol; \( r_t \) (SiO\(_2\), EtOAc/nHex) = 0.55 (10:90), 0.38 (5:95); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) [ppm] = 7.57-7.55 (m, 2H, 4-H), 7.46-7.44 (m, 2H, 3-H), 2.42 (t, 2H, \( ^3J_{3,4}= 7.1 \) Hz, 3´-H), 1.64-1.57 (m, 2H, 4´-H), 1.48-1.41 (m, 2H, 5´-H), 1.36-1.26 (m, 4H, 6´-H, 7´-H), 0.92-0.89 (m, 3H, 8´-H); 13C-NMR (100 MHz, CDCl\(_3\)) \( \delta \) [ppm] = 132.03 (C-3), 131.85 (C-4), 129.13 (C-2), 118.60 (C-6), 110.72 (C-5), 95.68 (C-2´), 79.39 (C-1´), 31.27 (C-6´), 28.55 (C-3´), 28.37 (C-4´), 22.49 (C-7´), 19.47 (C-5´), 14.00 (C-8´); GC-MS (CI, 70 eV) m/z [u] (\%) = 240 (6, [M+Et]^+), 226 (22, [M+Me]^+), 212 [M+H]^+), 182 (32, [M-Et]^+), 168 (41, [M-Pr]^+), 154 (26, [M-Bu]^+), 142 (24), 140 (24, [M-Pen]^+), 127 (11, [4-NC(C\(_6\)H\(_4\)]CCH]^+), 116 (23), 95 (16, [heptadienyl]^+), 81 (11, [hexadienyl]^+), 69 (20, [pentenyl]^+), 67 (13, [pentadienyl]^+), 55 (13, [butenyl]^+).

The NMR data is in match with the literature.\(^{[30]}\)
\(^1\)H-NMR spectrum of 1-(4-cyanophenyl)-2-nonyl-1-one (400 MHz, CDCl\(_3\)).

\(^{13}\)C-NMR spectrum of 1-(4-cyanophenyl)-2-nonyl-1-one (100 MHz, CDCl\(_3\)).
Mass spectrum of 1-(4-cyanophenyl)-2-nonyne-1-one (CI, 70 eV).

$^1$H-NMR spectrum of 1-(4-cyanophenyl)-1-octyne (400 MHz, CDCl$_3$).
$^{13}$C-NMR spectrum of 1-(4-cyanophenyl)-1-octyne (100 MHz, CDCl$_3$).

Mass spectrum of 1-(4-cyanophenyl)-1-octyne (CI, 70 eV).
3.3.4.7 Synthesis of 1-(4-nitrophenyl)-2-nonyn-1-one (15g)

**PH4250:** Following general procedure 3 (chapter 3.2.5 on page 42) the ynone 15g was synthesized from 1-iodo-4-nitrobenzene (247 mg, 0.992 mmol, 1.0 equiv) and 1-octyne (220 µL, 165 mg, 1.5 equiv) using Pd(PPh₃)₂Cl₂ (5 mol%) in THF (3.3 mL, 0.3 M) under stirring for 13 h at room temperature, whereby CO was formed from 1.5 equiv HCO₂H in DMF. Aqueous work up furnished the crude ketone 15g as a dark black oil (332 mg, 129%), of which ¹H-NMR confirmed full conversion and a ratio of 15g with respect to 1-(4-nitrophenyl)-1-octyne 18g of 81:19. In addition, 5 mol% of 1-(4-nitrophenyl)-2,4-nondien-1-one with respect to the title ketone were detected.

In the end, column chromatographic purification employing silica gel (26.8 g, mass ratio crude product/SiO₂ 1:81) with EtOAc/nHex 5:95 as eluent mixture gave the title alkyne 15g as a red oil in 59% yield (151.0 mg, 0.582 mmol). ¹H-NMR indicated negligible traces of 1-(4-nitrophenyl)-2,4-nondien-1-one of ≤2 mol% (r in eluent = 0.23). In order to charge the silica gel column, the crude material was not adsorbed on silica gel but diluted with EtOAc (0.25 mL) and the eluent (0.25 mL).

**PH4251:** The title ynone was prepared as described above from 4-nitrophenyliodide (251 mg, 1.008 mmol, 1.0 equiv). ¹H-NMR of the crude product (black oil, 330 mg, 126%) with dibenzylether as internal standard revealed full consumption of the starting aryl iodide and ynone 15g in 66% yield. In addition, 1-(4-nitrophenyl)-1-octyne 18g and 1-(4-nitrophenyl)-2,4-nondien-1-one were observed in 15% and ≤2% yield, respectively (15g/18g 82:18).

Eventually, purification by means of column chromatography on silica gel (28.2 g, ratio mass crude product/SiO₂ 1:85) using EtOAc/nHex 5:95 furnished the ketone 15g as a red oil (159.3 mg) containing minor traces of 1-(4-nitrophenyl)-2,4-nondien-1-one ≤2 mol%. Under consideration of 4 mol% residual dibenzyl ether as judged by ¹H-NMR the product 3 was obtained in 59% yield:

\[ n(3) = \frac{159.3 \text{mg}}{259.3 \frac{g}{mol} + 0.04 \cdot 198.3 \frac{g}{mol}} = 0.596 \text{mmol} \]

**PH4256:** In accordance with general procedure 3 (chapter 3.2.5 on page 42) the ynone 15g was produced from 1-iodo-4-nitrobenzene (1.00 mmol, 1.0 equiv) and 1-octyne (1.5 equiv) using Pd(PPh₃)₂Cl₂ (5 mol%) and NEt₃ (4.5 equiv) in THF (0.3 M) under stirring at room temperature for 6 h. Thereby, CO was synthesized from 2.5 equiv formic acid in DMF at ambient temperature. ¹H-NMR of the crude product (320 mg, 123%, black oil) indicated 91% conversion of 1-iodo-4-nitrobenzene and a ratio of 15g and 18g of 90:10. Ultimately, column
chromatographic purification employing silica gel (27.9 g, mass ratio crude material:SiO$_2$ 1:87) with EtOAc/nHex 5:95 delivered the title ynone as a red oil in a yield of 62% (160.1 mg, 0.617 mmol).

**M** (C$_{15}$H$_{17}$NO$_3$) = 259.31 g/mol; **r$_f$** (SiO$_2$, EtOAc/nHex 5:95) = 0.30; **$^1$H-NMR** (400 MHz, CDCl$_3$) δ [ppm] = 8.34-8.32 (m, 2H, 4-H), 8.30-8.28 (m, 2H, 3-H), 2.55 (t, 3J$_{3',4'}$ = 7.2 Hz, 2H, 3'-H), 1.74-1.67 (m, 2H, 4'-H), 1.53-1.45 (m, 2H, 5'-H), 1.37-1.31 (m, 4H, 6'-H, 7'-H), 0.93-0.90 (m, 3H, 8'-H); **$^{13}$C-NMR** (125 MHz, CDCl$_3$) δ [ppm] = 175.99 (C-1), 150.70 (C-5), 141.01 (C-2), 130.36 (C-3), 123.67 (C-4), 99.44 (C-2'), 79.36 (C-1'), 31.14 (C-6'), 28.62 (C-5'), 27.61 (C-4'), 22.43 (C-7'), 19.27 (C-3'), 13.97 (C-8').

The NMR data is in match with the literature.$^{[31]}$

$^1$H-NMR spectrum of 1-(4-nitrophenyl)-2-nonyl-1-one (500 MHz, CDCl$_3$).
$^{13}$C-NMR spectrum of 1-(4-nitrophenyl)-2-nonyl-1-one (125 MHz, CDCl₃).
3.3.4.8 Synthesis of 1-(3-Formylphenyl)-2-nonyn-1-one (15h)

| entry | conditions | 15h/18h% | Yield 15h [%] |
|-------|------------|----------|---------------|
| 1     | CO chamber: HCO₂H (2.5 equiv), TCT (95 mol%), DMF (2 M), 48 h rt/ Coupling chamber: Pd(PPh₃)₂Cl₂ (5 mol%), 8h (1.0 equiv), 1-octyne (1.5 equiv), NEt₃ (4.5 equiv), THF (0.3 M), 48 h rt | ≥98:2 | 72 |
| 2     | CO chamber: HCO₂H (2.5 equiv), TCT (95 mol%), DMF (2 M), 20 h rt/ Coupling chamber: Cul (2 mol%), Pd(PPh₃)₂Cl₂ (5 mol%), 8h (1.0 equiv), 1-octyne (1.5 equiv), NEt₃ (4.5 equiv), THF (0.3 M), 20 h rt | 85:15 | 71 |
| 3     | CO chamber: HCO₂H (1.5 equiv), TCT (95 mol%), DMF (2 M), 24 h rt/ Coupling chamber: Cul (3 mol%), Pd(PPh₃)₂Cl₂ (5 mol%), 8h (1.0 equiv), 1-octyne (1.5 equiv), NEt₃ (3.5 equiv), THF (0.3 M), 24 h rt | 73:27 | 62 |

a. Determined from the ¹H-NMR of the crude material. b. Isolated yield after chromatographic purification. 8h = 3-iodobenzaldehyde, 18h = 1-(3-formylphenyl)-1-octyne.

The best chemoselectivity 15h/18h (= 1-(3-formylphenyl)-1-octyne) was accomplished without Cul (entry 1), which afforded an increased reaction duration of 2 d in order to achieve full consumption of aryl iodide 8h. The isolated product contained traces of (2E,4E)1-(3-formylphenyl)-2,4-nonadien-1-one, which were considered in the determination of the yield of 15h. Low amounts of Cul still provided 15h in a good yield of 71% (entry 2), while reduction of the amount of formic acid for the CO formation from 2.5 to 1.5 equiv resulted in a reduced yield of 62% (entry 3).

An increase of the amount of formic acid from 1.5 to 2.5 equiv and TCT from 57 to 95 mol% allowed an improvement of the yield of the title compound from 62% (PH4130) to 71% (PH4140).

**Entry 1, PH4176:** Following general protocol 3 (chapter 3.2.5 on page 42) the title compound was produced from 3-iodobenzaldehyde (8h, 232 mg, 1.00 mmol, 1.0 equiv) and 1-octyne (220 µL, 165 mg, 1.5 equiv) **without Cul** harnessing Pd(PPh₃)₂Cl₂ (5 mol%) in THF (0.3 M) at room temperature under stirring for 48 h.[26] Thereby, CO was liberated from **2.5 equiv HCO₂H** in DMF. From an aqueous work up the crude ketone 15h arose as a black oil (339 mg, 140%), of which ¹H-NMR proved full consumption of 8h and a chemoselectivity 15h/18h (= 1-(3-formylphenyl)-1-octyne) ≥98:2. In addition, 10 mol% (2E,4E)1-(3-formylphenyl)-2,4-nonadien-1-one were detected with respect to ynone.

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[26] A reaction duration of 19 h resulted in 87% conversion of 8h (PH4173).
15h. Finally, purification with the aid of column chromatography on silica gel (29.7 g, ratio of masses crude product/SiO₂ 1:87) with EtOAc/nHex 13:87 as eluent system afforded ynone 15h as a red oil (184.1 mg). Under consideration of 6 mol% residual (2E,4E)1-(3-formylphenyl)-2,4-nonadien-1-one as judged by ¹H-NMR, the title ketone was obtained in 72% yield:

\[
n(18e) = \frac{184.1 \text{ mg}}{242.3 \text{ g mol}^{-1} + 0.06 \cdot 242.3 \text{ g mol}^{-1}} = 0.717 \text{ mmol}
\]

In order to charge the silica gel column, the crude material was dissolved in a mixture of EtOAc (0.25 mL) and the eluent (0.25 mL).

**Entry 2, PH4140:** As delineated in general protocol 3 (chapter 3.2.5 on page 42) the alkynone 15h was formed from 3-iodobenzaldehyde (1.00 mmol, 1.0 equiv) and 1-octyne (1.5 equiv) under stirring for 20 h at ambient temperature utilizing Cul (3.8 mg, 20 μmol, 2 mol%) and Pd(PPh₃)₂Cl₂ (5 mol%) in THF (0.3 M). In this experiment, CO preparation was carried out utilizing 2.5 equiv formic acid in DMF at room temperature. In the following, work up resulted in the crude ketone 15h (344 mg) as a black oil, whereby ¹H-NMR attested complete consumption of 3-iodobenzaldehyde and a ratio of the ynone 15h with regard to 1-(3-formylphenyl)-1-octyne of 85:15). Ultimately, purification by means of column chromatography with silica gel (26.9 g, mass ratio crude 15h/SiO₂ 1:78) as stationary phase and EtOAc/nHex 13:87 as mobile phase gave rise of the title alkyne as a red oil (172.6 mg, 0.71 mmol) in a yield of 71%. To load the crude material onto the silica gel column, it was adsorbed on silica gel (0.84 g, relation of crude 15h/SiO₂ 1:2.5).

**Entry 3, PH4130:** In accordance with general protocol 3 (chapter 3.2.5 on page 42) the title alkyne was accessed from 3-iodobenzaldehyde (1.00 mmol, 1.0 equiv) and 1-octyne (1.5 equiv) employing Cul (6.3 mg, 33 μmol, 3 mol%) and Pd(PPh₃)₂Cl₂ (5 mol%) in THF (3.3 mL, 0.3 M) at room temperature under stirring for 24 h. In doing so, carbon monoxide was synthesized from 1.5 equiv formic acid in DMF at ambient temperature. Next, work up provided ketone 15h as a black oil (341 mg, of which ¹H-NMR indicated full conversion of 3-iodobenzaldehyde and a chemoselectivity 15h/1-(3-formylphenyl)-1-octyne of 73:27. Eventually, chromatographic purification using silica gel (27.3 g, mass relation crude 15h/SiO₂ 1:80) applying EtOAc/nHex 12:88 as eluent mixture furnished ketone 15h a red oil (150.2 mg, 0.62 mmol, 62%). Thereby, the crude product was adsorbed on silica gel (0.90 g, ratio of weights crude 15h with respect to SiO₂ 1:2.6).

\[
\text{M} (C_{16}H_{18}O_2) = 242.32 \text{ g/mol}; \quad r_1 \text{ (SiO}_2, \text{ EtOAc/nHex)} = 0.28 (12:88), 0.33 (13:87); \quad ^1\text{H-NMR} (400 \text{ MHz, CDCl}_3) \delta [\text{ppm}] = 10.11 \text{ (s, 1H, 8-H)}, 8.62 \text{ (br. s, 1H, 1-H), 8.39-}
\]

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8.37 (m, 1H, 7-H), 8.14-8.12 (m, 1H, 5-H), 7.67 (ψ-t, 3J = 7.7 Hz, 1H, 6-H), 2.54 (t, 3J_2,3 = 7.1 Hz, 2H, 3’-H), 1.74-1.67 (m, 2H, 4’-H), 1.54-1.46 (m, 2H, 5’-H), 1.36-1.32 (m, 4H, 6’-H, 7’-H), 0.93-0.89 (m, 3H, 8’-H); \(^{13}\text{C-NMR}\) (100 MHz, CDCl\(_3\)) \(\delta\) [ppm] = 191.14 (C-8), 176.82 (C-1), 137.61 (C-2), 136.56 (C-4), 134.62 (C-7), 133.82 (C-5), 131.00 (C-3), 129.33 (C-6), 98.32 (C-2’), 79.32 (C-1’), 31.17 (C-6’), 28.63 (C-5’), 27.66 (C-4’), 22.43 (C-7’), 19.24 (C-3’), 13.96 (C-8’); \(\text{GC-MS}\) (Cl, 70 eV) m/z [u] (%) = 271 (1, [M+Et]\(^+\)), 257 (11, [M+Me]\(^+\)), 243 (100, [M]\(^+\)), 213 (26, [M-Et]\(^+\)), 199 (8, [M-Pr]\(^+\)), 185 (19, [M-Bu]\(^+\)), 172 (8), 133 (62, [3-OHC(C\(_6\)H\(_4\))CO]\(^+\)), 105 (9, [PhCO]\(^+\)), 91 (6, [Bn]\(^+\)), 67 (18, [pentadienyl]\(^+\)), 55 (8, [butenyl]\(^+\)); \(\text{HR-MS}\) (Cl, [C\(_{16}\)H\(_{19}\)O\(_2\)]\(^+\)) calc. 238.1380 u found: 243.1397 u.

\(^1\text{H-NMR}\) spectrum of 1-(3-formylphenyl)-2-nonyl-1-one (400 MHz, CDCl\(_3\)).
$^{13}$C-NMR spectrum of 1-(3-formylphenyl)-2-nonyl-1-one (100 MHz, CDCl$_3$).

Mass spectrum of 1-(3-formylphenyl)-2-nonyl-1-one (CI, 70 eV).
3.3.4.9 Synthesis of 1-(3-Methylphenyl)-3-phenyl-2-propyn-1-one (15i)

After cross coupling without using CuI, ynone 15i was isolated in an excellent yield of 91% (PH4175). Application of CuI (2 mol%) effected a drastically reduced yield of 55%, which is reasoned Sonogashira coupling without incorporation of CO (PH4131).

**PH4175:** In accordance with general procedure 3 (chapter 3.2.5 on page 42) the title compound was accessed from 3-iodotoluene (128 µL, 218 mg, 1.00 mmol, 1.0 equiv) and phenylacetylene (165 µL, 153 mg, 1.5 mmol, 1.5 equiv) under use of Pd(PPh3)2Cl2 (5 mol%) without CuI in THF (0.3 M) under stirring at ambient temperature for 48 h.\(^{(27)}\) Thereby, carbon monoxide was produced from 2.5 equiv HCO2H in DMF at room temperature. Aqueous work up furnished the crude material as a black oil (332 mg, 151%), of which \(^1\)H-NMR demonstrated 94% consumption of meta-tolyl iodide and a ratio of target ketone 15i and 1-(3-methylphenyl)-1-octyne 18i of ≥98:2. Eventually, purification by means of column chromatography based on silica gel (26.4 g, relation of weight crude material/SiO2 1:80) with EtOAc/nHex 7:93 as eluent mixture delivered ynone 15i as a yellow oil in 91% yield (200.1 mg, 0.908 mmol). In order to load the crude product onto the SiO2-column, it was dissolved in a mixture of EtOAc (0.25 mL) and the eluent (0.25 mL).

**PH4131:** As given in general protocol 3 (chapter 3.2.5 on page 42) ynone 15i was synthesized from 3-iodotoluene (1.00 mmol, 1.0 equiv) and phenylacetylene (1.5 equiv) with CuI (3.8 mg, 20 µmol, 2 mol%) and Pd(PPh3)2Cl2 (5 mol%) in THF (3.3 mL, 0.3 M) under stirring for 24 h at room temperature. In doing so, carbon monoxide was accessed from 1.5 equiv formic acid in DMF at ambient temperature. Aqueous work up yielded the crude title compound as a black oil (309 mg, 140%), whereby \(^1\)H-NMR verified 97% conversion of 3-iodotoluene and a ratio of carbonylation product 15i with respect of 1-(3-methylphenyl)-2-phenylethyne of 59:41. Subsequently, purification through column chromatography on silica gel (26.3 g, ratio weight crude product with respect to SiO2 1:85) employing EtOAc/nHex 7:93 delivered the product 15i as a yellow oil in 55% yield (122.0 mg, 0.55 mmol). To charge the silica gel column, the crude ketone 15i was adsorbed on silica gel (0.97 g, ratio of masses crude material/SiO2 1:3.1).

\[ M (C_{16}H_{12}O) = 220.27 \text{ g/mol}; \ r (SiO2, EtOAc/nHex 7:93) = 0.35; \]
\[ ^1\text{H-NMR} (400 \text{ MHz, CDCl}_3) \delta [ppm] = 8.05-8.01 (m, 2H, 3-H, 7-H), 7.69-7.67 (m, 2H, 4'-H), 7.50-7.38 (m, 5H, 5-H, 6-H, 5'-H, 6'-H), \]

\(^{(27)}\) In a separate but identical experiment with a shorter reaction time of 28 h only 84% conversion of 11f were reached. Afterwards the product was isolated in 78% yield upon chromatographic purification (PH4175).
2.44 (s, 3H, 8-H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ [ppm] = 178.15 (C-1), 138.44 (C-4), 136.88 (C-6), 134.92 (C-5), 132.99 (C-4'), 130.69 (C-6'), 129.73 (C-3), 128.63 (C-5'), 128.47 (C-6), 127.06 (C-7), 120.17 (C-9), 92.81 (C-2'), 86.98 (C-1'), 21.29 (C-8); GC-MS (Cl, 70 eV) m/z [u] (%) = 249 (2, [M+Et]$^+$), 235 (12, [M+Me]$^+$), 221 (93, [M+H]$^+$), 220 (100, [M]$^+$), 205 (12, [M+Me]$^+$), 192 (70), 143 (4, [M-Ph]$^+$), 129 (53, [PhCCCO]$^+$), 119 (24, [3-(H$_3$C)(C$_6$H$_4$)CO]$^+$), 91 (5, [H$_3$C(C$_6$H$_4$)]$^+$), 75 (6), 65 (3, [Cp]$^+$).

