

Supporting information for:

The First Aza Diels-Alder Reaction Involving an α,β -unsaturated Hydrazone as the Dienophile: Stereoselective Synthesis of C-4 Functionalized 1,2,3,4-Tetrahydroquinolines Containing a Quaternary Stereocenter

Vellaisamy Sridharan,[§] Paramasivan T. Perumal,^{§,‡} Carmen Avendaño[§] and J. Carlos Menéndez^{§,*}

[§]Departamento de Química Orgánica y Farmacéutica, Facultad de Farmacia, Universidad Complutense, 28040 Madrid, Spain.

[‡]Permanent address: Organic Chemistry Division, Central Leather Research Institute, Chennai 600 020, India

Contents

Characterization data of compounds 3	S2
Representative spectra of compounds 3	S7

Characterization data for compounds 3

(±)-(2*S,4*S**)-4-Methyl-6-methoxy-2-phenyl-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3a).** Mp 92-93 °C. IR (neat) 3362.8, 2952.1, 2827.5, 1602.6, 1503.9, 1275.6, 1043.6 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 1.63 (s, 3H), 1.87 (dd, *J* = 13.1, 2.5 Hz, 1H), 2.12 (dd, *J* = 13.1, 11.8 Hz, 1H), 2.78 (s, 6H), 3.77 (s, 3H), 3.96 (bs, 1H), 4.55 (dd, *J* = 11.8, 2.5 Hz, 1H), 6.58 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.69-6.73 (m, 3H), 7.33-7.52 (m, 5H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 28.6, 41.5, 43.9, 44.8, 53.7, 56.3, 113.9, 114.8, 116.0, 127.2, 128.1, 128.5, 129.1, 138.9, 144.6, 144.9, 152.5. Anal. Calcd. for C₂₀H₂₅N₃O: C, 74.27; H, 7.79; N, 12.99. Found: C, 74.35; H, 7.60; N, 12.97.

(±)-(2*S,4*S**)-4,6-Dimethyl-2-phenyl-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3b).** Mp 117-118 °C. IR (neat) 3376.0, 2967.5, 2852.8, 1616.8, 1505.6, 1311.3, 1010.8 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 1.64 (s, 3H), 1.87 (dd, *J* = 13.0, 2.5 Hz, 1H), 2.12 (dd, *J* = 13.0, 11.6 Hz, 1H), 2.29 (s, 3H), 2.81 (s, 6H), 4.08 (bs, 1H), 4.59 (dd, *J* = 11.6, 2.5 Hz, 1H), 6.57 (d, *J* = 7.7 Hz, 1H), 6.73 (s, 1H), 6.90-6.94 (m, 2H), 7.29-7.53 (m, 5H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 21.0, 28.4, 41.2, 43.9, 44.9, 53.6, 115.2, 127.2, 127.3, 128.1, 128.6, 129.1, 129.6, 142.4, 144.7, 145.4 (one aromatic carbon signal is merged with others). Anal. Calcd. for C₂₀H₂₅N₃: C, 78.14; H, 8.20; N, 13.67. Found: C, 78.11; H, 8.12; N, 13.63.

(±)-(2*S,4*S**)-2-(4-Chlorophenyl)-4,6-dimethyl-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3c).** Mp 128-129 °C. IR (neat) 3356.2, 2967.9, 2852.5, 1615.8, 1505.9, 1282.2, 1013.8 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 1.59 (s, 3H), 1.81 (dd, *J* = 13.0, 2.5 Hz, 1H), 2.04 (dd, *J* = 13.0, 11.6 Hz, 1H), 2.26 (s, 3H), 2.78 (s, 6H), 4.01 (bs, 1H), 4.54 (dd, *J* = 11.6, 2.5 Hz, 1H), 6.55 (d, *J* = 8.7 Hz, 1H), 6.68 (s, 1H), 6.87-6.90 (m, 2H), 7.36 (d, *J* = 8.7 Hz, 2H), 7.42 (d, *J* = 8.7 Hz, 2H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 21.0, 28.5, 41.1, 43.9, 44.9, 53.0,

115.2, 127.2, 127.6, 128.5, 128.6, 129.2, 129.5, 133.6, 142.1, 143.2, 145.0. Anal. Calcd. for $C_{20}H_{24}ClN_3$: C, 70.26; H, 7.08; N, 12.29. Found: C, 70.35; H, 6.89; N, 12.29.

