Radical Hydroxymethylation of Alkyl Iodides Using Formaldehyde as a C1 Synthon

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1 General Experimental Details

All required fine chemicals were used directly without purification unless stated otherwise. All air and moisture sensitive reactions were carried out under nitrogen atmosphere using standard Schlenk manifold technique. All solvents were bought from Acros as 99.8% purity. \(^1\)H and \(^{13}\)C Nuclear Magnetic Resonance (NMR) spectra were acquired at various field strengths as indicated and were referenced to CHCl\(_3\) (7.26 and 77.0 ppm for \(^1\)H and \(^{13}\)C respectively). \(^1\)H NMR coupling constants are reported in Hertz and refer to apparent multiplicities and not true coupling constants. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, qi = quintet, sx = sextet, sp = septet, m = multiplet, dd = doublet of doublets, etc.), proton assignment (determined by 2D NMR experiments: COSY, HSQC and HMBC) where possible. High resolution mass spectra were obtained using a JEOL JMS-700 spectrometer or a Fissions VG Trio 2000 quadrupole mass spectrometer. Spectra were obtained using electron impact ionization (EI) and chemical ionization (CI) techniques, or positive electrospray (ES). Analytical TLC: aluminium backed plates pre-coated (0.25 mm) with Merck Silica Gel 60 F254. Compounds were visualized by exposure to UV-light or by dipping the plates in permanganate (KMnO\(_4\)), ninhydrin or phosphomolybdic acid stains followed by heating. Flash column chromatography was performed using Merck Silica Gel 60 (40–63 μm). All mixed solvent eluents are reported as v/v solutions. Absorption and emission spectra were obtained using a Horiba Duetta spectrometer and 1 mm High Precision Cell made of quartz from Hellma Analytics. The LEDs used are Kessil PR 160 440 nm. All the reactions were conducted in CEM 10 mL glass microwave tubes.
2 Starting Material Synthesis

General Procedure for the Appel Iodination – GP1

A round-bottom flask equipped with a stirring bar was charged with the alcohol (1.0 equiv.), Ph$_3$P (1.2 equiv.) and imidazole (1.2 equiv.). The flask was evacuated and refilled with N$_2$. CH$_2$Cl$_2$ (0.1 M) was added, and the reaction was cooled to 0 °C with an ice-water bath. I$_2$ (1.2 equiv.) was added portion-wise and then the cooling bath was removed. The reaction was stirred 16 hours at room temperature and then diluted with H$_2$O. The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (x 3). The combined organic layers were washed with Na$_2$S$_2$O$_3$ sat., brine, dried (MgSO$_4$), filtered and evaporated. Purification by flash column chromatography on silica gel gave the products.

**tert-Butyl 4-Iodoazepane-1-carboxylate (S1)**

Following GP1, tert-butyl 4-hydroxyazepane-1-carboxylate (500 mg, 2.32 mmol) gave S1 as a solid (547 mg, 72%). $^1$H NMR (500 MHz, CDCl$_3$, rotamers) δ 4.48 (1H, bs), 3.49–3.38 (2H, m), 3.36–3.26 (2H, m), 2.24 (2H, bs), 2.15–2.04 (2H, m), 1.84 (1H, bs), 1.76–1.68 (1H, m), 1.46 (9H, s); $^{13}$C NMR (126 MHz, CDCl$_3$, rotamers) δ 155.6, 79.7, 46.1, 45.7, 45.2, 41.8, 41.3, 38.8, 33.3, 28.6, 27.9, 27.7. LRMS (GCMS): Found M 325.0, C$_{11}$H$_{20}$O$_2$NI requires 325.0539.

**1-(tert-Butyl) 2-Methyl (2S,4S)-4-Iodopyrrolidine-1,2-dicarboxylate (S2)**

Following GP1, 1-(tert-butyl) 2-methyl (2S,4R)-4-hydroxypyrrolidine-1,2-dicarboxylate (3.55 g, 10.00 mmol) gave S2 as a solid (2.33g, 66%). $^1$H NMR (500 MHz, CDCl$_3$, rotamers) δ 4.28 (0.5H, t, $J = 7.50$ Hz), 4.20 (0.5H, t, $J = 7.50$ Hz), 4.10–4.00 (2H, m), 3.72 (3H, s), 3.63 (1H, dd, $J = 10.2$, 8.2), 2.85–2.82 (1H, m), 2.35–2.26 (1H, m), 1.43 (4.5H, s), 1.38 (4.5H, s); $^{13}$C NMR (126 MHz, CDCl$_3$, rotamers) δ 172.1, 171.8, 153.2, 152.6, 80.7, 59.1, 58.6, 57.0, 56.6, 52.4, 52.2, 42.8, 41.9, 28.3, 28.2, 12.7, 11.9. Data in accordance with the literature.
4-Iodotetrahydro-2H-thiopyran (S3)

S3 is commercially available [CAS: 281204-90-8] but was prepared. Following GP1, tetrahydrothiopyran-4-ol (0.96 g, 8.2 mmol) gave S3 as an oil (1.41 g, 75%). $^1$H NMR (400 MHz, CDCl$_3$) δ 4.55–4.40 (1H, m), 2.90–2.74 (2H, m), 2.65–2.45 (2H, m), 2.40–2.15 (4H, m); $^{13}$C NMR (126 MHz, CDCl$_3$, rotamers) δ 33.8, 31.0, 28.1. Data in accordance with the literature.$^2$

cis-(4-Iodocyclohexyl)benzene (S4)

Following GP1, 4-phenylcyclohexan-1-ol (1.76 g, 10.00 mmol) gave S4 as a mixture of diastereoisomers as a solid (1.37 g, 48%). cis:trans 94:6. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.26–7.02 (5H, m), 4.85 (0.94H, p, J = 3.4 Hz), 4.12 (0.06H, tt, J = 12, 3.4 Hz), 2.58–2.40 (1H, m), 2.18–2.03 (2H, m), 2.02-1.87 (2H, m), 1.77–1.55 (4H, m); $^{13}$C NMR (126 MHz, CDCl$_3$, rotamers) δ 146.6, 146.1, 128.4, 126.8, 126.6, 126.2, 126.1, 43.8, 42.8, 40.7, 36.5, 36.0, 30.0, 29.0. Data in accordance with the literature.$^3$

tert-Butyl cis-(4-Iodocyclohexyl)carbamate (S5)

Following GP1, tert-butyl trans-(4-hydroxycyclohexyl)carbamate (1.00 g, 4.64 mmol) gave S5 as a mixture of diastereomers as a solid (401 mg, 27%). $^1$H NMR (500 MHz, CDCl$_3$) δ 4.68 (1H, bs), 4.56 (1H, bs), 3.54 (1H, bs), 2.14–1.99 (2H, m), 1.89–1.55 (6H, m), 1.43 (9H, s); $^{13}$C NMR (126 MHz, CDCl$_3$, rotamers) δ 155.3, 79.4, 48.2, 35.5, 33.4, 30.2, 28.5. Data in accordance with the literature.$^2$

tert-Butyl (3-Iodocyclobutyl)carbamate (S6)

S6 is commercially available [CAS: 1389264-12-3] but was prepared. Following GP1, tert-butyl (3-hydroxycyclobutyl)carbamate (0.94 g, 5.00 mmol) gave S6 as a solid (1.05 g, 71) as a
mixture of diastereomers. cis:trans 1:1. \(^1\)H NMR (400 MHz, CDCl\(_3\), diastereomers) \(\delta\) 4.88 (0.5H, br s), 4.83 (0.5H, br s), 4.63–4.45 (0.5H, m), 4.37 (0.5H, tt, \(J = 7.7\), 3.8 Hz), 4.20–4.08 (0.5H, m), 4.03 (0.5H, tt, \(J = 9.1\), 7.3 Hz), 3.16–3.01 (1H, m), 2.78–2.66 (1H, m), 2.64–2.52 (1H, m), 2.49–2.38 (1H, m), 1.42 (4.5H, s), 1.41 (4.5H, s); \(^{13}\)C NMR (126 MHz, CDCl\(_3\), diastereomers) \(\delta\) 155.0, 154.6, 46.0, 45.7, 43.8, 28.5, 11.0, 4.0; HRMS (ASAP): Found M+H\(^+\) 298.0293, \(\text{C}_{9}\text{H}_{17}\text{O}_2\)NI requires 298.0298.

**tert-Butyl 2-Iodo-7-azaspiro[3.5]nonane-7-carboxylate (S7)**

S7 is commercially available [CAS: 1638764-90-5] but was prepared. Following GP1, tert-butyl 2-hydroxy-7-azaspiro[3.5]nonane-7-carboxylate (0.96 g, 4.00 mmol) gave S7 as a solid (0.23 g, 16%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.49 (1H, p, \(J = 8.3\) Hz), 3.35–3.29 (2H, m), 3.29–3.25 (2H, m), 2.70–2.61 (2H, m), 2.46–2.38 (2H, m), 1.72–1.63 (2H, m), 1.59–1.52 (2H, m), 1.44 (9H, s); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\)154.8, 46.3, 40.8, 39.8, 39.5, 35.2, 28.4, 9.5. Data in accordance with the literature.\(^3\)

**tert-Butyl 6-Iodo-2-azaspiro[3.3]heptane-2-carboxylate (S8)**

S8 is commercially available [CAS: 2059140-61-1] but was prepared. Following GP1, tert-butyl 6-hydroxy-2-azaspiro[3.3]heptane-2-carboxylate (0.85 g, 4.0 mmol) gave S8 as a solid (0.97 g, 75%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.29 (1H, p, \(J = 7.8\) Hz), 3.94 (4H, d, \(J = 12.3\) Hz), 2.96–2.87 (2H, m), 2.74–2.66 (2H, m), 1.42 (9H, s); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 156.1, 79.6, 47.1, 38.4, 28.4, 7.5. Data in accordance with the literature.\(^3\)
**tert-Butyl 5-Iodohexahydrocyclopenta[c]pyrrole-2(1H)-carboxylate (S9)**

Following GP1 tert-butyl-5-hydroxyhexahydrocyclopenta[c]pyrrole-2(1H)-carboxylate (250 mg, 1.1 mmol) gave S9 as an oil (126 mg, 34%). Rf 0.52 [pentane:EtOAc (8.5:1.5)]; $^1$H NMR (400 MHz, CDCl$_3$) δ 4.42 (1H, p, J = 5.5 Hz), 3.58–3.42 (2H, m), 3.21 (2H, dd, J = 11.5, 2.9 Hz), 2.90 (2H, dt, J = 4.1, 8.0, 8.0 Hz), 2.44–2.26 (2H, m), 2.00 (2H, dt, J = 14.2, 5.4 Hz), 1.45 (9H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 154.7, 79.6, 51.6, 46.5, 42.2, 26.2; HRMS (ESI): Found M+Na$^+$ 360.0417, C$_{12}$H$_{20}$INO$_2$Na requires 360.0431.

