New Highly Nucleophilic and Practically Accessible Chlorocarbenoids for Carbonyl Olefination

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Supporting Information

Page 1.....List of Contents:

Page 2.....General Information

**Typical procedure for chloromethylenation of 1a-d, 1f-i, 1k, and 1n.
Preparation of 2a. Spectra data for 2a**

Page 3.....Procedure for the chloromethylenation of fenchone 1j

Spectra data for 2j, 2b, and 2c

Page 4.....Procedure for chloromethylenation of 1e, 1l-m.

Spectra data for 2d, 2e, 2f, 2g

Page 5.....Spectra data for 2h, 2i, 2k

Page 6-7.....Spectra data for 2l, 2m, 2n

Page 8-16.....Copies of ¹H NMR Spectra for compounds 2a-n

General Information. Dichloromethane was distilled from P₂O₅ prior to use. Commercially available ketones, and aldehydes were used as received (Lancaster, Acros, Aldrich, Tedia, RDH). Titanium tetrachloride was purchased from Fluka Chemie AG. Magnesium powder (ca 50 mesh) was purchased from Lancaster Synthesis Ltd. Substrates **1i**¹ and **1l**² were prepared according to the reported procedures. Substrate **1k**³ was prepared from 1,2-*O*-isopropylidene-3,5-cyclohexadiene via a cycloaddition protocol. Flash chromatography was performed on silica gel 60 (230-400 mesh). All reactions were carried out under an atmosphere of N₂.

¹Yan, T.-H.; Tan, C.-W.; Lee, H.-C.; Lo, H.-C.; Huang, T.-Y. *J. Am. Chem. Soc.* **1993**, *115*, 2613.

²Liu, H.; Cohen, T. *J. Org. Chem.* **1995**, *60*, 2022.

³Elango, S.; Yan, T.-H. *J. Org. Chem.* **2002**, *67*, 6954.

Typical procedure for chloromethylenation of 1a-d, 1f-i, 1k, and 1n. Preparation of 2a:

To a suspension consisting of Mg (192 mg, 8 mmol), TiCl₄ (570 mg, 0.31 mL, 3 mmol) and CHCl₃ (4 mL) at 10-15 °C was added a solution of 4-*tert*-butylcyclohexanone **1a** (154 mg, 1 mmol) in CHCl₃ (1 mL) and THF (1 mL). The black slurry was stirred for 1 h, then cooled to 0 °C, and carefully poured into ice-cold saturated potassium carbonate solution (10 mL). The resulting mixture was stirred with 20 mL of ether and the phases were separated. After this procedure was repeated twice, the combined extracts were dried, evaporated, and purified by chromatography on silica gel (elution with hexane) to give 4-*tert*-butyl-1-(chloromethylene)cyclohexane **2a** (123 mg, 66% yield) as a colorless oil: IR (neat) 3065, 2976, 2842, 1620, 1480, 1444, 1394, 1360 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.74 (t, *J* = 1.6 Hz, 1 H), 2.98-2.93 (m, 1 H), 2.35-2.30 (m, 1 H), 2.03-1.91 (m, 1 H), 1.90-1.85 (m, 2 H), 1.76-1.68 (m, 1 H), 1.20-1.16 (m, 1 H), 1.08-0.97 (m, 2 H), 0.85 (s, 9 H); ¹³C NMR (75.5 MHz, CDCl₃) δ 142.1, 108.1, 48.0, 34.0, 32.4, 28.6, 28.4, 27.6, 27.4; high-resolution MS *m/e* Calcd for C₁₁H₁₉Cl: 186.1172. Found: 186.1175.

