Transition Metal-Free Addition of Ketones or Nitriles to 1,3-Dienes

Jean-Marc Gaudin,* and Pascal Millet

Supplementary Data

General. All reactions were performed under N₂. GLC and prep GLC: Hewlett Packard 6890 instrument equipped with a flame ionization detector (250°C) coupled to a Hewlett Packard Chemstation 6.03; capillary columns Chrompack. DB-Wax (15 m, 0.25 mm), and DB-1 (15 m, 0.25 mm). Silica gel for flash chromatography is a 60 Å quality in prepacked cartridges from Interchim. Bulb-to-bulb distillation: Büchi GKR-50 oven; b.p. correspond to the air temp. NMR: Bruker WH-400, Bruker AMX-360; ¹H at 400 and ¹³C at 90 MHz in CDCl₃; chemical shifts in ppm rel. to TMS. MS: Varian MAT-112 spectrometer (ca. 70 eV); intensities in % rel to the base peak (100%).

Large scale procedure for the production of 7. A 5 L plastic coated pyrex reactor with screw cap (7 bars max.) is charged with 2,4-dimethyl-3-pentanone (864 g), 2,3-dimethyl-1,3-butadiene (520 g), tBuOK (400g), DMF (1.6 L) and heated at 80°C during 72 h (internal pressure less than 1 bar). Then the reaction mixture (4 litres) was cooled down and poured into 6 litres of water and 3 litres of cyclohexane. The organic layer was washed two times with 2 litres of water. After solvent evaporation, 1.29 kg of crude product was obtained and distilled with 100 g of Primol as ballast (7mbar, Eb 85°C) affording 1.03 kg of pure (99.8 GC %) 7 (83% yield).

Typical procedure for the hydrogenation. Molar solutions of olefins in ethylacetate in the presence of 10% weight of Pd/C 5% humid - Degussa were shaken in a Parr apparatus under 3 bar of hydrogen. The mixtures were filtered and the filtrates evaporated, affording the reduced compound in nearly quantitative yields (95–100%).

\[ \text{7 2,4,4,6,7-PENTAMETHYL-6-OCTEN-3-ONE} \]

MS: m/z (%): 196 [M⁺] (15), 178 (1), 153 (5), 135 (7), 125 (16), 114 (100), 99 (22), 83 (78), 71 (20), 69 (57), 55 (33), 43 (26), 41 (27). ¹³C-NMR: \( \delta = 20.3 (q, 2C), 20.9 (q), 21.0 (q), 21.5 (q), 24.3 (q, 2C), 34.4 (d), 42.3 (t), 49.5 (s), 124.5 (s), 128.3 (s), 220.3 \text{ppm} (s) \). ¹H-NMR: \( \delta = 1.05 (d, J=6Hz, 6H), 1.13 (s, 6H), 1.61 (s, 3H), 1.66 (s, 6H), 2.34 (s, 2H), 3.16 \text{ppm} (m, 1H) \).
10a 3-(2,3-DIMETHYLBUT-2-ENYL)-1-METHYLPYRROLIDIN-2-ONE
MS: \( m/z \) (%): 181 \([\text{M}^+](19)\), 166 (3), 152 (1), 138 (1), 112 (6), 99 (100), 98 (67), 67 (5), 55 (11), 41 (12). \(^{13}\text{C-NMR}: \delta = 18.0 (q), 20.5 (q), 20.7 (q), 24.3 (t), 29.8 (q), 35.3 (t), 41.0 (d), 47.7 (t), 125.3 (s), 126.1 (s), 176.9 \text{ppm} \). \(^{1}H\text{-NMR}: \delta = 1.63 (s, 3H), 1.66 \text{ppm} \).  