**tert-Butyl 5-Iodo-2-methylpiperidine-1-carboxylate (S10)**

Following GP, tert-butyl 5-hydroxy-2-methylpiperidine-1-carboxylate (250 mg, 1.2 mmol) gave S10 (78 mg, 21%) as an oil. Rf 0.4 [pentane:EtOAc 9:1]; $^1$H NMR (400 MHz, CDCl$_3$, rotamers) δ 4.47 (0.35H, br s), 4.33 (0.35H, br s), 4.09–3.79 (1.65H, m), 3.54 (0.65H, br s), 3.36–2.97 (1H, m), 2.30–2.11 (0.8H, m), 2.09–1.94 (1.2H, m), 1.93–1.72 (1H, m), 1.64–1.53 (1H, m), 1.47 & 1.45 (9H, s), 1.25 (2H, d, J = 6.2 Hz), 1.17 (1H, d, J = 6.9 Hz); $^{13}$C NMR (101 MHz, CDCl$_3$, rotamers) δ 154.7, 154.1, 80.1, 79.8, 59.7, 55.1, 33.0, 33.0, 31.4, 30.2, 28.6, 28.5, 15.5, 11.4; HRMS (ESI): Found M+Na$^+$ 348.0420 C$_{11}$H$_{20}$INO$_2$Na requires 348.0431.

**7-(2-Iodopropyl)-1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione (S11)**

Following GP1, 7-(2-hydroxypropyl)-1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione (1.00 g, 4.20 mmol) gave S11 as a solid (1.08 g, 74%). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.65 (1H, s), 4.61–4.54 (1H, m), 4.50 (1H, dd, J = 14.1, 5.0 Hz), 4.37 (1H, dd, J = 14.1, 9.0 Hz), 3.60 (3H, s), 3.40 (3H, s), 1.96 (3H, d, J = 6.9 Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 155.4, 151.7, 149.4, 141.6, 106.7, 56.8, 30.0, 28.2, 25.4, 25.0; HRMS (APCI): Found 349.0156 C$_{10}$H$_{14}$N$_4$O$_2$ requires 349.0162.
**tert-Butyl 3-exo-Iodo-8-azabicyclo[3.2.1]octane-8-carboxylate (S12)**

Following GP1 tert-butyl endo-3-hydroxy-8-azabicyclo[3.2.1]octane-8-carboxylate (1.56 g, 6.93 mmol) gave S12 as a solid (1.69 g, 73%). \( R_f \) 0.56 [petrol:EtOAc (8:2)]. \(^1\)H NMR (400 MHz, CDCl\(_3\), rotamers) \( \delta \) 4.51 (1H, tt, \( J = 11.9, 5.7 \) Hz), 4.14–4.04 (1H, m), 4.04–3.92 (1H, m), 2.47–2.23 (2H, m), 2.22–2.14 (2H, m), 1.98–1.83 (2H, m), 1.71–1.57 (2H, m), 1.47 (9H, s); \(^{13}\)C NMR (101 MHz, CDCl\(_3\), rotamers) \( \delta \) 150.2, 81.2, 56.2, 55.6, 45.3, 44.5, 28.5, 27.7, 27.1, 18.5; HRMS (ASAP): Found M+H\(^+\) 338.0612, C\(_{12}\)H\(_{21}\)INO\(_2\) requires 338.0611.

**\( \alpha \)-Cholesteryl Iodide (S13)**

S13 is commercially available [CAS: 2930-80-5] but was prepared. Following GP1 cholesterol (3.87 g, 10.00 mmol) gave S13 as a solid (3.57 g, 72%). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.32 (1H, d, \( J = 5.6 \) Hz), 4.07–4.00 (1H, m), 2.96–2.89 (1H, m), 2.70–2.64 (1H, m), 2.30–0.85 (38H, m), 0.66 (3H, s); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 142.9, 121.8, 56.8, 56.2, 50.5, 46.5, 42.4, 42.0, 39.8, 39.6, 36.7, 36.6, 36.3, 35.9, 31.8, 31.7, 30.7, 28.3, 28.1, 24.4, 23.9, 22.9, 22.7, 20.9, 19.3, 18.8, 11.9. Data in accordance with the literature.\(^4\)

**2-(4-Bromophenyl)-4-iodotetrahydro-2H-pyran (S14)**

A round bottomed flask equipped with a stirring bar was charged with 4-bromobenzaldehyde (0.3 g, 1.6 mmol), CH\(_2\)Cl\(_2\) (16 mL), 3-buten-1-ol (0.28 mL, 3.2 mmol) and HI (0.4 mL, 55 wt% solution in water, 3.2 mmol). The mixture was stirred at room temperature for 4 h when it was judged complete (TLC analysis). The mixture was diluted with H\(_2\)O (30 mL), the layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 x 30 mL). The combined organic layers were washed with Na\(_2\)S\(_2\)O\(_3\) (30 mL, 10% solution), brine (30 mL), dried (MgSO\(_4\)), filtered, and evaporated. Purification by flash column chromatography on silica gel gave S14 (0.29 g, 49%) as a solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.46 (d, \( J = 8.5 \) Hz, 2H), 7.22 (d, \( J = \)}
8.5 Hz, 2H), 4.91 (t, J = 3.3 Hz, 1H), 4.80 (dd, J = 10.6, 2.1 Hz, 1H), 4.05 (t, J = 5.6 Hz, 2H), 2.18 (dt, J = 14.7, 2.7 Hz, 1H), 1.96 (dt, J = 5.3, 2.7 Hz, 2H), 1.81 (dd, J = 14.5, 10.6, 3.5 Hz, 1H); 13C NMR (101 MHz, CDCl3) δ 140.4, 131.8, 127.6, 121.8, 80.7, 69.6, 47.6, 39.6, 29.9.

Data in accordance with the literature.5

N-(4-iodooctahydropentalen-1-yl)acetamide (S15)

A solution of I2 (7.6 g, 30 mmol, 1.5 equiv.) and COD (2.2 g, 20 mmol, 1.0 equiv.) in CH3CN (50 mL, 0.4 M) was stirred at room temperature for 24 h. The mixture was diluted with aqueous NaCl (150 mL), the layers were separated and the aqueous layer was extracted with CHCl3 (3 x 30 mL). The combined organic layers were washed with aqueous Na2S2O3 (50 mL), brine (50 mL), dried (MgSO4), filtered, and evaporated. Purification by flash column chromatography on silica gel gave S15 (2.3 g, 39%) as a solid as a mixture of diastereomers. dr 1:1. 1H NMR (400 MHz, CDCl3, diastereomers) δ 5.55 (1H, s), 5.47 (1H, s), 4.42 (0.5H, dt, J = 8.5, 6.2 Hz), 4.35–4.22 (0.5H, m), 4.06 (0.5H, ddd, J = 11.8, 7.5, 5.8 Hz), 3.91 (0.5H, td, J = 13.9, 12.7, 6.4 Hz), 2.77 (0.5 H, dq, J = 17.6, 9.9, 8.9 Hz), 2.70–2.61 (0.5H, m), 2.60–2.46 (0.5H, m), 2.13 (1.5 H, m), 2.00 (1.5H, s), 1.97 (1.5H, s), 1.89–1.37 (6.5H, m), 1.35–1.14 (0.5H, m); 13C NMR (101 MHz, CDCl3) δ 169.8, 58.8, 53.9, 48.6, 48.0, 47.4, 44.6, 39.3, 36.5, 35.9, 33.4, 32.9, 31.8, 30.8, 30.7, 25.7, 23.4, 23.2. Data in accordance with literature.6

1-(1-(tert-Butoxycarbonyl)piperidin-4-yl)-2,4,6-triphenylpyridin-1-ium
Tetrafluoroborate Salt (31)

An oven-dry tube equipped with a stirring bar was charged with 2,4,6-triphenylpyrylum tetrafluoroborate (1.00 g, 2.52 mmol, 1.0 equiv.), tert-butyl 4-aminopiperidine-1-carboxylate (607 mg, 3.02 mmol, 1.2 equiv.) and EtOH (2.5 mL, 1.0 M). The mixture was heated under reflux overnight and then was cooled to room temperature. The mixture was heated under Et2O (5 mL) and vigorously stirred for 15 minutes to precipitate product. The resultant solid was filtered, washed with Et2O (3 x 15 mL) and dried under vacuum to give 31 (993 mg, 68%) as a solid. 1H NMR (500 MHz, CDCl3) δ 7.86–7.69 (6H, m), 7.67 (2H, d, J = 7.2 Hz), 7.64–7.52
(6H, m), 7.52–7.46 (1H, m), 7.46–7.36 (2H, m), 4.82–4.69 (1H, m), 4.04–3.75 (2H, m), 2.27–1.95 (4H, m), 1.74–1.51 (2H, m), 1.30 (9H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 157.2, 155.5, 154.3, 134.0, 133.8, 132.1, 131.2, 129.7, 129.4, 129.1, 128.4, 128.3, 80.2, 70.0, 44.3, 32.8, 28.3. Data in accordance with the literature.$^7$

**tert-Butyl 4-((1H-Imidazole-1-carbonothioyl)oxy)piperidine-1-carboxylate (32)**

This procedure was adapted from a literature procedure:$^7$ a round-bottom flask equipped with a stirring bar was charged with tert-butyl 4-hydroxypiperidine-1-carboxylate (5.00 g, 24.8 mmol, 1.0 equiv.), DMAP (1.12 g, 9.94 mmol, 0.25 equiv.) and CH$_2$Cl$_2$ (75 mL, 0.33 M). Thiocarbonyldiimidazole (6.64 g, 37.3 mmol, 1.5 equiv.) was added and then the mixture was heated under reflux for 3 h. The mixture was cooled to r.t. and diluted with H$_2$O (100 mL). The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (75 mL). The combined organic layers were washed with brine (100 mL), dried (MgSO$_4$), filtered and evaporated. Purification by flash column chromatography on silica gel gave 32 (6.91 g, 90%) as a solid. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.33 (1H, s), 7.61 (1H, s), 7.03 (1H, s), 5.70–5.63 (1H, m), 3.76–3.70 (2H, m), 2.08–2.02 (2H, m), 1.90–1.82 (2H, m), 1.47 (9H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 183.1, 154.7, 136.9, 131.0, 117.9, 80.2, 79.5, 30.0, 28.5. Data in accordance with the literature.$^8$
3 Reaction Optimisations

3.1 Pictures of Reaction Set-Up

Figure S1.
3.2 Hydroxymethylation of Alkyl Iodides

General Procedure for the Hydroxymethylation of 1 – GP2

An oven-dry tube equipped with a stirring bar was charged with tert-butyl 4-iodopiperidine-1-carboxylate (31 mg, 0.1 mmol, 1.0 equiv.), photocatalyst (5 µmol, 5 mol%) and PR3 (0.3 mmol, 3.0 equiv.). The tube was capped with a Supelco aluminium crimp seal with septum (PTFE/butyl), evacuated and refilled with N2 (x 3). Dry and degassed organic solvent (1.0 mL, 0.1 M), H2O (100 µL), H2CO (31 µL, 0.4 mmol, 4 equiv.) and amine (0.3 mmol, 3.0 equiv.) were sequentially added. The tube was place in front of the blue LEDs (approx. 10 cm) and the lights were switched on. The mixture was stirred under continuous irradiation for 16 h whilst being cooled by a fan to give an internal temperature between 25–30 °C. The lights were switched off and the tube was opened. The mixture was diluted with brine (2 mL) and EtOAc (2 mL), then 1,3-dintrobenzene (1 mL, 0.05 M solution in EtOAc) was added as an internal standard and the mixture was vigorously shaken. The layers were separated and the aqueous layer was extracted with EtOAc (x 2). The combined organic layers were dried (MgSO4), filtered and evaporated. The crude was solubilised in CDCl3 and analysed by 1H NMR spectroscopy.

| Entry | Amine | PR3 | Solvent           | Yield (%) |
|-------|-------|-----|-------------------|-----------|
| 1     | Et3N  | –   | CH3CN–H2O (10:1) | 27        |
| 2     | i-Pr2NEt | – | CH3CN–H2O (10:1) | 35        |
| 3     | i-Pr2NH | – | CH3CN–H2O (10:1) | –         |
| 4     | TMP   | –   | CH3CN–H2O (10:1) | –         |
| 5     | PMP   | –   | CH3CN–H2O (10:1) | 11        |
| 6     | DABCO | –   | CH3CN–H2O (10:1) | –         |
| 7     | Ph3N  | –   | CH3CN–H2O (10:1) | –         |
| 8     | i-Pr2NEt | PPh3 | CH3CN–H2O (10:1) | 60        |
| 9a    | i-Pr2NEt | PPh3 | CH3CN–H2O (10:1) | 61        |
To further improve the efficiency of the process we have used the statistical software Ellistat for DoE. We investigated the effects of varying equivalents of amine, PPh₃, HCHO and H₂O leading us to the conditions reported in Scheme S1.

