Heterocycles Synthesis at Carbonylation of Acetylenic Compounds

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Abstract
The carbonylation of unsaturated hydrocarbons, alcohols, organic halides and other substrates catalyzed by transition metals, salts of transition metals and organometallic complexes is a wide used synthesis method of new carbonyl, carboxyl and alkoxycarbonyl containing compounds including creation or modification of heterocycles.

The data about synthesis of heterocycles at carbonylation of acetylenic compounds have been appeared at last 20 years and are demonstrated in our review.

Introduction of carbon monoxide in the catalytic reactions of acetylenic compounds permits to obtain in one step process the diverse heterocycles, having carbonyl, carboxyl or alkoxycarbonyl substitutes or containing these fragments inside of heterocycles.

Introduction
The carbonylation of unsaturated hydrocarbons, alcohols, organic halides and other substrates catalyzed by transition metals, salts of transition metals and organometallic complexes is a wide used synthesis method of new carbonyl, carboxyl and alkoxycarbonyl containing compounds synthesis including creation or modification of heterocycles [1-8]. However the data about synthesis of heterocycles at carbonylation of acetylenic compounds in these books and reviews practically are absent because ones mainly have appeared at last 25 years. These data are given in our review.

The synthesis of alkoxycarbonyl derivatives of dimethylenepyrrolidines

It is found by Chiusoli G.P. et al. that α,α-tetraalkylsubstituted dipropargylamines react with carbon monoxide and alcohols or water in the presence of PdCl₂ – thiourea complex forming alkoxycarbonyl derivatives of dimethylenepyrrolidines (1, 2) [9,10] (Scheme 1).

\[
\text{H}_2\text{N} + \text{CO} + \text{MeOH} \xrightarrow{\text{Cat}} \text{H}_2\text{N} + \text{COOMe}
\]

On using of PdCl₂ as catalyst in the presence of oxygen apart from carbon monoxide (CO/O₂ = 90:10) in methanol dimethoxycarbonyl dimethylenepyrrolidines (3 and 4) mainly are forming besides of monoalkoxycarbonyl derivatives 1 and 2. Similar picture is at catalysis by Pd⁰/C in the presence of KI and oxygen (CO/O₂ = 94:6). At that the third stereo isomer of methoxycarbonyl dimethylenepyrrolidine (5) is formed in a small amount [11] (Scheme 2).

Methoxycarbonylation of dipropargylmethylamine at catalysis by PdCl₂ – thiourea complex leads...
to both mono- and dimethoxycarbonyldimethylene pyrrolidines forming but with smaller yields [11].

At the oxidative alkoxycarbonylation of dipropargylamines and amides by mixture of CO/air at 4 bar pressure in the alcohole at Pd⁰/C catalysis in the presence of KI the mixture of 3,4-bis(alkoxycarbonyl-methylene)pyrrolidines 6 has been obtained. An isomerization of those in the various conditions leads to the forming of pyrrols 7 and free pyrrolo-3,4-di-acetic acids 8 [12] (Scheme 3).

\[
\text{NH} + \text{CO} + \text{MeOH} \xrightarrow{\text{Cat}} \begin{array}{c} \text{MeOOC} \\ \text{COOMe} \end{array} + \begin{array}{c} \text{MeOOC} \\ \text{COOMe} \end{array} + \begin{array}{c} \text{MeOOC} \\ \text{COOMe} \end{array}
\]

Scheme 2

\[
\begin{array}{c}
\text{N} \\
\text{H} \\
\text{H} \\
\text{N}
\end{array} + \begin{array}{c}
\text{COOMe} \\
\text{COOMe} \\
\text{COOMe}
\end{array} \rightarrow \begin{array}{c}
\text{N} \\
\text{H}
\end{array} + \begin{array}{c}
\text{COOMe} \\
\text{COOMe}
\end{array} + \begin{array}{c}
\text{COOMe}
\end{array}
\]

Scheme 3

**R¹ = alkyl, aryl, alkoxycarbonyl, tosyl; R² = alkyl**

i: CO/air, R'OH, Pd/C, KI;

ii: DMSO or MeCN/Et₃N, 25 – 70 °C, 3 – 70 h.

iii: R²OH, Et₃N, 25 – 80 °C, 5 – 70 h.

iv: (1) Ba(OH)₂/H₂O, 100°C, 15 h. (2) H₂SO₄/H₂O.

v: (1) NaOH/H₂O, 100°C, 30-40 min. (2) H₂SO₄/H₂O, 0°C.