The NMR data is in a fair agreement with reference data.$^{[32]}$

$^1$H-NMR spectrum of 1-(3-methylphenyl)-3-phenyl-2-propyn-1-one (400 MHz, CDCl$_3$).
$^1$H-NMR spectrum of 1-(3-methylphenyl)-3-phenyl-2-propyn-1-one (100 MHz, CDCl$_3$).

Mass spectrum of 1-(3-methylphenyl)-3-phenyl-2-propyn-1-one (CI, 70 eV).
3.3.5 Synthesis of Starting Materials

3.3.5.1 Synthesis of tert-Butyl 3-iodobenzoate (8d)

\[
\begin{align*}
\text{HO} & \quad \text{Boc}_2\text{O} (1.3 \text{ equiv}) \quad \text{DMAP} (10 \text{ mol\%}) \\
\text{THF} (1 \text{ M}) & \quad 17 \text{ h rt} \\
\text{I} & \quad \text{8d}
\end{align*}
\]

**BZ135:** In accordance with reference [33] a 25 mL flask was charged with 3-iodobenzoic acid (2.48 g, 10.0 mmol, 1.0 equiv) and suspended in reagent-grade THF (10 mL, 1 M). Subsequently, Boc\(_2\)O (3.0 mL, 13.0 mmol, 1.3 equiv) and DMAP (122 mg, 1.0 mmol, 10 mol\%) were added and the mixture was stirred at room temperature overnight (17 h).

Next, the reaction mixture was diluted with EtOAc (30 mL) and 1 N NaOH solution in water (25 mL) was added, the phases were separated, the organic phase was washed with brine (1 x 15 mL), dried over MgSO\(_4\) and concentrated under reduced pressure to yield the crude title compound as an orange solid (2.95 g, 97%). \(^1\)H-NMR indicated 64% conversion of 3-iodobenzoic acid. Chromatographic purification on silica gel (72.5 g, relation weight title compound with respect to SiO\(_2\) 1:25) using EtOAc/PE 1:99 finally afforded the ester 8d as pale green oil (1.84 g). The product contained 11 mol\% of Boc\(_2\)O and was thus isolated in 56% yield:

\[
\begin{align*}
\text{n(11f)} & = \frac{1.84 \text{ g}}{304.1 \text{ g/mol} + 0.11 \cdot 218.2 \text{ g/mol}} = 5.6 \text{ mmol}
\end{align*}
\]

In order to load the crude product on the silica gel column, it was dissolved in CH\(_2\)Cl\(_2\) (ca. 10 mL), silica gel was added (11.2 g, mass relation of crude product to SiO\(_2\) 1:4) and all volatile components were removed \textit{in vacuo}.

\textbf{M} \((C_{11}H_{13}I_2O_2) = 304.13 \text{ g/mol}; \textbf{r}_f (\text{SiO}_2, \text{EtOAc/PE 1:99}) = 0.29; \textbf{\textit{1H-NMR}} \ (400 \text{ MHz, CDCl}_3) \delta [\text{ppm}] = 8.31 (\text{\psi-t, } ^3J = 1.6 \text{ Hz, 1H, 2-H}), 7.95 (\text{\psi-dt, } J = 7.8 \text{ Hz, 1.2 Hz, 1H, 4-H}), 7.86-7.83 (m, ^3J = 7.9 \text{ Hz, }^4J = 1.7 \text{ Hz, 1.2 Hz, 1H, 6-H}), 7.16 (t, ^3J = 7.8 \text{ Hz, 1H, 5-H}), 1.59 (s, 9H, 9-H); \textbf{\textit{13C-NMR}} \ (100 \text{ MHz, CDCl}_3) \delta [\text{ppm}] = 164.16 \text{ (C-7), 141.20 (C-6), 138.29 (C-2), 133.89 (C-3), 129.86 (C-5), 128.57 (C-4), 93.67 (C-1), 81.66 (C-8), 28.10 (C-9); \textbf{GC-MS}} \ (\text{CI, 70 eV}) m/z [u] (%) = 305 (2, [M+H]+), 304 (5, [M]+), 277 (3), 263 (1), 249 (25, [M+H-H_2C=C(CH_3)_2]+), 248 (28, [M-H_2C=C(CH_3)_2]+), 231 (12, [M-OrBu]+), 92 (1, [BnH]+), 76 (2), 57 (100, [tBu]+).

The NMR data is in match with the literature.\[^{[34]}\]
$^1$H-NMR spectrum of tert-butyl 3-iodobenzoate (400 MHz, CDCl$_3$).

$^{13}$C-NMR spectrum of tert-butyl 3-iodobenzoate (100 MHz, CDCl$_3$).
Mass spectrum of tert-butyl 3-iodobenzoate (Cl, 70 eV).

3.3.5.2 Synthesis of N-(2-(Thiophen-2-yl)ethyl 3-Iodobenzamide (8i)

BZ131: According to reference [2] a 25 mL flask was charged with 3-iodobenzoic acid (2.48 g, 10.0 mmol, 1.0 equiv), FPyr (98 μL, 102 mg, 1.00 mmol, 10 mol%) and reagent-grade EtOAc (5 mL, 2 M) and TCT (715 mg, 3.8 mmol, 38 mol%) was added. The reaction apparatus was equipped with a reflux condenser and heated to 80 °C for 4 h, whereby no reflux was observed. Next, the oil bath was removed, the reaction suspension was diluted with more EtOAc (5 mL→1 M) and was cooled in an ice bath. Subsequently, 2-(thiophen-2-yl)ethylamine (1.29 mL, 11.0 mmol, 1.1 equiv) and NMM (1.44 mL, 13.0 mmol, 1.3 equiv) were added dropwise under vigorous stirring. After 15 min the cooling bath was removed and the reaction mixture was stirred for 4 h at ambient temperature.

Then, the reaction mixture was diluted with EtOAc (30 mL) and aqueous 1 N NaOH-solution (25 mL). The phases were separated, the organic phase was washed with brine (15 mL), dried over MgSO₄ and concentrated under reduced pressure. Afterwards the crude material (3.53 g, 99%, orange solid) was purified by means of column chromatography on silica gel (94 g, relation mass crude product with respect to SiO₂ 1:27) with EtOAc/PE 20:80, which furnished the title compound as a pale brownish solid (2.92 g, 8.17 mmol, 82%) after concentration with CH₂Cl₂ and drying in high vacuum. In order to charge the silica gel column, the crude material
was dissolved in CH$_2$Cl$_2$ (10 mL), silica gel was added (11.9 g, ratio of masses crude 8i/SiO$_2$
1:3.4) and all volatile components were removed under reduced pressure.

M (C$_{13}$H$_{12}$INOS) = 357.21 g/mol; mp. 88-90 °C; r$_f$ (SiO$_2$, EtOAc/PE 20:80) = 0.24; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ [ppm] = 8.06 ($\psi$-t, $^4$J = 1.6 Hz, 1H, 2-H), 7.80 (ddd, $^3$J$_{6,5}$ = 7.9 Hz, $^4$J = 1.6, 1.1 Hz, 1H, 6-H), 7.65 (ddd, $^3$J$_{5,6}$ = 7.8 Hz, $^4$J = 1.5, 1.1 Hz, 1H, 4-H), 7.19 (dd, $^3$J$_{13,12}$ = 5.1 Hz, $^4$J$_{13,11}$ = 1.1 Hz, 1H, 13-H), 7.14 (t, $^3$J = 7.8 Hz, 1H, 5-H), 6.97 (dd, $^3$J = 5.1, 3.4, 1H, 12-H), 6.87-6.86 (m, 1H, 11-H), 6.35 (br. s, 1H, NH), 3.70 ($\psi$-q, $^3$J = 6.5 Hz, 2H, 8-H), 3.14 (t, $^3$J$_{9,8}$ = 6.6 Hz, 2H, 9-H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ [ppm] = 165.96 (C-7), 141.02 (C-10), 140.31 (C-6), 136.49 (C-3), 136.01 (C-2), 130.19 (C-5), 127.15 (C-12), 125.95 (C-4), 125.50 (C-11), 124.10 (C-13), 94.27 (C-1), 41.41 (C-8), 29.78 (C-9).

$^1$H-NMR spectrum of N-(2-(thiophen-2-yl)ethyl 3-Iodobenzamide (400 MHz, CDCl$_3$).
13C-NMR spectrum of N-(2-(thiophen-2-yl)ethyl 3-iodobenzamide (100 MHz, CDCl3).

3.3.5.3 Synthesis of 1-Bromo-4-(2-(1,3-dioxan-2-yl)ethoxy) benzene (11a)

BZ178: According to reference [8] a 25 mL flask was charged with 4-bromophenol (1.73 g, 10.0 mmol, 1.0 equiv) and reagent-grade MeCN (10 mL, 1 M). The resulting solution was treated with 2-(2-bromoethyl)-1,3-dioxane (1.77 mL, 13.0 mmol, 1.3 equiv) and fine-powdered K$_2$CO$_3$ (1.93 g, 14.0 mmol, 1.4 equiv), the reaction flask was equipped with a reflux condenser and heated to 80 °C overnight (18 h). After cooling down to room temperature, the reaction suspension was transferred with EtOAc (20 mL) and water (20 mL) to a 100 mL extraction funnel, the phases were separated and the aqueous phase was extracted with EtOAc (2 x 10 mL). The collected organic phases were washed with brine (1 x 20 mL), dried over MgSO$_4$ and concentrated under reduced pressure to yield a yellow oil (3.01 g, 105%), of which $^1$H-NMR confirmed 96% conversion. At last, column chromatographic purification on silica gel (104 g, mass ratio crude material/SiO$_2$ 1:35) with EtOAc/PE 5:95, concentration with CH$_2$Cl$_2$ and drying in high vacuum allowed the isolation of the title compound as a yellow oil in 84% yield (2.47 g, 8.4 mmol). In order to charge the silica gel column, the crude product was
dissolved in CH₂Cl₂ (ca. 30 mL), silica gel (13.8 g, mass relation crude 11a with respect to silica gel 1:5) was added and concentrated to dryness.

\[ M (C_{12}H_{15}BrO_3) = 287.15 \text{ g/mol}; \] 
\[ \text{rl (SiO}_2, \text{ EtOAc/PE 5:95) } = 0.20; \]

\(^1\)H-NMR (400 MHz, CDCl\(_3\)) \( \delta \) [ppm] = 7.38-7.34 (m, 2H, 2-H), 6.80-6.76 (m, 2H, 3-H) 4.76 (t, \( ^3\)J\(_{\text{H},\text{H}} = 5.2 \text{ Hz}, 1\text{H}, 7\text{-H}), 4.13-4.09 (m, 2H, 8\text{a-H}), 4.03 (t, \( ^3\)J\(_{\text{H},\text{H}} = 6.4 \text{ Hz}, 2\text{H}, 5\text{-H}), 3.81-3.75 (m, 2H, 8\text{b-H}), 2.15-2.04 (m, 3H, 6-H, 9\text{a-H}), 1.38-1.33 (m, 1H, 9\text{b-H}); \]

\(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) \( \delta \) [ppm] = 158.01 (C-4), 132.18 (C-2), 116.31 (C-3), 112.74 (C-1), 99.38 (C-7), 66.90 (C-8), 63.52 (C-6), 34.96 (C-5), 25.76 (C-9); 

HR-MS (Cl, [C\(_{12}H_{15}O_3^{79}\)Br\(^+\)]) calc. 286.0205 u found 286.0204 u.

\(^1\)H-NMR spectrum of 1-bromo-4-(2-(1,3-dioxan-2-yl)ethoxy) benzene (400 MHz, CDCl\(_3\)).
$^{13}$C-NMR spectrum of 1-bromo-4-(2-(1,3-dioxan-2-yl)ethoxy) benzene (100 MHz, CDCl$_3$).
3.4 Gas Volumetry

3.4.1 Gas Formation in DMF at Room Temperature

Table S7. Gas formation using 1.0 equiv formic acid and 41 mol% TCT in DMF (1 M) at room temperature.

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|----------------------|
| 0.25    | 0.7    | 0.028         | 6                    |
| 0.50    | 1.6    | 0.062         | 13                   |
| 0.75    | 2.5    | 0.102         | 21                   |
| 1.00    | 3.4    | 0.135         | 28                   |
| 1.50    | 5.1    | 0.203         | 41                   |
| 1.75    | 5.8    | 0.231         | 47                   |
| 2.00    | 6.4    | 0.254         | 52                   |
| 2.25    | 6.8    | 0.271         | 55                   |
| 2.50    | 7.2    | 0.288         | 59                   |
| 2.75    | 7.5    | 0.299         | 61                   |
| 3.0     | 7.6    | 0.305         | 62                   |
| 3.5     | 8.0    | 0.322         | 66                   |
| 4.0     | 8.2    | 0.327         | 67                   |
| 4.5     | 8.5    | **0.339**     | **69**               |
| 5.0     | 8.6    | 0.344         | 70                   |
| 5.5     | 8.7    | 0.350         | 71                   |
| 6.0     | 8.9    | 0.355         | 73                   |
| 6.5     | 8.9    | 0.355         | 73                   |
| 7.0     | 9.0    | 0.361         | 74                   |
| 7.5     | 9.2    | 0.367         | 75                   |
| 8.0     | 9.3    | 0.372         | 76                   |
| 8.5     | 9.3    | 0.372         | 76                   |
| 9.0     | 9.5    | 0.378         | 77                   |
| 9.5     | 9.5    | 0.378         | 77                   |
| 10.0    | 9.6    | 0.384         | 78                   |
| 11.0    | 9.7    | 0.389         | 79                   |
| 12.0    | 9.9    | 0.395         | 81                   |
| 13.0    | 10.0   | 0.401         | 82                   |

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|----------------------|
| 14      | 10.2   | 0.406         | 83                   |
| 15      | 10.2   | 0.406         | 83                   |
| 16      | 10.30  | 0.412         | 84                   |
| 17      | 10.4   | 0.418         | 85                   |
| 18      | 10.4   | 0.418         | 85                   |
| 19      | 10.6   | 0.423         | 86                   |
| 20      | 10.7   | 0.429         | 88                   |
| 22      | 10.7   | 0.429         | 88                   |
| 24      | 10.9   | 0.434         | 89                   |
| 26      | 11.0   | 0.440         | 90                   |
| 28      | 11.4   | 0.446         | 91                   |
| 30      | 11.3   | 0.451         | 92                   |
| 35      | 11.4   | 0.457         | 93                   |
| 40      | 11.6   | 0.463         | 94                   |
| 45      | 11.7   | 0.468         | 96                   |
| 50      | 11.7   | 0.468         | 96                   |
| 55      | 11.9   | 0.474         | 97                   |
| 60      | 11.9   | 0.474         | 97                   |
| 65      | 11.9   | 0.474         | 97                   |
| 70      | 11.9   | 0.474         | 97                   |
| 75      | 12.0   | 0.480         | 98                   |
| 80      | 12.0   | 0.480         | 98                   |
| 85      | 12.0   | 0.480         | 98                   |
| 90      | 12.0   | 0.480         | 98                   |
| 105     | 12.0   | 0.480         | 98                   |
| 120     | 12.0   | 0.480         | 98                   |
| 180     | 12.1   | 0.485         | 99                   |
| 220     | 12.1   | 0.485         | 99                   |

**PH3960**: According to general procedure 6 (chapter 3.2.8, page 47) a 0.980 M solution of formic acid in DMF (500 µL, 490 µmol, 1.0 equiv) was combined with TCT (37.6 mg, 202 µmol, 41 mol%) and stirred at 297 K at an ambient pressure of 988 mbar. *Italic* = data points used for regression line, **blue** = time for formation of 1 equiv of CO when 1.5 equiv of HCO₂H are used.
Table S8. Gas volumetry using 2.0 equiv formic acid and 33.3 mol% TCT in DMF (2 M with respect for HCO₂H) at room temperature.

\[
\text{H}_2\text{COOH} \rightarrow \text{O} + \text{HCl}
\]

(2.0 equiv)  

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|--------|-------|--------------|------------------------|
| 0.25   | 0.6   | 0.023        | 5                      |
| 0.50   | 1.1   | 0.045        | 9                      |
| 0.75   | 1.7   | 0.068        | 14                     |
| 1.00   | 2.3   | 0.090        | 18                     |
| 1.25   | 3.0   | 0.118        | 24                     |
| 1.50   | 3.5   | 0.141        | 28                     |
| 1.75   | 4.4   | 0.175        | 35                     |
| 2.00   | 4.7   | 0.186        | 37                     |
| 2.25   | 5.1   | 0.203        | 41                     |
| 2.50   | 5.5   | 0.220        | 44                     |
| 2.75   | 5.8   | 0.231        | 46                     |
| 3.0    | 5.9   | 0.237        | 47                     |
| 3.5    | 6.3   | 0.254        | 51                     |
| 4.0    | 6.6   | 0.265        | 53                     |
| 4.5    | 6.8   | 0.271        | 54                     |
| 5.0    | 6.9   | 0.276        | 55                     |
| 5.5    | 7.1   | 0.282        | 56                     |
| 6.0    | 7.2   | 0.288        | 57                     |
| 6.5    | 7.3   | 0.293        | 59                     |
| 7.0    | 7.3   | 0.293        | 59                     |
| 7.5    | 7.5   | 0.299        | 60                     |
| 8.0    | 7.6   | 0.305        | 61                     |
| 8.5    | 7.6   | 0.305        | 61                     |
| 9.0    | 7.8   | 0.310        | 62                     |
| 9.5    | 7.9   | 0.316        | 63                     |
| 10     | 7.9   | 0.316        | 63                     |
| 11     | 8.0   | 0.322        | 64                     |
| 12     | 8.2   | 0.327        | 65                     |

| t [min] | V [mL] | n(gas) [mmol] | Δn(gas)/n₀(HCO₂H) [%] |
|--------|-------|--------------|-----------------------|
| 13     | 8.3   | 0.333        | 66                    |
| 14     | 8.5   | 0.339        | 68                    |
| 15     | 8.5   | 0.339        | 68                    |
| 16     | 8.6   | 0.344        | 69                    |
| 17     | 8.7   | 0.350        | 70                    |
| 18     | 8.7   | 0.350        | 70                    |
| 19     | 8.9   | 0.355        | 71                    |
| 20     | 8.9   | 0.355        | 71                    |
| 22     | 9.0   | 0.361        | 72                    |
| 24     | 9.2   | 0.367        | 73                    |
| 26     | 9.3   | 0.372        | 74                    |
| 28     | 9.4   | 0.378        | 75                    |
| 30     | 9.4   | 0.378        | 75                    |
| 35     | 9.6   | 0.384        | 77                    |
| 40     | 9.6   | 0.384        | 77                    |
| 45     | 9.7   | 0.389        | 78                    |
| 50     | 9.7   | 0.389        | 78                    |
| 55     | 9.9   | 0.395        | 79                    |
| 60     | 9.9   | 0.395        | 79                    |
| 65     | 9.9   | 0.395        | 79                    |
| 70     | 9.9   | 0.395        | 79                    |
| 75     | 9.9   | 0.395        | 79                    |
| 80     | 9.9   | 0.395        | 79                    |
| 85     | 10.0  | 0.401        | 80                    |
| 90     | 10.0  | 0.401        | 80                    |
| 105    | 10.7  | 0.429        | 86                    |
| 110    | 10.7  | 0.429        | 86                    |
| 115    | 10.7  | 0.429        | 86                    |