![Scheme S1.](image)

Further screening was performed using the conditions described below (Scheme S2) according to GP2, which is detailed in Table S2.

![Scheme S2.](image)

### Table S2.

| Entry | Photocatalyst | PR₃ | Solvent                | Yield (%) |
|-------|---------------|-----|-----------------------|-----------|
| 10    | 4CzIPN        | PPh₃| CH₃CN–H₂O (20:1)       | 86        |
| 11    | 4CzIPN        | P(4-F-C₆H₄)₃| CH₃CN–H₂O (20:1) | 78        |
| 12    | 4CzIPN        | P(4-CF₃-C₆H₄)₃| CH₃CN–H₂O (20:1) | 76        |
| 13    | 4CzIPN        | P(C₆F₅)₃| CH₃CN–H₂O (20:1)      | 26        |
| 14    | 4CzIPN        | P(4-MeO-C₆H₄)₃| CH₃CN–H₂O (20:1) | 70        |
| 15    | 4CzIPN        | P(1-Nap)₃| CH₃CN–H₂O (20:1)      | 40        |
| 16    | 4CzIPN        | PCy₃ | CH₃CN–H₂O (20:1)       | 65        |
| 17    | 4CzIPN        | P(t-Bu)₃| CH₃CN–H₂O (20:1)      | 43        |
| 18    | 4CzIPN        | P(OEt)₃| CH₃CN–H₂O (20:1)      | 40        |
| 19    | 4CzIPN        | P(OPh)₃| CH₃CN–H₂O (20:1)       | 74        |
| 20    | 4CzIPN        | Ph₂PO| CH₃CN–H₂O (20:1)       | 48        |
| 21    | 4CzIPN        | BPh₃ | CH₃CN–H₂O (20:1)       | –         |
| 22a   | 4CzIPN        | –   | CH₃CN–H₂O (20:1)       | –         |
|   | Compound     | Ligand | Solvent           | Conversion (%) |
|---|--------------|--------|-------------------|----------------|
|23 | 4CzIPN       | PPh₃   | DMF–H₂O (20:1)    | 58             |
|24 | 4CzIPN       | PPh₃   | DMSO–H₂O (20:1)   | 67             |
|25 | 4CzIPN       | PPh₃   | toluene–H₂O (20:1)| –              |
|26 | Ru(bpy)₃Cl₂  | PPh₃   | CH₃CN–H₂O (20:1)  | 18             |
|27 | Eosin Y (Na salt) | PPh₃ | CH₃CN–H₂O (20:1)  | 36             |
|28 | Rhodamine 6G | PPh₃   | CH₃CN–H₂O (20:1)  | 36             |
|29 | Ir(ppy)₃     | PPh₃   | CH₃CN–H₂O (20:1)  | 59             |
|30 | Ir(ppy)₂(dtbbpy)PF₆ | PPh₃ | CH₃CN–H₂O (20:1)  | 73             |
|31 | –            | PPh₃   | CH₃CN–H₂O (20:1)  | 25             |
|32a| 4CzIPN       | PPh₃   | CH₃CN–H₂O (20:1)  | –              |
|33b| 4CzIPN       | PPh₃   | CH₃CN–H₂O (20:1)  | –              |

a = no amine; b = no light
3.3 Hydroxymethylation of Katritzky’s Pyridiniums

General Procedure for the Hydroxymethylation of 31 via Photoredox Catalysis – GP3

An oven-dry tube equipped with a stirring bar was charged with 31 (54 mg, 0.1 mmol, 1.0 equiv.), the photocatalyst (5 µmol, 5 mol%) and the phosphine (0.3 mmol, 3.0 equiv.). The tube was capped with a Supelco aluminium crimp seal with septum (PTFE/butyl), evacuated and refilled with N\textsubscript{2} (x 3). Dry and degassed CH\textsubscript{3}CN (1.0 mL, 0.1 M), H\textsubscript{2}O (100 µL), and H\textsubscript{2}CO (78 µL, 1.0 mmol, 10 equiv.) were sequentially added. The tube was place in front of the blue LEDs and the lights were switched on. The reaction setup was covered in aluminium foil and the mixture was stirred under continuous irradiation for 16 h. The lights were switched off and the tube was opened. The mixture was diluted with brine (2 mL) and EtOAc (2 mL), then 1,3-dinitrobenzene (1 mL, 0.05 M solution in EtOAc) was added as an internal standard and the mixture was vigorously shaken. The layers were separated, and the aqueous layer was extracted with EtOAc (x 2). The combined organic layers were dried (MgSO\textsubscript{4}), filtered and evaporated. The crude was solubalised in CDCl\textsubscript{3} and analysed by \textsuperscript{1}H NMR spectroscopy.

| Entry | Photocatalyst          | Phosphine | Additive               | Yield (%) |
|-------|------------------------|-----------|------------------------|-----------|
| 1\textsuperscript{a} | 4CzIPN                 | PPh\textsubscript{3} | Na-ascorbate (2 eq.)   | 5         |
| 2\textsuperscript{a} | [Ir(dtbbpy)(ppy)\textsubscript{2}]PF\textsubscript{6} | PPh\textsubscript{3} | Na-ascorbate (2 eq.)   | 12        |
| 3\textsuperscript{a} | [Ir(dF(CF\textsubscript{3})ppy)\textsubscript{2}(dtbbpy)]PF\textsubscript{6} | PPh\textsubscript{3} | Na-ascorbate (2 eq.)   | 10        |
| 4\textsuperscript{a} | [Ru(bpy)\textsubscript{3}]Cl\textsubscript{2} | PPh\textsubscript{3} | Na-ascorbate (2 eq.)   | 10        |
| 5\textsuperscript{a} | Rose Bengal            | PPh\textsubscript{3} | Na-ascorbate (2 eq.)   | 9         |
| 6\textsuperscript{a} | Ir(ppy)\textsubscript{3} | PPh\textsubscript{3} | Na-ascorbate (2 eq.)   | 8         |
| 7\textsuperscript{b} | Ir(ppy)\textsubscript{3} | PPh\textsubscript{3} | Na-ascorbate (2 eq.)   | 56        |
| 8\textsuperscript{b} | Ir(ppy)\textsubscript{3} | PPh\textsubscript{3} | Ph\textsubscript{3}N    | 59        |
| 9\textsuperscript{b} | [Ir(dtbbpy)(ppy)\textsubscript{2}]PF\textsubscript{6} | PPh\textsubscript{3} | Ph\textsubscript{3}N    | 62        |
| 10\textsuperscript{b} | Ir(ppy)\textsubscript{3} | PPh\textsubscript{3} | –                      | 69        |
| 11\textsuperscript{b} | [Ir(dtbbpy)(ppy)\textsubscript{2}]PF\textsubscript{6} | PPh\textsubscript{3} | –                      | 45        |
| 12\textsuperscript{b} | Ir(ppy)\textsubscript{3} | P(4-CF\textsubscript{3}-C\textsubscript{6}H\textsubscript{4})\textsubscript{3} | –         | 10        |
| 13\textsuperscript{b} | Ir(ppy)\textsubscript{3} | PCy\textsubscript{3} | –                      | 27        |
| Entry | Electron Donor | Solvent            | Concentration | Yield (%) |
|-------|----------------|--------------------|---------------|-----------|
| 1a    | Et$_3$N        | CH$_3$CN–H$_2$O (20:1) | 0.1 M         | 22        |
| 2a    | i-Pr$_2$NEt    | CH$_3$CN–H$_2$O (20:1) | 0.1 M         | 37        |
| 3a    | HE             | CH$_3$CN–H$_2$O (20:1) | 0.1 M         | 10        |
| 4a    | HE             | CH$_3$CN–H$_2$O (20:1) | 0.2 M         | 10        |
| 5     | HE             | CH$_3$CN–H$_2$O (10:1)| 0.5 M         | 31        |
| 6     | HE             | DMA–H$_2$O (10:1)    | 0.5 M         | 28        |
| 7     | HE             | HFIP–H$_2$O (10:1)   | 0.5 M         | 41        |

* room temperature, $^\text{b}$ 60°C
| 8 | 4-Me-HE | HFIP–H₂O (10:1) | 0.5 M | 72 |
|---|---|---|---|---|
|   | a = K₂CO₃ (1.5 equiv.) |   |   |   |

![Diagram of chemical structures](image)
3.4 Hydroxymethylation of Thiocarbamates

**General Procedure for the Hydroxymethylation of 33 – GP5**

An oven-dry tube equipped with a stirring bar was charged with 33 (31 mg, 0.1 mmol, 1.0 equiv.), the photocatalyst (1-5 µmol, 1-5 mol%) and the phosphine (0.3 mmol, 3.0 equiv.). The tube was capped with a Supelco aluminium crimp seal with septum (PTFE/butyl), evacuated and refilled with N₂ (x 3). Dry and degassed CH₃CN (1.0 mL, 0.1 M), H₂O (100 µL), H₂CO (78 µL, 1.0 mmol, 10 equiv.) and the amine (0.2 mmol, 2.0 equiv.) were sequentially added. The tube was place in front of the blue LEDs (approx. 10 cm) and the lights were switched on. The mixture was stirred under continuous irradiation for 16 h whilst being cooled by a fan to give an internal temperature between 25–30 °C. The lights were switched off and the tube was opened. The mixture was diluted with brine (2 mL) and EtOAc (2 mL), then 1,3-dintrobenzene (1 mL, 0.05 M solution in EtOAc) was added as an internal standard and the mixture was vigorously shaken. The layers were separated and the aqueous layer was extracted with EtOAc (x 2). The combined organic layers were dried (MgSO₄), filtered and evaporated. The crude was solubilised in CDCl₃ and analysed by ¹H NMR spectroscopy.