The polycyclic heterocycles formation

Chiusoli G.P. with co-workers have founded, that the polycyclic products 10-12 were formed at carbonylation of 1,6-diynes 9 in the presence of Pd⁰ on charcoal [13] (Scheme 4).

Reaction proceeds at the room temperature and atmospheric pressure of carbon monoxide. Polycyclic compounds 11 are formed at dimerization of cyclopentadienone 10. When the reaction is carried out in a base – alcohol medium (at X = NH, NMe, R = alkyl) the cyclopentadienone 10 “is caught” by alkoxyl group with the forming of corresponding alkoxycyclopentenones 12. Application of various alkenes and alkynes as dienophiles, using for “catching” of cyclopentadienones 10, allows to extend the number of obtaining heteropolycyclic compounds 13-15 (Scheme 5) [14].

Palladium on charcoal (10%), complexes of Pd⁰ such as Pd₂(dba)₃ (dba – dibenzylidenacetone) or palladium salts lightly reducing in reaction conditions up to metallic Pd are used as catalysts. The using of alkynes as dienophiles leads to obtaining of products those are spontaneously aromatized at the heating.
The better yields of polycyclic compounds 13 and 15 (up to 98%) are observed in reaction of alkenes and alkynes with terminal double and triple bonds. In the absence of CO in the same reaction conditions any reactions not proceed. But at the using of Ni and Co complexes as catalysts the cycloaromatization reaction of dialkynes 9 has proceeded [15].

**The methoxycarbonylation of N,N-dipropargylarylamines**

We have shown, that at oxidative methoxy-carbonylation of N,N-dipropargylarylamines by carbon monoxide in methanol at PdCl₂ catalysis in the presence of CuCl₂ and AcONa cyclic compounds – dimethyl-1-aryl-5-methoxycarbonylmethylene-1,2,5,6-tetrahydropyridine-3,4-dicarboxylates 17 are formed besides of alicyclic diesters of aminodicarboxylic acids 16 (Scheme 6) [16,17].

\[
\text{Scheme 6}
\]

\[
\text{Scheme 4}
\]

\[
\text{Scheme 5}
\]

\[
\text{Scheme 6}
\]

\[
\text{Scheme 6}
\]
The forming of cyclic aminotriesters 17 takes place by additive methoxycarbonylation of one from arylaminodiesters 16 triple bonds followed by cyclization. Observing dependence for cyclic 17 and allicyclic arylamineosters 16 forming from electron nature and position of substituent X (at X = p-CH₃, p-OCH₃ and p-Br cyclic compound 17 yet unforms) in aryl ring apparently is caused by stability of intermediate complexes of aminodiesters 16 with catalyst PdCl₂ [17].

**High stereoselective cyclization/carbonylation of propargylallylamines**

Oppolzer W. et al. have shown that catalyzed by nickel and palladium complexes high stereoselective cyclization/carbonylation reaction of propargylallylamines 18 a, b furnishes mono- 19 and bicyclic 20, 21 derivatives of pyrrolidines (Scheme 7) depending on used catalyst and reaction conditions [18,19] (in the Table 1).

| N | Catalyst          | Reaction conditions | Products yields, % |
|---|-------------------|---------------------|--------------------|
| 1 | a Ni(CO)₂PPh₃     | A (20)              | 69                 |
| 2 | a Ni(COD)₂/dppb   | A (12)              | 23 57              |
| 3 | b Pd(db)₂[PPh₃]   | B (2)               | 13 50 16           |

a. A: 25 mol % Ni(0), THF / MeOH 4:1, CO (1 atm) room temp.
b. B: 10 mol % Pd(0), HOAc, CO (1 atm), 45°C.

**Synthesis of indoles and benzofurans**

Palladium chloride catalyzed carbonylation of o-hexynyl anilines 22 and phenols 24 gives the methyl-2-butyldiene-3-carboxylate 23 and methyl-2-butyldienolated-3-carboxylate 25 correspondingly [20] (Scheme 8).