**PH3961:** According to general procedure 6 (chapter 3.2.8, page 47) a 2.04 M solution of formic acid (500 μL, 1021 μmol, 2.0 equiv) was combined with TCT (31.1 mg, 167 μmol, 33.3 mol% → 1 equiv = 501 μmol) and stirred at 298 K at an ambient pressure of 988 mbar. *Italic numbers* = data points used for regression line, *red numbers* = heating to 70 °C started after 100 min reaction duration, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO₂H are used.
### 3.4.2 Solvent Screening

Table S9. Monitoring of gas generation using 10 mol% of FPy.

| t [min] | V [mL] | n(gas) | n(gas)/n₀(HCO₂H) [%] | n(MeCN) | Δn(gas) | Δn(gas)/n₀(HCO₂H) [%] |
|---------|--------|--------|-----------------------|---------|---------|------------------------|
| 0.25    | 0.6    | 0.0223 | 8                     | 0.0279  | -0.0056 | -2                     |
| 0.50    | 0.8    | 0.0334 | 11                    | 0.0390  | -0.0056 | -2                     |
| 0.75    | 1.3    | 0.0502 | 17                    | 0.0446  | 0.0056  | 2                      |
| 1.00    | 1.6    | 0.0613 | 21                    | 0.0557  | 0.0056  | 2                      |
| 1.25    | 1.7    | 0.0669 | 23                    | 0.0613  | 0.0056  | 2                      |
| 1.50    | 2.0    | 0.0780 | 27                    | 0.0669  | 0.0111  | 4                      |
| 1.75    | 2.1    | 0.0836 | 29                    | 0.0724  | 0.0111  | 4                      |
| 2.00    | 2.4    | 0.0947 | 32                    | 0.0780  | 0.0167  | 6                      |
| 2.25    | 2.5    | 0.1003 | 34                    | 0.0780  | 0.0223  | 8                      |
| 2.50    | 2.7    | 0.1059 | 36                    | 0.0836  | 0.0223  | 8                      |
| 2.75    | 2.8    | 0.1114 | 38                    | 0.0892  | 0.0223  | 8                      |
| 3.00    | 3.1    | 0.1226 | 42                    | 0.0892  | 0.0334  | 11                     |
| 3.50    | 3.4    | 0.1337 | 46                    | 0.0892  | 0.0446  | 15                     |
| 4.00    | 3.7    | 0.1449 | 50                    | 0.0947  | 0.0502  | 17                     |
| 4.50    | 3.8    | 0.1505 | 52                    | 0.0947  | 0.0557  | 19                     |
| 5.00    | 4.1    | 0.1616 | 55                    | 0.0947  | 0.0669  | 23                     |
| 5.50    | 4.4    | 0.1727 | 59                    | 0.1003  | 0.0724  | 25                     |
| 6.00    | 4.5    | 0.1783 | 61                    | 0.1003  | 0.0780  | 27                     |
| 6.50    | 4.8    | 0.1895 | 65                    | 0.1003  | 0.0892  | 30                     |
| 7.00    | 4.9    | 0.1950 | 67                    | 0.1003  | 0.0947  | 32                     |
| 7.50    | 5.2    | 0.2062 | 71                    | 0.1003  | 0.1059  | 36                     |
| 8.00    | 5.4    | 0.2118 | 73                    | 0.1003  | 0.1114  | 38                     |
| 8.50    | 5.6    | 0.2229 | 76                    | 0.1003  | 0.1226  | 42                     |
| 9.00    | 5.8    | 0.2285 | 78                    | 0.1003  | 0.1282  | 44                     |
| 9.50    | 5.9    | 0.2340 | 80                    | 0.1003  | 0.1337  | 45                     |
| 10.00   | 6.1    | 0.2396 | 82                    | 0.1003  | 0.1393  | 47                     |
| 11.00   | 6.3    | 0.2508 | 86                    | 0.1003  | 0.1505  | 51                     |
| 12.00   | 6.6    | 0.2619 | 90                    | 0.1003  | 0.1616  | 55                     |
| 13.00   | 6.8    | 0.2675 | 92                    | 0.1003  | 0.1672  | 57                     |
| 14.00   | 7.1    | 0.2786 | 95                    | 0.1003  | 0.1783  | 61                     |
| 15.00   | 7.2    | 0.2842 | 97                    | 0.1003  | 0.1839  | 63                     |
| 16.00   | 7.5    | 0.2953 | 101                   | 0.1003  | 0.1950  | 66                     |
| 17.00   | 7.6    | 0.3099 | 103                   | 0.1003  | 0.2006  | 68                     |
| 18.00   | 7.9    | 0.3121 | 107                   | 0.1003  | 0.2118  | 72                     |
| 19.00   | 8.0    | 0.3176 | 109                   | 0.1003  | 0.2173  | 74                     |
| 20.00   | 8.2    | 0.3232 | 111                   | 0.1003  | 0.2229  | 76                     |
| 22.00   | 8.5    | 0.3343 | 115                   | 0.1003  | 0.2340  | 80                     |
| 24.00   | 8.7    | 0.3455 | 118                   | 0.1003  | 0.2452  | 83                     |
| 26.00   | 9.2    | 0.3622 | 124                   | 0.1003  | 0.2619  | 89                     |
| 28.00   | 9.3    | 0.3678 | 126                   | 0.1003  | 0.2675  | 91                     |
| 30.00   | 9.7    | 0.3845 | 132                   | 0.1003  | 0.2842  | 97                     |
PH3941: As described in general protocol 6 (chapter 3.2.8, page 47) a solution of formic acid (0.974 M, 300 μL, 292 μmol, 1.0 equiv) and FPyr (0.102 M, 31 μmol, 10 mol%) in dry MeCN was combined with TCT (23.2 mg, 125 μmol, 43 mol%) and the resulting suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 979 mbar). n(MeCN) was obtained from the measurement of a HCO₂H/FPyr solution in MeCN at 70 °C without TCT in Table S22 (page 173). Italic = data points used for regression line, blue = time for formation of 1 equiv of CO when 1.5 equiv of HCO₂H are used, blue numbers = at ambient temperature after removal of the heating bath.

Figure S25. Determination of the initial rate for the CO formation in the presence of 10 mol% FPyr. Only the filled data points were considered for the regression line (for underlying data see Table S9).
Table S10. Second study on gas formation using 10 mol% of FPy in MeCN to ensure reproducibility.

![Diagram of the reaction](image)

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n_0(HCO_2H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n_0(HCO_2H) [%] |
|---------|--------|---------------|--------------------------|---------------|----------------|--------------------------|
| 0.25    | 0.4    | 0.0168        | 6                        | 0.0279        | -0.0111        | -4                       |
| 0.50    | 0.7    | 0.0279        | 10                       | 0.0390        | -0.0111        | -4                       |
| 0.75    | 1.0    | 0.0391        | 13                       | 0.0446        | -0.0055        | -2                       |
| 1.00    | 1.1    | 0.0447        | 15                       | 0.0557        | -0.0110        | -4                       |
| 1.25    | 1.4    | 0.0559        | 19                       | 0.0613        | -0.0054        | -2                       |
| 1.50    | 1.7    | 0.0671        | 23                       | 0.0669        | 0.0002         | 0                        |
| 1.75    | 1.8    | 0.0727        | 25                       | 0.0724        | 0.0002         | 0                        |
| 2.00    | 2.1    | 0.0838        | 29                       | 0.0780        | 0.0058         | 2                        |
| 2.25    | 2.4    | 0.0950        | 33                       | 0.0780        | 0.0170         | 6                        |
| 2.50    | 2.5    | 0.1006        | 34                       | 0.0836        | 0.0170         | 6                        |
| 2.75    | 2.8    | 0.1118        | 38                       | 0.0892        | 0.0226         | 8                        |
| 3.00    | 3.0    | 0.1174        | 40                       | 0.0892        | 0.0282         | 10                       |
| 3.50    | 3.2    | 0.1286        | 44                       | 0.0892        | 0.0394         | 13                       |
| 4.00    | 3.5    | 0.1397        | 48                       | 0.0947        | 0.0450         | 15                       |
| 4.50    | 3.8    | 0.1509        | 52                       | 0.0947        | 0.0562         | 19                       |
| 5.00    | 4.1    | 0.1621        | 56                       | 0.0947        | 0.0674         | 23                       |
| 5.50    | 4.4    | 0.1733        | 59                       | 0.1003        | 0.0730         | 25                       |
| 6.00    | 4.5    | 0.1789        | 61                       | 0.1003        | 0.0786         | 27                       |
| 6.50    | 4.8    | 0.1900        | 65                       | 0.1003        | 0.0897         | 31                       |
| 7.00    | 4.9    | 0.1956        | 67                       | 0.1003        | 0.0953         | 33                       |
| 7.50    | 5.1    | 0.2012        | 69                       | 0.1003        | 0.1009         | 35                       |
| 8.00    | 5.4    | 0.2124        | 73                       | 0.1003        | 0.1121         | 38                       |
| 8.50    | 5.5    | 0.2180        | 75                       | 0.1003        | 0.1177         | 40                       |
| 9.00    | 5.8    | 0.2292        | 78                       | 0.1003        | 0.1289         | 44                       |
| 9.50    | 5.9    | 0.2348        | 80                       | 0.1003        | 0.1345         | 46                       |
| 10.00   | 6.1    | 0.2403        | 82                       | 0.1003        | 0.1400         | 48                       |
| 11.00   | 6.3    | 0.2515        | 86                       | 0.1003        | 0.1512         | 52                       |
| 12.00   | 6.6    | 0.2627        | 90                       | 0.1003        | 0.1624         | 56                       |
| 13.00   | 6.8    | 0.2683        | 92                       | 0.1003        | 0.1680         | 58                       |
| 14.00   | 7.1    | 0.2795        | 96                       | 0.1003        | 0.1792         | 61                       |
| 15.00   | 7.3    | 0.2907        | 100                      | 0.1003        | 0.1904         | 65                       |
| **16.00** | **7.5** | **0.2962** | **101** | **0.1003** | **0.1959** | **67** |
| 17.00   | 7.8    | 0.3074        | 105                      | 0.1003        | 0.2071         | 71                       |
| 18.00   | 7.9    | 0.3130        | 107                      | 0.1003        | 0.2127         | 73                       |
| 19.00   | 8.0    | 0.3186        | 109                      | 0.1003        | 0.2183         | 75                       |
| 20.00   | 8.2    | 0.3242        | 111                      | 0.1003        | 0.2239         | 77                       |
| 22.00   | 8.6    | 0.3410        | 117                      | 0.1003        | 0.2407         | 82                       |
| 24.00   | 8.7    | 0.3465        | 119                      | 0.1003        | 0.2462         | 84                       |
| 26.00   | 9.2    | 0.3633        | 124                      | 0.1003        | 0.2630         | 90                       |
| 28.00   | 9.4    | 0.3745        | 128                      | 0.1003        | 0.2742         | 94                       |
| 30.00   | 9.7    | 0.3857        | 132                      | 0.1003        | 0.2854         | 98                       |
PH3943: According to general procedure 6 (chapter 3.2.8, page 47) a solution of formic acid (0.974 M, 300 µL, 292 µmol, 1.0 equiv) and FPyr (0.102 M, 31 µmol, 10 mol%) in dry MeCN was treated with TCT (22.4 mg, 120 µmol, 41 mol%) and the resulting suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 982 mbar). n(MeCN) was obtained from the measurement of a HCO$_2$H/FPyr solution in MeCN at 70 °C without TCT in Table S22 (page 173). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO$_2$H are used, *blue numbers* = at ambient temperature after removal of the heating bath.

Figure S26. Second determination of the initial rate for the CO formation in the presence of 10 mol% FPyr to prove reproducibility. Only the filled data points were considered for the regression line (for underlying data see Table S10).
Table S11. Gas formation in THF using 10 mol% of FPyr.

![Diagram](image)

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/nₐ(HCO₂H) [%] | n(THF) [mmol] | Δn(gas) [mmol] | Δn(gas)/nₐ(HCO₂H) [%] |
|---------|--------|---------------|------------------------|--------------|---------------|------------------------|
| 0.25    | 5.8    | 0.0226        | 8                      | 0.0395       | -0.0169       | -6                     |
| 0.50    | 6.1    | 0.0395        | 13                     | 0.0678       | -0.0283       | -9                     |
| 0.75    | 6.5    | 0.0620        | 21                     | 0.0847       | -0.0227       | -8                     |
| 1.00    | 6.8    | 0.0790        | 26                     | 0.1016       | -0.0226       | -8                     |
| 1.25    | 7.0    | 0.0903        | 30                     | 0.1186       | -0.0283       | -9                     |
| 1.50    | 7.3    | 0.1072        | 36                     | 0.1355       | -0.0283       | -9                     |
| 1.75    | 7.5    | 0.1185        | 39                     | 0.1468       | -0.0283       | -9                     |
| 2.00    | 7.7    | 0.1297        | 43                     | 0.1581       | -0.0284       | -9                     |
| 2.25    | 7.9    | 0.1410        | 47                     | 0.1694       | -0.0284       | -9                     |
| 2.50    | 8.1    | 0.1523        | 51                     | 0.1807       | -0.0284       | -9                     |
| 2.75    | 8.3    | 0.1636        | 55                     | 0.1863       | -0.0227       | -8                     |
| 3.0    | 8.4    | 0.1692        | 56                     | 0.1976       | -0.0284       | -9                     |
| 3.5    | 8.7    | 0.1861        | 62                     | 0.2089       | -0.0228       | -8                     |
| 4.0    | 9.0    | 0.2031        | 68                     | 0.2202       | -0.0171       | -6                     |
| 4.5    | 9.2    | 0.2143        | 71                     | 0.2259       | -0.0116       | -4                     |
| 5.0    | 9.4    | 0.2256        | 75                     | 0.2315       | -0.0059       | -2                     |
| 5.5    | 9.6    | 0.2369        | 79                     | 0.2371       | 0.0002        | 0                      |
| 6.0    | 9.7    | 0.2426        | 81                     | 0.2371       | 0.0055        | 2                      |
| 6.5    | 9.8    | 0.2482        | 83                     | 0.2428       | 0.0054        | 2                      |
| 7.0    | 10.0   | 0.2595        | 86                     | 0.2484       | 0.0111        | 4                      |
| 7.5    | 10.1   | 0.2651        | 88                     | 0.2484       | 0.0167        | 6                      |
| 8.0    | 10.2   | 0.2708        | 90                     | 0.2484       | 0.0224        | 7                      |
| 8.5    | 10.3   | 0.2764        | 92                     | 0.2484       | 0.0280        | 9                      |
| 9.0    | 10.5   | 0.2877        | 96                     | 0.2428       | 0.0449        | 15                     |
| 9.5    | 10.6   | 0.2933        | 98                     | 0.2428       | 0.0505        | 17                     |
| 10     | 10.7   | 0.2990        | 100                    | 0.2428       | 0.0562        | 19                     |
| 11     | 10.9   | 0.3102        | 103                    | 0.2428       | 0.0674        | 22                     |
| 12     | 11.1   | 0.3215        | 107                    | 0.2371       | 0.0844        | 28                     |
| 13     | 11.4   | 0.3384        | 113                    | 0.2315       | 0.1069        | 36                     |
| 14     | 11.6   | 0.3497        | 117                    | 0.2315       | 0.1182        | 39                     |
| 15     | 11.7   | 0.3554        | 118                    | 0.2259       | 0.1295        | 43                     |
| 16     | 11.9   | 0.3666        | 122                    | 0.2259       | 0.1407        | 47                     |
| 17     | 12.0   | 0.3723        | 124                    | 0.2259       | 0.1464        | 49                     |
| 18     | 12.3   | 0.3892        | 130                    | 0.2259       | 0.1633        | 54                     |
| 19     | 12.5   | 0.4005        | 133                    | 0.2259       | 0.1746        | 58                     |
| 20     | 12.6   | 0.4061        | 135                    | 0.2259       | 0.1802        | 60                     |
| 22     | 12.9   | 0.4231        | 141                    | 0.2202       | 0.2029        | 68                     |
| 24     | 13.2   | 0.4400        | 147                    | 0.2202       | 0.2198        | 73                     |
| 26     | 13.3   | 0.4456        | 149                    | 0.2259       | 0.2197        | 73                     |
| 28     | 13.5   | 0.4569        | 152                    | 0.2259       | 0.2310        | 77                     |
| 30     | 13.6   | 0.4625        | 154                    | 0.2259       | 0.2366        | 79                     |
| t [min] | V [mL] | n(gas) [mmol] | n(gas)/ n₀(HCO₂H) [%] | n(THF) [mmol] | Δn(gas) [mmol] | Δn(gas)/ n₀(HCO₂H) [%] |
|--------|--------|--------------|------------------------|--------------|----------------|-------------------------|
| 35     | 13.8   | 0.4738       | 158                    | 0.2202       | 0.2536         | 85                      |
| 40     | 14.0   | 0.4851       | 162                    | 0.2259       | 0.2592         | 86                      |
| 45     | 14.2   | 0.4964       | 165                    | 0.2259       | 0.2705         | 90                      |
| 50     | 14.2   | 0.4964       | 165                    | 0.2259       | 0.2705         | 90                      |
| 55     | 14.2   | 0.4964       | 165                    | 0.2259       | 0.2705         | 90                      |
| 60     | 14.2   | 0.4964       | 165                    | 0.2259       | 0.2705         | 90                      |
| 65     | 12.3   | 0.3892       | 130                    | 0.1129       | 0.2763         | 92                      |
| 70     | 12.0   | 0.3723       | 124                    | 0.1016       | 0.2707         | 90                      |
| 75     | 11.9   | 0.3666       | 122                    | 0.096        | 0.2706         | 90                      |
| 80     | 11.9   | 0.3666       | 122                    | 0.0903       | 0.2763         | 92                      |
| 85     | 11.9   | 0.3666       | 122                    | 0.0903       | 0.2763         | 92                      |
| 90     | 11.9   | 0.3666       | 122                    | 0.0903       | 0.2763         | 92                      |

**PH4242**: In alignment to general protocol 6 (chapter 3.2.8, page 47) TCT (22.4 mg, 120 μmol, 40 mol%) was combined with a solution of formic acid (1.00 M, 300 μL, 300 μmol, 1.0 equiv) and FPyr (0.100 M, 30 μmol, 10 mol%) in reagent-grade THF and the resulting solution was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 991 mbar). n(THF) was obtained from the measurement of a HCO₂H/FPyr solution in THF at 70 °C without TCT in Table S12 (page 149). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO₂H are used, *blue numbers* = at ambient temperature after removal of the heating bath.
Table S12. Gas formation during heating of a solution of formic acid and FPyr in THF to 70 °C.

\[
\begin{array}{cccc}
\text{t [min]} & \text{V [mL]} & \text{n(gas) [mmol]} & \text{n(gas)/n(HCO}_2\text{H)} [%]
\end{array}
\]

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n(HCO}_2\text{H)} [%] |
|---------|--------|---------------|-------------------------------|
| 0.25    | 6.1    | 0.0395        | 14                            |
| 0.50    | 6.6    | 0.0678        | 24                            |
| 0.75    | 6.9    | 0.0847        | 29                            |
| 1.00    | 7.2    | 0.1016        | 35                            |
| 1.25    | 7.5    | 0.1186        | 41                            |
| 1.50    | 7.8    | 0.1355        | 47                            |
| 1.75    | 8.0    | 0.1468        | 51                            |
| 2.00    | 8.2    | 0.1581        | 55                            |
| 2.25    | 8.4    | 0.1694        | 59                            |
| 2.50    | 8.6    | 0.1807        | 63                            |
| 2.75    | 8.7    | 0.1863        | 65                            |
| 3.0     | 8.9    | 0.1976        | 69                            |
| 3.5     | 9.1    | 0.2089        | 73                            |
| 4.0     | 9.3    | 0.2202        | 76                            |
| 4.5     | 9.4    | 0.2259        | 78                            |
| 5.0     | 9.5    | 0.2315        | 80                            |
| 5.5     | 9.6    | 0.2371        | 82                            |
| 6.0     | 9.6    | 0.2371        | 82                            |
| 6.5     | 9.7    | 0.2428        | 84                            |
| 7.0     | 9.8    | 0.2484        | **86**                        |
| 7.5     | 9.8    | 0.2484        | 86                            |
| 8.0     | 9.8    | 0.2484        | 86                            |
| 8.5     | 9.8    | 0.2484        | 86                            |
| 9.0     | 9.7    | 0.2428        | 84                            |
| 9.5     | 9.7    | 0.2428        | 84                            |
| 10      | 9.7    | 0.2428        | 84                            |
| 11      | 9.7    | 0.2428        | 84                            |

\[
\begin{array}{cccc}
\text{t [min]} & \text{V [mL]} & \text{n(gas) [mmol]} & \text{n(gas)/n(HCO}_2\text{H)} [%]
\end{array}
\]