| Entry | Photocatalyst (mol%) | PR₃    | Amine       | Yield (%) |
|-------|----------------------|--------|-------------|-----------|
| 1     | 4CzIPN (5%)          | PPh₃   | i-Pr₂NEt    | 22        |
| 2     | Ir(ppy)₃ (5%)        | PPh₃   | i-Pr₂NEt    | 29        |
| 3     | [Ir(dtbbpy)(ppy)₂]PF₆ (5%) | PPh₃ | i-Pr₂NEt    | 12        |
| 4     | fluorescein (5%)     | PPh₃   | i-Pr₂NEt    | –         |
| 5     | eosin Y (Na salt) (5%) | PPh₃ | i-Pr₂NEt    | –         |
| 6     | rose bengal (5%)     | PPh₃   | i-Pr₂NEt    | –         |
| 7     | rhodamine 6G (5%)    | PPh₃   | i-Pr₂NEt    | –         |
| 8     | Ir(ppy)₃ (1%)        | PPh₃   | i-Pr₂NEt    | 30        |
| 9     | Ir(ppy)₃ (1%)        | PPh₃   | Et₃N        | 25        |
| 10    | Ir(ppy)₃ (1%)        | PPh₃   | i-Pr₂NMe    | 27        |
| 11    | Ir(ppy)₃ (1%)        | PPh₃   | n-Bu₃N      | 28        |
|   | Reactant | Ligand | Additive | Yield |
|---|----------|--------|----------|-------|
| 12 | Ir(ppy)$_3$ (1%) | PPh$_3$ | $i$-Bu$_3$N | 14 |
| 13 | Ir(ppy)$_3$ (1%) | PPh$_3$ | PMP | 13 |
| 14 | Ir(ppy)$_3$ (1%) | PPh$_3$ | Bn$_3$N | – |
| 15$^a$ | Ir(ppy)$_3$ (1%) | PPh$_3$ | $i$-Pr$_2$NEt | 15 |
| 16 | Ir(ppy)$_3$ (1%) | P(4-OMe-C$_6$H$_4$)$_3$ | $i$-Pr$_2$NEt | 16 |
| 17 | Ir(ppy)$_3$ (1%) | P(4-F-C$_6$H$_4$)$_3$ | $i$-Pr$_2$NEt | – |
| 18$^b$ | Ir(ppy)$_3$ (1%) | PPh$_3$ | $i$-Pr$_2$NEt | 47 |
| 19 | Ir(ppy)$_3$ (1%) | PPh$_3$ | $i$-Pr$_2$NEt | 22 |
| 20 | Ir(ppy)$_3$ (1%) | PPh$_3$ | $i$-Pr$_2$NEt | – |

$a = 20$ mol% $i$-Pr$_2$NEt; $b =$ reaction concentration 0.05 M
4 Mechanistic Considerations

4.1 Proposed Mechanism for Hydroxymethylation of Alkyl Iodides

Scheme S3.
4.2 Stern-Volmer Quenching Studies

Stern-Volmer experiments were carried out monitoring the emission intensity of argon-degassed solutions of 4CzIPN (3 x 10^{-5} M solution in CH3CN) containing variable amounts of the quencher in dry acetonitrile. The reported excited-state lifetime for 4CzIPN in CH3CN (1.4 \text{s})^{9} was used for $k_q$ calculations (see Table S6). These experiments show the $i$-Pr$_2$NEt quenches *4CzIPN at faster rates than any other reagent (Figure S2 and Table S6).

![Figure S2.](image)

**Table S6.**

| Entry | Quencher | $K_q \times 10^{-7}$ (M$^{-1}$ s$^{-1}$) |
|-------|----------|--------------------------------------|
| 1     | $i$-Pr$_2$NEt | 156 |
| 2     | PPh$_3$ | 14.8 |
| 3     | 2.31 |
| 4     | 0.814 |
4.3 Ruling Out the Formation of Electron Donor-Acceptor (EDA) Complexes
To rule out the formation of EDA complexes between the alkyl iodide and the amine that might be absorbing in the visible region, we have performed UV/Vis absorption spectroscopy studies (Figure S3). These studies demonstrate that there is not EDA complexation between the amine and the alkyl iodide.

![Figure S3](image-url)
4.4 Evidences Supporting XAT by the Phosphoranyl Radical

In order to obtain supporting evidences on the ability of phosphoranyl radicals to sustain a chain-propagation based on XAT, we evaluated the hydroxymethylation of 1 in the absence of amines as well as any other possible reductant (e.g. *4CzIPN or 4CzIPN⁻).

We speculated that by treatment of 1, HCHO and PPh₃ with (t-BuO)₂, the phosphoranyl radical X could be obtained upon O–O bond homolysis (photochemical or thermal) and diffusion-controlled reaction of t-BuO• with PPh₃ (Scheme S4). X would then act as an initiating species for the generation of the alkyl radical F upon XAT on 1. Reaction of F with HCHO followed by fast trap of the O-radical H with PPh₃ would provide the chain carrier phosphoranyl radical J from which product formation can occur.

Pleasingly, irradiation of 1, HCHO, PPh₃ and (t-BuO)₂ with purple LEDs (390 nm) led to the formation of 3 in 50% yield (Scheme 5A). Control experiments in the absence of (t-BuO)₂ resulted in full starting material recovery thus proving the homolytic activation of the sp³ C–I bond was not taking place under these conditions (Scheme 5B).

Under these conditions we monitored the reaction by NMR to detect formation of MeI or acetone, formed from β-fragmentation of the phosphoranyl radical X. Neither of these side-products were detected, ruling out the possibility that Me• was generated and acted as XAT agent/initiator.
Procedure for the Peroxide Initiated Hydroxymethylation of 1

An oven-dry tube equipped with a stirring bar was charged with tert-butyl 4-iodopiperidine-1-carboxylate (31 mg, 0.1 mmol, 1.0 equiv.) and PPh₃ (78 mg, 0.3 mmol, 3.0 equiv.). The tube was capped with a Supelco aluminium crimp seal with septum (PTFE/butyl), evacuated and refilled with N₂ (x 3). Dry and degassed CH₃CN (1.0 mL, 0.1 M), H₂O (100 µL), H₂CO (78 µL, 1.0 mmol, 10 equiv.) and (t-BuO)₂ (9.2 µL, 0.05 mmol, 0.5 equiv.) were sequentially added. The tube was place in front of the purple LEDs (approx. 10 cm) and the lights were switched on. The mixture was stirred under continuous irradiation overnight whilst either being cooled by a fan or in an oil bath at 70 °C. The lights were switched off and the tube was opened. The mixture was diluted with brine (2 mL) and EtOAc (2 mL), then 1,3-dintrobenzene (1 mL, 0.05 M solution in EtOAc) was added as an internal standard and the mixture was vigorously shaken. The layers were separated and the aqueous layer was extracted with EtOAc (x 2). The combined organic layers were dried (MgSO₄), filtered and evaporated. The crude was solubilised in CDCl₃ and analysed by ¹H NMR spectroscopy.
4.5 Quantum Yield (Φ) Determination

The quantum yield (Φ) of the photochemical hydroxymethylation reaction of 1 was determined at 50 ºC following procedures described in literature (Scheme S6). Elevated temperatures were required to accelerate the reaction for quantum yield determination, as it was not possible to record an accurate quantum yield at room temperature due to the reaction progressing slowly. The degassed reaction tube was irradiated using blue LEDs plates (λmax = 444 nm) and product yield was determined by 1H NMR spectroscopy analysis. The photon flux of the blue LEDs used was determined by standard ferrioxalate actinometry.11

Reactions where a radical chain propagations is present are typically expected to provide a Φ > 1. In our case we have observed that the hydroxymethylation reaction displays a significant induction time that might account for the low Φ observed (Figure S4).

Figure S4.
4.6 Hydroxymethylation of Alkyl Bromide 30

We have evaluated the reactivity of alkyl bromide 30 under our standard conditions since \( \alpha \)-aminoalkyl radical-mediated XAT is feasible.\(^{12}\) However, the desired product 2 was obtained in low yield with remaining 30 accounting for the remaining mass balance (Scheme S7).

![Scheme S7](image)

Despite considerable efforts aimed at optimising this reactivity changing all reaction parameters we did not succeed in engaging this class of derivatives in higher yield. According to our proposed mechanism we speculated that there might have been an issue with one of the two XAT steps: either the one mediated with the \( \alpha \)-aminoalkyl radical or the one mediated by the phosphoranyl radical. Various alkylamines were screened to evaluate their impact in the reactivity (Table S7).

| Entry | Amine      | Yield (%) |
|-------|------------|-----------|
| 1     | \( i\)-Pr\(_2\)NEt | 25        |
| 2     | PMP        | 25        |
| 3     | \( i\)-Pr\(_2\)NMe | 14        |
| 4     | \( i\)-Pr\(_2\)NH | –         |
| 5     | Et\(_3\)N  | –         |
| 6     | \( n\)-Bu\(_3\)N | –         |
| 7     | \( i\)-Bu\(_3\)N | –         |
| 8     | Bn\(_3\)N  | –         |
| 9     | Me\(_3\)N  | –         |
| 10    | Cy\(_3\)N  | –         |
| 11    | PhNMe\(_2\) | –         |
| 12    | BnNPh\(_2\) | –         |
As shown in Table S7, this led to no improvement in the reaction yield. Interestingly, we detected the hydroxymethylation of some amines by mass spectrometry analysis of the reaction crudes. This suggests that in the case of the alkyl bromides were XAT is slower, the nucleophilic α-aminoalkyl radical can trap HCHO and undergo PPh₃-mediated hydroxymethylation. To obtain further evidences on this reactivity we have performed DFT studies to determine the reaction parameters for the addition step. As shown in Scheme S8, the reaction of an α-aminoalkyl radical derived from Et₃N should undergo a feasible addition to HCHO.

![Scheme S8](image)

Depending on the structure of the amine, mono- or tri-hydroxymethylation was observed.

2-(Diisopropylamino)propan-1-ol (S16)

HRMS (ESI): Found M+H⁺ 160.1691, C₉H₂₂NO requires 160.1696.

2,2',2''-Nitrilotris(pentan-1-ol) (S17)

HRMS (ESI): Found M-H⁻ 274.2393, C₁₅H₃₂NO₃ requires 274.2382.