The mechanism of process includes the formation of intermediate bicyclic Pd complex, carboxylating by CO into acylyl palladium complex, giving in reaction with methanol the final product and Pd⁰ species. Catalyst regeneration happens in result of Pd⁰ into Pd²⁺ oxidation with participation of CuCl₂ [20].

Lately the sphere of reaction application has extended and the series of 2-substituted 3-methoxycarbonylindoles and benzofurans 26 has been obtained. Only lactams 27 have formed from 2-alkynylformilnilides in these conditions [21] (Scheme 9).
The palladium-catalyzed reaction of readily accessible 2-alkynyltrifluoracetanilides with aryl halides and vinyl triflates under a carbon monoxide atmosphere (1 or 7 atm) in the presence of potassium carbonate produces 2-substituted-3-acyl indoles in fair to good yield. The acidity of the nitrogen-hydrogen bond proved to be primary importance for the success of the reaction. The methodology has been applied to the synthesis of pravadole \(30\), a drug that shows analgesic activity against postoperative pain in man. Pravadole \(30\) was prepared from acylindole \(29\), which was obtained by palladium-catalyzed carbonylative cyclization of alkynyltrifluoracetanilide \(28\) with \(p\)-iodanisole \([22]\) (Scheme 10).

**Synthesis of substituted furans**

2-R\(^2\)-3-(4-R-benzoyl)-5-(4-R’-phenyl)furans \(32\) are synthesized by palladium-catalyzed cross-coupling of aryl iodides and 1-aryl-2-alkynyl-1-ones \(31\) with CO in benzene in the presence of \(\text{PdCl}_2(\text{PPh}_3)_2\) at 120°C (Scheme 11). Analogously 2-R\(^2\)-3-thienoyl-5-phenyl furans \(33\) were obtained from 2-bromothiophene and arylalkynylketones \(31\) \([23]\).

\[
\text{Scheme 9}
\]

\[
\text{Scheme 10}
\]

\[
\text{Scheme 11}
\]
Synthesis of 2-aryl-4-quinolones

Carbonylation of o-iodoaniline and terminal aryl-acetylenes in the presence of palladium complexes leads to 2-aryl-4-quinolones \[34\] \cite{24} (Scheme 12).

The alteration of pressure, amines, solvents and catalysts allows to find the best conditions those are given at the Scheme 12. The best catalyst is \(\text{PdCl}_2\) (dpff) complex (dpff is 1,1’-bis(diphenylphosphino)ferrocene).

Synthesis of aurone or chromones

Carbonylation of o-iodophenol in the presence of phenyl acetylene, potassium acetate and \(\text{Pd(PPh}_3\)\)\) in anisole at 1 atm CO leads to aurone \[35\] formation (Scheme 13) \cite{25}.

Reaction carrying out in the secondary amine (the best one – is \(\text{Et}_2\text{NH}\)) at 20 atm CO and catalysis by 2 mol % \(\text{PdCl}_2\)(dpff) leads to flavone \[36\] (scheme 13) \cite{26}. Selective formation of aurone or flavone at carbonylation of o-iodophenole and phenylacetylene depends on reaction conditions (temperature, CO pressure) and used bases. The influence of the nature of a solvent, amine, catalyst, carbon monoxide pressure, and temperature on the yield of the flavone was studied \cite{26,27}.

Palladium – catalysed coupling of o-iodophenols proceeds either with aryl or heteroaryl halides and alkylacetylenes giving the corresponding 2-substituted chromones \[37\] in good yields (scheme 13) \cite{27}.

Synthesis of (E)- and (Z)-substituted methylene-3,4-dihydro-2H-1-benzopyrans

A stereocontrolled synthetic approach to (E)- and (Z)-substituted methylene-3,4-dihydro-2H-1-benzopyrans \[39\] \textit{a-c} is developed from o-iodoalkynes \[38\] \textit{a, b} using as a key palladium-catalyzed intramolecular cyclic carbopalladation of iodoalkynes \[38\] followed by carbonylation or a hydride ion capture process (Scheme 14) \cite{28}.