(±)-(2*S,4*S**)-2-(4-Chlorophenyl)-4-methyl-6-methoxy-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3d).** Mp 120-121 °C. IR (neat) 3363.1, 2950.3, 2850.9, 1615.0, 1503.7, 1278.1, 1013.8 cm^{-1} . 1H -NMR ($CDCl_3$, 250 MHz) δ 1.60 (s, 3H), 1.81 (dd, $J = 13.2, 2.6$ Hz, 1H), 2.05 (dd, $J = 13.2, 11.6$ Hz, 1H), 2.77 (s, 6H), 3.76 (s, 3H), 3.95 (bs, 1H), 4.51 (dd, $J = 11.6, 2.6$ Hz, 1H), 6.58 (d, $J = 9.4$ Hz, 1H), 6.66 (s, 1H), 6.67-6.71 (m, 2H), 7.35 (d, $J = 8.7$ Hz, 2H), 7.42 (d, $J = 8.7$ Hz, 2H). ^{13}C -NMR ($CDCl_3$, 62.9 MHz) δ 28.7, 41.5, 43.8, 44.8, 53.2, 56.3, 113.9, 114.7, 116.1, 128.5, 129.2, 133.5, 138.7, 143.1, 144.6, 152.6 (one aromatic carbon signal is merged with others). Anal. Calcd. for $C_{20}H_{24}ClN_3O$: C, 67.12; H, 6.76; N, 11.74. Found: C, 66.97; H, 6.52; N, 11.80.

(±)-(2*S,4*S**)-4-Methyl-2-(4-methylphenyl)-6-methoxy-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3e).** Mp 110-111 °C. IR (neat) 3360.8, 2950.8, 2851.0, 1612.0, 1504.0, 1469.0, 1277.4, 1043.9 cm^{-1} . 1H -NMR ($CDCl_3$, 250 MHz) δ 1.62 (s, 3H), 1.84 (dd, $J = 13.0, 2.5$ Hz, 1H), 2.09 (dd, $J = 13.0, 12.0$ Hz, 1H), 2.40 (s, 3H), 2.77 (s, 6H), 3.77 (s, 3H), 3.92 (bs, 1H), 4.50 (dd, $J = 12.0, 2.5$ Hz, 1H), 6.57 (dd, $J = 7.5, 1.6$ Hz, 1H), 6.68-6.72 (m, 3H), 7.22 (d, $J = 8.0$ Hz, 2H), 7.38 (d, $J = 8.0$ Hz, 2H). ^{13}C -NMR ($CDCl_3$, 62.9 MHz) δ 21.6, 28.6, 41.6, 43.9, 44.7, 53.4, 56.3, 113.9, 114.8, 115.9, 127.1, 128.5, 129.7, 137.7, 139.1, 141.6, 145.1, 152.4. Anal. Calcd. for $C_{21}H_{27}N_3O$: C, 74.74; H, 8.06; N, 12.45. Found: C, 74.58; H, 7.77; N, 12.48.

(±)-(2*S,4*S**)-2-(4-Chlorophenyl)-4-methyl-8-methoxy-1,2,3,4-tetrahydroquinoline-4-carbaldehyde (3f).** Viscous liquid. IR (neat) 3388.1, 2954.6, 2849.4, 1586.4, 1489.3, 1335.5, 1245.4, 1013.9 cm^{-1} . 1H -NMR ($CDCl_3$, 250 MHz) δ 1.60 (s, 3H), 1.84 (dd, $J = 12.8, 2.5$ Hz, 1H), 2.08 (dd, $J = 12.8, 11.6$ Hz, 1H), 2.78 (s, 6H), 3.87 (s, 3H), 4.53 (dd, $J = 11.6, 2.5$ Hz, 1H), 4.65 (bs, 1H), 6.68-6.79 (m, 4H), 7.37 (d, $J = 8.5$ Hz, 2H),

7.46 (d, $J = 8.5$ Hz, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 62.9 MHz) δ 28.5, 41.2, 43.8, 44.6, 52.5, 55.9, 108.1, 116.9, 121.1, 127.2, 128.6, 129.2, 133.6, 134.4, 143.1, 144.9, 146.6. Anal. Calcd. for $\text{C}_{20}\text{H}_{24}\text{ClN}_3\text{O}$: C, 67.12; H, 6.76; N, 11.74. Found: C, 66.89; H, 6.50; N, 11.51.