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n(HCO}_2\text{H)} [%] |
|---------|--------|---------------|-------------------------------|
| 12      | 9.6    | 0.2371        | 82                            |
| 13      | 9.5    | 0.2315        | 80                            |
| 14      | 9.5    | 0.2315        | 80                            |
| 15      | 9.4    | 0.2259        | 78                            |
| 16      | 9.4    | 0.2259        | 78                            |
| 17      | 9.4    | 0.2259        | 78                            |
| 18      | 9.4    | 0.2259        | 78                            |
| 19      | 9.4    | 0.2259        | 78                            |
| 20      | 9.4    | 0.2259        | 78                            |
| 21      | 9.4    | 0.2259        | 78                            |
| 22      | 9.3    | 0.2202        | 76                            |
| 23      | 9.3    | 0.2202        | 76                            |
| 24      | 9.3    | 0.2202        | 76                            |
| 25      | 9.4    | 0.2259        | 78                            |
| 26      | 9.4    | 0.2259        | 78                            |
| 27      | 9.4    | 0.2259        | 78                            |
| 28      | 9.4    | 0.2259        | 78                            |
| 29      | 9.4    | 0.2259        | 78                            |
| 30      | 9.4    | 0.2259        | 78                            |
| 31      | 9.3    | 0.2202        | 76                            |
| 32      | 9.3    | 0.2202        | 76                            |
| 33      | 9.4    | 0.2259        | 78                            |
| 34      | 9.4    | 0.2259        | 78                            |
| 35      | 9.4    | 0.2259        | 78                            |
| 36      | 9.4    | 0.2259        | 78                            |
| 37      | 9.4    | 0.2259        | 78                            |
| 38      | 9.4    | 0.2259        | 78                            |
| 39      | 9.4    | 0.2259        | 78                            |
| 40      | 9.4    | 0.2259        | 78                            |
| 41      | 9.4    | 0.2259        | 78                            |
| 42      | 9.4    | 0.2259        | 78                            |
| 43      | 9.4    | 0.2259        | 78                            |
| 44      | 9.4    | 0.2259        | 78                            |
| 45      | 9.4    | 0.2259        | 78                            |
| 46      | 9.4    | 0.2259        | 78                            |
| 47      | 9.4    | 0.2259        | 78                            |
| 48      | 9.4    | 0.2259        | 78                            |
| 49      | 9.4    | 0.2259        | 78                            |
| 50      | 9.4    | 0.2259        | 78                            |
| 51      | 9.4    | 0.2259        | 78                            |
| 52      | 9.4    | 0.2259        | 78                            |
| 53      | 9.4    | 0.2259        | 78                            |
| 54      | 9.4    | 0.2259        | 78                            |
| 55      | 9.4    | 0.2259        | 78                            |
| 56      | 9.4    | 0.2259        | 78                            |
| 57      | 9.4    | 0.2259        | 78                            |
| 58      | 9.4    | 0.2259        | 78                            |
| 59      | 9.4    | 0.2259        | 78                            |
| 60      | 9.4    | 0.2259        | 78                            |

**PH4239:** In alignment to general protocol 6 (chapter 3.2.8, page 47) a solution of formic acid (1.00 M, 300 µL, 300 µmol, 1.0 equiv) and FPyr (0.100 M, 30 µmol, 10 mol%) in reagent-grade THF was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 991 mbar). *Italic* = data points used for regression line, **blue** = maximum gas evolution, **blue numbers** = at ambient temperature after removal of the heating bath.
Table S13. Gas formation during heating a mixture of formic acid and TCT in THF to 70 °C.

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|-----------------------|
| 0.25    | 0.7    | 0.0281        | 9                     |
| 0.50    | 1.0    | 0.0394        | 13                    |
| 0.75    | 1.4    | 0.0562        | 19                    |
| 1.00    | 1.7    | 0.0675        | 22                    |
| 1.25    | 2.0    | 0.0787        | 26                    |
| 1.50    | 2.3    | 0.0900        | 30                    |
| 1.75    | 2.7    | 0.1068        | 36                    |
| 2.00    | 2.8    | 0.1125        | 37                    |
| 2.25    | 3.0    | 0.1181        | 39                    |
| 2.50    | 3.2    | 0.1293        | 43                    |
| 2.75    | 3.4    | 0.1350        | 45                    |
| 3.0     | 3.5    | 0.1406        | 47                    |
| 3.5     | 3.8    | 0.1518        | 51                    |
| 4.0     | 4.1    | 0.1631        | 54                    |
| 4.5     | 4.2    | 0.1687        | 56                    |
| 5.0     | 4.4    | 0.1743        | 58                    |
| 5.5     | 4.5    | 0.1800        | 60                    |
| **6.0** | **4.7**| **0.1856**    | **62**                |
| 6.5     | 4.7    | 0.1856        | 62                    |
| 7.0     | 4.7    | 0.1856        | 62                    |
| 7.5     | 4.7    | 0.1856        | 62                    |
| 8.0     | 4.7    | 0.1856        | 62                    |
| 8.5     | 4.7    | 0.1856        | 62                    |
| 9.0     | 4.7    | 0.1856        | 62                    |
| 9.5     | 4.7    | 0.1856        | 62                    |
| 10      | 4.7    | 0.1856        | 62                    |
| 11      | 4.7    | 0.1856        | 62                    |

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|-----------------------|
| 12      | 4.7    | 0.1856        | 62                    |
| 13      | 4.7    | 0.1856        | 62                    |
| 14      | 4.7    | 0.1856        | 62                    |
| 15      | 4.7    | 0.1856        | 62                    |
| 16      | 4.7    | 0.1856        | 62                    |
| 17      | 4.7    | 0.1856        | 62                    |
| 18      | 4.7    | 0.1856        | 62                    |
| 19      | 4.7    | 0.1856        | 62                    |
| 20      | 4.7    | 0.1856        | 62                    |
| 22      | 4.7    | 0.1856        | 62                    |
| 24      | 4.7    | 0.1856        | 62                    |
| 26      | 4.7    | 0.1856        | 62                    |
| 28      | 4.7    | 0.1856        | 62                    |
| 30      | 4.7    | 0.1856        | 62                    |
| 32      | 4.7    | 0.1856        | 62                    |
| 35      | 4.8    | 0.1912        | 64                    |
| 40      | 4.7    | 0.1856        | 62                    |
| 45      | 4.7    | 0.1856        | 62                    |
| 50      | 4.7    | 0.1856        | 62                    |
| 55      | 4.8    | 0.1912        | 64                    |
| 60      | 4.8    | 0.1912        | 64                    |
| 65      | 2.7    | 0.1068        | 36                    |
| 70      | 2.4    | 0.0956        | 32                    |
| 75      | 2.1    | 0.0844        | 28                    |
| 80      | 2.1    | 0.0844        | 28                    |
| 85      | 2.1    | 0.0844        | 28                    |
| 90      | 2.1    | 0.0844        | 28                    |

**PH3966**: Following general protocol 6 (chapter 3.2.8, page 47) a mixture of formic acid (0.994 M, 300 μL, 298 μmol, 1.0 equiv) and TCT (22.4 mg, 120 μmol, 40 mol%) in reagent-grade THF was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 988 mbar). *Italic* = data points used for regression line, *blue* = maximum gas evolution, *blue numbers* = at ambient temperature after removal of the heating bath.
Figure S27. Monitoring of the gas generation in THF using 10 mol% of FPyr (green), without TCT (blue) and without FPyr (red, data extracted from Table S11 to Table S13).

Figure S28. Formation of gas in THF under consideration of the evaporated solvent (for data see Table S11).
Figure S29. Estimation of the initial rate for the gas formation in THF. Only the filled data points were considered for the regression line (for underlying data see Table S11).

As recognizable from Figure S29, the slope increased at 20% gas formation. This suggests an increase of the rate of the CO formation.
Table S14. Gas formation with 10 mol% of FPy in EtOAc.

![ Chemical Reaction Diagram ]

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n0(HCO₂H) [%] | n(EtOAc) [mmol] | Δn(gas) [mmol] | Δn(gas)/n0(HCO₂H) [%] |
|---------|--------|---------------|-----------------------|----------------|----------------|------------------------|
| 0.25    | 0.4    | 0.0167        | 4                     | 0.0278         | 0.0167         | -3                     |
| 0.50    | 0.7    | 0.0279        | 7                     | 0.0389         | 0.0279         | -3                     |
| 0.75    | 0.8    | 0.0334        | 9                     | 0.05           | 0.0334         | -4                     |
| 1.00    | 1.0    | 0.0390        | 10                    | 0.0611         | 0.039          | -6                     |
| 1.25    | 1.1    | 0.0446        | 11                    | 0.0666         | 0.0446         | -6                     |
| 1.50    | 1.3    | 0.0502        | 13                    | 0.0722         | 0.0502         | -6                     |
| 1.75    | 1.4    | 0.0557        | 14                    | 0.0833         | 0.0557         | -7                     |
| 2.00    | 1.6    | 0.0613        | 16                    | 0.0888         | 0.0613         | -7                     |
| 2.25    | 1.7    | 0.0669        | 17                    | 0.0944         | 0.0669         | -7                     |
| 2.50    | 1.8    | 0.0725        | 18                    | 0.0944         | 0.0725         | -6                     |
| 2.75    | 2.0    | 0.0780        | 20                    | 0.0999         | 0.078          | -6                     |
| 3.00    | 2.0    | 0.0780        | 20                    | 0.1055         | 0.078          | -7                     |
| 3.50    | 2.3    | 0.0892        | 23                    | 0.111          | 0.0892         | -6                     |
| 4.00    | 2.4    | 0.0948        | 24                    | 0.1166         | 0.0948         | -6                     |
| 4.50    | 2.5    | 0.1003        | 26                    | 0.1221         | 0.1003         | -6                     |
| 5.00    | 2.8    | 0.1115        | 28                    | 0.1221         | 0.1115         | -3                     |
| 5.50    | 3.0    | 0.1171        | 30                    | 0.1221         | 0.1171         | -1                     |
| 6.00    | 3.1    | 0.1226        | 31                    | 0.1277         | 0.1226         | -1                     |
| 6.50    | 3.2    | 0.1282        | 33                    | 0.1277         | 0.1282         | 0                      |
| 7.00    | 3.5    | 0.1394        | 36                    | 0.1277         | 0.1394         | 3                      |
| 7.50    | 3.7    | 0.1449        | 37                    | 0.1277         | 0.1449         | 4                      |
| 8.00    | 3.8    | 0.1505        | 38                    | 0.1333         | 0.1505         | 4                      |
| 8.50    | 4.1    | 0.1617        | 41                    | 0.1333         | 0.1617         | 7                      |
| 9.00    | 4.2    | 0.1672        | 43                    | 0.1333         | 0.1672         | 9                      |
| 9.50    | 4.5    | 0.1784        | 46                    | 0.1333         | 0.1784         | 12                     |
| 10.00   | 4.7    | 0.1840        | 47                    | 0.1333         | 0.184          | 13                     |
| 11.00   | 5.1    | 0.2007        | 51                    | 0.1388         | 0.2007         | 16                     |
| 12.00   | 5.4    | 0.2118        | 54                    | 0.1388         | 0.2118         | 19                     |
| 13.00   | 5.8    | 0.2286        | 58                    | 0.1388         | 0.2286         | 23                     |
| 14.00   | 6.1    | 0.2397        | 61                    | 0.1388         | 0.2397         | 26                     |
| 15.00   | 6.5    | 0.2564        | 65                    | 0.1388         | 0.2564         | 30                     |
| 16.00   | 6.8    | 0.2676        | 68                    | 0.1444         | 0.2676         | 31                     |
| 17.00   | 7.1    | 0.2787        | 71                    | 0.1444         | 0.2787         | 34                     |
| 18.00   | 7.3    | 0.2899        | 74                    | 0.1444         | 0.2899         | 37                     |
| 19.00   | 7.6    | 0.3010        | 77                    | 0.1444         | 0.301          | 40                     |
| 20.00   | 7.9    | 0.3122        | 80                    | 0.1444         | 0.3122         | 43                     |
| 21.00   | 8.5    | 0.3345        | 85                    | 0.1444         | 0.3345         | 48                     |
| 22.00   | 9.0    | 0.3568        | 91                    | 0.1499         | 0.3568         | 53                     |
| 23.00   | 9.4    | 0.3735        | 95                    | 0.1499         | 0.3735         | 57                     |
| 24.00   | 9.9    | 0.3902        | 100                   | 0.1499         | 0.3902         | 61                     |
| 25.00   | 10.3   | 0.4070        | 104                   | 0.1499         | 0.407          | 66                     |
| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n_0(HCO_2H) [%] | n(EtOAc) [mmol] | Δn(gas) [mmol] | Δn(gas)/n_0(HCO_2H) [%] |
|---------|--------|---------------|--------------------------|-----------------|----------------|--------------------------|
| 35      | 11.1   | 0.4404        | 112                      | 0.1499          | 0.4404        | 74                       |
| 40      | 12.0   | 0.4739        | 121                      | 0.1499          | 0.4739        | 83                       |
| 45      | 12.6   | 0.4962        | 127                      | 0.1499          | 0.4962        | 88                       |
| 50      | 13.3   | 0.5240        | 134                      | 0.1499          | 0.524         | 95                       |
| 55      | 13.7   | 0.5408        | 138                      | 0.1444          | 0.5408        | 101                      |
| 60      | 14.1   | 0.5575        | 142                      | 0.1444          | 0.5575        | 105                      |
| 65      | 11.6   | 0.4571        | 117                      | 0.0833          | 0.4571        | 95                       |
| 70      | 10.6   | 0.4181        | 107                      | 0.0611          | 0.4181        | 91                       |
| 75      | 10.2   | 0.4014        | 102                      | 0.0555          | 0.4014        | 88                       |
| 80      | 10.0   | 0.3958        | 101                      | 0.0555          | 0.3958        | 87                       |
| 85      | 9.9    | 0.3902        | 100                      | 0.0555          | 0.3902        | 85                       |
| 90      | 9.9    | 0.3902        | 100                      | 0.0555          | 0.3902        | 85                       |

**PH3909:** In accordance with general protocol 6 (chapter 3.2.8, page 47) TCT (31.3 mg, 168 μmol, 42 mol%) was combined with a solution of formic acid (0.980 M, 400 μL, 392 μmol, 1.0 equiv) and FPyr (0.100 M, 40 μmol, 10 mol%) in reagent-grade EtOAc and the resulting suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 300 K, atmospheric pressure p = 986 mbar). n(EtOAc) was obtained from the measurement of a HCO_2/H/FPyr solution in EtOAc at 70 °C without TCT in Table S15 (page 155). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO_2H are used, *blue numbers* = at ambient temperature after removal of the heating bath.
Table S15. Progress of gas generation during heating of a formic acid and FPyr solution in EtOAc.

![Chemical structure](image)

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n\(_0\)(HCO\(_2\)H) [%] |
|---------|--------|---------------|------------------------------|
| 0.25    | 0.7    | 0.0278        | 7                            |
| 0.50    | 1.0    | 0.0389        | 10                           |
| 0.75    | 1.3    | 0.0500        | 13                           |
| 1.00    | 1.6    | 0.0611        | 16                           |
| 1.25    | 1.7    | 0.0666        | 17                           |
| 1.50    | 1.8    | 0.0722        | 18                           |
| 1.75    | 2.1    | 0.0833        | 21                           |
| 2.00    | 2.3    | 0.0888        | 23                           |
| 2.25    | 2.4    | 0.0944        | 24                           |
| 2.50    | 2.4    | 0.0944        | 24                           |
| 2.75    | 2.5    | 0.0999        | 25                           |
| 3.00    | 2.7    | 0.1055        | 27                           |
| 3.50    | 2.8    | 0.1110        | 28                           |
| 4.00    | 3.0    | 0.1166        | 30                           |
| 4.50    | 3.1    | 0.1221        | 31                           |
| 5.00    | 3.1    | 0.1221        | 31                           |
| 5.50    | 3.1    | 0.1221        | 31                           |
| 6.00    | 3.2    | 0.1277        | 33                           |
| 6.50    | 3.2    | 0.1277        | 33                           |
| 7.00    | 3.2    | 0.1277        | 33                           |
| 7.50    | 3.2    | 0.1277        | 33                           |
| 8.00    | 3.4    | 0.1333        | 34                           |
| 8.50    | 3.4    | 0.1333        | 34                           |
| 9.00    | 3.4    | 0.1333        | 34                           |
| 9.50    | 3.4    | 0.1333        | 34                           |
| 10.00   | 3.4    | 0.1333        | 34                           |
| 11.00   | 3.5    | 0.1388        | 35                           |

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n\(_0\)(HCO\(_2\)H) [%] |
|---------|--------|---------------|------------------------------|
| 12      | 3.5    | 0.1388        | 35                           |
| 13      | 3.5    | 0.1388        | 35                           |
| 14      | 3.5    | 0.1388        | 35                           |
| 15      | 3.5    | 0.1388        | 35                           |
| 16      | 3.7    | 0.1444        | 37                           |
| 17      | 3.7    | 0.1444        | 37                           |
| 18      | 3.7    | 0.1444        | 37                           |
| 19      | 3.7    | 0.1444        | 37                           |
| 20      | 3.7    | 0.1444        | 37                           |
| 22      | 3.7    | 0.1444        | 37                           |
| 24      | 3.8    | 0.1499        | 38                           |
| 26      | 3.8    | 0.1499        | 38                           |
| 28      | 3.8    | 0.1499        | 38                           |
| 30      | 3.8    | 0.1499        | 38                           |
| 35      | 3.8    | 0.1499        | 38                           |
| 40      | 3.8    | 0.1499        | 38                           |
| 45      | 3.8    | 0.1499        | 38                           |
| 50      | 3.8    | 0.1499        | 38                           |
| 55      | 3.7    | 0.1444        | 37                           |
| 60      | 3.7    | 0.1444        | 37                           |
| 65      | 2.1    | 0.0833        | 21                           |
| 70      | 1.6    | 0.0611        | 16                           |
| 75      | 1.4    | 0.0555        | 14                           |
| 80      | 1.4    | 0.0555        | 14                           |
| 85      | 1.4    | 0.0555        | 14                           |
| 90      | 1.4    | 0.0555        | 14                           |

**PH3910**: In alignment to general protocol 6 (chapter 3.2.8, page 47) a solution of formic acid (0.980 M, 400 µL, 392 µmol, 1.0 equiv) and FPyr (0.100 M, 40 µmol, 10 mol%) in reagent-grade EtOAc was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 300 K, atmospheric pressure p = 986 mbar). *Italic* = data points used for regression line, *blue* = maximum gas evolution, *blue numbers* = at ambient temperature after removal of the heating bath.
Figure S30. Observation of the gas evolution in EtOAc employing 10 mol% of FPyr (green) and without TCT (blue, data taken from Table S14 and Table S15).

Figure S31. Development of gas evolution in EtOAc taking evaporated solvent into account (for data see Table S14).
Figure S32. Determination of the initial rate for the CO formation with 10 mol% FPy in EtOAc. Only the filled data points were considered for the regression line (for underlying data see Table S14).
Table S16. Gas formation applying 10 mol% of FPyr in dry dioxane.