The influence of various solvents, catalysts and additives on the yields of benzopyrans \[39\] was studied. The best reaction conditions were (i) for obtaining benzopyran \[39\] \textit{a} (79% yield) and (ii) for benzopyran \[39\] \textit{b} (79% yield).

Facile stereoselective synthesis of oxathiolanes

The stereoselective interaction of alkynols \[40\] with elemental sylfur, carbon monoxide and triethyl amine gives the salts \[41\], those are cyclized into 4-alkylidene-2-oxo-1,3-oxathiolanes \[42\] in the presence of catalytic amounts of catalyst (scheme 15). CuJ shows the best activity among studied catalysts (CuCl, CuCl\(_2\), CuBr, CuBr\(_2\), Cul, CuSO\(_4\), FeCl\(_2\)4H\(_2\)O, FeCl\(_3\), CoCl\(_2\), CoBr\(_2\), Co\(_3\), NiCl\(_2\), ZnCl\(_2\), ZnBr\(_2\), ZnI\(_2\), PdCl\(_2\)) \cite{29}. 

\[ \text{R} = \text{H}, \text{R}’ = \text{OMe}, \text{HC}_{3}H_{11}; \quad \text{R} = \text{Me}, \text{R}’ = \text{Ph} \]
Formation of unsaturated lactams

\( \alpha \)-Methylene-\( \beta \)-lactams 43 are formed at carbonylation of \( \alpha,\alpha \)-disubstituted propargylalkylamines, then \( \gamma \)-lactams 44 are formed from unsubstituted or acylated amines [30] (Scheme 16).

The same authors have shown for the first time that on simultaneously interaction of the propargylalkylamines with a carbon monoxide and a carbon dioxide catalyzed by \( \text{PdI}_2 \) or \( \text{Pd}_0/\text{C} \) in the presence of KI consistent carboxylation and alkoxycarbonylation reactions proceed leading to Z- and E-[(alkoxycarbonyl)methylene]oxazolidin-2-ones 45 a and 45 b [31,32] (Scheme 17).

In the absence of carbon monoxide only oxazolidinone 46 has been formed (Scheme 18).

\( \alpha \)-Methylene-\( \gamma \)-butyrolactones synthesis

Interest in the synthesis methods of \( \alpha \)-methylene-\( \gamma \)-butyrolactones is supported owing to high biological activity and the wide spectrum of physiological action of natural products, containing \( \alpha \)-methylene-lactonic unit [33, 34]. For example, elephantopin, euparotin acetate and vernolepin show antitumor activity [33], as a natural sesquiterpene lactone phan- томolin shows cytotoxic activity [34].

Among other synthetic methods for such struct-
ural imis catalytic cyclocarbonylation of acetylene alcohols at first had not great importance, because of it gave low yields of \( \alpha \)-methylene-\( \gamma \)-butyrolactone 47 by reaction of 3-butyn-1-ol with stoichiometric amount of nickel tetracarbonyl [35] (Scheme 19).

Norton J.R., Murray T.F. et al. have given a general method of \( \alpha \)-methylene lactones 48 synthesis in mild conditions, that has been in cyclocarbonylation of ethynyl alcohols at organopalladium complexes catalysis [36,37] (Scheme 20).
Comparative study of the ability of the various catalytic systems to cyclocarbonylate of acyclic and cyclic alcohols has shown that system PdCl$_2$, anhydrous SnCl$_2$ and 2 equiv. of tertiary phosphine in acetonitrile is the best one. At that not only $\alpha$-methylene $\gamma$-lactones, but $\delta$-lactones of various structure in cis- and trans-fused rings can be made with rather high yields, if the substrate concentration is kept sufficiently low (0.1-1 M), to direct the reaction into intramolecular cyclization way. Study of cyclocarbonylation mechanism shows at first carboalkoxy intermediate species is formed from Pd(II), CO and acetylene alcohol, followed by intramolecular cis addition to the triple bond [37,38] (Scheme 21).

