

Supporting Information

Two-step stereocontrolled synthesis of cyclic β -aminoesters containing four stereocenters, based on a sequential three-component reaction

Vellaisamy Sridharan and J. Carlos Menéndez*

[§]Departamento de Química Orgánica y Farmacéutica, Facultad de Farmacia, Universidad Complutense, 28040 Madrid, Spain. E-mail, josecm@farm.ucm.es.

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Experimental Section

General experimental information

All reagents (Aldrich, Fluka, SDS, Probus) and solvents (SDS) were of commercial quality and were used as received. Reactions were monitored by thin layer chromatography, on aluminium plates coated with silica gel with fluorescent indicator (SDS CCM221254). Separations by flash chromatography were performed on silica gel (SDS 60 ACC 40-63 μm). Melting points were measured on a Reichert 723 hot stage microscope, and are uncorrected. Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrophotometer, with all compounds examined as thin films on NaCl disks. NMR spectra were obtained on a Bruker Avance 250 spectrometer operating at 250 MHz for ^1H and 63 MHz for ^{13}C (CAI de Resonancia Magnética Nuclear, Universidad Complutense). Elemental analyses were determined by the CAI de Microanálisis Elemental, Universidad Complutense, using a Leco 932 CHNS combustion microanalyzer. The X-Ray diffraction study of compound **5c** was performed at the Physical Chemistry Department, Madurai Tamaraj University, Madurai, Tamil Nadu, India.

General procedure for the synthesis of compounds (**5**)

To a stirred solution of amine **2** (3.9 mmol, 1.3 eq) and β -keto ester **3** (3 mmol, 1 eq) in ethanol (5 mL) was added CAN (5 mol %). Stirring was continued for 30 min at room temperature. Chalcone **4** (3.3 mmol, 1.1 eq) was then added to the stirred solution and the stirring was continued for the time periods specified in Table 1. After completion of the reaction, as indicated by TLC, the mixture was dissolved in CH_2Cl_2 (30 mL), washed with water, brine, dried (anhydrous Na_2SO_4), and the solvent was evaporated under reduced pressure. Pure products **5** were obtained by rapid column chromatography on neutral alumina (activity grade II-III), eluting with a petroleum ether-ethyl acetate mixture (90:10, v/v).

2-Butylamino-4-hydroxy-4,6-diphenylcyclohex-1-enecarboxylic acid ethyl ester (5a). Mp 98-99 °C. IR (neat) 3446.1, 3271.5, 3024.7, 2930.9, 1627.6, 1593.9, 1453.0, 1245.6, 1060.5 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.75 (t, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H), 1.36-1.51 (m, 2H), 1.55-1.67 (m, 2H), 1.99 (dd, *J* = 13.6, 11.0 Hz, 1H), 2.30 (dd, *J* = 13.6, 7.0 Hz, 1H), 2.39 (s, 1H), 2.80 (s, 2H), 3.13-3.29 (m, 2H), 3.72-3.93 (m, 2H), 4.10 (dd, *J* = 11.0, 7.0 Hz, 1H), 7.14-7.41 (m, 8H), 7.54 (d, *J* = 7.5 Hz, 2H), 9.12 (bt, *J* = 4.6 Hz, 1H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.1, 14.3, 20.6, 32.8, 39.9, 41.6, 42.9, 46.1, 58.9, 72.2, 91.5, 124.9, 125.6, 127.1, 127.7, 128.5, 128.8, 146.9, 150.0, 157.9, 170.9. Anal. Calcd for C₂₅H₃₁NO₃: C, 76.30; H, 7.94; N, 3.56. Found: C, 76.53; H, 7.84; N, 3.65.

2-Butylamino-4-(4-chlorophenyl)-4-hydroxy-6-phenylcyclohex-1-enecarboxylic acid ethyl ester (5b). Mp 117-118 °C. IR (neat) 3423.1, 3275.9, 3025.7, 2931.2, 1627.0, 1595.4, 1453.2, 1246.0, 1094.1, 1013.5 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.75 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H), 1.36-1.51 (m, 2H), 1.55-1.65 (m, 2H), 1.95 (dd, *J* = 13.7, 11.2 Hz, 1H), 2.26 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.47 (s, 1H), 2.75 (s, 2H), 3.13-3.27 (m, 2H), 3.72-3.93 (m, 2H), 4.08 (dd, *J* = 11.2, 6.8 Hz, 1H), 7.12-7.35 (m, 7H), 7.47 (d, *J* = 8.4 Hz, 2H), 9.12 (bt, *J* = 4.7 Hz, 1H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.1, 14.3, 20.6, 32.8, 39.8, 41.5, 42.9, 45.9, 59.0, 71.9, 91.5, 125.7, 126.6, 127.1, 128.6, 128.9, 133.5, 145.5, 149.7, 157.5, 170.8. Anal. Calcd for C₂₅H₃₀ClNO₃: C, 70.16; H, 7.07; N, 3.27. Found: C, 70.12; H, 6.94; N, 3.46.