![Dioxane diagram](image)

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n(HCO₂H) [%] | n(dioxane) [mmol] | Δn(gas)/n(HCO₂H) [%] |
|---------|--------|----------------|----------------------|------------------|----------------------|
| 0.25    | 0.3    | 0.0111         | 3                    | 0.0056           | 0.0055               |
| 0.50    | 0.4    | 0.0167         | 4                    | 0.0112           | 0.0055               |
| 0.75    | 0.6    | 0.0222         | 6                    | 0.0168           | 0.0054               |
| 1.00    | 0.6    | 0.0222         | 6                    | 0.0168           | 0.0054               |
| 1.25    | 0.7    | 0.0278         | 7                    | 0.0168           | 0.0110               |
| 1.50    | 0.8    | 0.0333         | 8                    | 0.0224           | 0.0109               |
| 1.75    | 0.8    | 0.0333         | 8                    | 0.0224           | 0.0109               |
| 2.00    | 0.8    | 0.0333         | 8                    | 0.0280           | 0.0053               |
| 2.25    | 1.0    | 0.0389         | 10                   | 0.0280           | 0.0109               |
| 2.50    | 1.0    | 0.0389         | 10                   | 0.0280           | 0.0109               |
| 2.75    | 1.0    | 0.0389         | 10                   | 0.0280           | 0.0109               |
| 3.00    | 1.1    | 0.0445         | 11                   | 0.0336           | 0.0109               |
| 3.50    | 1.1    | 0.0445         | 11                   | 0.0336           | 0.0109               |
| 4.00    | 1.3    | 0.0500         | 13                   | 0.0392           | 0.0108               |
| 4.50    | 1.3    | 0.0500         | 13                   | 0.0392           | 0.0108               |
| 5.00    | 1.3    | 0.0500         | 13                   | 0.0392           | 0.0108               |
| 5.50    | 1.4    | 0.0556         | 14                   | 0.0392           | 0.0164               |
| 6.00    | 1.4    | 0.0556         | 14                   | 0.0392           | 0.0164               |
| 6.50    | 1.6    | 0.0611         | 15                   | 0.0392           | 0.0219               |
| 7.00    | 1.6    | 0.0611         | 15                   | 0.0392           | 0.0219               |
| 7.50    | 1.6    | 0.0611         | 15                   | 0.0392           | 0.0219               |
| 8.00    | 1.7    | 0.0667         | 17                   | 0.0392           | 0.0275               |
| 8.50    | 1.7    | 0.0667         | 17                   | 0.0447           | 0.0220               |
| 9.00    | 1.8    | 0.0723         | 18                   | 0.0447           | 0.0276               |
| 9.50    | 1.8    | 0.0723         | 18                   | 0.0447           | 0.0276               |
| 10.00   | 2.0    | 0.0778         | 20                   | 0.0447           | 0.0331               |
| 11.00   | 2.1    | 0.0834         | 21                   | 0.0447           | 0.0387               |
| 12.00   | 2.3    | 0.0889         | 22                   | 0.0447           | 0.0442               |
| 13.00   | 2.4    | 0.0945         | 24                   | 0.0447           | 0.0498               |
| 14.00   | 2.5    | 0.1000         | 25                   | 0.0447           | 0.0553               |
| 15.00   | 2.7    | 0.1056         | 27                   | 0.0447           | 0.0609               |
| 16.00   | 2.8    | 0.1112         | 28                   | 0.0447           | 0.0665               |
| 17.00   | 3.0    | 0.1167         | 29                   | 0.0447           | 0.0720               |
| 18.00   | 3.2    | 0.1278         | 32                   | 0.0447           | 0.0831               |
| 19.00   | 3.4    | 0.1334         | 34                   | 0.0447           | 0.0887               |
| 20.00   | 3.5    | 0.1389         | 35                   | 0.0447           | 0.0942               |
| 22.00   | 3.9    | 0.1556         | 39                   | 0.0447           | 0.1109               |
| 24.00   | 4.4    | 0.1723         | 44                   | 0.0447           | 0.1276               |
| 26.00   | 4.7    | 0.1834         | 46                   | 0.0503           | 0.1331               |
| 28.00   | 5.1    | 0.2001         | 51                   | 0.0503           | 0.1498               |
| 30.00   | 5.4    | 0.2112         | 53                   | 0.0503           | 0.1609               |
| t [min] | V [mL] | n(gas) | n(gas)/n_0(HCO_2H) [%] | n(dioxane) | Δn(gas) | Δn(gas)/n_0(HCO_2H) [%] |
|---------|--------|--------|-------------------------|------------|----------|--------------------------|
| 35      | 6.1    | 0.2390 | 60                      | 0.0503     | 0.1887   | 48                       |
| 40      | 6.8    | 0.2668 | 67                      | 0.0503     | 0.2165   | 55                       |
| 45      | 7.3    | 0.2890 | 73                      | 0.0503     | 0.2387   | 61                       |
| 50      | 7.9    | 0.3112 | 79                      | 0.0503     | 0.2609   | 67                       |
| 55      | 8.3    | 0.3279 | 83                      | 0.0503     | 0.2776   | 71                       |
| 60      | 8.7    | 0.3446 | 87                      | 0.0503     | 0.2943   | 75                       |
| 65      | 7.5    | 0.2946 | 74                      | 0.0168     | 0.2778   | 71                       |
| 70      | 6.9    | 0.2723 | 69                      | 0.0112     | 0.2611   | 67                       |
| 75      | 6.8    | 0.2668 | 67                      | 0.0056     | 0.2612   | 67                       |
| 80      | 6.6    | 0.2612 | 66                      | 0.0056     | 0.2556   | 65                       |
| 85      | 6.6    | 0.2612 | 66                      | 0.0056     | 0.2556   | 65                       |
| 90      | 6.6    | 0.2612 | 66                      | 0.0056     | 0.2556   | 65                       |

**PH3907:** As delineated in general protocol 6 (chapter 3.2.8, page 47) a solution of formic acid (0.990 M, 400 μL, 396 μmol, 1.0 equiv) and FPyr (0.095 M, 38 μmol, 10 mol%) in dry dioxane was combined with TCT (30.2 mg, 160 μmol, 40 mol%) and the resulting solution was stirred at 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 300 K, atmospheric pressure p = 983 mbar). n(dioxane) was obtained from the measurement of a HCO_2H/FPyr solution in dioxane at 70 °C without TCT in Table S17 (page 160). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO_2H are used, *blue numbers* = at ambient temperature after removal of the heating bath.
Table S17. Gas formation during heating of a formic acid and FPyr solution in dioxane.

\[
\text{H}_2\text{CO}_2\text{H} \quad \text{no TCT} \\
+ \text{FPyr (10 mol%)} \\
\text{dioxane (1 M)} \\
70 ^\circ \text{C}
\]

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n(HCO\textsubscript{2}H) [%] |
|---------|--------|---------------|----------------------------------|
| 0.25    | 0.1    | 0.0056        | 1                                |
| 0.50    | 0.3    | 0.0112        | 3                                |
| 0.75    | 0.4    | 0.0168        | 4                                |
| 1.00    | 0.4    | 0.0168        | 4                                |
| 1.25    | 0.4    | 0.0168        | 4                                |
| 1.50    | 0.6    | 0.0224        | 6                                |
| 1.75    | 0.6    | 0.0224        | 6                                |
| 2.00    | 0.7    | 0.0280        | 7                                |
| 2.25    | 0.7    | 0.0280        | 7                                |
| 2.50    | 0.7    | 0.0280        | 7                                |
| 2.75    | 0.7    | 0.0280        | 7                                |
| 3.00    | 0.7    | 0.0280        | 7                                |
| 3.50    | 0.8    | 0.0336        | 9                                |
| 4.00    | 0.8    | 0.0336        | 9                                |
| 4.50    | 1.0    | 0.0392        | 10                               |
| 5.00    | 1.0    | 0.0392        | 10                               |
| 5.50    | 1.0    | 0.0392        | 10                               |
| 6.00    | 1.0    | 0.0392        | 10                               |
| 6.50    | 1.0    | 0.0392        | 10                               |
| 7.00    | 1.0    | 0.0392        | 10                               |
| 7.50    | 1.0    | 0.0392        | 10                               |
| 8.00    | 1.0    | 0.0392        | 10                               |
| 8.50    | 1.1    | 0.0447        | 11                               |
| 9.00    | 1.1    | 0.0447        | 11                               |
| 9.50    | 1.1    | 0.0447        | 11                               |
| 10.00   | 1.1    | 0.0447        | 11                               |
| 11.00   | 1.1    | 0.0447        | 11                               |

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n(HCO\textsubscript{2}H) [%] |
|---------|--------|---------------|----------------------------------|
| 12      | 1.1    | 0.0447        | 11                               |
| 13      | 1.1    | 0.0447        | 11                               |
| 14      | 1.1    | 0.0447        | 11                               |
| 15      | 1.1    | 0.0447        | 11                               |
| 16      | 1.1    | 0.0447        | 11                               |
| 17      | 1.1    | 0.0447        | 11                               |
| 18      | 1.1    | 0.0447        | 11                               |
| 19      | 1.1    | 0.0447        | 11                               |
| 20      | 1.1    | 0.0447        | 11                               |
| 21      | 1.1    | 0.0447        | 11                               |
| 24      | 1.1    | 0.0447        | 11                               |
| 26      | 1.3    | 0.0503        | 13                               |
| 28      | 1.3    | 0.0503        | 13                               |
| 30      | 1.3    | 0.0503        | 13                               |
| 35      | 1.3    | 0.0503        | 13                               |
| 40      | 1.3    | 0.0503        | 13                               |
| 45      | 1.3    | 0.0503        | 13                               |
| 50      | 1.3    | 0.0503        | 13                               |
| 55      | 1.3    | 0.0503        | 13                               |
| 60      | 1.3    | 0.0503        | 13                               |
| 65      | 0.4    | 0.0168        | 4                                |
| 70      | 0.3    | 0.0112        | 3                                |
| 75      | 0.1    | 0.0056        | 1                                |
| 80      | 0.1    | 0.0056        | 1                                |
| 85      | 0.1    | 0.0056        | 1                                |
| 90      | 0.1    | 0.0056        | 1                                |

PH3908: Following general protocol 6 (chapter 3.2.8, page 47) a solution of formic acid (0.990 M, 400 µL, 392 µmol, 1.0 equiv) and FPyr (0.095 M, 38 µmol, 10 mol%) in dry dioxane was stirred at 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 299 K, atmospheric pressure p = 986 mbar). *Italic* = data points used for regression line, *blue* = maximum gas evolution, *blue numbers* = at ambient temperature after removal of the heating bath.
Figure S33. Monitoring of the gas generation in dioxane utilizing 10 mol% of FPyr (green) and without TCT (blue, data taken from Table S16 and Table S17).

Figure S34. Formation of gas in dioxane under consideration of evaporated solvent (for data see Table S16).
Figure S35. Determination of the initial rate for the gas formation with 10 mol% FPyr and in EtOAc. Only the filled data points were considered for the regression line (for underlying data see Table S16).

As apparent from Figure S35, the slope increased at 20% gas formation. This suggests an increase of the rate of the CO formation.
### Table S18. Development of gas engaging 10 mol% of FPyr in 2-MeTHF.

![Chemical reaction diagram](image)

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n_0(HCO₂H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n_0(HCO₂H) [%] |
|---------|--------|---------------|------------------------|---------------|----------------|------------------------|
| 0.25    | 0.6    | 0.0223        | 6                      | 0.0169        | 0.0054         | 1                      |
| 0.50    | 0.7    | 0.0279        | 7                      | 0.0282        | -0.0003        | 0                      |
| 0.75    | 1.0    | 0.0390        | 10                     | 0.0395        | -0.0005        | 0                      |
| 1.00    | 1.3    | 0.0502        | 13                     | 0.0507        | -0.0005        | 0                      |
| 1.25    | 1.4    | 0.0558        | 14                     | 0.0564        | -0.0006        | 0                      |
| 1.50    | 1.7    | 0.0669        | 17                     | 0.062         | 0.0049         | 1                      |
| 1.75    | 1.8    | 0.0725        | 19                     | 0.0676        | 0.0049         | 1                      |
| 2.00    | 2.0    | 0.0781        | 20                     | 0.0789        | -0.0008        | 0                      |
| 2.25    | 2.1    | 0.0836        | 22                     | 0.0846        | -0.0010        | 0                      |
| 2.50    | 2.3    | 0.0892        | 23                     | 0.0902        | -0.0010        | 0                      |
| 2.75    | 2.4    | 0.0948        | 24                     | 0.0958        | -0.0010        | 0                      |
| 3.00    | 2.5    | 0.1004        | 26                     | 0.0958        | 0.0046         | 1                      |
| 3.50    | 2.8    | 0.1115        | 29                     | 0.1015        | 0.0100         | 3                      |
| 4.00    | 3.0    | 0.1171        | 30                     | 0.1127        | 0.0044         | 1                      |
| 4.50    | 3.1    | 0.1227        | 32                     | 0.1184        | 0.0043         | 1                      |
| 5.00    | 3.2    | 0.1283        | 33                     | 0.1184        | 0.0099         | 3                      |
| 5.50    | 3.4    | 0.1338        | 34                     | 0.1240        | 0.0098         | 3                      |
| 6.00    | 3.5    | 0.1394        | 36                     | 0.1240        | 0.0154         | 4                      |
| 6.50    | 3.7    | 0.1450        | 37                     | 0.1296        | 0.0154         | 4                      |
| 7.00    | 3.7    | 0.1450        | 37                     | 0.1296        | 0.0154         | 4                      |
| 7.50    | 3.8    | 0.1506        | 39                     | 0.1296        | 0.0210         | 5                      |
| 8.00    | 3.9    | 0.1561        | 40                     | 0.1296        | 0.0265         | 7                      |
| 8.50    | 3.9    | 0.1561        | 40                     | 0.1296        | 0.0265         | 7                      |
| 9.00    | 3.9    | 0.1561        | 40                     | 0.1296        | 0.0265         | 7                      |
| 9.50    | 4.1    | 0.1617        | 42                     | 0.1296        | 0.0321         | 8                      |
| 10.00   | 4.1    | 0.1617        | 42                     | 0.1296        | 0.0321         | 8                      |
| 11.00   | 4.2    | 0.1673        | 43                     | 0.1296        | 0.0377         | 10                     |
| 12.00   | 4.4    | 0.1729        | 45                     | 0.1296        | 0.0433         | 11                     |
| 13.00   | 4.5    | 0.1784        | 46                     | 0.1296        | 0.0488         | 12                     |
| 14.00   | 4.7    | 0.1840        | 47                     | 0.1296        | 0.0544         | 14                     |
| 15.00   | 4.8    | 0.1896        | 49                     | 0.1296        | 0.0600         | 15                     |
| 16.00   | 4.8    | 0.1896        | 49                     | 0.1296        | 0.0600         | 15                     |
| 17.00   | 4.9    | 0.1952        | 50                     | 0.1296        | 0.0656         | 17                     |
| 18.00   | 5.1    | 0.2008        | 52                     | 0.1296        | 0.0712         | 18                     |
| 19.00   | 5.2    | 0.2063        | 53                     | 0.1240        | 0.0823         | 21                     |
| 20.00   | 5.4    | 0.2119        | 55                     | 0.1240        | 0.0879         | 22                     |
| 22.00   | 5.6    | 0.2231        | 57                     | 0.1240        | 0.0991         | 25                     |
| 24.00   | 5.8    | 0.2286        | 59                     | 0.1240        | 0.1046         | 27                     |
| 26.00   | 6.1    | 0.2398        | 62                     | 0.1240        | 0.1158         | 30                     |
| 28.00   | 6.3    | 0.2509        | 65                     | 0.1240        | 0.1269         | 32                     |
| 30.00   | 6.5    | 0.2565        | 66                     | 0.1240        | 0.1325         | 34                     |
| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n₀(HCO₂H) [%] |
|--------|-------|---------------|-----------------------|----------------|----------------|------------------------|
| 35     | 6.9   | 0.2732        | 70                    | 0.1240         | 0.1492         | 38                     |
| 40     | 7.2   | 0.2844        | 73                    | 0.1240         | 0.1604         | 41                     |
| 45     | 7.6   | 0.3011        | 78                    | 0.1240         | 0.1771         | 45                     |
| 50     | 7.9   | 0.3123        | 80                    | 0.1240         | 0.1883         | 48                     |
| 55     | 8.0   | 0.3179        | 82                    | 0.1240         | 0.1939         | 49                     |
| 60     | 8.3   | 0.3290        | 85                    | 0.1240         | 0.2050         | 52                     |
| 65     | 6.6   | 0.2621        | 68                    | 0.0564         | 0.2057         | 52                     |
| 70     | 6.1   | 0.2398        | 62                    | 0.0451         | 0.1947         | 50                     |
| 75     | 5.8   | 0.2286        | 59                    | 0.0395         | 0.1891         | 48                     |
| 80     | 5.6   | 0.2231        | 57                    | 0.0395         | 0.1836         | 47                     |
| 85     | 5.6   | 0.2231        | 57                    | 0.0338         | 0.1893         | 48                     |
| 90     | 5.5   | 0.2175        | 56                    | 0.0338         | 0.1837         | 47                     |

**PH3926**: According to general protocol 6 (chapter 3.2.8, page 47) a Schlenk tube was charged with TCT (31.3 mg, 168 μmol, 43 mol%) and a solution of formic acid (0.970 M, 400 μL, 388 μmol, 1.0 equiv) and FPyr (0.100 M, 40 μmol, 10 mol%) in reagent-grade 2-MeTHF and the resulting solution was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 299 K, atmospheric pressure p = 983 mbar). n(2-MeTHF) was obtained from the measurement of a HCO₂H/FPyr solution in 2-MeTHF at 70 °C without TCT in Figure S27 (page 151). *Italic* = data points used for regression line, *blue numbers* = at ambient temperature after removal of the heating bath.
Table S19. Gas propagation when a formic acid and FPyr solution in 2-MeTHF was heated to 70 °C.

![Chemical structure](image)

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|----------------------|
| 0.25    | 0.4    | 0.0169        | 4                    |
| 0.50    | 0.7    | 0.0282        | 7                    |
| 0.75    | 1.0    | 0.0395        | 10                   |
| 1.00    | 1.3    | 0.0507        | 13                   |
| 1.25    | 1.4    | 0.0564        | 15                   |
| 1.50    | 1.6    | 0.0620        | 16                   |
| 1.75    | 1.7    | 0.0676        | 17                   |
| 2.00    | 2.0    | 0.0789        | 20                   |
| 2.25    | 2.1    | 0.0846        | 22                   |
| 2.50    | 2.3    | 0.0902        | 29                   |
| 2.75    | 2.4    | 0.0958        | 25                   |
| 3.0     | 2.4    | 0.0958        | 25                   |
| 3.5     | 2.5    | 0.1015        | 29                   |
| 4.0     | 2.8    | 0.1127        | 31                   |
| 4.5     | 3.0    | 0.1184        | 31                   |
| 5.0     | 3.0    | 0.1184        | 31                   |
| 5.5     | 3.1    | 0.1240        | 32                   |
| 6.0     | 3.1    | 0.1240        | 32                   |
| 6.5     | 3.2    | 0.1296        | 33                   |
| 7.0     | 3.2    | 0.1296        | 33                   |
| 7.5     | 3.2    | 0.1296        | 33                   |
| 8.0     | 3.2    | 0.1296        | 33                   |
| 8.5     | 3.2    | 0.1296        | 33                   |
| 9.0     | 3.2    | 0.1296        | 33                   |
| 9.5     | 3.2    | 0.1296        | 33                   |
| 10      | 3.2    | 0.1296        | 33                   |
| 11      | 3.2    | 0.1296        | 33                   |

**PH3927:** In orientation on general protocol 6 (chapter 3.2.8, page 47) a solution of formic acid (0.970 M, 400 µL, 388 µmol, 1.0 equiv) and FPyr (0.102 M, 40 µmol, 10 mol%) in reagent-grade 2-MeTHF was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature \( T = 298 \) K, atmospheric pressure \( p = 987 \) mbar). *Italic* = data points used for regression line, *blue* = maximum gas evolution, *blue numbers* = at ambient temperature after removal of the heating bath.
Figure S36. Monitoring of the gas evolution in 2-MeTHF harnessing 10 mol% of FPyr (green) and without TCT (blue, data taken from Table S18 and Table S19).