Competitive intermolecular insertion of the triple bond in another substrate can occur, leading to obtaining of dimeric and, eventually, polymeric products. Cleavage of the vinyl-palladium bond by the proton generated in the first reaction removes the product and regenerates the initial Pd(II) complex. In the course of mechanism studies the authors design a much more efficient Pd(II) catalyst system with SnCl$_2$ as a cocatalyst, that of role is in labilizing of palladium coordination sphere. As at use of PdI$_2$/Bu$_3$P/MeCN catalyst system the rate-determining step evidently being the uptake of CO by Pd, then for second catalyst system case (PdCl$_2$/2Ph$_3$P/SnCl$_2$/MeCN) the rate-determining step is coordination of the substrate, followed by
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rapid uptake of CO and completion of the cyclocarbylation reaction [38] (Scheme 22).

\[
\text{[PdL}_2\text{(SnCl}_3\text{)]}^+ \text{Cl}^- + \text{HOCH}_2\text{CH}_2\text{C=CR} \xrightarrow{k} \text{[L}_2\text{Pd(SnCl}_3\text{)(HOCH}_2\text{CH}_2\text{C=CR)}^+\text{Cl}^- + \text{CO}
\]

\[
\xrightarrow{+\text{CO}} \text{[L}_2\text{Pd(SnCl}_3\text{)(HOCH}_2\text{CH}_2\text{C=CR)(CO)}^+\text{Cl}^- + \text{HCl}
\]

\[
\xrightarrow{+\text{HCl}} \text{[PdL}_2\text{(SnCl}_3\text{)]}^+ \text{Cl}^- \quad \text{here L = PPh}_3
\]

Scheme 22

**Stereoselective synthesis of (Z)-α-(alkoxy-carbonyl) methylene β- and γ-lactones**

(Z)-α-(Alkoxycarbonyl)methylene β- 50 and γ-lactones 52 can be obtained in fair to excellent yields and with high catalytic efficiencies by PdI2/KI catalyzed oxidative dialkoxycarbonylation of propynyl alcohols (α,α-diallyl substituted, or α-monoalkyl substituted) with a sufficiently bulky alkyl group 49 and but-3-yn-1-ols 51, respectively. Reactions are carried out in alcoholic media under mild conditions (70-80°C and 20 atm of a 3:1 mixture of carbon monoxide and air) (Scheme 23) [39,40]. Possible reaction pathways are discussed.

The presence of alkyl substituents α to the triple bond is essential in order to achieve good selectivities for β-lactones 50. Yields of β-lactones deriving from α-monoalkylsubstituted propynyl alcohols are very low if the alkyl group is not sterically demanding. Thus, but-3-yn-2-ol 49f yielded only 2% of the corresponding β-lactone 50f at 80% conversion. Maleic diester 53 (50%), its cyclic tautomer 54 (9%), the fumaric derivative 55 (12%) and γ-lactone 56 (6%) accounted for the converted substrate (Scheme 24).

In contrast to the propynyl alcohols, substitution α to the triple bond of but-3-yn-1-ols 51 is not necessary in order to direct the carbonylation process towards ring closure to give γ-lactones selectively. But-3-yn-1-ol 51, pent-4-yn-2-ol 51b and cis-2-ethyl-cyclopentan-1-ol 51d were, in fact, converted into their corresponding γ-lactones 52a, 52b and 52d in
excellent yields. Where there was dialkyl substitution α to the triple bond as in 51c, the reaction was slower, and the product yield of the γ-lactone 52 lower. When cyclization is disfavoured by molecular geometry, as in the case of trans-2-ethynylcyclpentan-1-ol 51, product distribution changes in favour of maleate, the γ-lactone 52e being obtained as by – product [39].

Palladium (II)-catalized dicarbonylation of 4-(trimethylsilyl)-3-butyn-1-ols 57a and 57b in the presence of propylene oxide and ethyl orthoacetate in methanol-dichloromethane under carbon monoxide at atmospheric pressure afforded cis-dicarboxylated α-methylene-γ-butyrolactones 58a, b respectively. 4-Alkyl- and 4-aryl-3-butyn-1-ols 57c-g, on the other hand, undergo trans alkoxycarbonylation across the triple bond and selectively furnish E-tetrasubstituted α-methylene-γ-butyrolactones 59c-g (Scheme 25) [41].