(±)-(2*S,4*S**)-4,6-Dimethyl-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3g).** Mp 119-120 °C. IR (neat) 3366.4, 2956.1, 2852.5, 1612.1, 1506.5, 1467.1, 1247.4, 1172.8, 1034.2 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 1.59 (s, 3H), 1.80 (dd, $J = 13.1, 2.6$ Hz, 1H), 2.07 (dd, $J = 13.1, 11.6$ Hz, 1H), 2.25 (s, 3H), 2.78 (s, 6H), 3.85 (s, 3H), 4.00 (bs, 1H), 4.51 (dd, $J = 11.6, 2.6$ Hz, 1H), 6.53 (d, $J = 8.3$ Hz, 1H), 6.70 (s, 1H), 6.86-6.89 (m, 2H), 6.93 (d, $J = 8.7$ Hz, 2H), 7.40 (d, $J = 8.7$ Hz, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 62.9 MHz) δ 20.9, 28.4, 41.2, 43.9, 44.8, 52.9, 55.8, 114.4, 115.0, 127.1, 127.2, 128.2, 128.5, 129.6, 136.7, 142.5, 145.5, 159.5. Anal. Calcd. for $\text{C}_{21}\text{H}_{27}\text{N}_3\text{O}$: C, 74.74; H, 8.06; N, 12.45. Found: C, 74.35; H, 7.93; N, 12.41.

(±)-(2*S,4*S**)-4-Methyl-6-methoxy-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3h).** Mp 94-95 °C. IR (neat) 3363.2, 2950.8, 2831.5, 1611.1, 1503.3, 1466.3, 1246.4, 1172.4, 1035.5 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 1.60 (s, 3H), 1.81 (dd, $J = 13.2, 2.5$ Hz, 1H), 2.08 (dd, $J = 13.2, 11.6$ Hz, 1H), 2.77 (s, 6H), 3.76 (s, 3H), 3.85 (s, 3H), 3.89 (bs, 1H), 4.48 (dd, $J = 11.6, 2.5$ Hz, 1H), 6.56 (dd, $J = 7.5, 1.4$ Hz, 1H), 6.67-6.70 (m, 3H), 6.93 (d, $J = 8.7$ Hz, 2H), 7.40 (d, $J = 8.7$ Hz, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 62.9 MHz) δ 28.6, 41.6, 43.9, 44.7, 53.0, 55.8, 56.3, 113.9, 114.4, 114.8, 115.9, 128.2, 128.5, 136.7, 139.1, 145.1, 152.5, 159.5. Anal. Calcd. for $\text{C}_{21}\text{H}_{27}\text{N}_3\text{O}_2$: C, 71.36; H, 7.70; N, 11.89. Found: C, 71.28; H, 7.48; N, 11.95.

(±)-(2*S,4*S**)-2-(4-Chlorophenyl)-4,6,8-trimethyl-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3i).** Mp 125-126 °C. IR (neat) 3396.4, 2917.9, 2850.9, 1612.0, 1485.9, 1442.6, 1261.4, 1088.0, 1014.0 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 1.60 (s, 3H), 1.82 (dd, $J = 13.0, 2.5$ Hz, 1H), 2.05 (dd, $J = 13.0, 11.6$ Hz, 1H), 2.15 (s, 3H), 2.25 (s, 3H), 2.78 (s, 6H), 3.84 (bs, 1H), 4.57 (dd, $J = 11.6, 2.5$ Hz, 1H),

6.69 (s, 1H), 6.81-6.83 (m, 2H), 7.38 (d, $J = 8.6$ Hz, 2H), 7.47 (d, $J = 8.6$ Hz, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 62.9 MHz) δ 17.9, 20.9, 28.4, 41.2, 43.9, 44.7, 53.1, 122.1, 126.7, 126.8, 127.3, 128.6, 129.2, 129.9, 133.6, 140.1, 143.5, 145.3. Anal. Calcd. for $\text{C}_{21}\text{H}_{26}\text{ClN}_3$: C, 70.87; H, 7.36; N, 11.81. Found: C, 70.88; H, 7.21; N, 12.06.