Figure S37. Evolution of gas in 2-MeTHF under consideration of solvent in the gas phase (for data see Table S18).
Figure S38. Determination of the initial rate for the CO formation in 2-MeTHF. Only the filled data points were considered for the regression line (for underlying data see Table S18).
Table S20. Gas formation using 10 mol% of FPyr in toluene.

```
| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] | n(toluene) [mmol] | Δn(gas) [mmol] | Δn(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|-----------------------|------------------|---------------|-----------------------|
| 0.25    | 0.1    | 0.0056        | 1                     | 0.0057           | -0.0001       | 0                     |
| 0.50    | 0.3    | 0.0113        | 1                     | 0.0113           | 0.0000        | 0                     |
| 0.75    | 0.4    | 0.0169        | 2                     | 0.017            | -0.0001       | 0                     |
| 1.00    | 0.6    | 0.0225        | 2                     | 0.0226           | -0.0001       | 0                     |
| 1.25    | 0.6    | 0.0225        | 2                     | 0.0283           | -0.0058       | -1                    |
| 1.50    | 0.7    | 0.0282        | 3                     | 0.0339           | -0.0057       | -1                    |
| 1.75    | 0.7    | 0.0282        | 3                     | 0.0339           | -0.0057       | -1                    |
| 2.00    | 0.8    | 0.0338        | 3                     | 0.0396           | -0.0058       | -1                    |
| 2.25    | 0.8    | 0.0338        | 3                     | 0.0396           | -0.0058       | -1                    |
| 2.50    | 1.0    | 0.0394        | 4                     | 0.0452           | -0.0058       | -1                    |
| 2.75    | 1.0    | 0.0394        | 4                     | 0.0452           | -0.0058       | -1                    |
| 3.0     | 1.1    | 0.0451        | 4                     | 0.0509           | -0.0058       | -1                    |
| 3.5     | 1.1    | 0.0451        | 4                     | 0.0509           | -0.0058       | -1                    |
| 4.0     | 1.3    | 0.0507        | 5                     | 0.0565           | -0.0058       | -1                    |
| 4.5     | 1.4    | 0.0564        | 6                     | 0.0565           | -0.0001       | 0                     |
| 5.0     | 1.4    | 0.0564        | 6                     | 0.0565           | -0.0001       | 0                     |
| 5.5     | 1.6    | 0.0620        | 6                     | 0.0622           | -0.0002       | 0                     |
| 6.0     | 1.6    | 0.0620        | 6                     | 0.0622           | -0.0002       | 0                     |
| 6.5     | 1.6    | 0.0620        | 6                     | 0.0622           | -0.0002       | 0                     |
| 7.0     | 1.7    | 0.0676        | 7                     | 0.0622           | 0.0054        | 1                     |
| 7.5     | 1.7    | 0.0676        | 7                     | 0.0622           | 0.0054        | 1                     |
| 8.0     | 1.7    | 0.0676        | 7                     | 0.0622           | 0.0054        | 1                     |
| 8.5     | 1.8    | 0.0733        | 7                     | 0.0622           | 0.0111        | 1                     |
| 9.0     | 1.8    | 0.0733        | 7                     | 0.0622           | 0.0111        | 1                     |
| 9.5     | 2.0    | 0.0789        | 8                     | 0.0622           | 0.0167        | 2                     |
| 10      | 2.0    | 0.0789        | 8                     | 0.0622           | 0.0167        | 2                     |
| 11      | 2.1    | 0.0845        | 8                     | 0.0622           | 0.0223        | 2                     |
| 12      | 2.1    | 0.0845        | 8                     | 0.0622           | 0.0223        | 2                     |
| 13      | 2.3    | 0.0902        | 9                     | 0.0622           | 0.0280        | 3                     |
| 14      | 2.4    | 0.0958        | 9                     | 0.0622           | 0.0336        | 3                     |
| 15      | 2.5    | 0.1014        | 10                    | 0.0622           | 0.0392        | 4                     |
| 16      | 2.5    | 0.1014        | 10                    | 0.0622           | 0.0392        | 4                     |
| 17      | 2.7    | 0.1071        | 11                    | 0.0622           | 0.0449        | 4                     |
| 18      | 2.8    | 0.1127        | 11                    | 0.0622           | 0.0505        | 5                     |
| 19      | 3.0    | 0.1183        | 12                    | 0.0622           | 0.0561        | 6                     |
| 20      | 3.0    | 0.1183        | 12                    | 0.0622           | 0.0561        | 6                     |
| 22      | 3.2    | 0.1296        | 13                    | 0.0622           | 0.0674        | 7                     |
| 24      | 3.5    | 0.1409        | 14                    | 0.0622           | 0.0787        | 8                     |
| 26      | 3.7    | 0.1465        | 15                    | 0.0622           | 0.0843        | 8                     |
| 28      | 3.9    | 0.1578        | 16                    | 0.0622           | 0.0956        | 9                     |
| 30      | 4.1    | 0.1634        | 16                    | 0.0622           | 0.1012        | 10                    |
```
| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] | n(toluene) [mmol] | Δn(gas) [mmol] | Δn(gas)/n₀(HCO₂H) [%] |
|--------|--------|---------------|----------------------|------------------|----------------|----------------------|
| 35     | 4.7    | 0.1860        | 18                   | 0.0622           | 0.1238         | 12                   |
| 40     | 5.1    | 0.2029        | 20                   | 0.0622           | 0.1407         | 14                   |
| 45     | 5.4    | 0.2141        | 21                   | 0.0622           | 0.1519         | 15                   |
| 50     | 5.8    | 0.2310        | 23                   | 0.0622           | 0.1688         | 17                   |
| 55     | 6.3    | 0.2536        | 25                   | 0.0622           | 0.1914         | 19                   |
| 60     | 6.8    | 0.2705        | 27                   | 0.0622           | 0.2083         | 21                   |
| 65     | 5.4    | 0.2141        | 21                   | 0.0283           | 0.1858         | 18                   |
| 70     | 4.8    | 0.1916        | 19                   | 0.017            | 0.1746         | 17                   |
| 75     | 4.7    | 0.1860        | 18                   | 0.017            | 0.1690         | 17                   |
| 80     | 4.5    | 0.1803        | 18                   | 0.0113           | 0.1690         | 17                   |
| 85     | 4.4    | 0.1747        | 17                   | 0.0113           | 0.1634         | 16                   |
| 90     | 4.4    | 0.1747        | 17                   | 0.0113           | 0.1634         | 16                   |

**PH4240:** As described in general protocol 6 (chapter 3.2.8, page 47) CO was prepared using a solution of FPyr (0.099 M, 1000 μL, 100 μmol, 10 mol%) in dry toluene, formic acid (38 μL, 47.1 mg, 1010 μmol, 1.0 equiv) and TCT (75.0 mg, 400 μmol, 40 mol%) under stirring for 1 h at 70 °C, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 990 mbar). n(toluene) was obtained from the measurement of a HCO₂H/FPy solution in toluene at 70 °C without TCT in Table S21 (page 170). *Italic* = data points used for regression line, *blue numbers* = at ambient temperature after removal of the heating bath.
Table S21. Progress of gas generation during heating of a formic acid and FPyr solution in toluene.

Table S21: As given in general protocol 6 (chapter 3.2.8, page 47) formic acid (38 µL, 47.1 mg, 1010 µmol, 1.0 equiv) and a solution of FPyr (0.099 M, 1000 µL, 100 µmol, 10 mol%) in dry toluene was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 300 K, atmospheric pressure p = 984 mbar). *Italic* = data points used for regression line, *blue* = maximum gas evolution, *blue numbers* = at ambient temperature after removal of the heating bath.

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n$_0$(HCO$_2$H) [%] |
|---------|--------|---------------|-----------------------------|
| 0.25    | 0.1    | 0.0057        | 1                           |
| 0.50    | 0.3    | 0.0113        | 1                           |
| 0.75    | 0.4    | 0.0170        | 2                           |
| 1.00    | 0.6    | 0.0226        | 2                           |
| 1.25    | 0.7    | 0.0283        | 3                           |
| 1.50    | 0.8    | 0.0339        | 3                           |
| 1.75    | 0.8    | 0.0339        | 3                           |
| 2.00    | 1.0    | 0.0396        | 4                           |
| 2.25    | 1.0    | 0.0396        | 4                           |
| 2.50    | 1.1    | 0.0452        | 4                           |
| 2.75    | 1.1    | 0.0452        | 4                           |
| 3.0     | 1.3    | 0.0509        | 5                           |
| 3.5     | 1.3    | 0.0509        | 5                           |
| 4.0     | 1.4    | 0.0565        | 6                           |
| 4.5     | 1.4    | 0.0565        | 6                           |
| 5.0     | 1.4    | 0.0565        | 6                           |
| 5.5     | 1.6    | 0.0622        | 6                           |
| 6.0     | 1.6    | 0.0622        | 6                           |
| 6.5     | 1.6    | 0.0622        | 6                           |
| 7.0     | 1.6    | 0.0622        | 6                           |
| 7.5     | 1.6    | 0.0622        | 6                           |
| 8.0     | 1.6    | 0.0622        | 6                           |
| 8.5     | 1.6    | 0.0622        | 6                           |
| 9.0     | 1.6    | 0.0622        | 6                           |
| 9.5     | 1.6    | 0.0622        | 6                           |
| 10      | 1.6    | 0.0622        | 6                           |
| 11      | 1.6    | 0.0622        | 6                           |

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n$_0$(HCO$_2$H) [%] |
|---------|--------|---------------|-----------------------------|
| 12      | 1.6    | 0.0622        | 6                           |
| 13      | 1.6    | 0.0622        | 6                           |
| 14      | 1.6    | 0.0622        | 6                           |
| 15      | 1.6    | 0.0622        | 6                           |
| 16      | 1.6    | 0.0622        | 6                           |
| 17      | 1.6    | 0.0622        | 6                           |
| 18      | 1.6    | 0.0622        | 6                           |
| 19      | 1.6    | 0.0622        | 6                           |
| 20      | 1.6    | 0.0622        | 6                           |
| 22      | 1.6    | 0.0622        | 6                           |
| 24      | 1.6    | 0.0622        | 6                           |
| 26      | 1.6    | 0.0622        | 6                           |
| 28      | 1.6    | 0.0622        | 6                           |
| 30      | 1.6    | 0.0622        | 6                           |
| 35      | 1.6    | 0.0622        | 6                           |
| 40      | 1.6    | 0.0622        | 6                           |
| 45      | 1.6    | 0.0622        | 6                           |
| 50      | 1.6    | 0.0622        | 6                           |
| 55      | 1.6    | 0.0622        | 6                           |
| 60      | 1.6    | 0.0622        | 6                           |
| 65      | 0.7    | 0.0283        | 3                           |
| 70      | 0.4    | 0.0170        | 2                           |
| 75      | 0.4    | 0.0170        | 2                           |
| 80      | 0.3    | 0.0113        | 1                           |
| 85      | 0.3    | 0.0113        | 1                           |
| 90      | 0.3    | 0.0113        | 1                           |
Figure S39. Observation of the gas evolution in EtOAc employing 10 mol% of FPyr (green) and without TCT (blue, data taken from Table S20 and Table S21).

Figure S40. Development of gas in toluene taking evaporated solvent into account (for data see Table S20).
Figure S41. Determination of the initial rate for the CO formation in toluene. Only the filled data points were considered for the regression line (for underlying data see Table S20).
### 3.4.3 Variation of FPyr Amount

Gas monitoring with 10 mol% FPyr given in Table S9 and Table S10 on page 143 and 145).

**Table S22.** Gas formation by means of heating a solution of formic acid and FPyr in MeCN to 70 °C.

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|----------------------|
| 0.25    | 0.7    | 0.0279        | 10                   |
| 0.50    | 1.0    | 0.0390        | 13                   |
| 0.75    | 1.1    | 0.0446        | 15                   |
| 1.00    | 1.4    | 0.0557        | 19                   |
| 1.25    | 1.6    | 0.0613        | 21                   |
| 1.50    | 1.7    | 0.0669        | 23                   |
| 1.75    | 1.8    | 0.0724        | 25                   |
| 2.00    | 2.0    | 0.0780        | 27                   |
| 2.25    | 2.0    | 0.0780        | 27                   |
| 2.50    | 2.1    | 0.0836        | 29                   |
| 2.75    | 2.3    | 0.0892        | 31                   |
| 3.0     | 2.3    | 0.0892        | 31                   |
| 3.5     | 2.3    | 0.0892        | 31                   |
| 4.0     | 2.4    | 0.0947        | 32                   |
| 4.5     | 2.4    | 0.0947        | 32                   |
| 5.0     | 2.4    | 0.0947        | 32                   |
| **5.5** | **2.5**| **0.1003**    | **34**               |
| 6.0     | 2.5    | 0.1003        | 34                   |
| 6.5     | 2.5    | 0.1003        | 34                   |
| 7.0     | 2.5    | 0.1003        | 34                   |
| 7.5     | 2.5    | 0.1003        | 34                   |
| 8.0     | 2.5    | 0.1003        | 34                   |
| 8.5     | 2.5    | 0.1003        | 34                   |
| 9.0     | 2.5    | 0.1003        | 34                   |
| 9.5     | 2.5    | 0.1003        | 34                   |
| 10.0    | 2.5    | 0.1003        | 34                   |
| 11.0    | 2.5    | 0.1003        | 34                   |

**PH3939:** According to general procedure 6 (chapter 3.2.8, page 47) a solution of formic acid (0.974 M, 300 µL, 292 µmol, 1.0 equiv) and FPyr (0.102 M, 31 µmol, 10 mol%) in dry MeCN was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 982 mbar). **Blue numbers** = at ambient temperature after removal of the heating bath. **Blue** = maximum gas evolution.
An experiment with 1 mL instead of 0.3 mL of a 1 M HCO₂H and 0.1 M FPy solution in MeCN showed that the molar amount of the evaporated solvent with 106 μmol instead of 100 μmol stays approximately the same. Therefore, the solvent amount in the gas phase is virtually not impacted by the solvent volume used.

Table S23. Gas formation by means of heating a solution of formic acid and FPy using 1 mL MeCN instead of 300 μL to 70 °C.

| t [min] | V [mL] | n(gas) [mmol] |
|--------|--------|---------------|
| 0.25   | 0.6    | 0.0224        |
| 0.50   | 0.7    | 0.0279        |
| 0.75   | 1.0    | 0.0391        |
| 1.00   | 1.1    | 0.0447        |
| 1.25   | 1.3    | 0.0503        |
| 1.50   | 1.4    | 0.0559        |
| 1.75   | 1.7    | 0.0671        |
| 2.00   | 1.8    | 0.0727        |
| 2.25   | 2.0    | 0.0783        |
| 2.50   | 2.0    | 0.0783        |
| 2.75   | 2.1    | 0.0838        |
| 3.0    | 2.3    | 0.0894        |
| 3.5    | 2.4    | 0.0950        |
| 4.0    | 2.5    | 0.1006        |
| 4.5    | 2.5    | 0.1006        |
| 5.0    | 2.5    | 0.1006        |
| **5.5**| **2.7**| **0.1062**    |
| 6.0    | 2.7    | 0.1062        |
| 6.5    | 2.7    | 0.1062        |
| 7.0    | 2.7    | 0.1062        |
| 7.5    | 2.7    | 0.1062        |
| 8.0    | 2.7    | 0.1062        |
| 8.5    | 2.7    | 0.1062        |
| 9.0    | 2.7    | 0.1062        |
| 9.5    | 2.7    | 0.1062        |
| 10     | 2.7    | 0.1062        |
| 11     | 2.7    | 0.1062        |

PH3944: According to general procedure 6 (chapter 3.2.8, page 47) a solution of formic acid (0.987 M, 1000 μL, 987 μmol, 1.0 equiv) and FPy (0.105 M, 105 μmol, 10 mol%) in dry MeCN was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 982 mbar). Blue numbers = at ambient temperature after removal of the heating bath. Blue = maximum gas evolution.
Table S24. Gas formation during heating of MeCN to 70 °C.

| t [min] | V [mL] | n(gas) [mmol] | t [min] | V [mL] | n(gas) [mmol] |
|---------|--------|---------------|---------|--------|---------------|
| 0.25    | 0.4    | 0.0168        | 12      | 0.4    | 0.0168        |
| 0.50    | 0.8    | 0.0336        | 13      | 0.8    | 0.0336        |
| 0.75    | 1.1    | 0.0449        | 14      | 1.1    | 0.0449        |
| 1.00    | 1.4    | 0.0561        | 15      | 1.4    | 0.0561        |
| 1.25    | 1.6    | 0.0617        | 16      | 1.6    | 0.0617        |
| 1.50    | 1.7    | 0.0673        | 17      | 1.7    | 0.0673        |
| 1.75    | 1.8    | 0.0729        | 18      | 1.8    | 0.0729        |
| 2.00    | 2.0    | 0.0785        | 19      | 2.0    | 0.0785        |
| 2.25    | 2.1    | 0.0841        | 20      | 2.1    | 0.0841        |
| 2.50    | 2.3    | 0.0897        | 21      | 2.3    | 0.0897        |
| 2.75    | 2.4    | 0.0953        | 22      | 2.4    | 0.0953        |
| 3.0     | 2.4    | 0.0953        | 23      | 2.4    | 0.0953        |
| 3.5     | 2.5    | 0.1009        | 24      | 2.5    | 0.1009        |
| 4.0     | 2.7    | 0.1065        | 25      | 2.7    | 0.1065        |
| 4.5     | 2.7    | 0.1065        | 26      | 2.7    | 0.1065        |
| 5.0     | 2.8    | 0.1121        | 27      | 2.8    | 0.1121        |
| 5.5     | 2.8    | 0.1121        | 28      | 2.8    | 0.1121        |
| 6.0     | 2.8    | 0.1121        | 29      | 2.8    | 0.1121        |
| 6.5     | 2.8    | 0.1121        | 30      | 2.8    | 0.1121        |
| 7.0     | 2.8    | 0.1121        | 31      | 2.8    | 0.1121        |
| 7.5     | 2.8    | 0.1121        | 32      | 2.8    | 0.1121        |
| 8.0     | 2.8    | 0.1121        | 33      | 2.8    | 0.1121        |
| 8.5     | 2.8    | 0.1121        | 34      | 2.8    | 0.1121        |
| 9.0     | 2.8    | 0.1121        | 35      | 2.8    | 0.1121        |
| 9.5     | 2.8    | 0.1121        | 36      | 2.8    | 0.1121        |
| 10      | 2.8    | 0.1121        | 37      | 2.8    | 0.1121        |
| 11      | 2.8    | 0.1121        | 38      | 2.8    | 0.1121        |

PH3953: According to general procedure 6 (chapter 3.2.8, page 47) dry MeCN (300 μL) was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 298 K, atmospheric pressure p = 985 mbar). Blue numbers = at ambient temperature after removal of the heating bath. Blue = maximum gas evolution.
Table S25. Gas formation by heating a mixture of formic acid and TCT in MeCN to 70 °C.

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|------------------------|
| 0.25    | 0.7    | 0.0278        | 9                      |
| 0.50    | 0.8    | 0.0333        | 11                     |
| 0.75    | 1.1    | 0.0444        | 15                     |
| 1.00    | 1.3    | 0.0500        | 17                     |
| 1.25    | 1.4    | 0.0555        | 19                     |
| 1.50    | 1.6    | 0.0611        | 21                     |
| 1.75    | 1.7    | 0.0666        | 23                     |
| 2.00    | 1.8    | 0.0722        | 24                     |
| 2.25    | 1.8    | 0.0722        | 24                     |
| 2.50    | 2.0    | 0.0777        | 26                     |
| 2.75    | 2.0    | 0.0777        | 26                     |
| 3.0     | 2.1    | 0.0833        | 28                     |
| 3.5     | 2.1    | 0.0833        | 28                     |
| 4.0     | 2.3    | 0.0888        | 30                     |
| 4.5     | 2.3    | 0.0888        | 30                     |
| 5.0     | 2.3    | 0.0888        | 30                     |
| **5.5** | **2.4**| **0.0944**    | **32**                 |
| 6.0     | 2.4    | 0.0944        | 32                     |
| 6.5     | 2.4    | 0.0944        | 32                     |
| 7.0     | 2.4    | 0.0944        | 32                     |
| 7.5     | 2.4    | 0.0944        | 32                     |
| 8.0     | 2.4    | 0.0944        | 32                     |
| 8.5     | 2.4    | 0.0944        | 32                     |
| 9.0     | 2.4    | 0.0944        | 32                     |
| 9.5     | 2.4    | 0.0944        | 32                     |
| 10      | 2.4    | 0.0944        | 32                     |
| 11      | 2.4    | 0.0944        | 32                     |

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|------------------------|
| 12      | 2.4    | 0.0944        | 32                     |
| 13      | 2.4    | 0.0944        | 32                     |
| 14      | 2.4    | 0.0944        | 32                     |
| 15      | 2.4    | 0.0944        | 32                     |
| 16      | 2.4    | 0.0944        | 32                     |
| 17      | 2.4    | 0.0944        | 32                     |
| 18      | 2.4    | 0.0944        | 32                     |
| 19      | 2.4    | 0.0944        | 32                     |
| 20      | 2.4    | 0.0944        | 32                     |
| 22      | 2.4    | 0.0944        | 32                     |
| 24      | 2.4    | 0.0944        | 32                     |
| 26      | 2.4    | 0.0944        | 32                     |
| 28      | 2.4    | 0.0944        | 32                     |
| 30      | 2.4    | 0.0944        | 32                     |
| 35      | 2.4    | 0.0944        | 32                     |
| 40      | 2.4    | 0.0944        | 32                     |
| 45      | 2.4    | 0.0944        | 32                     |
| 50      | 2.4    | 0.0944        | 32                     |
| 55      | 2.3    | 0.0888        | 30                     |
| 60      | 2.3    | 0.0888        | 30                     |
| 65      | 0.8    | 0.0333        | 11                     |
| 70      | 0.6    | 0.0222        | 8                      |
| 75      | 0.6    | 0.0222        | 8                      |
| 80      | 0.6    | 0.0222        | 8                      |
| 85      | 0.6    | 0.0222        | 8                      |
| 90      | 0.6    | 0.0222        | 8                      |

**PH3906:** According to general procedure 6 (chapter 3.2.8, page 47) a solution of formic acid (0.990 M, 400 µL, 396 µmol, 1.0 equiv) in dry MeCN was combined with TCT (31.8 mg, 168 µmol, 42 mol%) and heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 300 K, atmospheric pressure p = 982 mbar). Blue numbers = at ambient temperature after removal of the heating bath. Blue = maximum gas evolution.