**Formation of α-(triorganosilyl)methylene β-, γ-, and δ-lactones**

Cyclocarbonylation of acetylenic alcohols 60, 63,
gives $\alpha$-(triorganosilyl)methylene $\beta$- 61, $\gamma$- 65, and $\delta$- 66 lactones with the assistance of an appropriate base and Rh$_4$(CO)$_{12}$. Lactone formation depends on both steric and electronic factors. In fact, the ratio of $\beta$-lactone 61 to 3-silylpropenal 62 was remarkably affected by the silane and base employed in the carbonylation of acetylenic alcohols 60. Improvement of the selectivity for $\beta$-lactone was attained by the use of either a bulkier silane, as t-BuMe$_2$SiH, or stronger base, such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) [42] (Scheme 26). Carbonylation of 60 without of base, however, results in the formation of 62 selectively.

$\gamma$-Lactone 65 is derived from homopropargyl type alcohols 63 by a similar operation even more easily than 61 already with employment of Me$_2$PhSiH and Et$_3$N. This operation is also applicable to the synthesis of six-membered $\alpha$-silylmethylene lactones 66, although a combined use of t-BuMe$_2$SiH and Et$_3$N is required for the selective formation of $\delta$-lactone 66.

**Scheme 25**

**Scheme 26**

| R, R' | R = TMS (trimethylsilyl), R' = H; a | R = TMS, R' = Me; b | R = Me, R' = H; c | R = Et, R' = Me; d | R = t-Bu, R' = Me; e | R = Ph, R' = Me; f | CO (1 atm), PdCl$_2$ (0.01 – 0.1 equiv.), CuCl$_2$ (3 equiv.), propylene oxide (5 equiv.), MeC(OEt)$_2$ (0.4 equiv.), MeOH, room temp. g | CO (15-40 kg/sm$^2$), base (1 equiv. Et$_3$N, 0.1 equiv. DBU or DABCO – 1,4-diazabicyclo[2,2,2]octane, Rh$_4$(CO)$_{12}$ (0.001 equiv.) at 100°C in benzene. |
Intermediate A may be proposed as the common intermediate to give lactone and propenal derivatives.

**Synthesis of 3(2H)-furanones**

At catalysis of transition metals triphenylphosphyn complexes (Fe, Co, Ni, Ru, Rh, Pt, the best PdCl₂(PPh₃)₂) 3(2H)-furanones 72 are formed from 1,1-dimethylprop-2-ynol 69, carbon monoxide and RX in the carbon dioxide atmosphere. Reaction mechanism includes intermediate producing of acetylenic ketone 70, followed by the forming of the cyclic carbonate 71 from ketone and CO₂, that of decarboxylates quantitatively into furanone 72 [43] (Scheme 27). It was not possible to cyclize 1-methylprop-2-ynol or prop-2-ynol by similar manner.

**Selective synthesis of furan-2(5H)-ones**

The rhodium catalysed carbonylation of acetylenes in alcohols giving 5-alkoxyfuran-2-(5H)-ones in satisfactory yields has been reported [44,45].

The reaction of acetylene homologs 73 and alkenes 74 with CO in the presence of Rh-cat and organophosphoric compounds [PR’R”R”R”(OR’)OR”(OR“)OR”(OR”)R” OR” or R”R”PR(CHR)PR”R”R”, for R” = R” = H, alkyl, n = 1-4] gives lactones 75 with high yield (Scheme 28) [46].

The general method of selective synthesis of furan-2(5H)-ones 76 and 77 from acetylenes has been proposed, being in elaboration of lasts by water gas and carbon monoxide (100 atm) in THF containing triethylamine at 100°C in the presence of rhodium carbonyl cluster catalyst [47,48] (Scheme 29).

The isomer ratio of the formed furanones 76 and 77 depends on electronic and steric nature of the substituents. As catalysts, rhodium carbonyl clusters such as Rh₄(CO)₁₂ and Rh₆(CO)₁₆ are the best among the tested transition metal complexes. Ruthenium carbonyls showed a very low activity, but cobalt and iron carbonyls were almost inactive for the present reaction. The presence of amines such as diethylamine or triethylamine is essential for the selective synthe-
sis of furanones. The absence of amines resulted in a marked decrease in both catalytic activity and product selectivity.