2,2',2''-Nitrilotris(propan-1-ol) (S18)

HRMS (ESI): Found M-H⁺ 190.1451, C₉H₂₀NO₃ requires 190.1449.
4.7 Cyclic Voltammetry Studies

General Experimental Details

Cyclic voltammetry was conducted on an EmStat (PalmSens) potentiostat using a 3-electrode cell configuration. A glassy carbon working electrode was employed alongside a platinum wire counter electrode and a Ag/AgCl reference electrode. All the solutions were degassed by bubbling Ar prior to measurements. 10 mM solutions of the desired compounds were freshly prepared in dry acetonitrile along with 0.1 M of tetrabutylammonium hexafluorophosphate as supporting electrolyte and were examined at a scan rate of 0.1 V s\(^{-1}\). Ferrocene (\(E_{1/2} = +0.42\) V vs SCE\(^{13}\)) was added at the end of the measurements as an internal standard to determine the precise potential scale. Potential values are given versus the saturated calomel electrode (SCE). When irreversible waves were obtained the potentials were estimated at half the maximum current, as previously described by Nicewicz.\(^{14}\)

### Table S8.

| Entry | Substrate | \(E_{\text{red}}\) (V vs SCE) |
|-------|-----------|-----------------------------|
| 1     | (Ph\(_3\)POMe)OTf | –1.65                       |
| 2     | ![Substrate 2](image) | –0.89                       |
| 3     | ![Substrate 3](image) | –1.71                       |
5 Reaction Scope

General Procedure for the Hydroxymethylation of Alkyl Iodides – GP6

An oven-dry tube equipped with a stirring bar was charged with the alkyl iodide (0.1 mmol, 1.0 equiv.), 4CzIPN (4 mg, 5 μmol, 5 mol%) and PPh₃ (78 mg, 0.3 mmol, 3.0 equiv.). The tube was capped with a Supelco aluminium crimp seal with septum (PTFE/butyl), evacuated and refilled with N₂ (x 3). Dry and degassed CH₃CN (1.0 mL, 0.1 M), H₂O (50 μL), H₂CO (78 μL, 1.0 mmol, 10 equiv.) and (i-Pr)₂NEt (53 μL, 0.3 mmol, 3.0 equiv.) were sequentially added. The tube was placed in front of the blue LEDs (approx. 10 cm) and the lights were switched on. The mixture was stirred under continuous irradiation for 16 h whilst being cooled by a fan to give an internal temperature between 25–30 °C. The lights were switched off and the tube was opened. The mixture was diluted with brine (2 mL) and EtOAc (2 mL), then 1,3-dintrobenzene (1 mL, 0.05 M solution in EtOAc) was added as an internal standard and the mixture was vigorously shaken. The layers were separated and the aqueous layer was extracted with EtOAc (x 2). The combined organic layers were dried (MgSO₄), filtered and evaporated. Purification by flash column chromatography on silica gel gave the products.

*tert*-Butyl 4-(Hydroxymethyl)piperidine-1-carboxylate (2)

Following GP6, *tert*-butyl 4-iodopiperidine-1-carboxylate (31 mg, 0.1 mmol) gave 2 (19 mg, 86%) as an oil. ¹H NMR (500 MHz, CDCl₃) δ 4.14–4.09 (2H, m), 3.48 (2H, d, J = 6.3 Hz), 2.72–2.69 (2H, m), 1.74–1.67 (4H, m), 1.44 (9H, s), 1.14–1.09 (2H, m); ¹³C NMR (126 MHz, CDCl₃) δ 155.0, 79.5, 67.6, 43.9, 38.9, 28.7, 28.6. Data in accordance with the literature.¹⁵

*tert*-Butyl 3-(Hydroxymethyl)piperidine-1-carboxylate (3)

Following GP6, *tert*-butyl 3-iodopiperidine-1-carboxylate (31 mg, 0.1 mmol) gave 3 (18 mg, 85%) as an oil. ¹H NMR (500 MHz, CDCl₃) δ 3.78–3.50 (4H, m), 3.06–2.95 (2H, m), 1.81–
1.53 (4H, m), 1.45 (9H, s), 1.33–1.24 (1H, m); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 155.3, 79.5, 64.5, 46.5, 44.8, 38.1, 28.5, 26.9, 23.9. Data in accordance with literature.$^{16}$

**tert-Butyl 4-(Hydroxymethyl)azepane-1-carboxylate (4)**

![Diagram of tert-Butyl 4-(Hydroxymethyl)azepane-1-carboxylate]

Following GP6, *S1* (33 mg, 0.1 mmol) gave 4 (21 mg, 90%) as an oil. R$_f$ 0.4 [EtOAc:pentane 7:3]. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.55 (1H, dt, $J$ = 14.2, 5.0 Hz), 3.51–3.43 (3H, m), 3.30–3.22 (2H, m), 1.93–1.81 (3H, m), 1.62–1.51 (2H, m), 1.45 (9H, s), 1.34–1.25 (1H, m), 1.17–1.10 (1H, m). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 155.7, 79.2, 68.2, 46.7, 45.5, 41.8, 31.4, 29.8, 28.7, 27.2. A HRMS could not be obtained for this compound.

**tert-Butyl 3-(Hydroxymethyl)pyrrolidine-1-carboxylate (5)**

![Diagram of tert-Butyl 3-(Hydroxymethyl)pyrrolidine-1-carboxylate]

Following GP6, tert-butyl 3-iodopyrrolidine-1-carboxylate (30 mg, 0.1 mmol) gave 5 (13 mg, 65%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.65–3.58 (2H, m), 3.52–3.35 (2H, m), 3.34–3.22 (1H, m), 3.10–3.04 (1H, m), 2.65 (1H, s), 2.42–2.32 (1H, m), 2.01–1.85 (1H, m), 1.73–1.56 (1H, m), 1.42 (9H, s); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 154.6, 79.0, 63.7, 48.6, 48.1, 45.3, 44.9, 41.1, 40.3, 28.3. Data in accordance with the literature.$^{17}$

**1-(tert-Butyl) 2-Methyl 4-(hydroxymethyl)pyrrolidine-1,2-dicarboxylate (6)**

![Diagram of 1-(tert-Butyl) 2-Methyl 4-(hydroxymethyl)pyrrolidine-1,2-dicarboxylate]

Following GP6, *S2* (36 mg, 0.1 mmol) gave 6 (16 mg, 62%) as an oil as a mixture of diastereomers. *trans:cis* 1.5:1. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.39 (0.4H, $J$ = 8.6, 2.8 Hz), 4.29 (0.6H, dd, $J$ = 7.5, 4.9 Hz), 3.70–3.60 (3H, m), 3.25 (0.6H, dd, $J$ = 10.4, 7.3 Hz), 3.19 (0.4H, dd, $J$ = 10.4, 8.0 Hz), 2.67–2.47 (1H, m), 2.17–1.59 (2H, m), 1.46 (3.6H, s), 1.41 (5.4H, s); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 173.6, 173.5, 154.6, 154.0, 80.2, 80.1, 63.7, 63.5, 59.0, 58.7, 52.2, 52.0, 49.1, 48.7, 39.8, 39.0, 33.0, 32.3, 28.4, 28.3. Data in accordance with literature.$^{18}$
**tert-Butyl 3-(Hydroxymethyl)azetidine-1-carboxylate (7)**

Following GP6, tert-butyl 3-iodoazetidine-1-carboxylate (28 mg, 0.1 mmol) gave 7 (12 mg, 66%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.99 (2H, t, $J = 8.5$ Hz), 3.78 (2H, d, $J = 6.6$ Hz), 3.68 (2H, dd, $J = 8.8$, 5.2 Hz), 2.74–2.67 (1H, m), 1.43 (9H, s); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 156.6, 79.6, 64.8, 30.6, 28.5. Data in accordance with the literature.$^{19}$

**(Tetrahydro-2H-pyran-4-yl)methanol (8)**

Following GP6, 4-iodotetrahydro-2H-pyran (21 mg, 0.1 mmol) gave 8 (10 mg, 84%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.00 (2H, dd, $J = 11.7$, 4.6 Hz), 3.51 (2H, d, $J = 6.4$ Hz), 3.41 (2H, td, $J = 11.7$, 2.1 Hz), 1.81–1.71 (1H, m), 1.68–1.62 (3H, m), 1.37 (1H, dd, $J = 12.1$, 4.5 Hz), 1.31 (1H, dd, $J = 12.1$, 4.5 Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 67.9, 67.7, 37.7, 29.4. Data in accordance with literature.$^{20}$

**(2-(4-Bromophenyl)tetrahydro-2H-pyran-4-yl)methanol (9)**

Following GP6, S14 (37 mg, 0.1 mmol) gave 9 (20 mg, 74%) as an oil as a mixture of diastereomers. cis:trans 3:1. $R$y 0.41 [EtOAc:Pentane 1:1; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.54–7.35 (2H, m), 7.26–7.16 (2H, m), 4.61 (0.25H, dd, $J = 9.0$, 3.4 Hz), 4.31 (0.75H, dd, $J = 11.2$, 2.1 Hz), 4.20 (0.75H, ddd, $J = 11.5$, 4.7, 1.6 Hz), 3.93 (0.25H, ddd, $J = 10.9$, 6.3, 4.5 Hz), 3.81–3.72 (0.5H, m), 3.62 (0.75H, ddd, $J = 12.5$, 11.5, 2.3 Hz), 3.58–3.43 (1.5H, m), 2.06 (0.25H, tt, $J = 7.4$, 4.8 Hz), 1.99–1.87 (1.5H, m), 1.87–1.77 (0.5H, m), 1.71 (0.75H, ddq, $J = 13.3$, 3.9, 2.0 Hz), 1.44–1.35 (0.75H, m), 1.35–1.17 (1.5H, m); $^{13}$C NMR (126 MHz, CDCl$_3$, diastereomers) $\delta$ 142.14, 141.54, 131.60, 131.55, 131.54, 128.01, 127.66, 121.27, 121.14, 78.83, 73.85, 68.22, 67.92, 64.63, 63.38, 38.52, 37.26, 33.59, 33.53, 28.99, 27.24.
(Tetrahydro-2H-thiopyran-4-yl)methanol (10)

Following **GP6, S3** (23 mg, 0.1 mmol) gave 10 (10 mg, 73%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 3.47 (2H, d, J = 6.4 Hz), 2.70 (2H, ddd, J = 14.3, 11.9, 2.6 Hz), 2.64–2.58 (2H, m), 2.07 (2H, dd, J = 13.5, 3.5 Hz), 1.59 (1H, br s), 1.57–1.48 (1H, m), 1.39 (1H, dtd, J = 13.1, 11.8, 3.5 Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 68.4, 40.2, 30.8, 28.3. Data in accordance with literature.\textsuperscript{21}

4-(Hydroxymethyl)cyclohexan-1-one (11)

Following **GP6**, 4-iodocyclohexan-1-one (22 mg, 0.1 mmol) gave 11 (8 mg, 63%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 3.58 (2H, d, J = 6.6 Hz), 2.48–2.34 (4H, m), 2.13–2.08 (2H, m), 2.06–1.89 (1H, m), 1.45 (2H, dq, J = 12.1, 5.5 Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 212.9, 66.5, 40.4, 38.5, 29.1. Data in accordance with literature.\textsuperscript{22}

(4-Phenylcyclohexyl)methanol (12)