11 (±)-2,4,4,6,7-PENTAMETHYL-7-OCTEN-3-ONE
MS: \( m/z \) (%): 196 \([\text{M}^+](1)\), 178 (1), 153 (2), 135 (4), 125 (4), 114 (51), 99 (7), 83 (21), 71 (20), 69 (100), 55 (10), 43 (31), 41 (35). \(^{13}\text{C-NMR}: \delta = 18.6 (q), 20.0 (q), 20.3 (q), 22.1 (q), 24.3 (q), 24.9 (q), 34.3 (d), 38.2 (d), 44.0 (t), 48.2 (s), 109.9 (t), 150.9 (s), 219.8 \text{ppm} \). \(^{1}H\text{-NMR}: \delta = 0.98 (d, J=7\text{Hz}, 3H), 1.03 (d, J=7\text{Hz}, 6H), 1.16 (d, J=7\text{Hz}, 6H), 1.49 (dd, J=14, 7\text{Hz}, 1H), 1.65 (s, 3H), 1.76 (dd, J=14, 7\text{Hz}, 1H), 2.22 (m, 1H), 3.09 \text{ppm} \).  

Table 2

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14 (±)-R-2-(2,3-DIMETHYL-2-BUTENYL)-2,T-6-DIMETHYLCYCLOHEXANONE
MS: \( m/z \) (%): 208 \([\text{M}^+](4)\), 193 (2), 126 (100), 111 (25), 83 (35), 55 (25), 41 (13).

15 (±)-R-2-(2,3-DIMETHYL-2-BUTENYL)-2,C-6-DIMETHYLCYCLOHEXANONE
MS: \( m/z \) (%): 208 \([\text{M}^+](8)\), 190 (6), 126 (100), 111 (28), 83 (37), 55 (35), 41 (13).

16 (±)-6-(2,3-DIMETHYL-2-BUTENYL)-2,2-DIMETHYLCYCLOHEXANONE
MS: \( m/z \) (%): 208 \([\text{M}^+](62)\), 193 (20), 190 (20), 175 (5), 165 (28), 137 (19), 126 (100), 111 (95), 95 (37), 83 (45), 70 (45), 55 (64), 41 (48). \(^{13}\text{C-NMR}: \delta = 18.4 (q), 20.6 (q), 20.7 (q), 21.7 (t), 25.4 (q), 25.8 (q), 33.7 (t), 33.8 (t), 41.9 (t), 44.9 (d), 45.4 (s), 125.3 (s), 125.8 (s), 217.1 \text{ppm} \). \(^{1}H\text{-NMR}: \delta = 1.05 (s, 3H), 1.18 (s, 3H), 1.21 (m, 1H), 1.52 (m,
1H), 1.57 (s, 3H), 1.61 (s, 3H), 1.63 (s, 3H), 1.66 (m, 1H), 1.76 (m, 1H), 1.81 (m, 1H), 2.03 (m, 1H), 2.12 (dd, J=14, 8Hz, 1H), 2.35 (dd, J=14, 1Hz, 1H), 2.64 ppm (m, 1H).

17 1-(2,3-DIMETHYL-2-BUTENYL)CYCLOPROPANECARBONITRILE
MS: m/z (%): 149 [M+] (48), 134 (100), 119 (28), 106 (25), 83 (65), 55 (77), 41 (58). 13C-NMR: δ = 9.0 (s), 13.7 (t, 2C), 18.8 (q), 20.7 (q, 2C), 38.4 (t), 123.4 (s), 123.8 (s), 128.7 ppm (s). 1H-NMR: δ = 1.15 (m, 1H), 1.25 (m, 2H), 1.62 (m, 2H), 1.68 (s, 3H), 1.70 (s, 3H), 1.70 (s, 3H), 1.82 (s, 3H), 1.95 (d, J=13Hz, 2H), 2.35 ppm (s, 2H).

18 (±)-2-ETHYL-2,4,5-TRIMETHYL-4-HEXENENITRILE
MS: m/z (%): 165 [M+] (10), 83 (100), 55 (50), 41 (19). 13C-NMR: δ = 9.4 (s), 20.4 (q), 20.9 (q), 21.4 (q), 23.8 (q), 33.3 (t), 37.6 (s), 43.6 (t), 123.1 (s), 125.0 (s), 130.1 ppm (s). 1H-NMR: δ = 1.09 (t, J=7Hz, 3H), 1.27 (s, 3H), 1.50 (dq, J=14, 7Hz, 1H), 1.70 (s, 6H), 1.70 (m, 1H), 1.82 (s, 3H), 2.28 (d, J=14Hz, 1H), 2.40 ppm (d, J=14Hz, 1H).