Carbonylation of 2-methylbut-3-yn-2-ol catalyzed by \( \text{Co}_2(\text{CO})_8 \) in benzene proceeds with low yield, but 100% selectively giving 5,5-dimethylfuran-2(5H)-one \( 78 \) (Scheme 30) [49].

\[ \text{H}_3\text{C}-\overline{\text{C}}-\text{C}=\text{CH}+\text{CO}+\text{H}_2\text{O} \xrightarrow{150^\circ\text{C}, 100 \text{ atm}, \text{Co}_2(\text{CO})_8 \ (5 \text{ mol} \% \text{ benzene})} \]

\[ 78 \ (15.3\%) \]

**Scheme 30**

**Synthesis of but-2-enolide**

Alkynes \( 79 \) react smoothly with CO and \( \text{CH}_3\text{J} \) in a liquid-liquid two-phase system to yield regioselectively the corresponding but-2-enolide \( 80 \), most probably via the intermediate formation of acylcobalt complex (Scheme 31) [50,51].

\[ \text{Co}_2(\text{CO})_8 - \text{OH}^- \xrightarrow{\text{CH}_3\text{I}} \text{Co}(\text{CO})_4^+ \xrightarrow{\text{CO}} \text{CH}_3\text{CCo}(\text{CO})_4 + \text{I}^- \]

\[ \text{R = Ph, (CH}_2)_5\text{CH, 17-testosteronyl} \]

\( i \ 5\text{N NaOH/benzene, CTAB (Cetyltrimethylammonium bromide), room temp, 1 atm.} \)

**Scheme 31**

When benzylbromide was used, no but-2-enolide was formed, due to the fast hydrolysis of the acylcobalt intermediate prior to the alkyne complexation. Thus phenylacetic acid was the only product obtained. This inconvenience was circumvented by performing the reaction in the absence of water in a solid-liquid system using a new kind of chelating agent, \( \text{Ni}[\text{(CH}_2)_2\text{O}(\text{CH}_2)_2\text{OCH}_3]_3 \) (TDA), which has the same properties as a crown ether but without the toxicity and the work-up difficulties encountered with the macrocyclic catalysts [52] (Scheme 32).

\[ \text{PhCH}_2\text{Br} + \text{PhC}==\text{CH} \xrightarrow{\text{CO}, i} \]

\[ 40\% \]

**Scheme 32**

**(E)-and (Z)-2,2-bifurylidene-5,5'-diones**

Two groups independently announced the discovery of a catalytic reaction between CO and certain simple alkynes [53-56] (acetylene [53,54,56], propyne [53,55], hex-1-yne and some ary lacetylenes [53]) that produces (E)- and (Z)- 2,2'-bifurylidene-5,5'-diones \( 81, 82 \) (or bifuran diones [53], octatrienedi olides [54-56], 5-(oxo furan-2(5H)-ylidene) furan-2(5H)-ones according previous and systematic nomenclature) (Scheme 33).

The catalyst is \( [\text{CO}_4(\text{CO})_6] \), and the reaction has been run at temperatures around 100°C and CO pressures of 100-300 and up to 1000 bar. Polar aprotic solvents as MeCN, MeNO\(_2\), acetone, N,N,N',N'-tetramethylurea, esters and ethers appear to be most suitable. The yields in acetone as the solvent have been improved by adding phosphines or phosphates [57]. In 1975, it was shown that Co complexes are

\[ 2\text{R} - \overline{\text{C}}\equiv\text{CH} + 4\text{CO} \xrightarrow{i} \]

\[ 81 \ (R = H) \]

\[ 82 \ (R = \text{Me, n-Bu, Ar}) \]

\( i \ \text{Co}_2(\text{CO})_8, 90-120^\circ\text{C}, 100-300 \text{ bar} \)