Procedure for chloromethylenation of fenchone 1j: 2-(chloromethylene)-1,3,3-Trimethylbicyclo[2.2.1]heptane 2j: To a suspension consisting of Mg (192 mg, 8 mmol), TiCl₄ (570 mg, 0.31 mL, 3 mmol) and CHCl₃ (4 mL) at 40-50 °C was added a solution of fenchone **1j** (152 mg, 1 mmol) in CHCl₃ (1 mL) and THF (1 mL). The reaction was stirred for 1 h at ambient temperature, and recooled to 0 °C. Saturated potassium carbonate solution (10 mL) was added and the mixture was diluted with ether (20 mL). The organic layer was separated, dried, evaporated, and purified by chromatography on silica gel (elution with hexane) to give 110 mg (60%) of 2-(chloromethylene)-1,3,3-Trimethylbicyclo[2.2.1]heptane **2j** as a 14:86 *Z/E* mixture along with recovered fenchone **1j** (60 mg). **2j**: IR (neat) 3020, 2920, 1668, 1558, 1129 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.61 and 5.58 (2 s, total 1 H, ratio 14:86), 1.76-1.68 (m, total 1 H), 1.59-1.53 (m, total 1 H), 1.52 and 1.44 (2 s, total 3 H), 1.53-1.40 (m, total 2 H), 1.25-1.14 (m, total 3 H), 1.28, 1.21, 1.05, and 1.03 (4 s, total 6 H); major isomer ¹³C NMR (75.5 MHz, CDCl₃) δ 157.3, 106.7, 51.5, 47.6, 45.9, 45.6, 35.1, 29.5, 26.6, 25.3, 20.4; high-resolution MS *m/e* Calcd for C₁₁H₁₇Cl: 184.1019. Found: 184.1011.

2-(Chloromethylene)adamantane 2b: As described above, 150 mg (1 mmol) of **1b** and Mg (8 mmol)/TiCl₄ (2 mmol)/CHCl₃ (4 mL)/THF (1 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 145 mg (80%) of **2b** as a colorless oil: IR (neat) 3050, 2925, 2849, 1651, 1449 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.73 (s, 1 H), 3.10 (bs, 1 H), 2.47 (bs, 1 H), 1.94-1.71 (m, 12 H); ¹³C NMR (75.5 MHz, CDCl₃) δ 149.6, 103.9, 39.3, 37.9, 36.8, 31.8, 28.2; high-resolution MS *m/e* Calcd for C₁₁H₁₅Cl: 182.0863. Found: 182.0856.

2-(Chloromethylene)-1-isopropyl-4-methylcyclohexane 2c: As described above, 154 mg (1 mmol) of **1c** and Mg (8 mmol)/TiCl₄ (3 mmol)/CHCl₃ (4 mL)/THF (1 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 158 mg (85%) of **2c** as a 1:1 mixture: IR (neat) 3068, 2949, 2803, 2761, 1625, 1541, 1423 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.81 and 5.73 (2 bs, total 1 H, ratio 1:1), 2.72-2.69 and 2.53-2.48 (2 m, total 1 H), 2.06-1.14 (m, total 8 H), 0.95 and 0.93 (2 s, total 3 H), 0.89 and 0.88 (2 d, *J* = 2.4 Hz, total 3 H), 0.80 and 0.73 (2 d, *J* = 6.4 Hz, total 3 H); ¹³C NMR (75.5 MHz, CDCl₃) δ 145.1, 144.9, 109.5, 108.8, 49.8, 46.6, 42.7, 39.3, 35.0, 33.6, 33.2, 29.9, 29.6, 29.1, 27.9, 26.7, 26.2, 22.6, 22.4, 21.5, 20.7, 20.5; high-resolution MS *m/e* Calcd for C₁₁H₁₉Cl: 186.1175. Found: 186.1171.

2-(Chloromethylene)-1,3-dimethylcyclohexane 2d: As described above, 126 mg (1 mmol) of **1d** and Mg (8 mmol)/TiCl₄ (3 mmol)/CHCl₃ (4 mL)/THF (1 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 134 mg (85%) of **2d** as a 4:1 mixture: IR (neat) 3059, 2962, 2931, 2867, 1621, 1461 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.78 and 5.66 (2 bs, total 1 H, ratio 4:1), 3.31-2.27 and 3.10-3.03 (2 m, total 1 H), 2.55-2.47 and 2.33-2.25 (2 m, total 1 H), 1.77-1.68 (m, 1 H), 1.59-1.45 (m, 4 H), 1.42-1.36 (m, 1 H), 1.14, 1.12, 1.05, and 1.00 (4 d, *J* = 6.4 Hz, total 6 H); major isomer ¹³C NMR (75.5 MHz, CDCl₃) δ 148.7, 110.6, 35.8, 32.5, 31.8, 30.1, 22.4, 19.9, 16.2; high-resolution MS *m/e* Calcd for C₉H₁₅Cl: 158.0862. Found: 158.0859.