In Figure S42 the gas development at 70 °C of solutions in MeCN of formic acid and FPyr, and formic acid and TCT are compared.
Figure S42. Gas volume formed though heating formic acid and FPyr solutions and formic acid and TCT solutions in MeCN and pure MeCN, respectively, to 70 °C for 1 h (for numerical values see Table S22 to Table S25).
Table S26. Gas monitoring using DMF (10 mol%).

\[
\begin{align*}
\text{H-O} & \quad \text{DMF (10 mol%)} \\
& \quad \text{TCT (41 mol%)} \\
& \quad \text{MeCN (1 M), 70 °C}
\end{align*}
\]

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n(HCO_2H) [%] | n(MeCN) [mmol] | \( \Delta n(\text{gas})/n(\text{HCO}_2\text{H}) \) [%] |
|---------|--------|----------------|------------------------|----------------|----------------------------------|
| 0.25    | 0.4    | 0.0168         | 6                      | 0.0279         | -0.0110 -4                      |
| 0.50    | 0.7    | 0.0280         | 10                     | 0.0390         | -0.0110 -4                      |
| 0.75    | 1.0    | 0.0393         | 13                     | 0.0446         | -0.0053 -2                      |
| 1.00    | 1.3    | 0.0505         | 17                     | 0.0557         | -0.0052 -2                      |
| 1.25    | 1.4    | 0.0561         | 19                     | 0.0613         | -0.0052 -2                      |
| 1.50    | 1.6    | 0.0617         | 21                     | 0.0669         | -0.0052 -2                      |
| 1.75    | 1.7    | 0.0673         | 23                     | 0.0724         | -0.0051 -2                      |
| 2.00    | 1.8    | 0.0729         | 25                     | 0.0780         | -0.0051 -2                      |
| 2.25    | 2.0    | 0.0785         | 27                     | 0.0780         | 0.0005 0                        |
| 2.50    | 2.1    | 0.0841         | 29                     | 0.0836         | 0.0005 0                        |
| 2.75    | 2.3    | 0.0897         | 31                     | 0.0892         | 0.0006 0                        |
| 3.0     | 2.3    | 0.0897         | 31                     | 0.0892         | 0.0006 0                        |
| 3.5     | 2.5    | 0.1009         | 34                     | 0.0892         | 0.0118 4                        |
| 4.0     | 2.7    | 0.1066         | 36                     | 0.0947         | 0.0118 4                        |
| 4.5     | 2.8    | 0.1122         | 38                     | 0.0947         | 0.0174 6                        |
| 5.0     | 3.0    | 0.1178         | 40                     | 0.0947         | 0.0230 8                        |
| 5.5     | 3.1    | 0.1234         | 42                     | 0.1003         | 0.0231 8                        |
| 6.0     | 3.2    | 0.1290         | 44                     | 0.1003         | 0.0287 10                       |
| 6.5     | 3.4    | 0.1346         | 46                     | 0.1003         | 0.0343 12                       |
| 7.0     | 3.5    | 0.1402         | 48                     | 0.1003         | 0.0399 14                       |
| 7.5     | 3.5    | 0.1402         | 48                     | 0.1003         | 0.0399 14                       |
| 8.0     | 3.7    | 0.1458         | 50                     | 0.1003         | 0.0455 15                       |
| 8.5     | 3.8    | 0.1514         | 52                     | 0.1003         | 0.0511 17                       |
| 9.0     | 3.9    | 0.1570         | 54                     | 0.1003         | 0.0567 19                       |
| 9.5     | 4.1    | 0.1626         | 56                     | 0.1003         | 0.0623 21                       |
| 10      | 4.1    | 0.1626         | 56                     | 0.1003         | 0.0623 21                       |
| 11      | 4.4    | 0.1739         | 59                     | 0.1003         | 0.0736 25                       |
| 12      | 4.5    | 0.1795         | 61                     | 0.1003         | 0.0792 27                       |
| 13      | 4.7    | 0.1851         | 63                     | 0.1003         | 0.0848 29                       |
| 14      | 4.8    | 0.1907         | 65                     | 0.1003         | 0.0904 31                       |
| 15      | 5.1    | 0.2019         | 69                     | 0.1003         | 0.1016 35                       |
| 16      | 5.2    | 0.2075         | 71                     | 0.1003         | 0.1072 36                       |
| 17      | 5.4    | 0.2131         | 73                     | 0.1003         | 0.1128 38                       |
| 18      | 5.5    | 0.2187         | 75                     | 0.1003         | 0.1184 40                       |
| 19      | 5.6    | 0.2243         | 77                     | 0.1003         | 0.1240 42                       |
| 20      | 5.8    | 0.2299         | 78                     | 0.1003         | 0.1296 44                       |
| 22      | 5.9    | 0.2355         | 80                     | 0.1003         | 0.1352 46                       |
| 24      | 6.2    | 0.2468         | 84                     | 0.1003         | 0.1465 50                       |
| 26      | 6.5    | 0.2580         | 88                     | 0.1003         | 0.1577 54                       |
| 28      | 6.6    | 0.2636         | 90                     | 0.1003         | 0.1633 56                       |
| 30      | 6.9    | 0.2748         | 94                     | 0.1003         | 0.1745 59                       |
According to general procedure 6 (chapter 3.2.8, page 47) to a solution of formic acid (0.990 M, 300 µL, 297 µmol, 1.0 equiv) and DMF (0.099 M, 30 µmol, 10 mol%) in dry MeCN was added TCT (22.5 mg, 121 µmol, 41 mol%) and the resulting suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 297 K, atmospheric pressure p = 982 mbar). n(MeCN) was obtained from the measurement of a HCO$_2$H/FPyr solution in MeCN at 70 °C without TCT in Table S22 (page 173). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO$_2$H are used, *blue numbers* = at ambient temperature after removal of the heating bath.

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n$_0$(HCO$_2$H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n$_0$(HCO$_2$H) [%] |
|---------|--------|---------------|-----------------------------|----------------|----------------|-------------------------------|
| 35      | 7.5    | 0.2972        | 101                         | 0.1003         | 0.1969         | 67                            |
| 40      | 8.0    | **0.3197**    | **109**                     | **0.1003**     | **0.2194**     | **75**                        |
| 45      | 8.3    | 0.3309        | 113                         | 0.1003         | 0.2306         | 78                            |
| 50      | 8.7    | 0.3477        | 119                         | 0.1003         | 0.2474         | 84                            |
| 55      | 9.2    | 0.3645        | 124                         | 0.1003         | 0.2642         | 90                            |
| 60      | 9.4    | 0.3758        | 128                         | 0.1003         | 0.2755         | 94                            |
| 65      | 7.3    | 0.2916        | 100                         | 0.0446         | 0.2471         | 84                            |
| 70      | 6.9    | 0.2748        | 94                          | 0.0334         | 0.2414         | 82                            |
| 75      | 6.8    | 0.2692        | 92                          | 0.0279         | 0.2413         | 82                            |
| 80      | 6.8    | 0.2692        | 92                          | 0.0223         | 0.2469         | 84                            |
| 85      | 6.6    | 0.2636        | 90                          | 0.0223         | 0.2413         | 82                            |
| 90      | 6.6    | 0.2636        | 90                          | 0.0223         | 0.2413         | 82                            |

**PH3942**: Determination of the initial rate for the CO formation in the presence of 10 mol% DMF. Only the filled data points were considered for the regression line (for underlying data see Table S26).

**Figure S43.** Determination of the initial rate for the CO formation in the presence of 10 mol% DMF. Only the filled data points were considered for the regression line (for underlying data see Table S26).
Table S27. Gas formation in the presence of 5 mol% FPyr.

| t [min] | V [mL] | n(gas) [mmol] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n₀(HCO₂H) [%] |
|---------|--------|----------------|----------------|----------------|------------------------|
| 0.25    | 0.6    | 0.0223 8       | 0.0279         | -0.0055 -2     |                        |
| 0.50    | 0.8    | 0.0335 11     | 0.0390         | -0.0055 -2     |                        |
| 0.75    | 1.0    | 0.0391 13     | 0.0446         | -0.0055 -2     |                        |
| 1.00    | 1.3    | 0.0503 17     | 0.0557         | -0.0055 -2     |                        |
| 1.25    | 1.6    | 0.0614 21     | 0.0613         | 0.0001 0       |                        |
| 1.50    | 1.7    | 0.0670 23     | 0.0669         | 0.0002 0       |                        |
| 1.75    | 1.8    | 0.0726 25     | 0.0724         | 0.0002 0       |                        |
| 2.00    | 2.1    | 0.0838 28     | 0.0780         | 0.0058 2       |                        |
| 2.25    | 2.3    | 0.0894 30     | 0.0780         | 0.0114 4       |                        |
| 2.50    | 2.4    | 0.0950 32     | 0.0836         | 0.0114 4       |                        |
| 2.75    | 2.5    | 0.1005 34     | 0.0892         | 0.0114 4       |                        |
| 3.0     | 2.7    | 0.1061 36     | 0.0892         | 0.0170 6       |                        |
| 3.5     | 3.0    | 0.1173 40     | 0.0892         | 0.0281 10      |                        |
| 4.0     | 3.1    | 0.1229 42     | 0.0947         | 0.0281 10      |                        |
| 4.5     | 3.2    | 0.1285 44     | 0.0947         | 0.0337 11      |                        |
| 5.0     | 3.4    | 0.1341 46     | 0.0947         | 0.0393 13      |                        |
| 5.5     | 3.5    | 0.1396 47     | 0.1003         | 0.0393 13      |                        |
| 6.0     | 3.7    | 0.1452 49     | 0.1003         | 0.0449 15      |                        |
| 6.5     | 3.8    | 0.1508 51     | 0.1003         | 0.0505 17      |                        |
| 7.0     | 3.9    | 0.1564 53     | 0.1003         | 0.0561 19      |                        |
| 7.5     | 4.1    | 0.1620 55     | 0.1003         | 0.0617 21      |                        |
| 8.0     | 4.2    | 0.1676 57     | 0.1003         | 0.0673 23      |                        |
| 8.5     | 4.4    | 0.1731 59     | 0.1003         | 0.0728 25      |                        |
| 9.0     | 4.5    | 0.1787 61     | 0.1003         | 0.0784 27      |                        |
| 9.5     | 4.5    | 0.1787 61     | 0.1003         | 0.0784 27      |                        |
| 10      | 4.7    | 0.1843 63     | 0.1003         | 0.0840 29      |                        |
| 11      | 4.9    | 0.1955 66     | 0.1003         | 0.0952 32      |                        |
| 12      | 5.1    | 0.2011 68     | 0.1003         | 0.1008 34      |                        |
| 13      | 5.4    | 0.2122 72     | 0.1003         | 0.1119 38      |                        |
| 14      | 5.5    | 0.2178 74     | 0.1003         | 0.1175 40      |                        |
| 15      | 5.6    | 0.2234 76     | 0.1003         | 0.1231 42      |                        |
| 16      | 5.9    | 0.2346 80     | 0.1003         | 0.1343 46      |                        |
| 17      | 6.1    | 0.2402 82     | 0.1003         | 0.1399 48      |                        |
| 18      | 6.2    | 0.2458 84     | 0.1003         | 0.1455 49      |                        |
| 19      | 6.5    | 0.2569 87     | 0.1003         | 0.1566 53      |                        |
| 20      | 6.6    | 0.2625 89     | 0.1003         | 0.1622 55      |                        |
| 22      | 6.8    | 0.2681 91     | 0.1003         | 0.1678 57      |                        |
| 24      | 7.1    | 0.2793 95     | 0.1003         | 0.1790 61      |                        |
| 26      | 7.3    | 0.2904 99     | 0.1003         | 0.1901 65      |                        |
| 28      | 7.6    | 0.3016 103    | 0.1003         | 0.2013 68      |                        |
| 30      | 7.8    | 0.3072 104    | 0.1003         | 0.2069 70      |                        |
According to general procedure 6 (chapter 3.2.8, page 47) a solution of formic acid (0.979 M, 300 μL, 294 μmol, 1.0 equiv) and FPy (0.051 M, 15 μmol, 5 mol%) in dry MeCN was treated with TCT (22.4 mg, 120 μmol, 41 mol%) and the resulting suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 297 K, atmospheric pressure p = 978 mbar). n(MeCN) was obtained from the measurement of a HCO2H/FPy solution in MeCN at 70 °C without TCT in Table S22 (page 173). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO2H are used, *blue numbers* = at ambient temperature after removal of the heating bath.

**Figure S44.** Determination of the initial rate for the CO formation in the presence of 5 mol% FPy. Only the filled data points were considered for the regression line (for underlying data see Table S27).
Table S28. Gas formation in the presence of 10 mol% of FPyr and a formic acid concentration of 0.3 M.

```
| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n_0(HCO_2H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n_0(HCO_2H) [%] |
|---------|--------|---------------|-------------------------|---------------|----------------|---------------------------|
| 0.25    | 0.4    | 0.0167        | 6                       | 0.0279        | -0.0112        | -4                        |
| 0.50    | 0.6    | 0.0222        | 7                       | 0.0390        | -0.0168        | -6                        |
| 0.75    | 0.8    | 0.0333        | 11                      | 0.0446        | -0.0112        | -4                        |
| 1.00    | 1.0    | 0.0389        | 13                      | 0.0557        | -0.0168        | -6                        |
| 1.25    | 1.3    | 0.0500        | 17                      | 0.0613        | -0.0113        | -4                        |
| 1.50    | 1.4    | 0.0556        | 19                      | 0.0669        | -0.0113        | -4                        |
| 1.75    | 1.6    | 0.0611        | 21                      | 0.0724        | -0.0113        | -4                        |
| 2.00    | 1.7    | 0.0667        | 22                      | 0.0780        | -0.0113        | -4                        |
| 2.25    | 1.8    | 0.0722        | 24                      | 0.0780        | -0.0058        | -2                        |
| 2.50    | 2.0    | 0.0778        | 26                      | 0.0836        | -0.0058        | -2                        |
| 2.75    | 2.1    | 0.0833        | 28                      | 0.0892        | -0.0058        | -2                        |
| 3.0     | 2.3    | 0.0889        | 30                      | 0.0892        | -0.0003        | 0                         |
| 3.5     | 2.4    | 0.0944        | 32                      | 0.0892        | 0.0053         | 2                         |
| 4.0     | 2.7    | 0.1056        | 36                      | 0.0947        | 0.0108         | 4                         |
| 4.5     | 2.8    | 0.1111        | 37                      | 0.0947        | 0.0164         | 6                         |
| 5.0     | 3.0    | 0.1167        | 39                      | 0.0947        | 0.0219         | 8                         |
| 5.5     | 3.1    | 0.1222        | 41                      | 0.1003        | 0.0219         | 8                         |
| 6.0     | 3.2    | 0.1278        | 43                      | 0.1003        | 0.0275         | 9                         |
| 6.5     | 3.4    | 0.1333        | 45                      | 0.1003        | 0.0330         | 11                        |
| 7.0     | 3.5    | 0.1389        | 47                      | 0.1003        | 0.0386         | 13                        |
| 7.5     | 3.7    | 0.1444        | 49                      | 0.1003        | 0.0441         | 15                        |
| 8.0     | 3.8    | 0.1500        | 51                      | 0.1003        | 0.0497         | 17                        |
| 8.5     | 3.9    | 0.1555        | 52                      | 0.1003        | 0.0552         | 19                        |
| 9.0     | 3.9    | 0.1555        | 52                      | 0.1003        | 0.0552         | 19                        |
| 9.5     | 4.1    | 0.1611        | 54                      | 0.1003        | 0.0608         | 21                        |
| 10      | 4.2    | 0.1667        | 56                      | 0.1003        | 0.0664         | 23                        |
| 11      | 4.4    | 0.1722        | 58                      | 0.1003        | 0.0719         | 25                        |
| 12      | 4.5    | 0.1778        | 60                      | 0.1003        | 0.0775         | 27                        |
| 13      | 4.7    | 0.1833        | 62                      | 0.1003        | 0.0830         | 28                        |
| 14      | 4.8    | 0.1889        | 64                      | 0.1003        | 0.0886         | 30                        |
| 15      | 5.1    | 0.2000        | 67                      | 0.1003        | 0.0997         | 34                        |
| 16      | 5.2    | 0.2055        | 69                      | 0.1003        | 0.1052         | 36                        |
| 17      | 5.4    | 0.2111        | 71                      | 0.1003        | 0.1108         | 38                        |
| 18      | 5.4    | 0.2111        | 71                      | 0.1003        | 0.1108         | 38                        |
| 19      | 5.6    | 0.2222        | 75                      | 0.1003        | 0.1219         | 42                        |
| 20      | 5.8    | 0.2278        | 77                      | 0.1003        | 0.1275         | 44                        |
| 22      | 5.9    | 0.2333        | 79                      | 0.1003        | 0.1330         | 46                        |
| 24      | 6.2    | 0.2444        | 82                      | 0.1003        | 0.1441         | 49                        |
| 26      | 6.3    | 0.2500        | 84                      | 0.1003        | 0.1497         | 51                        |
| 28      | 6.6    | 0.2611        | 88                      | 0.1003        | 0.1608         | 55                        |
| 30      | 6.8    | 0.2667        | 90                      | 0.1003        | 0.1664         | 57                        |
```
PH3952: Following general protocol 6 (chapter 3.2.8, page 47) TCT (23.0 mg, 123 μmol, 41 mol%) was combined with a solution of formic acid (0.297 M, 1000 μL, 297 μmol, 1.0 equiv) and FPyr (0.030 M, 30 μmol, 10 mol%) in dry MeCN and the resulting suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 299 K, atmospheric pressure p = 976 mbar). n(MeCN) was obtained from the measurement of a HCO₂H/FPyr solution in MeCN at 70 °C without TCT in Table S22 (page 173). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO₂H are used, *blue numbers* = at ambient temperature after removal of the heating bath.

| t [min] | V [mL] | n(gas) [mmol] | n(gas) / n₀(HCO₂H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas) / n₀(HCO₂H) [%] |
|---------|--------|---------------|-------------------------|----------------|---------------|-------------------------|
| 35      | 7.2    | 0.2833        | 95                      | 0.1003         | 0.1830        | 63                      |
| 40      | 7.6    | **0.3000**    | **101**                 | **0.1003**     | **0.1997**    | **68**                 |
| 45      | 7.9    | 0.3111        | 105                     | 0.1003         | 0.2108        | 72                      |
| 50      | 8.2    | 0.3222        | 108                     | 0.1003         | 0.2219        | 76                      |
| 55      | 8.6    | 0.3389        | 114                     | 0.1003         | 0.2386        | 82                      |
| 60      | 8.9    | 0.3500        | 118                     | 0.1003         | 0.2497        | 86                      |
| 65      | 7.3    | 0.2889        | 97                      | 0.0446         | 0.2443        | 84                      |
| 70      | 6.6    | 0.2611        | 88                      | 0.0334         | 0.2277        | 78                      |
| 75      | 6.5    | 0.2555        | 86                      | 0.0279         | 0.2277        | 78                      |
| 80      | 6.3    | 0.2500        | 84                      | 0.0223         | 0.2277        | 78                      |
| 85      | 6.2    | 0.2444        | 82                      | 0.0223         | 0.2221        | 76                      |
| 90      | 6.2    | 0.2444        | 82                      | 0.0223         | 0.2221        | 76                      |