**Scheme 33**
intermediates in the catalytic reactions that leads to the bifurylidenediones [58,59]. In the course of the reinvestigation of this [Co₄(CO)₈]-catalized reaction between propyne and CO in acetone at 110°C and 170 bar five major products are produced: (E)-3,4'-dimethyl-2,2-bifurylidene-5,5-dione 83, 3,5,8-trimethylcoumarin 84, 3a,7a-dihydro-2,4,7,7a-tetramethylcoumarin 85, 2,6-dimethyl-5H-furo[3,2-b]pyran-5-one 86, and 2,7-dimethyl-5H-furo[3,2-b]pyran-5-one 87 [60] (Scheme 34), and it has found that products distribution is strongly affected by CO pressure and propyne concentration. The structures of 85, 86 and 88 were established by X-ray diffraction [60].

\[ \text{Scheme 34} \]

\[ \text{83} \quad \text{84} \quad \text{85} \quad \text{86} \quad \text{87} \]

**γ-Butyrolactones synthesis**

Alkynes 88 a-e react with methyl iodide, bromo-pentacarbonylmanganese (or dimanganese decacarbonyl), and carbon monoxide, under phase-transfer catalysis conditions, to give 2,4-disubstituted γ-butyrolactones 89 a-e. The reaction conditions are mild [35°C (1 atm)], and the process is a regiospecific one (Scheme 35) [61].

\[ \text{Scheme 35} \]

\[ \text{RC} = \text{CH} + \text{CH}_3\text{J} + 2\text{CO} \quad \text{i} \quad \text{88 a-e} \quad 35\text{-78%} \]

\[ \begin{align*}
\text{a} & \quad R = \text{Ph}, \quad \text{b} & \quad R = (\text{CH}_2)_2\text{Ph}, \quad \text{c} & \quad R = \text{n-Bu}, \quad \text{d} & \quad R = \text{n-Hex}, \\
& \quad \text{e} & \quad R = p-\text{CH}_3\text{C}_6\text{H}_4 \\
& \quad \text{i} & \quad \text{Mn(CO)}_5\text{Br} (1 \text{ equiv.}), \quad 5\text{N NaOH}, \quad [\text{PhCH}_2\text{NEt}_3]^+\text{Cl}^-, \\
& \quad \text{CH}_2\text{Cl}_2, \quad 35^\circ\text{C}, \quad 1 \text{ atm CO} 
\end{align*} \]

\[ \text{Anhydrides synthesis} \]

The carbonylation of propargyl alcohol in benzene gives only resinous substances, but substituted propargyl alcohols such as 1-pentyn-3-ol 90a, 2-methyl-3-buten-2-ol 90b and 1-ethynyl-cyclohexanol 90c give substituted itaconic acid anhydrides selectively. The products are anhydrides of propyldienesuccinic acid 88 (19%), teraconic acid 89 (42%) and cyclohexyldienesuccinic acid 90 (45%) (Scheme 36) [61].

\[ \text{Scheme 36} \]

\[ \text{RC} = \text{CH} + \text{CH}_3\text{J} + 2\text{CO} \quad \text{i} \quad \text{90 a-c} \quad 35\text{-78%} \]

\[ \begin{align*}
\text{a} & \quad R = \text{H}, \quad R' = \text{Et}; \\
\text{b} & \quad R = R' = \text{Me}; \\
\text{c} & \quad R - R' = (\text{CH}_2)_5 \\
i & \quad \text{PdCl}_2 (10\text{-20%}), \quad \text{benzene, CO (100 atm), 100°C}. 
\end{align*} \]

The carbonylation of 2,5-dimethyl-3-hexyn-2,5-diol in benzene proceeds smoothly to give the anhydride of diisopropylidenesuccinic acid 92 (49%), as a main product accompanied by bis(1-hydroxy-1-methylthyl)furanic acid dilactone 93 (14%) (Scheme 36) [62].

The reaction of alkynes 94 with CO/O₂ in diox-
ane gives anhydrides 95 (Scheme 37) [63].

\[
\begin{align*}
\text{RC} + \text{CH + CO + O}_2 & \rightarrow \text{RCO} \iff \text{RCOO} \\
\text{94} & \rightarrow \text{95} \\
\end{align*}
\]

R = Ph; 4-MeC\text{H}_2; 4-ClC\text{H}_2; t-Bu, Hex, C\text{H}_3CH(OH) i
Pd(OAc)\_2/HQCl/NPMoV; MeSO\_3H, 25\degree \text{C}, 15h.

**Scheme 37**

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Received 22 January 2003.