Following **GP6, S4** (29 mg, 0.1 mmol) gave 12 (19 mg, quant.) as an oil as a mixture of diastereomers. cis:trans 1.5:1. $^1$H NMR (500 MHz, CDCl$_3$, diastereomers) δ 7.31–7.28 (2H, d, J = 6.6 Hz), 2.64–2.60 (0.6H, m), 2.52–2.46 (0.4H, m), 2.03–1.33 (8.2H, m), 1.27–1.04 (0.8H, m); $^{13}$C NMR (126 MHz, CDCl$_3$, diastereomers) δ 147.4, 147.1, 128.3, 128.2, 126.9, 126.7, 125.8, 68.2, 64.2, 44.4, 43.3, 40.0, 35.8, 33.7, 29.8, 29.1, 26.9. Data in accordance with literature.\textsuperscript{23}

(Adamantan-2-yl)methanol (13)

Following **GP6**, 2-iodoadamantane (26 mg, 0.1 mmol) gave 13 (13 mg, 79%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 3.74 (2H, d, J = 7.1 Hz), 1.94–1.90 (1H, m), 1.89–1.84 (4H, m),

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1.83–1.79 (3H, m), 1.79–1.77 (1H, m), 1.75–1.72 (2H, m), 1.57 (1H, br s), 1.55 (3H, br s); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 65.3, 47.3, 39.1, 38.2, 31.9, 29.2, 28.4, 27.9. Data in accordance with literature.$^{21}$

(Adamantan-1-yl)methanol (14)

Following GP6, 1-iodoadamantane (26 mg, 0.1 mmol) gave 14 (14 mg, 85%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 3.20 (2H, s), 2.01–1.95 (3H, m), 1.76–1.69 (3H, m), 1.67–1.60 (3H, m), 1.54–1.46 (6H, m), 1.32 (1H, br s); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 73.9, 39.1, 37.3, 34.6, 28.3. Data in accordance with literature.$^{24}$

tert-Butyl (4-(hydroxymethyl)cyclohexyl)carbamate (15)

Following GP6, S5 (33 mg, 0.1 mmol) gave 15 (23 mg, quant.) as an oil as a mixture of diastereomers. cis:trans 1.5:1. $^1$H NMR (500 MHz, CDCl$_3$) δ 4.40 (1H, s), 3.45 (2H, d, $J$ = 6.3 Hz), 3.38 (1H, s), 2.05–2.02 (2H, m), 1.84–1.81 (2H, m), 1.44 (10H, s), 1.17–1.01 (4H, m). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 155.4, 79.3, 68.2, 67.3, 50.1, 46.5, 39.8, 38.8, 33.1, 29.8, 29.7, 28.6, 24.4. Data in accordance with literature.$^{25}$

tert-Butyl (3-(Hydroxymethyl)cyclobutyl)carbamate (16)

Following GP6, S6 (22 mg, 0.1 mmol) gave 16 (12 mg, 60%) as an oil as a mixture of diastereomers. cis:trans 1:1. $^1$H NMR (400 MHz, CDCl$_3$, diastereomers) δ 4.70 (1H, br. s), 4.17 (0.5H, br. s), 4.01 (0.5H, s), 3.67 (1H, d, $J$ = 7.3 Hz), 3.57 (1H, d, $J$ = 5.7 Hz), 2.48–2.39 (1H, m), 2.37–2.27 (2H, m), 2.05–1.93 (2H, m), 1.75–1.51 (1H, m), 1.66-1.54 (1H, m) 1.43 (9H, s). $^{13}$C NMR (101 MHz, CDCl$_3$, diastereomers) δ 155.09, 154.86, 79.71, 79.49, 66.59, 66.30, 44.21, 42.40, 33.65, 32.71, 30.80, 30.24, 28.54. Data in accordance with literature.$^{26}$
**tert-Butyl 2-(Hydroxymethyl)-7-azaspiro[3.5]nonane-7-carboxylate (17)**

Following **GP6, S7** (35 mg, 0.1 mmol) gave 17 (21 mg, 81%) as an oil. $R_f$ 0.35 [EtOAc:Pentane 1:1]; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.60 (2H, d, $J = 6.6$ Hz), 3.40–3.31 (2H, m), 3.29–3.21 (2H, m), 2.54–2.40 (1H, m), 1.95–1.85 (2H, m), 1.60–1.48 (6H, m), 1.44 (9H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 155.2, 79.4, 68.0, 40.6, 39.3, 36.8, 34.3, 30.6, 28.6. HRMS (ESI): Found M+Na$^+$ 278.1718, C$_{14}$H$_{25}$O$_3$NNa requires 278.1713.

**tert-Butyl 6-(Hydroxymethyl)-2-azaspiro[3.3]heptane-2-carboxylate (18)**

Following **GP6, S8** (32 mg, 0.1 mmol) gave 18 (12 mg, 55%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 3.92 (2H, s), 3.82 (2H, s), 3.56 (2H, d, $J = 6.4$ Hz), 2.35 (1H, hept, $J = 7.1$ Hz), 2.26–2.22 (2H, m), 1.96–1.92 (2H, m), 1.42 (9H, s); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 156.4, 79.4, 66.8, 62.4, 61.5, 35.4, 34.5, 31.5, 28.5; HRMS (ESI): Found M+Na$^+$ 250.1402, C$_{12}$H$_{21}$O$_3$NNa requires 250.1414.

**N-(4-(Hydroxymethyl)octahydropentalen-1-yl)acetamide (19)**

Following **GP6, S15** (29 mg, 0.1 mmol) gave 19 (12 mg, 62%) as an oil as a mixture of diastereomers. dr 1:1. $R_f$ 0.25 [CH$_2$Cl$_2$:MeOH 9:1]. $^1$H NMR (400 MHz, CDCl$_3$, diastereomers) $\delta$ 5.61 (2H, bs), 4.16–4.02 (1H, m), 3.88 (1H, ddd, $J = 7.6$, 5.6, 3.7 Hz), 3.67–3.45 (4H, m), 2.74–2.63 (1H, p, $J = 7.8$ Hz), 2.20 (1H, tt, $J = 5.8$, 3.0 Hz), 2.14–2.07 (1H, m), 1.96 (3H, s), 1.94 (3H, s), 1.84–1.17 (19H, m); $^{13}$C NMR (126 MHz, CDCl$_3$, diastereomers) $\delta$ 170.0, 169.8, 167.4, 164.5, 57.4, 53.3, 51.9, 51.1, 50.3, 45.2, 45.1, 44.8, 33.0, 30.9, 30.7, 30.0, 29.9, 29.3, 27.3, 23.7, 23.6.
**tert-Butyl 5-(Hydroxymethyl)hexahydrocyclopenta[c]pyrrole-2(1H)-carboxylate (21)**

Following **GP6, S9** (34 mg, 0.1 mmol) gave 21 (17 mg, 72%) as an oil as a mixture of diastereomers. dr 10:1. $^1$H NMR (400 MHz, CDCl$_3$) δ 3.53 (4H, d, $J = 6.8$ Hz), 3.13 (2H, m), 2.70 (2H, q, $J = 3.9$ Hz), 2.33 (1H, dq, $J = 15.2, 7.8$ Hz), 1.71–1.52 (4H, m), 1.45 (9H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 154.7, 79.2, 66.8, 44.8, 41.3, 35.2, 29.9, 28.7. Data in accordance with the literature.

**tert-Butyl (2S,5S)-5-(Hydroxymethyl)-2-methylpiperidine-1-carboxylate (23)**

Following **GP6, S10** (33 mg, 0.1 mmol) gave 23 (6 mg, 26%) as an oil as a mixture of diastereomers. trans:cis 3.3:1. $^1$H NMR (500 MHz, CDCl$_3$, diastereomers) δ 4.32 (0.22H, dd, $J = 12.6, 3.9$ Hz), 4.21 (0.78H, tt, $J = 10.3, 5.1$ Hz), 3.97 (0.22H, d, $J = 12.8$ Hz), 3.88 (0.78H, dd, $J = 14.3, 1.3$ Hz), 3.53–3.42 (2H, m), 2.95 (0.78H, dd, $J = 14.3, 3.5$ Hz), 2.47 (0.22H, t, $J = 12.4$ Hz) 2.05–1.45 (4H, m), 1.40 (9H, s), 1.12 (2.34H, d, $J = 6.9$ Hz), 1.04 (0.66H, d, $J = 6.9$ Hz); $^{13}$C NMR (126 MHz, CDCl$_3$, diastereomers) δ 156.1, 79.9, 79.4, 66.2, 62.2, 47.3, 39.3, 38.1, 37.3, 35.8, 32.1, 29.9, 28.6, 26.0, 22.8, 22.1, 20.5, 16.8, 14.3. Data in accordance with literature.

**7-(3-Hydroxy-2-methylpropyl)-1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione (25)**

Following **GP6, S11** (35 mg, 0.1 mmol) gave 25 (8.0 mg, 32%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 7.59 (1H, s), 4.38 (1H, dd, $J = 13.9, 6.9$ Hz), 4.26 (1H, dd, $J = 13.9, 5.4$ Hz), 3.60 (3H, s), 3.50 (1H, dd, $J = 11.5, 3.8$ Hz), 3.41 (3H, s), 3.38 (1H, dd, $J = 11.6, 6.5$ Hz), 2.22–2.15 (1H, m), 0.98 (3H, d, $J = 6.9$ Hz); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 156.0, 151.6, 149.1, 107.4, 63.5, 48.8, 37.6, 30.0, 28.3, 14.3; HRMS (APCI): Found M+H$^+$ 253.1295, C$_{11}$H$_{17}$O$_3$N$_4$ requires 253.1301.
**tert-Butyl 3-(Hydroxymethyl)-8-azabicyclo[3.2.1]octane-8-carboxylate (27)**

Following **GP6, S12** (34 mg, 0.1 mmol) gave 27 (17 mg, 70%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 4.36–4.14 (2H, m), 3.43 (2H, d, $J$ = 6.2 Hz) 2.15–1.99 (2H, m), 1.95 (2H, dt, $J$ = 7.5, 2.8 Hz), 1.75–1.61 (3H, m), 1.61–1.52 (2H, m), 1.45 (9H, s); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 153.6, 79.2, 77.2, 68.2, 31.5, 28.7. Note: some peaks aren’t visible due to the conformation flip of the compound. Data in accordance with literature.$^{29}$

**((85,95,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl) 2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)methanol (29)**

Following **GP6, S13** (50 mg, 0.1 mmol) gave 29 (16 mg, 40%) as an oil as a mixture of diastereomers. dr 2.3:1 $^1$H NMR (500 MHz, CDCl$_3$, diastereomers) $\delta$ 5.32–5.27 (1H, m), 3.57–3.46 (2H, m), 2.53–2.44 (1H, m), 2.10–0.85 (41H, m), 0.67 (3H, d, $J$ = 2.4 Hz); $^{13}$C NMR (126 MHz, CDCl$_3$, diastereomers) $\delta$ 142.0, 140.2, 121.3, 119.9, 68.4, 63.8, 56.7, 56.1, 50.4, 50.3, 42.2, 42.0, 39.8, 39.7, 39.4, 38.9, 37.4, 37.3, 36.7, 36.1, 35.7, 34.3, 33.7, 31.8, 28.2, 27.9, 25.3, 24.2, 23.8, 23.1, 22.8, 22.5, 20.9, 20.7, 19.4, 19.3, 18.6, 11.8. Data in accordance with literature.$^4$
6 Computational Studies