Figure S45. determination of the initial rate for the CO formation with 10 mol% FPyr and [HCO₂H] = 0.3 mol/L. Only the filled data points were considered for the regression line (for underlying data see Table S28).
Table S29. Gas formation in the presence using 20 mol% of FPyr.

\[
\text{H} \xrightarrow{\text{FPyr (20 mol\%)} \text{TCT (41 mol\%)}} \text{O} \xrightarrow{\text{MeCN (1 M), 70 °C}} \text{C} + \text{HCl}
\]

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n(HCO}_2\text{H}) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n(HCO}_2\text{H}) [%] |
|--------|--------|----------------|-------------------------------|----------------|----------------|-------------------------------|
| 0.25   | 0.7    | 0.0278         | 9                             | 0.0279         | -0.0001        | 0                             |
| 0.50   | 1.0    | 0.0389         | 13                            | 0.0390         | -0.0001        | 0                             |
| 0.75   | 1.4    | 0.0555         | 19                            | 0.0446         | 0.0110         | 4                             |
| 1.00   | 1.7    | 0.0666         | 22                            | 0.0557         | 0.0109         | 4                             |
| 1.25   | 2.1    | 0.0833         | 28                            | 0.0613         | 0.0220         | 7                             |
| 1.50   | 2.4    | 0.0944         | 32                            | 0.0669         | 0.0275         | 9                             |
| 1.75   | 2.7    | 0.1055         | 35                            | 0.0724         | 0.0331         | 11                            |
| 2.00   | 3.0    | 0.1166         | 39                            | 0.0780         | 0.0386         | 13                            |
| 2.25   | 3.4    | 0.1333         | 45                            | 0.0780         | 0.0553         | 19                            |
| 2.50   | 3.7    | 0.1444         | 48                            | 0.0836         | 0.0608         | 21                            |
| 2.75   | 3.8    | 0.1500         | 50                            | 0.0892         | 0.0608         | 21                            |
| 3.0    | 4.1    | 0.1611         | 54                            | 0.0892         | 0.0719         | 24                            |
| 3.5    | 4.4    | 0.1722         | 58                            | 0.0892         | 0.0830         | 28                            |
| 4.0    | 4.8    | 0.1888         | 63                            | 0.0947         | 0.0941         | 32                            |
| 4.5    | 5.1    | 0.1999         | 67                            | 0.0947         | 0.1052         | 36                            |
| 5.0    | 5.4    | 0.2110         | 71                            | 0.0947         | 0.1163         | 40                            |
| 5.5    | 5.8    | 0.2277         | 76                            | 0.1003         | 0.1274         | 43                            |
| 6.0    | 6.1    | 0.2388         | 80                            | 0.1003         | 0.1385         | 47                            |
| 6.5    | 6.3    | 0.2499         | 84                            | 0.1003         | 0.1496         | 51                            |
| 7.0    | 6.6    | 0.2610         | 88                            | 0.1003         | 0.1607         | 55                            |
| 7.5    | 6.9    | 0.2721         | 91                            | 0.1003         | 0.1718         | 58                            |
| 8.0    | 7.1    | 0.2777         | 93                            | 0.1003         | 0.1774         | 60                            |
| 8.5    | 7.3    | 0.2888         | 97                            | 0.1003         | 0.1885         | 64                            |
| 9.0    | 7.6    | **0.2999**     | **101**                       | **0.1003**     | **0.1996**     | **68**                       |
| 9.5    | 7.8    | 0.3055         | 103                           | 0.1003         | 0.2052         | 70                            |
| 10     | 8.0    | 0.3166         | 106                           | 0.1003         | 0.2163         | 74                            |
| 11     | 8.3    | 0.3277         | 110                           | 0.1003         | 0.2274         | 77                            |
| 12     | 8.7    | 0.3443         | 116                           | 0.1003         | 0.2440         | 83                            |
| 13     | 9.0    | 0.3554         | 119                           | 0.1003         | 0.2551         | 87                            |
| 14     | 9.3    | 0.3665         | 123                           | 0.1003         | 0.2662         | 91                            |
| 15     | 9.7    | 0.3832         | 129                           | 0.1003         | 0.2829         | 96                            |
| 16     | 10.0   | 0.3943         | 132                           | 0.1003         | 0.2940         | 100                           |
| 17     | 10.3   | 0.4054         | 136                           | 0.1003         | 0.3051         | 104                           |
| 18     | 10.4   | 0.4110         | 138                           | 0.1003         | 0.3107         | 106                           |
| 19     | 10.7   | 0.4221         | 142                           | 0.1003         | 0.3218         | 109                           |
| 20     | 10.9   | 0.4276         | 144                           | 0.1003         | 0.3273         | 111                           |
| 22     | 11.1   | 0.4387         | 147                           | 0.1003         | 0.3384         | 115                           |
| 24     | 11.4   | 0.4499         | 151                           | 0.1003         | 0.3496         | 119                           |
| 26     | 11.6   | 0.4554         | 153                           | 0.1003         | 0.3551         | 121                           |
| 28     | 11.8   | 0.4665         | 157                           | 0.1003         | 0.3662         | 125                           |
| 30     | 12.1   | 0.4776         | 160                           | 0.1003         | 0.3773         | 128                           |
In accordance with general protocol 6 (chapter 3.2.8, page 47) TCT (22.8 mg, 122 μmol, 41 mol%) was combined with a solution of formic acid (0.995 M, 300 μL, 298 μmol, 1.0 equiv) and FPy (0.200 M, 60 μmol, 20 mol%) in dry MeCN and the resulting suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature \( T = 298 \, \text{K} \), atmospheric pressure \( p = 979 \, \text{mbar} \)). \( n(\text{MeCN}) \) was obtained from the measurement of a \( \text{HCO}_2\text{H}/\text{FPyr} \) solution in MeCN at 70 °C without TCT in Table S22 (page 173). \textit{Italic} = data points used for regression line, \textcolor{blue}{blue} = time for formation of 1 equiv of CO when 1.5 equiv of \( \text{HCO}_2\text{H} \) are used, \textcolor{blue}{blue numbers} = at ambient temperature after removal of the heating bath.

\[ y = 9.67x - 4.84 \quad R^2 = 0.966 \]

**Figure S46.** Determination of the initial rate for the CO formation with 20 mol% FPy. Only the filled data points were considered for the regression line (for underlying data see Table S29).
Table S30. Gas evolution using 20 mol% of FPyr to test levels of reproducibility.

\[
\text{FPyr (20 mol%) \quad \text{TCT (41 mol%) \quad \text{MeCN (1 M), 70 °C}}
\]

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|------------------------|----------------|---------------|------------------------|
| 0.25    | 0.3    | 0.0111        | 4                      | 0.0279         | -0.0168       | -6                     |
| 0.50    | 0.6    | 0.0221        | 8                      | 0.0390         | -0.0169       | -6                     |
| 0.75    | 0.8    | 0.0332        | 11                     | 0.0446         | -0.0114       | -4                     |
| 1.00    | 1.1    | 0.0442        | 15                     | 0.0557         | -0.0115       | -4                     |
| 1.25    | 1.6    | 0.0608        | 21                     | 0.0613         | -0.0005       | 0                      |
| 1.50    | 1.8    | 0.0719        | 25                     | 0.0669         | 0.0050        | 2                      |
| 1.75    | 2.3    | 0.0885        | 30                     | 0.0724         | 0.0160        | 5                      |
| 2.00    | 2.5    | 0.0995        | 34                     | 0.0780         | 0.0215        | 7                      |
| 2.25    | 2.8    | 0.1106        | 38                     | 0.0780         | 0.0325        | 11                     |
| 2.50    | 3.1    | 0.1216        | 42                     | 0.0836         | 0.0380        | 13                     |
| 2.75    | 3.4    | 0.1327        | 45                     | 0.0892         | 0.0435        | 15                     |
| 3.0     | 3.7    | 0.1437        | 49                     | 0.0892         | 0.0546        | 19                     |
| 3.5     | 4.1    | 0.1603        | 55                     | 0.0892         | 0.0712        | 24                     |
| 4.0     | 4.4    | 0.1714        | 58                     | 0.0947         | 0.0766        | 26                     |
| 4.5     | 4.7    | 0.1824        | 62                     | 0.0947         | 0.0877        | 30                     |
| 5.0     | 5.1    | 0.1990        | 68                     | 0.0947         | 0.1043        | 35                     |
| 5.5     | 5.4    | 0.2101        | 72                     | 0.1003         | 0.1098        | 37                     |
| 6.0     | 5.8    | 0.2267        | 77                     | 0.1003         | 0.1264        | 43                     |
| 6.5     | 6.1    | 0.2377        | 81                     | 0.1003         | 0.1374        | 47                     |
| 7.0     | 6.3    | 0.2488        | 85                     | 0.1003         | 0.1485        | 50                     |
| 7.5     | 6.6    | 0.2598        | 89                     | 0.1003         | 0.1595        | 54                     |
| 8.0     | 6.8    | 0.2654        | 91                     | 0.1003         | 0.1650        | 56                     |
| 8.5     | 7.1    | 0.2764        | 94                     | 0.1003         | 0.1761        | 60                     |
| 9.0     | 7.3    | 0.2875        | 98                     | 0.1003         | 0.1872        | 64                     |
| 9.5     | 7.6    | 0.2985        | 102                    | 0.1003         | 0.1982        | 67                     |
| **10**  | **7.8**| **0.3040**    | **104**                | **0.1003**     | **0.2037**    | **69**                  |
| 11      | 8.2    | 0.3206        | 109                    | 0.1003         | 0.2203        | 75                     |
| 12      | 8.6    | 0.3372        | 115                    | 0.1003         | 0.2369        | 81                     |
| 13      | 9.0    | 0.3538        | 121                    | 0.1003         | 0.2535        | 86                     |
| 14      | 9.3    | 0.3649        | 125                    | 0.1003         | 0.2646        | 90                     |
| 15      | 9.6    | 0.3759        | 128                    | 0.1003         | 0.2756        | 94                     |
| 16      | 9.9    | 0.3870        | 132                    | 0.1003         | 0.2867        | 98                     |
| 17      | 10.2   | 0.3980        | 136                    | 0.1003         | 0.2977        | 101                    |
| 18      | 10.3   | 0.4036        | 138                    | 0.1003         | 0.3033        | 103                    |
| 19      | 10.6   | 0.4146        | 142                    | 0.1003         | 0.3143        | 107                    |
| 20      | 10.7   | 0.4201        | 143                    | 0.1003         | 0.3198        | 109                    |
| 22      | 11.0   | 0.4312        | 147                    | 0.1003         | 0.3309        | 113                    |
| 24      | 11.3   | 0.4423        | 151                    | 0.1003         | 0.3419        | 116                    |
| 26      | 11.6   | 0.4533        | 155                    | 0.1003         | 0.3530        | 120                    |
| 28      | 11.7   | 0.4588        | 157                    | 0.1003         | 0.3585        | 122                    |
| 30      | 11.8   | 0.4644        | 158                    | 0.1003         | 0.3641        | 124                    |
### Table S22

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n₀(HCO₂H) [%] |
|---------|--------|----------------|-----------------------|----------------|----------------|------------------------|
| 35      | 12.3   | 0.4809         | 164                   | 0.1003         | 0.3806         | 129                    |
| 40      | 12.4   | 0.4865         | 166                   | 0.1003         | 0.3862         | 131                    |
| 45      | 12.7   | 0.4975         | 170                   | 0.1003         | 0.3972         | 135                    |
| 50      | 12.7   | 0.4975         | 170                   | 0.1003         | 0.3972         | 135                    |
| 55      | 12.6   | 0.4920         | 168                   | 0.1003         | 0.3917         | 133                    |
| 60      | 12.6   | 0.4920         | 168                   | 0.1003         | 0.3917         | 133                    |
| 65      | 10.3   | 0.4036         | 138                   | 0.0446         | 0.3590         | 122                    |
| 70      | 9.6    | 0.3759         | 128                   | 0.0334         | 0.3425         | 116                    |
| 75      | 9.3    | 0.3649         | 125                   | 0.0279         | 0.3370         | 115                    |
| 80      | 9.3    | 0.3649         | 125                   | 0.0223         | 0.3426         | 117                    |
| 85      | 9.2    | 0.3593         | 123                   | 0.0223         | 0.3370         | 115                    |
| 90      | 9.2    | 0.3593         | 123                   | 0.0223         | 0.3370         | 115                    |

**PH3933:** In agreement with general protocol 6 (chapter 3.2.8, page 47) a solution of formic acid (0.977 M, 300 μL, 301 μmol, 1.0 equiv) and FPyr (0.197 M, 79 μmol, 20 mol%) in dry MeCN was treated with TCT (22.5 mg, 121 μmol, 41 mol%) and the resulting suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 299 K, atmospheric pressure p = 976 mbar). n(MeCN) was obtained from the measurement of a HCO₂H/FPyr solution in MeCN at 70 °C without TCT in Table S22 (page 173). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO₂H are used, *blue numbers* = at ambient temperature after removal of the heating bath.

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**Figure S47.** Determination of the initial rate for the CO formation with 20 mol% FPyr, second measurement to probe levels of reproducibility. Only the filled data points were considered for the regression line (for underlying data see Table S30).
Table S31. Gas production employing 30 mol% of FPyr.

![Chemical reaction diagram](image)

| t [min] | V [mL] | n(gas) [mmol] | n(gas)/n₀(HCO₂H) [%] | n(MeCN) [mmol] | Δn(gas) [mmol] | Δn(gas)/n₀(HCO₂H) [%] |
|---------|--------|---------------|------------------------|----------------|----------------|------------------------|
| 0.25    | 0.7    | 0.0277        | 9                      | 0.0279         | -0.0001        | 0                      |
| 0.50    | 1.1    | 0.0444        | 15                     | 0.0390         | 0.0054         | 2                      |
| 0.75    | 1.6    | 0.0610        | 21                     | 0.0446         | 0.0164         | 6                      |
| 1.00    | 2.0    | 0.0777        | 27                     | 0.0557         | 0.0219         | 7                      |
| 1.25    | 2.4    | 0.0943        | 32                     | 0.0613         | 0.0330         | 11                     |
| 1.50    | 2.8    | 0.1109        | 38                     | 0.0669         | 0.0441         | 15                     |
| 1.75    | 3.2    | 0.1276        | 44                     | 0.0724         | 0.0551         | 19                     |
| 2.00    | 3.7    | 0.1442        | 49                     | 0.0780         | 0.0662         | 23                     |
| 2.25    | 4.1    | 0.1609        | 55                     | 0.0780         | 0.0828         | 28                     |
| 2.50    | 4.4    | 0.1719        | 59                     | 0.0836         | 0.0884         | 30                     |
| 2.75    | 4.5    | 0.1775        | 61                     | 0.0892         | 0.0883         | 30                     |
| 3.00    | 4.8    | 0.1886        | 64                     | 0.0892         | 0.0994         | 34                     |
| 3.50    | 5.2    | 0.2052        | 70                     | 0.0892         | 0.1161         | 39                     |
| 4.00    | 5.8    | 0.2274        | 78                     | 0.0947         | 0.1327         | 45                     |
| 4.50    | 6.1    | 0.2385        | 81                     | 0.0947         | 0.1438         | 49                     |
| 5.00    | 6.5    | 0.2551        | 87                     | 0.0947         | 0.1604         | 55                     |
| 5.50    | 6.8    | 0.2662        | 91                     | 0.1003         | 0.1659         | 56                     |
| 6.00    | 7.1    | 0.2773        | 95                     | 0.1003         | 0.1770         | 60                     |
| 6.50    | 7.3    | 0.2884        | 98                     | 0.1003         | 0.1881         | 64                     |
| 7.00    | 7.6    | 0.2995        | 102                    | 0.1003         | 0.1992         | 68                     |
| 7.50    | 7.9    | 0.3106        | 106                    | 0.1003         | 0.2103         | 72                     |
| 8.00    | 8.2    | 0.3217        | 110                    | 0.1003         | 0.2214         | 75                     |
| 8.50    | 8.5    | 0.3328        | 114                    | 0.1003         | 0.2325         | 79                     |
| 9.00    | 8.7    | 0.3439        | 117                    | 0.1003         | 0.2436         | 83                     |
| 9.50    | 9.0    | 0.3550        | 121                    | 0.1003         | 0.2547         | 87                     |
| 10.00   | 9.2    | 0.3605        | 123                    | 0.1003         | 0.2602         | 89                     |
| 11.00   | 9.6    | 0.3772        | 129                    | 0.1003         | 0.2769         | 94                     |
| 12.00   | 10.0   | 0.3938        | 134                    | 0.1003         | 0.2935         | 100                    |
| 13.00   | 10.4   | 0.4104        | 140                    | 0.1003         | 0.3101         | 105                    |
| 14.00   | 10.7   | 0.4215        | 144                    | 0.1003         | 0.3212         | 109                    |
| 15.00   | 10.9   | 0.4271        | 146                    | 0.1003         | 0.3268         | 111                    |
| 16.00   | 11.1   | 0.4382        | 150                    | 0.1003         | 0.3379         | 115                    |
| 17.00   | 11.3   | 0.4437        | 151                    | 0.1003         | 0.3434         | 117                    |
| 18.00   | 11.4   | 0.4493        | 153                    | 0.1003         | 0.3490         | 119                    |
| 19.00   | 11.6   | 0.4548        | 155                    | 0.1003         | 0.3545         | 121                    |
| 20.00   | 11.8   | 0.4659        | 159                    | 0.1003         | 0.3656         | 124                    |
| 22.00   | 12.0   | 0.4715        | 161                    | 0.1003         | 0.3712         | 126                    |
| 24.00   | 12.1   | 0.4770        | 163                    | 0.1003         | 0.3767         | 128                    |
| 26.00   | 12.3   | 0.4826        | 165                    | 0.1003         | 0.3822         | 130                    |
| 28.00   | 12.4   | 0.4881        | 167                    | 0.1003         | 0.3878         | 132                    |
| 30.00   | 12.4   | 0.4881        | 167                    | 0.1003         | 0.3878         | 132                    |
As described in general protocol 6 (chapter 3.2.8, page 47) a solution of formic acid (0.975 M, 300 μL, 293 μmol, 1.0 equiv) and FPyr (0.295 M, 89 μmol, 30 mol%) in dry MeCN was added to TCT (22.9 mg, 124 μmol, 42 mol%) and the suspension was heated to 70 °C for 1 h, after which the heating bath was removed (ambient temperature T = 300 K, atmospheric pressure p = 981 mbar). n(MeCN) was obtained from the measurement of a HCO₂H/FPyr solution in MeCN at 70 °C without TCT in Table S22 (page 173). *Italic* = data points used for regression line, *blue* = time for formation of 1 equiv of CO when 1.5 equiv of HCO₂H are used, *blue numbers* = at ambient temperature after removal of the heating bath.

**Figure S48.** Determination of the initial rate for the CO liberation applying 20 mol% FPyr. Only the filled data points were considered for the regression line (for underlying data see Table S31).
4 Appendix

4.1 List of Abbreviations

2-MeTHF = 2-methyltetrahydrofurane
aq. = aqueous
bp. = boiling point
BzCl = benzoyl chloride
Cbz = benzyloxycarbonyl
conv. = conversion
d = diameter
DMF = dimethylformamide
dioxane = 1,4-dioxane
DMF = dimethylformamide
equiv = equivalents
FPyr = 1-formylpyrrolidine
g = gaseous
i.r. = initial rate
MeCN = acetonitrile
MTBE = methyl-\textit{tert}-butylether
n = molar amount of substance
NMR = nuclear magnetic resonance
p = pressure
PMP = para-methoxyphenyl
Py = pyridine
r = radius
R = Avogadro constant = 6.02214\times10^{13} \text{ mol}^{-1}
s = solid
solv. = solvated
TCT = 2,4,6-trichloro-1,3,4-triazine
TFA = trifluoroacetyl
THF = tetrahydrofurane
V = volume
4.2 References

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