2-Butylamino-4-hydroxy-4,6-diphenylcyclohex-1-enecarboxylic acid *t*-butyl ester (5c). Mp 135-136 °C. IR (neat) 3460.2, 3266.6, 3023.7, 2928.4, 1643.3, 1595.9, 1451.9, 1245.9, 1163.8, 1049.9 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.97 (t, *J* = 7.3 Hz, 3H), 1.10 (s, 9H), 1.35-1.49 (m, 2H), 1.56-1.68 (m, 2H), 1.94 (dd, *J* = 13.7, 11.2 Hz, 1H), 2.27 (dd, *J* = 13.7, 6.7 Hz, 1H), 2.44 (s, 1H), 2.78 (s, 2H), 3.11-3.30 (m, 2H), 4.04 (dd, *J* = 11.2, 6.7 Hz, 1H), 7.16-7.41 (m, 8H), 7.54 (d, *J* = 7.4 Hz, 2H), 9.05 (bt, *J* = 4.6 Hz, 1H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.3, 20.6, 28.5,

33.0, 40.3, 41.6, 42.9, 46.2, 72.1, 79.0, 92.8, 125.0, 125.7, 127.3, 127.6, 128.5, 128.8, 147.0, 150.4, 157.0, 170.7. Anal. Calcd for $C_{27}H_{35}NO_3$: C, 76.92; H, 8.37; N, 3.32. Found: C, 76.90; H, 8.17; N, 3.43.

2-Butylamino-4-(4-chlorophenyl)-4-hydroxy-6-phenylcyclohex-1-enecarboxylic acid *t*-butyl ester (5d). Mp 143-144 °C. IR (neat) 3445.2, 3272.7, 3018.5, 2930.8, 1643.4, 1597.5, 1452.9, 1246.7, 1163.5, 1094.4, 1012.3 cm^{-1} . 1H -NMR ($CDCl_3$, 250 MHz) δ 0.97 (t, $J = 7.2$ Hz, 3H), 1.09 (s, 9H), 1.35-1.49 (m, 2H), 1.56-1.67 (m, 2H), 1.89 (dd, $J = 13.7, 11.2$ Hz, 1H), 2.23 (dd, $J = 13.7, 6.6$ Hz, 1H), 2.49 (s, 1H), 2.74 (s, 2H), 3.11-3.25 (m, 2H), 4.02 (dd, $J = 11.2, 6.6$ Hz, 1H), 7.13-7.34 (m, 7H), 7.47 (d, $J = 8.7$ Hz, 2H), 9.04 (bt, $J = 4.4$ Hz, 1H). ^{13}C -NMR ($CDCl_3$, 62.9 MHz) δ 14.3, 20.6, 28.4, 33.0, 40.2, 41.6, 42.9, 46.1, 71.9, 79.1, 92.7, 125.8, 126.6, 127.2, 128.5, 128.9, 133.4, 145.5, 150.1, 156.6, 170.7. Anal. Calcd for $C_{27}H_{34}ClNO_3$: C, 71.11; H, 7.52; N, 3.07. Found: C, 70.91; H, 7.41; N, 3.12.