6.1 Computational Methods

Density functional theory (DFT)\textsuperscript{30} calculations were performed using Gaussian 09 (revision E.01)\textsuperscript{31} and the Gaussview\textsuperscript{3} was used to generate input geometries and visualize output structures. Geometry optimizations and frequency calculations for the calculation of reaction energies were performed using the B3LYP functional\textsuperscript{32} and an atom-pairwise dispersion correction (D3)\textsuperscript{33} with a flexible triplet zeta basis set (def2-TZVP)\textsuperscript{34} using acetonitrile to model solvation effect by applying the most commonly used integral equation formalism (IEF) version of polarized continuum model (PCM).\textsuperscript{35} The bond distance \([d(C–C)]\) between the carbon radical centre and carbon atom of CO or CH\textsubscript{2}O was calculated from the transition states structures and the amount of charge transfer (\(\delta^{TS}\)) from the carbon radical to the carbon atom of CO or CH\textsubscript{2}O in the transition states was evaluated from the Mulliken charges. For calculation of electronic properties of phosphoranyl radical, global and local electrophilicity index, B3LYP functional.\textsuperscript{32b,32d,36} was used and the geometry of studied radical was optimized at the UB3LYP/6-311+G(d,p) level of theory, followed by frequency calculation at the same level.\textsuperscript{37} The computed Hirshfeld charges on the radicals were also calculated at the same level of theory.\textsuperscript{38} All stationary points were characterized as minima based on normal vibrational mode analysis. Thermal corrections were computed from unscaled frequencies, assuming a standard state of 298.15 K and 1 atm.
6.2 Electronic Properties of Phosphoranyl Radical

*DFT Method*: UB3LYP/6-311+G(d,p)

| Phosphoranyl Radical | Ionization Potential (IP, eV) | Electron affinity (EA, eV) | Electronegativity (χ, eV) | Electronic Chemical Potential (μ, eV) | Chemical Hardness (η, eV) | Chemical Softness (S, meV) | Global Electrophilicity Index (ω, eV) | Local Electrophilicity Index (ω(rc), eV) | Hirshfeld Charge |
|----------------------|-------------------------------|-----------------------------|----------------------------|---------------------------------------|---------------------------|---------------------------|----------------------------------------|------------------------------------------|----------------|
| ![Phosphoranyl Radical](image) | 4.20                          | 0.27                        | 2.23                       | -2.23                                 | 3.93                      | 254.31                    | 0.64                                   | 0.07                                     | 0.3621          |

**Computed Energies** [values are in Hartree]

| Phosphoranyl Radical | Total Electronic Energy | Sum of Electronic and Zero-point Energies | Sum of Electronic and Thermal Enthalpies | Gibbs Free Energy |
|----------------------|-------------------------|------------------------------------------|----------------------------------------|-------------------|
| ![Phosphoranyl Radical](image) | -1386.3564642           | -1385.892647                             | -1385.866697                           | -1385.950731      |
Optimized Structure and Cartesian Coordinates

| No. | Phosphoranyl Radical | Optimized Structure |
|-----|----------------------|---------------------|
| 1   | ![Phosphoranyl Radical](image) | ![Optimized Structure](image) |

**Cartesian Coordinates**

| Atomic Symbol | X (Angstrom) | Y (Angstrom) | Z (Angstrom) |
|---------------|--------------|--------------|--------------|
| C             | -3.08059200  | 0.38203900   | -0.26609100  |
| C             | -4.10383100  | 1.38502100   | 0.29859800   |
| C             | -5.48772600  | 1.21116200   | -0.34397300  |
| C             | -5.99936200  | -0.22993900  | -0.20981900  |
| C             | -4.98197800  | -1.23639600  | -0.76428600  |
| C             | -3.60080900  | -1.05823300  | -0.11791600  |
| H             | -6.19923000  | 1.91039400   | 0.10719900   |
| H             | -4.18927600  | 1.23929400   | 1.38427500   |
| H             | -3.74697900  | 2.40981000   | 0.14804600   |
| H             | -2.95101300  | 0.59255000   | -1.33644300  |
| H             | -6.18431500  | -0.45021600  | 0.84987500   |
| H             | -6.96071300  | -0.33900400  | -0.72245200  |
| H             | -5.33806300  | -2.26030300  | -0.61039700  |
| H             | -4.89213200  | -1.09862000  | -1.84971600  |
| H             | -3.66737000  | -1.30127300  | 0.95198200   |
| H             | -2.88323400  | -1.75796600  | -0.55471200  |
| H             | -5.42477400  | 1.47449200   | -1.40766800  |
| C             | -1.72244200  | 0.58522500   | 0.39640500   |
| H             | -1.41801300  | 1.63433600   | 0.31577900   |
| H             | -1.76787600  | 0.32214600   | 1.46039600   |
| O             | -0.74270000  | -0.24746200  | -0.26118500  |
| P             | 0.89215200   | 0.02607200   | 0.00024500   |
| C             | 1.51219600   | -1.11469300  | -1.27678900  |
| C             | 0.70739200   | -2.11644500  | -1.84189800  |
| C             | 2.88217800   | -1.08664000  | -1.58556400  |
| C             | 1.26536200   | -3.06028800  | -2.70314800  |
|   | X   | Y   | Z   |
|---|-----|-----|-----|
| H | -0.34961600 | -2.14125800 | -1.61686100 |
| C | 3.42733100  | -2.01761500  | -2.46156300  |
| H | 3.51847600  | -0.33091300  | -1.13878700  |
| C | 2.62071500  | -3.01286700  | -3.01973200  |
| H | 0.63392000  | -3.82950200  | -3.13421300  |
| H | 4.48349700  | -1.97380700  | -2.70249600  |
| H | 3.04932900  | -3.74636900  | -3.69328800  |
| C | 1.48946000  | 1.65358300   | -0.28274900  |
| C | 1.52893600  | 2.64267200   | 0.74781600   |
| C | 1.75155000  | 2.08948200   | -1.61833300  |
| C | 1.89830300  | 3.94475700   | 0.46518300   |
| H | 1.26424700  | 2.37796700   | 1.76380200   |
| C | 2.11791700  | 3.39890800   | -1.87647600  |
| H | 1.67227700  | 1.38817100   | -2.43980800  |
| C | 2.20982000  | 4.34282200   | -0.84454800  |
| H | 1.93433100  | 4.66900000   | 1.27224600   |
| H | 2.32948800  | 3.69485100   | -2.89868500  |
| H | 2.49183500  | 5.36679500   | -1.05689300  |
| C | 1.17438500  | -0.52737700  | 1.68215500   |
| C | 0.39437100  | -1.59402000  | 2.18665100   |
| C | 2.26438300  | -0.07152500  | 2.45699600   |
| C | 0.68197700  | -2.15530500  | 3.42666800   |
| H | -0.43464500 | -1.97615400  | 1.60386800   |
| C | 2.52705500  | -0.62563800  | 3.70042200   |
| H | 2.91027900  | 0.70867300   | 2.07465300   |
| C | 1.73858900  | -1.67234800  | 4.19733400   |
| H | 0.07088500  | -2.97217700  | 3.79533300   |
| H | 3.36168400  | -0.25190100  | 4.28333900   |
| H | 1.95551300  | -2.10842200  | 5.16537800   |
6.3 Reaction Energies

*DFT Method:* B3LYP-D3/def2-TZVP [solvent: CH$_3$CN, values are in Kcal mol$^{-1}$]

| Addition Reactions | $\Delta G^\#$ | $\Delta G$ | $d$(C–C) (Å) | $\delta^{TS}$ |
|--------------------|---------------|-------------|---------------|--------------|
| $\cdot + \text{C}=\text{O}$ | 10.2 | -0.7 | 2.27196 | 0.109536 |
| $\cdot + \text{H}_2\text{C}=\text{O}$ | 9.9 | 4.8 | 2.19618 | 0.128423 |
| $\cdot + \text{H}_2\text{C}=\text{O}$ | 3.9 | 4.6 | 2.00949 | 0.158047 |

**Computed Energies** [values are in Hartree]

| Species | Total Electronic Energy | Sum of Electronic and Zero-point Energies | Sum of Electronic and Thermal Enthalpies | Gibbs Free Energy |
|---------|-------------------------|------------------------------------------|------------------------------------------|------------------|
| $\cdot$ | -235.3134492 | -235.158424 | -235.151457 | -235.188113 |
| $\text{C}=\text{O}$ | -113.3631968 | -113.358162 | -113.354857 | -113.377278 |
| $\cdot$ | -348.6766246 | -348.513916 | -348.504598 | -348.549078 |
| $\cdot$ | -348.7006279 | -348.533770 | -348.525235 | -348.566516 |
| $\cdot$ | -114.5596746 | -114.533057 | -114.529246 | -114.554060 |
| $\cdot$ | -349.8782668 | -349.692471 | -349.683177 | -349.726337 |
| No. | Species | Optimized Structure |
|-----|---------|---------------------|
| 1   | ![Image](image1.png) | ![Image](image2.png) |

**Cartesian Coordinates**

|             | X    | Y    | Z    |
|-------------|------|------|------|
| C           | 1.26397300 | -0.71045000 | -0.24239500 |
| C           | 1.28286100 | 0.77605000 | 0.15890500 |
| C           | 0.00000100 | 1.45997600 | -0.17061900 |
| C           | -1.28286000 | 0.77605100 | 0.15890400 |
| C           | -1.26397400 | -0.71045000 | -0.24239400 |
| C           | 0.00000000 | -1.40798200 | 0.26742700 |
| H           | 1.45609800 | 0.82755100 | 1.24886100 |
| H           | 2.13003100 | 1.28862500 | -0.30343300 |
| H           | 1.29813000 | -0.78597100 | -1.33447200 |
| H           | 2.15786900 | -1.20990500 | 0.14011700 |
| H           | -1.45609900 | 0.82755400 | 1.24886000 |
| H           | -2.13002900 | 1.28862600 | -0.30343600 |
| H           | -2.15786900 | -1.20990400 | 0.14012000 |
| H           | -1.29813200 | -0.78597100 | -1.33447100 |
| H           | 0.00000000 | -1.39975200 | 1.36403100 |
| H           | -0.00000100 | -2.45748300 | -0.03895400 |
| H           | 0.00000100 | 2.51746400 | -0.40619000 |

2  ![Image](image3.png)

**Optimized Structures and Cartesian Coordinates**

- Species: 1
- Optimized Structure: ![Image](image4.png)

- Cartesian Coordinates:
  - C: 1.26397300, -0.71045000, -0.24239500
  - C: 1.28286100, 0.77605000, 0.15890500
  - C: 0.00000100, 1.45997600, -0.17061900
  - C: -1.28286000, 0.77605100, 0.15890400
  - C: -1.26397400, -0.71045000, -0.24239400
  - C: 0.00000000, -1.40798200, 0.26742700
  - H: 1.45609800, 0.82755100, 1.24886100
  - H: 2.13003100, 1.28862500, -0.30343300
  - H: 1.29813000, -0.78597100, -1.33447200
  - H: 2.15786900, -1.20990500, 0.14011700
  - H: -1.45609900, 0.82755400, 1.24886000
  - H: -2.13002900, 1.28862600, -0.30343600
  - H: -2.15786900, -1.20990400, 0.14012000
  - H: -1.29813200, -0.78597100, -1.33447100
  - H: 0.00000000, -1.39975200, 1.36403100
  - H: -0.00000100, -2.45748300, -0.03895400
  - H: 0.00000100, 2.51746400, -0.40619000
### Cartesian Coordinates