(±)-(2*S,4*S**)-2-4,6,8-Trimethyl-(4-methoxyphenyl)-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3j).** Mp 117-118 °C. IR (neat) 3386.0, 2931.1, 2852.3, 1611.3, 1511.8, 1485.2, 1302.1, 1246.2, 1174.1, 1033.9 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 1.60 (s, 3H), 1.82 (dd, $J = 13.0, 2.2$ Hz, 1H), 2.07 (dd, $J = 13.0, 11.6$ Hz, 1H), 2.14 (s, 3H), 2.25 (s, 3H), 2.78 (s, 6H), 3.84 (bs, 1H), 3.87 (s, 3H), 4.55 (dd, $J = 11.6, 2.2$ Hz, 1H), 6.71 (s, 1H), 6.81-6.83 (m, 2H), 6.96 (d, $J = 8.6$ Hz, 2H), 7.45 (d, $J = 8.6$ Hz, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 62.9 MHz) δ 17.9, 20.9, 28.4, 41.3, 43.9, 44.7, 52.9, 55.8, 114.4, 121.9, 126.4, 126.5, 127.3, 128.3, 129.9, 137.0, 140.4, 145.9, 159.5. Anal. Calcd. for $\text{C}_{22}\text{H}_{29}\text{N}_3\text{O}$: C, 75.18; H, 8.32; N, 11.96. Found: C, 75.35; H, 8.15; N, 11.99.

(±)-(2*S,4*S**)-2-4,6,8-Trimethyl-(4-methylphenyl)-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3k).** Mp 85-86 °C. IR (neat) 3398.7, 2919.7, 2852.1, 1612.1, 1484.7, 1261.9, 1017.8 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 1.62 (s, 3H), 1.84 (dd, $J = 13.3, 2.3$ Hz, 1H), 2.09 (dd, $J = 13.3, 11.6$ Hz, 1H), 2.15 (s, 3H), 2.26 (s, 3H), 2.43 (s, 3H), 2.79 (s, 6H), 3.88 (bs, 1H), 4.58 (dd, $J = 11.6, 2.3$ Hz, 1H), 6.72 (s, 1H), 6.83-6.84 (m, 2H), 7.25 (d, $J = 8.0$ Hz, 2H), 7.44 (d, $J = 8.0$ Hz, 2H). $^{13}\text{C-NMR}$ (CDCl_3 , 62.9 MHz) δ 17.9, 20.9, 21.6, 28.3, 41.3, 43.9, 44.7, 53.3, 121.9, 126.4, 126.5, 127.1, 127.4, 129.8, 129.9, 137.8, 140.4, 142.0, 145.9. Anal. Calcd. for $\text{C}_{22}\text{H}_{29}\text{N}_3$: C, 78.76; H, 8.71; N, 12.53. Found: C, 79.10; H, 8.46; N, 12.36.

(±)-(2*S,4*S**)-2-(4-Bromophenyl)-4,6,8-trimethyl-1,2,3,4-tetrahydroquinoline-4-carbaldehyde *N,N*-dimethylhydrazone (3l).** Mp 131-132 °C. IR (neat) 3391.5, 2917.9, 2852.3, 1610.2, 1484.8, 1261.3, 1071.0, 1009.3 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 1.60 (s, 3H), 1.82 (dd, $J =$

13.0, 2.4 Hz, 1H), 2.05 (dd, $J = 13.0, 11.6$ Hz, 1H), 2.15 (s, 3H), 2.26 (s, 3H), 2.78 (s, 6H), 3.83 (bs, 1H), 4.56 (dd, $J = 11.6, 2.4$ Hz, 1H), 6.68 (s, 1H), 6.81-6.83 (m, 2H), 7.41 (d, $J = 8.5$ Hz, 2H), 7.54 (d, $J = 8.5$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 17.9, 20.9, 28.4, 41.2, 43.9, 44.6, 53.1, 121.7, 122.1, 126.7, 126.8, 127.3, 128.9, 130.0, 132.2, 140.1, 144.0, 145.3. Anal. Calcd. for $\text{C}_{21}\text{H}_{26}\text{BrN}_3$: C, 63.00; H, 6.55; N, 10.50. Found: C, 62.89; H, 6.39; N, 10.72.

Representative spectra of compounds 3