Procedure for chloromethylenation of 1e, 1l-m. Preparation of 2-(Chloromethylene)indane 2e: To a suspension consisting of Mg (288 mg, 12 mmol), TiCl₄ (570 mg, 0.31 mL, 3 mmol) and CHCl₃ (4 mL) at 10-15 °C was added a solution of indanone **1e** (132 mg, 1 mmol) in CHCl₃ (1 mL) and THF (0.5 mL). The mixture was stirred. After 15 min of stirring at room temperature, an additional 1 mL of THF was added. The black slurry was stirred for an additional 0.5 h, then cooled to 0 °C, and carefully poured into ice-cold saturated potassium carbonate solution (10 mL). The product was extracted into ether, and the combined extracts were dried and evaporated. Purification by flash chromatography (silica gel, hexane) afforded 111 mg (68%) of **2e** as a colorless oil: IR (neat) 3020, 2920, 1668, 1558, 1129 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.23-7.15 (m, 4H), 5.09 (quintet, *J* = 1.2 Hz, 1 H), 3.75 and 3.73 (2 d, *J* = 1.2 Hz, 4 H); ¹³C NMR (75.5 MHz, CDCl₃) δ 142.2, 141.1, 140.7, 126.8, 126.7, 124.7, 124.5, 110.9, 37.7, 37.6; high-resolution MS *m/e* Calcd for C₁₀H₉Cl: 164.0392. Found: 164.0394.

2-(Chloromethylene)-1,2,3,4-tetrahydronaphthalene 2f: Utilizing procedure for the chloromethylenation of **1a**, 146 mg (1 mmol) of **1f** and Mg (12 mmol)/TiCl₄ (3 mmol)/CHCl₃ (4 mL)/THF (3 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) gave **2f** (117 mg, 71%) as a 1:1 *E/Z* mixture: IR (neat) 3020, 2942, 2842, 1676, 1626, 1580, 1495, 736 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.17 (m, 4H), 6.10 and 6.06 (2 quintet, *J* = 1.2 Hz, total 1 H, ratio 1:1), 3.77 (s, 1 H), 3.55 (s, 1 H), 2.96-2.89 (m, total 2 H), 2.70 (dt, *J* = 6.4, 1.6 Hz, 1 H), 2.57 (t, *J* = 6.4 Hz, 1 H); ¹³C NMR (75.5 MHz, CDCl₃) δ 138.5, 138.4, 137.7, 136.8, 135.7, 134.5, 128.7, 128.4, 127.9, 127.5, 126.3, 126.2, 126.1, 125.8, 110.7, 110.7, 36.2, 31.4, 30.7, 30.4, 28.8, 26.5; high-resolution MS *m/e* Calcd for C₁₁H₁₁Cl: 178.0549. Found: 178.0543.

2-(Chloromethylene)-1,1-Dimethylcyclohexane 2g: Utilizing procedure for the chloromethylenation of **1a**, 126 mg (1 mmol) of **1g** and Mg (8 mmol)/TiCl₄ (3 mmol)/CHCl₃ (4 mL)/THF (1 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 113 mg (72%) of **2g** as a 85:15 *E/Z* mixture: IR (neat) 3022,

2978, 2928, 2856, 1614, 1462 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.80 and 5.73 (2 s, total 1 H, ratio 85:15), 2.40-2.37 and 2.14-2.10 (2 m, total 2 H, ratio 85:15), 1.60-1.48 (m, 4 H), 1.37-1.34 (m, 2 H), 1.06 and 1.08 (2 s, total 6 H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 148.7, 109.1, 41.5, 37.2, 27.5, 27.0, 25.3, 22.2; high-resolution MS m/e Calcd for $\text{C}_9\text{H}_{15}\text{Cl}$: 158.0862. Found: 158.0866.