#### 3

|   | C     | O     |
|---|-------|-------|
| C | 0.00000000 | 0.00000000 | -0.64266700 |
| O | 0.00000000 | 0.00000000 | 0.48200000 |

#### 4

|   | C     | O     |
|---|-------|-------|
| C | -1.86843800 | 0.47132800 | -0.39383600 |
| C | -0.71546000 | 1.44795300 | -0.14151000 |
| C | 0.18985600 | 0.96924400 | 0.99669500 |
| C | 0.69287400 | -0.46748300 | 0.76821800 |
| C | -0.46318100 | -1.44093600 | 0.48518700 |
SI-44

Cartesian Coordinates

C           -1.34967700   -0.94490900   -0.66022700
H           -0.12257300    1.55106100   -1.05589200
H           -1.10327500    2.44214500    0.09272900
H           -2.52482900    0.45290500    0.48381500
H           -2.47580400    0.81497800   -1.23472200
H           1.23739000   -0.81922000    1.65297800
H           -0.06725200   -2.43497800    0.26807300
H           -1.06052300   -1.52346700    1.39752000
H           -0.77311200   -0.95024300   -1.59289800
H           -2.18358900   -1.63557800   -0.80499800
H           1.03872600    1.64328500    1.12401300
H          -0.37157800   -0.97451600    1.93620400
C           1.75174000   -0.54647800   -0.32067500
O           2.37251700    0.31903500   -0.83374100

Cartesian Coordinates

C           0.00000000    0.00000000   -0.52939300
O           0.00000000    0.00000000    0.67536600
H           0.00000000   -0.93778400   -1.11328400
H           0.00000000    0.93778400   -1.11328400

Cartesian Coordinates

C           0.41183800    0.00086800    0.72013000
C           -0.07769000    1.26541300    0.09524400
C           -0.07642800   -1.26459800    0.09616500
H           0.52570300    0.00131200    1.80108500
C           -1.62641800    1.26526100    0.09356200
H           0.27149900    1.31646600   -0.94070500
H           0.30246300    2.14349900    0.61968300
C           -1.62514300   -1.26597300    0.09469000
H           0.27274200   -1.31596600   -0.93976600
H           0.30470200   -2.14194300    0.62114200

|    | C      |  H                  | H                  |
|----|--------|---------------------|---------------------|
|    | -2.17412000 | -1.98420900 | -1.98792100 |
|    | -0.00092600 | 2.15961600 | 1.32422200 |
|    | -0.56917300 | -0.42232600 | 1.12502700 |
|    | -2.16117200 | -0.216117200 | -0.42026600 |
|    | -1.32425300 | -1.12626200 | 1.12502700 |
|    | 0.56917300 | 2.42026600 | 1.32422200 |
|    | 0.00092600 | -0.42232600 | -0.216117200 |
|    | -0.12502700 | 0.56917300 | 1.32422200 |
|    | -0.56917300 | 1.32425300 | -1.12626200 |
|    | 2.42026600 | 0.56917300 | 1.32422200 |
|    | -0.42232600 | -0.216117200 | 1.12502700 |
|    | -0.216117200 | 0.56917300 | 1.32422200 |
|    | -1.98792100 | -1.98792100 | 1.12502700 |
|    | 0.56917300 | 2.42026600 | 1.32422200 |
|    | -0.42232600 | -0.216117200 | 1.12502700 |
|    | -0.216117200 | 0.56917300 | 1.32422200 |
|    | -1.98792100 | -1.98792100 | 1.12502700 |

**Cartesian Coordinates**

|    | C      | H                  | O                  |
|----|--------|---------------------|---------------------|
|    | -2.05368500 | -0.32356100 | 0.37682300 |
|    | 0.37682300 | -0.32356100 | 0.37682300 |
|    | -0.93520000 | 0.90954600 | 0.90954600 |
|    | 1.42155800 | 1.42155800 | 1.42155800 |
|    | 0.69528900 | 0.69528900 | 0.69528900 |
|    | 0.80954600 | 0.80954600 | 0.80954600 |
|    | -1.36463100 | 0.59671600 | 0.59671600 |
|    | -0.90147400 | -1.36463100 | -0.90147400 |
|    | -1.62920200 | 0.59671600 | 0.59671600 |
|    | -0.32356100 | 0.90954600 | 0.90954600 |
|    | 0.37682300 | -0.32356100 | 0.37682300 |
|    | -0.32356100 | 0.90954600 | 0.90954600 |
|    | 0.37682300 | -0.32356100 | 0.37682300 |
|    | -0.93520000 | 0.90954600 | 0.90954600 |
|    | 1.42155800 | 1.42155800 | 1.42155800 |
|    | 0.69528900 | 0.69528900 | 0.69528900 |
|    | 0.80954600 | 0.80954600 | 0.80954600 |
|    | -1.36463100 | 0.59671600 | 0.59671600 |
|    | -0.90147400 | -1.36463100 | -0.90147400 |
|    | -1.62920200 | 0.59671600 | 0.59671600 |
|    | -0.32356100 | 0.90954600 | 0.90954600 |
|    | 0.37682300 | -0.32356100 | 0.37682300 |
|    | -0.32356100 | 0.90954600 | 0.90954600 |
|    | 0.37682300 | -0.32356100 | 0.37682300 |

**Diagram**
Cartesian Coordinates

| Element |
|---------|
| C       |
| -0.84583400 | -1.11049900 | -0.45482600 |
| N       |
| -0.12060300 | -0.23894100 | 0.03355900  |
| C       |
| -1.43388000 | -0.23598700 | -0.60541800 |
| H       |
| -1.45366300 | -1.04061000 | -1.34096200 |
| H       |
| -1.58164500 | 0.69667800  | -1.16323900 |
| C       |
| -2.57442500 | -0.42760400 | 0.39091400  |
| H       |
| -2.58834800 | 0.36503600  | 1.14098600  |
| H       |
| -3.53614300 | -0.41251300 | -0.12720000 |
| H       |
| -2.47420000 | -1.38397900 | 0.90735100  |
| C       |
| 0.29344000  | 1.02296300  | 0.64013500  |
| H       |
| -0.57571100 | 1.45508500  | 1.13831800  |
| H       |
| 1.02305400  | 0.81402400  | 1.42398100  |
| C       |
| 2.15508600  | -1.25209000 | 0.24996200  |
| H       |
| 2.04467300  | -1.56672300 | 1.30125400  |
| H       |
| 2.76074200  | -2.00720500 | -0.25257600 |
| H       |
| 2.73679400  | -0.32499400 | 0.26427300  |
| C       |
| 0.87682500  | 2.03484400  | -0.35171300 |
| H       |
| 0.15300200  | 2.29096500  | -1.12747600 |
| H       |
| 1.15562600  | 2.95445200  | 0.16691900  |
| H       |
| 1.76542400  | 1.62977600  | -0.83796400 |
| H       |
| 0.43733600  | -1.98716700 | -0.94290600 |

Cartesian Coordinates

| Element |
|---------|
| C       |
| -0.57928100 | -0.47232000 | 0.71143600  |
| N       |
| 0.42756700  | -0.09952800 | -0.13426900 |
### Cartesian Coordinates

| Element | X        | Y        | Z        |
|---------|----------|----------|----------|
| C       | -0.61501100 | -0.52697200 | 0.64565600 |
| N       | 0.43262900   | -0.09099800   | -0.15221900 |
| C       | 1.38961400   | -1.07790200   | -0.64243800 |
| H       | 0.85641100   | -2.00354500   | -0.88128100 |
| C       | 0.38429500   | 1.22448600   | -0.77629400 |
| H       | 0.74260500   | 1.12555500   | -1.80295100 |
| H       | -0.66330300  | 1.52559800   | -0.83561000 |
| C       | -1.15752300  | 0.44746200   | 1.67235800 |
| H       | -1.52315800  | 1.36221200   | 1.21086200 |
|   |   |   |   |
|---|---|---|---|
| H | -1.98584700 | -0.01179000 | 2.21124600 |
| H | -0.37703200 | 0.70503800 | 2.39090600 |
| C | 1.21402800 | 2.28157200 | -0.04506900 |
| H | 2.26620100 | 1.99480400 | -0.01139600 |
| H | 1.13653100 | 3.23775900 | -0.56635400 |
| H | 0.86338000 | 2.41813800 | 0.97788400 |
| H | -0.36751600 | -1.48923900 | 1.09260400 |
| C | 2.50490600 | -1.36704600 | 0.36228100 |
| H | 3.18274900 | -2.12341100 | -0.03814100 |
| H | 3.07884100 | -0.46402900 | 0.57381500 |
| H | 2.09443500 | -1.74068900 | 1.30187600 |
| H | 1.81576700 | -0.70738400 | -1.57468800 |
| C | -1.99380700 | -1.00431900 | -0.37718000 |
| H | -1.49488500 | -1.72522600 | -1.05218500 |
| O | -2.55500100 | 0.02572600 | -0.92140000 |
| H | -2.57258600 | -1.53629600 | 0.40426900 |
7 NMR Spectra

S1 - $^1$H NMR (500 MHz, CDCl$_3$)

S1 - $^{13}$C NMR (101 MHz, CDCl$_3$)
S6 - $^1$H NMR (400 MHz, CDCl$_3$)

S6 - $^{13}$C NMR (101 MHz, CDCl$_3$)
S9 – $^1$H NMR (400 MHz, CDCl$_3$)

S9 – $^{13}$C NMR (101 MHz, CDCl$_3$)
S10 - $^1$H NMR (400 MHz, CDCl$_3$)

S10 - $^{13}$C NMR (101 MHz, CDCl$_3$)
S11 - $^1$H NMR (500 MHz, CDCl$_3$)

S11 - $^{13}$C NMR (101 MHz, CDCl$_3$)
S12 - $^1$H NMR (400 MHz, CDCl$_3$)

S12 - $^{13}$C NMR (101 MHz, CDCl$_3$)
4 - $^1$H NMR (400 MHz, CDCl$_3$)

4 - $^{13}$C NMR (101 MHz, CDCl$_3$)
9 – $^1$H NMR (400 MHz, CDCl$_3$)

9 – $^{13}$C NMR (126 MHz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (101 MHz, CDCl$_3$)
18 - $^1$H NMR (500 MHz, CDCl$_3$)

18 - $^{13}$C NMR (101 MHz, CDCl$_3$)
19 – $^1$H NMR (400 MHz, CDCl$_3$)

19 – $^{13}$C NMR (126 MHz, CDCl$_3$)
25 - $^1$H NMR (500 MHz, CDCl$_3$)

25 - $^{13}$C NMR (101 MHz, CDCl$_3$)
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