2-Hexylamino-4-hydroxy-4,6-diphenylcyclohex-1-enecarboxylic acid ethyl ester (5e). Mp 116-117 °C. IR (neat) 3443.7, 3277.0, 2929.4, 2858.2, 1628.2, 1594.3, 1453.3, 1245.8, 1061.6 cm^{-1} . 1H -NMR ($CDCl_3$, 250 MHz) δ 0.75 (t, $J = 7.1$ Hz, 3H), 0.92 (t, $J = 6.8$ Hz, 3H), 1.29-1.41 (m, 6H), 1.59-1.66 (m, 2H), 1.99 (dd, $J = 13.8, 11.2$ Hz, 1H), 2.30 (dd, $J = 13.8, 6.8$ Hz, 1H), 2.41 (s, 1H), 2.80 (s, 2H), 3.13-3.26 (m, 2H), 3.70-3.93 (m, 2H), 4.10 (dd, $J = 11.2, 6.8$ Hz, 1H), 7.17-7.41 (m, 8H), 7.54 (d, $J = 7.8$ Hz, 2H), 9.11 (bt, $J = 4.9$ Hz, 1H). ^{13}C -NMR ($CDCl_3$, 62.9 MHz) δ 14.1, 14.5, 22.9, 27.1, 30.7, 31.9, 39.9, 41.6, 43.2, 46.1, 58.9, 72.2, 91.5, 124.9, 125.6, 127.1, 127.7, 128.5, 128.8, 146.9, 150.0, 157.8, 170.8. Anal. Calcd for $C_{27}H_{35}NO_3$: C, 76.92; H, 8.37; N, 3.32. Found: C, 76.72; H, 8.14; N, 3.53.

2-Heptylamino-4-hydroxy-4,6-diphenylcyclohex-1-enecarboxylic acid ethyl ester (5f). Mp 88-89 °C. IR (neat) 3444.2, 3277.0, 2927.9, 2856.8, 1646.0, 1594.9, 1452.8, 1241.9, 1061.4 cm^{-1} . 1H -NMR ($CDCl_3$, 250 MHz) δ 0.76 (t, $J = 7.1$ Hz, 3H), 0.91 (t, $J = 6.7$ Hz, 3H), 1.30-1.42 (m, 8H), 1.57-1.68 (m, 2H), 1.99 (dd, $J = 13.8, 11.2$ Hz, 1H), 2.30 (dd, $J = 13.8, 6.7$ Hz, 1H), 2.40 (s, 1H), 2.80 (s, 2H), 3.12-3.28 (m, 2H), 3.70-

3.96 (m, 2H), 4.10 (dd, $J = 11.2, 6.7$ Hz, 1H), 7.11-7.41 (m, 8H), 7.54 (d, $J = 8.1$ Hz, 2H), 9.11 (bt, $J = 5.1$ Hz, 1H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 14.2, 14.5, 23.1, 27.4, 29.4, 30.7, 32.1, 39.9, 41.6, 43.2, 46.1, 58.9, 72.2, 91.5, 124.9, 125.6, 127.1, 127.7, 128.5, 128.8, 146.9, 150.0, 157.9, 170.9. Anal. Calcd for $\text{C}_{28}\text{H}_{37}\text{NO}_3$: C, 77.20; H, 8.56; N, 3.22. Found: C, 77.14; H, 8.44; N, 3.46.

4-(4-Chlorophenyl)-2-hexylamino-4-hydroxy-6-phenylcyclohex-1-enecarboxylic acid ethyl ester (5g). Mp 130-131 °C. IR (neat) 3424.1, 3277.0, 2929.1, 2858.1, 1627.4, 1596.2, 1453.0, 1246.2, 1094.4 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 0.75 (t, $J = 7.1$ Hz, 3H), 0.91 (t, $J = 6.9$ Hz, 3H), 1.29-1.45 (m, 6H), 1.56-1.64 (m, 2H), 1.95 (dd, $J = 13.7, 11.2$ Hz, 1H), 2.27 (dd, $J = 13.7, 6.8$ Hz, 1H), 2.46 (s, 1H), 2.75 (s, 2H), 3.12-3.25 (m, 2H), 3.70-3.93 (m, 2H), 4.08 (dd, $J = 11.0, 6.8$ Hz, 1H), 7.12-7.36 (m, 7H), 7.47 (d, $J = 8.5$ Hz, 2H), 9.11 (bt, $J = 5.2$ Hz, 1H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 14.1, 14.5, 22.9, 27.1, 30.7, 31.9, 39.8, 41.5, 43.2, 45.9, 59.0, 71.9, 91.5, 125.7, 126.6, 127.1, 128.6, 128.9, 133.5, 145.5, 149.7, 157.5, 170.8. Anal. Calcd for $\text{C}_{27}\text{H}_{34}\text{ClNO}_3$: C, 71.11; H, 7.52; N, 3.07. Found: C, 70.81; H, 7.37; N, 3.31.