(*E*)-2-(Chloromethylene)-1,7,7-trimethylbicyclo[2.2.1]heptane 2h: Utilizing procedure for the chloromethylenation of **1a**, 152 mg (1 mmol) of **1h** and Mg (8 mmol)/ TiCl_4 (3 mmol)/ CHCl_3 (4 mL)/THF (1 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded **2h** (169 mg, 92%) as a colorless oil. A NOESY spectrum reveals a positive NOE between the vinylic proton and 1-methyl group, substantiating (*E*)-**2h** as the correct structure. (*E*)-**2h**: IR (neat) 3078, 2961, 1651, 1469 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.66 (t, $J = 2.4$ Hz, 1 H), 2.39 (ddd, $J = 16, 2.4, 1.2$ Hz, 1 H), 1.90 (dd, $J = 16, 2.4$ Hz, 1 H), 1.82-1.74 (m, 2 H), 1.67-1.63 (m, 1 H), 1.30-1.27 (m, 1 H), 1.21-1.17 (m, 1 H), 1.15, 0.87, and 0.73 (3 s, 9 H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 153.1, 106.7, 52.5, 48.7, 44.3, 35.7, 34.5, 27.7, 19.5, 18.7, 12.4; high-resolution MS m/e Calcd for $\text{C}_{11}\text{H}_{17}\text{Cl}$: 184.1019. Found: 184.1018.

Methyl (*E*)-2-(chloromethylene)-7,7-dimethylbicyclo[2.2.1]heptane-1-carboxylate 2i: Utilizing procedure for the chloromethylenation of **1a**, 196 mg (1 mmol) of **1i** and Mg (10 mmol)/ TiCl_4 (5 mmol)/ CHCl_3 (4 mL)/THF (1 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded **2i** (207 mg, 91%) as a colorless oil. A NOESY spectrum reveals a positive NOE between the vinylic proton and *O*-methyl group, substantiating (*E*)-**2i** as the correct structure. (*E*)-**2i**: IR (neat) 3025, 2950, 1736, 1650, 1450 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.95 (t, $J = 2.4$ Hz, 1 H), 3.71 (s, 3 H), 2.53 (ddd, $J = 16, 2.4, 1.2$ Hz, 1 H), 2.33-2.27 (dt, $J = 12, 4.4$ Hz, 1 H), 1.96 (dd, $J = 16, 2.4$ Hz, 1 H), 1.94-1.82 (m, 2 H), 1.68-1.60 (m, 1 H), 1.29-1.23 (m, 1 H), 1.01 and 0.99 (2s, 6 H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 172.5, 147.0, 110.2, 62.3, 51.4, 51.4, 45.4, 36.1, 31.9, 27.3, 20.7, 19.5; high-resolution MS m/e Calcd for $\text{C}_{12}\text{H}_{17}\text{ClO}_2$: 228.0918. Found: 228.0925.

7-(2-Chloro-1-methylvinyl)-2,3-*O*-Isopropylidenebicyclo[2.2.2]hept-5-ene 2k: Utilizing procedure for the chloromethylenation of **1a**, 222 mg (1 mmol) of **1k** and Mg (8 mmol)/ TiCl_4 (3 mmol)/ CHCl_3 (4 mL)/THF (1 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded (*E*)-**2k** (120 mg, 48%) and (*Z*)-**2k** (88 mg, 34%): (*E*)-**2k**: IR (neat) 3098, 2994, 2988, 2938, 2887, 1640, 1454, 1380 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.14 (t, $J = 7.2$ Hz, 1 H), 5.99 (t, $J = 7.2$ Hz, 1 H), 5.77 (bs, 1 H), 4.18 (bs, 2 H), 2.84 (bs, 2 H), 2.21-1.17 (m, 1 H), 1.68 (d, $J = 1.2$ Hz, 3

H), 1.62-1.59 (m, 1 H), 1.31 and 1.25 (2s, 6 H), 1.16-1.11 (m, 1 H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 141.1, 131.4, 129.1, 112.9, 108.5, 79.0, 78.1, 40.0, 39.1, 35.0, 27.4, 25.4, 24.9, 16.2; (Z)-**2k**: IR (neat) 3052, 2936, 2868, 1620, 1456, 1380 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.17 (t, $J = 7.2$ Hz, 1 H), 6.02 (t, $J = 7.2$ Hz, 1 H), 5.70 (bs, 1 H), 4.30-4.21 (m, 2 H), 2.94-2.76 (m, 3 H), 1.55 (d, $J = 1.2$ Hz, 3 H), 1.62-1.58 (m, 1 H), 1.30 and 1.26 (2s, 6 H), 1.11-1.08 (m, 1 H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 141.4, 131.6, 129.5, 111.9, 108.3, 79.0, 78.1, 38.8, 35.1, 33.7, 26.6, 25.4, 24.9, 19.5; high-resolution MS m/e Calcd for $\text{C}_{14}\text{H}_{19}\text{ClO}_2$: 254.1074. Found: 254.1082.