19 1-(2,3-DIMETHYL-2-BUTENYL)CYCLOHEXANECARBONITRILE
MS: m/z (%): 191 [M+] (10), 109 (15), 83 (100), 55 (29), 41 (15). 13C-NMR: δ = 20.8 (q), 20.9 (q), 21.6 (q), 23.1 (t, 2C), 25.4 (t), 36.2 (t, 2C), 39.5 (s), 45.0 (t), 122.7 (s), 124.2 (d), 130.0 ppm (s). 1H-NMR: δ = 0.85 (m, 2H), 1.20 (m, 2H), 1.70 (s, 3H), 1.72 (s, 3H), 1.76 (s, 3H), 2.30 ppm (s, 2H).

Table 3

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20E/20Z 2,4,4-TRIMETHYL-6-OCTEN-3-ONE
Two identical MS spectra: m/z (%): 168 [M+] (5), 153 (2), 139 (1), 125 (52), 97 (85), 81 (11), 71 (27), 69 (27), 55 (100), 43 (46).
Minor isomer with a double bond in terminal position MS: m/z (%): 168 [M+] (0.2), 125 (3), 114 (76), 97 (52), 81 (12), 71 (28), 55 (100), 43 (46).

Hydrogenation of this mixture gives the single following compound: 2,4,4-TRIMETHYL-3-OCTANONE
MS: m/z (%): 114 (20), 99 (29), 71 (17), 57 (100), 43 (35), 41 (20). 13C-NMR: δ = 14.0 (q), 20.2 (q, 2C), 23.4 (t), 24.0 (q, 2C), 27.1 (t), 33.9 (d), 39.3 (t), 48.2 (s), 220.1 ppm (s).
**1H-NMR:** $\delta = 0.88 \ (t, J=8\text{Hz}, 3\text{H}), 1.02 \ (d, J=7\text{Hz}, 3\text{H}), 1.12 \ (s, 3\text{H}), 1.12 \ (m, 2\text{H}), 1.28 \ (m, 2\text{H}), 1.50 \ (m, 2\text{H}), 3.11 \text{ ppm} \ (sept, J=7\text{Hz}, 1\text{H}).$

**21E/21Z** $(\pm)$-2,3,3,5-TETRAMETHYL-7-NONEN-4-ONE

Two identical MS spectra: $m/z \ (%)$: 196 [M$^+$] (3), 154 (1), 113 (19), 111 (22), 85 (100), 83 (73), 55 (37), 43 (47). E major, based on the $^{13}$C-NMR shift of the methyl on the double bond ($17.8 \text{ ppm}$ for the E isomer and $12.8 \text{ ppm}$ for the Z isomer).

Hydrogenation of this mixture gives the single following compound: $(\pm)$-2,3,3,5-TETRAMETHYL-4-NONANONE

**22** $E_1$-[(2$E$)-2-BUTENYL]CYCLOHEXANECARBONITRILE

**23** $E$ MS: $m/z \ (%)$: 163 [M$^+$] (6), 109 (100), 82 (20), 67 (15), 55 (42), 41 (9). $^{13}$C-NMR: $\delta = 18.0 \ (q), 23.0 \ (t, 2\text{C}), 25.4 \ (t), 35.4 \ (t, 2\text{C}), 39.2 \ (s), 43.5 \ (t), 123.6 \ (s), 124.5 \ (d, 2\text{C}), 130.7 \text{ ppm} \ (d)$. $^1$H-NMR: $\delta = 0.86 \ (t, J=7\text{Hz}, 6\text{H}), 1.29 \ (s, 3\text{H}), 1.31–1.40 \ (m, 4\text{H}), 1.40–1.48 \ (m, 6\text{H}), 1.54–1.63 \text{ ppm} \ (m, 2\text{H}).$