4-(4-Chlorophenyl)-2-heptylamino-4-hydroxy-6-phenylcyclohex-1-enecarboxylic acid ethyl ester (5h). Mp 97-98 °C. IR (neat) 3420.2, 3277.0, 2927.9, 2856.9, 1627.3, 1596.0, 1452.9, 1242.5, 1094.1 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 0.75 (t, $J = 7.1$ Hz, 3H), 0.91 (t, $J = 6.8$ Hz, 3H), 1.30-1.42 (m, 8H), 1.56-1.68 (m, 2H), 1.95 (dd, $J = 13.7, 11.2$ Hz, 1H), 2.27 (dd, $J = 13.7, 6.7$ Hz, 1H), 2.46 (s, 1H), 2.75 (s, 2H), 3.12-3.27 (m, 2H), 3.70-3.96 (m, 2H), 4.08 (dd, $J = 11.1, 6.8$ Hz, 1H), 7.11-7.36 (m, 7H), 7.48 (d, $J = 8.5$ Hz, 2H), 9.11 (bt, $J = 5.1$ Hz, 1H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 14.1, 14.5, 23.0, 27.3, 29.4, 30.7, 32.1, 39.8, 41.5, 43.2, 45.9, 59.0, 71.9, 91.4, 125.7, 126.6, 127.1, 128.6, 128.9, 133.5, 145.5, 149.7, 157.5, 170.8. Anal. Calcd for $\text{C}_{28}\text{H}_{36}\text{ClNO}_3$: C, 71.55; H, 7.72; N, 2.98. Found: C, 71.48; H, 7.60; N, 3.19.

4-Hydroxy-2-(2-methylbutylamino)-4,6-diphenylcyclohex-1-enecarboxylic acid ethyl ester (5i). Mp 102-103 °C. IR (KBr) 3493.3, 3265.6, 2962.5, 2874.0, 1620.3, 1592.4, 1452.1, 1384.3, 1254.8, 1229.7, 1095.3, cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 0.75 (t, $J = 7.1$ Hz, 3H), 0.95 (t, $J = 7.3$ Hz, 3H), 1.01 (d, $J = 6.6$ Hz, 3H), 1.18-1.32 (m, 1H), 1.46-1.69 (m, 2H), 1.99 (dd, $J = 13.8, 11.2$ Hz, 1H), 2.30 (dd, $J = 13.8, 6.7$ Hz, 1H), 2.42 (s, 1H), 2.79 (s, 2H), 2.95-3.22 (m, 2H), 3.74-3.94 (m, 2H), 4.10 (dd, $J = 11.0, 6.7$ Hz, 1H), 7.13-7.42 (m, 8H), 7.54 (dd, $J = 8.0, 1.2$ Hz, 2H), 9.25 (bt, $J = 5.0$ Hz, 1H). $^{13}\text{C-NMR}$ (CDCl_3 , 62.9 MHz) δ 11.8, 14.2, 17.8, 17.9, 27.5, 36.0, 36.1, 40.0, 41.7, 46.2, 49.0, 58.9, 72.2, 91.5, 91.6, 125.0, 125.6, 127.2, 127.7, 128.5, 128.8, 147.1, 150.1, 158.1, 170.9. Anal. Calcd for $\text{C}_{26}\text{H}_{33}\text{NO}_3$: C, 76.62; H, 8.16; N, 3.44. Found: C, 76.69; H, 8.08; N, 3.72.

2-sec-Butylamino-4-hydroxy-4,6-diphenylcyclohex-1-enecarboxylic acid ethyl ester (5j, diastereoisomer A). Viscous liquid. IR (neat) 3257.5, 2968.0, 2867.4, 1724.6, 1645.0, 1574.4, 1435.8, 1238.6, 1076.4 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 0.76 (t, $J = 7.1$ Hz, 3H), 0.97 (t, $J = 7.5$ Hz, 3H), 1.24 (d, $J = 6.4$ Hz, 3H), 1.50-1.61 (m, 2H), 1.99 (dd, $J = 13.8, 11.2$ Hz, 1H), 2.32 (dd, $J = 13.8, 6.7$ Hz, 1H), 2.42 (s, 1H), 2.82 (s, 2H), 3.46-3.58 (m, 1H), 3.71-3.97 (m, 2H), 4.11 (dd, $J = 11.0, 6.9$ Hz, 1H), 7.16-7.41 (m, 8H), 7.55 (d, $J = 7.6$ Hz, 2H), 9.17 (d, $J = 8.8$ Hz, 1H). $^{13}\text{C-NMR}$ (CDCl_3 , 62.9 MHz) δ 10.8, 14.1, 22.1, 31.5, 40.0, 41.4, 46.2, 49.5, 58.9, 72.3, 91.4, 125.0, 125.6, 127.7, 128.2, 128.6, 128.8, 146.9, 150.1, 157.3, 170.9. Anal. Calcd for $\text{C}_{25}\text{H}_{31}\text{NO}_3$: C, 76.30; H, 7.94; N, 3.56. Found: C, 76.57; H, 7.69; N, 3.68.