2-(Chloromethylene)-4-(phenylthio)butane 2l: Utilizing procedure for the chloromethylenation of **1e**, 180 mg (1 mmol) of **1l** and Mg (12 mmol)/ TiCl_4 (3 mmol)/ CHCl_3 (5 mL)/THF (1.5 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 127 mg (60%) of **2l** as a 60:40 *E/Z* mixture: IR (neat) 3074, 2925, 2849, 1636, 1583, 1558, 1438 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.19 (m, 5 H), 5.85 and 5.86 (2 bs, total 1 H, ratio 60:40), 3.03-2.98 (m, 2 H), 2.54 and 2.38 (2 t, $J = 7.6$ Hz, total 2 H, ratio 60:40), 1.79 and 1.78 (2 s, total 3 H, ratio 60:40); ^{13}C NMR (75.5 MHz, CDCl_3) δ 136.6, 136.5, 136.1, 135.9, 129.6, 129.2, 128.9, 128.9, 126.2, 126.0, 113.9, 113.4, 36.7, 31.9, 31.8, 30.7, 21.0, 16.2; high-resolution MS m/e Calcd for $\text{C}_{11}\text{H}_{13}\text{ClS}$: 212.0426. Found: 212.0418.

5-(2-chlorovinyl)benzo[1,3]dioxole 2m: Utilizing procedure for the chloromethylenation of **1e**, 150 mg (1 mmol) of **1m** and Mg (16 mmol)/ TiCl_4 (5 mmol)/ CHCl_3 (6 mL)/THF (2 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 142 mg (78%) of **2m** as a 3:1 *E/Z* mixture: IR (neat) 3074, 3012, 2884, 1614, 1503, 1498, 1226, 1040 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.35-6.69 (m with bs at 7.35 and d at 6.71, $J = 13.2$ Hz, total 3.7 H), 6.51 and 6.46 (2 d, $J = 8.4$ and 13.2 Hz, total 1 H, ratio 1:3), 6.13 (d, $J = 8.4$ Hz, 0.3 H), 5.96 and 5.94 (2 s, total 2 H, ratio 1:3); ^{13}C NMR (75.5 MHz, CDCl_3) δ 148.1, 147.6, 147.5, 147.4, 132.8, 129.1, 128.7, 128.2, 124.0, 120.8, 116.9, 115.8, 109.1, 108.4, 108.1, 105.4, 101.2, 101.2; high-resolution MS m/e Calcd for $\text{C}_9\text{H}_7\text{ClO}_2$: 182.0134. Found: 182.0128.

1-Chloro-4-phenyl-1-butene 2n: Utilizing procedure for the chloromethylenation of **1a**, 134 mg (1 mmol) of **1n** and Mg (12 mmol)/ TiCl_4 (3 mmol)/ CHCl_3 (6 mL)/THF (2 mL) gave a crude reaction mixture. Purification by flash chromatography (silica gel, hexane) afforded 141 mg (85%) of **2n** as a 12:5 *E/Z* mixture: IR (neat) 3086, 3063, 3027, 2942, 2858, 1631, 1603, 1496, 1454 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.28-7.14 (m, total 5 H), 6.02-5.73 (dt at 6.02, $J = 6.8$, 1.2 Hz and q at 5.76, $J = 6.8$ Hz; 5.88-5.97, m (*E*)- $\text{HC}=\text{CH}$, total 2 H), 2.75-2.33 (m, 4 H); ^{13}C NMR (75.5 MHz, CDCl_3) δ 141.2, 140.9,

132.9, 130.7, 128.4, 126.1, 118.6, 117.6, 35.3, 34.4, 32.6, 28.6; high-resolution MS m/e
Calcd for C₁₀H₁₁Cl: 166.0550. Found: 166.0556.