**24EE** $(4E)$-2-[(2$E$)-2-BUTENYL]-2-METHYL-4-HEXENENITRILE

**24EZ** $E$ MS: $m/z \ (%)$: 167 [M$^+$] (0.2), 166 (1), 152 (4), 138 (2), 124 (13), 111 (62), 110 (40), 96 (46), 83 (33), 68 (100), 57 (30), 55 (21), 41 (43). $^{13}$C-NMR: $\delta = 13.9 \ (q, 2\text{C}), 22.8 \ (t, 2\text{C}), 24.0 \ (q), 27.0 \ (t, 2\text{C}), 39.2 \ (t, 2\text{C}), 36.7 \ (s), 124.7 \text{ ppm} \ (d)$. $^1$H-NMR: $\delta = 0.94 \ (t, J=7\text{Hz}, 6\text{H}), 1.29 \ (s, 3\text{H}), 1.31–1.40 \ (m, 4\text{H}), 1.40–1.48 \ (m, 6\text{H}), 1.54–1.63 \text{ ppm} \ (m, 2\text{H}).$
**Table 4**

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**25/26** 2,4,4,8-TETRAMETHYL-6-NONEN-3-ONE/2,4,4,8-TETRAMETHYL-7-NONEN-3-ONE

**25E** (40% of the mixture) MS: m/z (%): 196 [M⁺] (3), 153 (16), 125 (12), 114 (35), 83 (55), 69 (100), 55 (25), 43 (35), 41 (35).

**25Z** (10% of the mixture) MS: m/z (%): 196 [M⁺] (1), 181 (1), 167 (1), 153 (8), 125 (15), 114 (64), 83 (58), 69 (100), 55 (25), 43 (37), 41 (37).

**26** (50% of the mixture) MS: m/z (%): 114 (100), 99 (23), 69 (60), 43 (22), 41 (30).

Hydrogenation of this mixture gives the single following compound: 2,4,4,8-TETRAMETHYL-3-NONANONE

MS: m/z (%): 183 (1), 155 (1), 127 (27), 114 (38), 85 (36), 71 (100), 57 (53), 43 (65), 41 (32). 13C-NMR: δ = 20.2 (q), 22.6 (q, 2C), 22.7 (t), 24.0 (q, 2C), 27.8 (d), 33.9 (d), 39.7 (t), 39.8 (t), 48.3 (s), 220.2 ppm (s). 1H-NMR: δ = 0.85 (d, J=7Hz, 6H), 1.03 (d, J=7Hz, 6H), 1.05 (m, 1H), 1.12 (s, 6H), 1.14 (m, 4H), 1.49 (m, 2H), 3.11 ppm (sept, J=7Hz, 1H).

**27/28** 2,4,4-TRIMETHYL-6-NONEN-3-ONE/2,4,4-TRIMETHYL-7-NONEN-3-ONE

**27Z** (30% of the mixture) MS: m/z (%): 182 [M⁺] (2), 139 (5), 111 (38), 95 (5), 71 (21), 69 (100), 55 (15), 43 (24), 41 (20).

**27E** (50% of the mixture) MS: m/z (%): 182 [M⁺] (3), 139 (32), 111 (20), 95 (6), 71 (19), 69 (100), 55 (28), 43 (28), 41 (23).

Two identical spectra for **28E/28Z** (20% of the mixture) MS: m/z (%): 114 (100), 111 (14), 99 (19), 95 (9), 71 (21), 69 (63), 55 (60), 43 (33), 41 (20).

Hydrogenation of this mixture gives the single following compound: 2,4,4-TRIMETHYL-3-NONANONE

MS: m/z (%): 114 (32), 113 (28), 71 (100), 57 (82), 43 (55), 41 (30). 13C-NMR: δ = 14.0 (q), 20.2 (q, 2C), 22.6 (t), 24.0 (q, 2C), 24.6 (t), 32.5 (t), 33.9 (d), 39.6 (t), 48.3 (s), 220.2 ppm
ppm (s). $^1$H-NMR: $\delta = 0.87$ (t, J=7Hz, 3H), 1.02 (d, J=7Hz, 6H), 1.12 (s, 6H), 1.15 (m, 2H), 1.26 (m, 4H), 1.50 (m, 2H), 3.11 ppm (sept, J=7Hz, 1H).

29E/29Z 2,2,5-TRIMETHYL-4-HEPTENENITRILE
29Z (30% of the mixture) MS: m/z (%): 151 [M$^+$] (32), 136 (38), 123 (26), 108 (30), 95 (48), 83 (44), 69 (100), 55 (100), 41 (74).
29E (70% of the mixture) MS: m/z (%): 151 [M$^+$] (6), 136 (2), 109 (2), 95 (3), 83 (80), 69 (13), 55 (100), 41 (25).

30 2,4,4,7-TETRAMETHYL-6-OCTEN-3-ONE
MS: m/z (%): 182 [M$^+$] (11), 167 (4), 139 (52), 114 (34), 111 (67), 69 (100), 55 (25), 43 (28), 41 (29). $^{13}$C-NMR: $\delta = 17.9$ (q), 20.1 (q, 2C), 23.7 (q, 2C), 25.9 (q), 34.1 (d), 37.6 (t), 48.7 (s), 120.0 (d), 133.9 (s), 220.1 ppm (s). $^1$H-NMR: $\delta = 1.02$ (d, J=7Hz, 6H), 1.12 (s, 6H), 1.60 (s, 3H), 1.69 (s, 3H), 2.21 (d, J=7Hz, 2H), 3.09 (sept, J=7Hz, 1H), 5.00 ppm (m, 1H).

31 2,4,4,6-TETRAMETHYL-6-OCTEN-3-ONE
MS: m/z (%): 182 [M$^+$] (8), 167 (3), 153 (3), 139 (18), 114 (23), 111 (77), 69 (100), 55 (28), 43 (31), 41 (28). $^{13}$C-NMR: $\delta = 13.5$ (q), 17.9 (q), 20.2 (q, 2C), 24.0 (q), 24.6 (q), 34.5 (d), 37.7 (t), 48.6 (s), 123.1 (d), 132.4 (s), 220.0 ppm (s).

32/33/34 2-(1-CYCLOHEXEN-1-YL)-2-METHYLPROPANENITRILE/(±)-2-(2-CYCLOHEXEN-1-YL)-2-METHYLPROPANENITRILE/(±)-2-(3-CYCLOHEXEN-1-YL)-2-METHYLPROPANENITRILE
32 MS: m/z (%): 149 [M$^+$] (9), 134 (3), 120 (1), 107 (4), 91 (3), 81 (100), 79 (21), 77 (6), 69 (8), 53 (6). $^{13}$C-NMR: $\delta = 128.8$ (d), 136.6 ppm (s).
33 MS: m/z (%): 149 [M$^+$] (3), 81 (100), 79 (22), 77 (6), 69 (9), 53 (7). $^{13}$C-NMR: $\delta = 125.7$ (d), 131.1 ppm (d).
34 MS: m/z (%): 149 [M$^+$] (6), 134 (2), 117 (3), 107 (4), 91 (3), 81 (100), 79 (62), 71 (19), 69 (25), 56 (10), 54 (14), 53 (14). $^{13}$C-NMR: $\delta = 125.5$ (d), 126.9 ppm (d).

Hydrogenation of this mixture gives the single following compound: 2-CYCLOHEXYL-2-METHYLPROPANENITRILE
MS: m/z (%): 83 (20), 69 (100), 55 (36), 41 (18). $^{13}$C-NMR: $\delta = 24.5$ (q, 2C), 26.0 (t), 26.3 (t, 2C), 27.9 (t, 2C), 36.3 (s), 45.8 (d), 125.0 ppm (s). $^1$H-NMR: $\delta = 1.06$–1.35 (m, 6H), 1.31 (s, 3H), 1.69 (m, 1H), 1.80–1.93 ppm (m, 4H).