2-sec-Butylamino-4-hydroxy-4,6-diphenylcyclohex-1-enecarboxylic acid ethyl ester (5j, diastereoisomer B). Viscous liquid. IR (neat) 3263.4, 2968.2, 2874.0, 1731.6, 1645.1, 1574.8, 1447.0, 1240.4, 1075.3 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3 , 250 MHz) δ 0.76 (t, $J = 7.1$ Hz, 3H), 1.01 (t, $J = 7.4$ Hz, 3H), 1.21 (d, $J = 6.4$ Hz, 3H), 1.54-1.65 (m, 2H), 1.99 (dd, $J = 13.8, 11.2$ Hz, 1H), 2.32 (dd, $J = 13.8, 6.9$ Hz, 1H), 2.44 (s, 1H), 2.80 (s, 2H), 3.45-3.54 (m, 1H), 3.74-3.97 (m, 2H), 4.11 (dd, $J = 11.1, 7.0$ Hz, 1H), 7.18-7.42 (m, 8H), 7.54 (d, $J = 7.6$ Hz, 2H), 9.14 (d, $J = 9.1$ Hz, 1H).

^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 11.1, 14.2, 22.6, 31.4, 39.9, 41.6, 46.1, 49.8, 58.9, 72.3, 91.3, 125.0, 125.6, 127.1, 127.9, 128.5, 128.8, 146.9, 150.1, 157.3, 170.9. Anal. Calcd for $\text{C}_{25}\text{H}_{31}\text{NO}_3$: C, 76.30; H, 7.94; N, 3.56. Found: C, 76.07; H, 7.82; N, 3.69.

General procedure for the synthesis of compounds (9)

To a solution of the enamino ester **5** (1 mmol) in ethanol (10 mL) was added ammonium formate (10 mmol). The mixture was stirred at room temperature for 5 h. After completion of the reaction, the mixture was diluted with CH_2Cl_2 , washed with water and evaporated. The amino compounds **9** were purified by recrystallization from ethanol.

2-Amino-4-hydroxy-4,6-diphenylcyclohex-1-enecarboxylic acid ethyl ester (9a). Mp 140-141 °C. IR (KBr) 3474.0, 3328.5, 2982.0, 2924.5, 1654.3, 1608.6, 1531.0, 1360.2, 1262.9, 1065.7 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 0.78 (t, $J = 7.1$ Hz, 3H), 2.00 (dd, $J = 13.7, 11.3$ Hz, 1H), 2.29-2.35 (m, 2H), 2.41 (dd, $J = 16.8, 2.9$ Hz, 1H), 3.01 (d, $J = 16.8$ Hz, 1H), 3.73-4.00 (m, 2H), 4.07 (dd, $J = 11.0, 3.4$ Hz, 1H), 6.20 (bs, 2H), 7.12-7.40 (m, 8H), 7.52 (dd, $J = 8.1, 1.1$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 14.1, 39.9, 45.3, 46.6, 59.3, 72.5, 94.9, 124.9, 125.8, 127.3, 127.8, 128.6, 128.8, 146.5, 149.2, 154.7, 170.2. Anal. Calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_3$: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.67; H, 6.81; N, 4.12.

2-Amino-4-(4-chlorophenyl)-4-hydroxy-6-phenylcyclohex-1-enecarboxylic acid ethyl ester (9b). Mp 146-147 °C. IR (KBr) 3529.8, 3456.2, 3311.4, 2981.5, 2945.6, 1664.4, 1614.3, 1544.0, 1492.6, 1366.8, 1261.5, 1065.7 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 0.78 (t, $J = 7.1$ Hz, 3H), 1.96 (dd, $J = 13.7, 11.8$ Hz, 1H), 2.25-2.41 (m, 3H), 2.96 (d, $J = 17.1$ Hz, 1H), 3.75-3.97 (m, 2H), 4.06 (dd, $J = 10.5, 6.4$ Hz, 1H), 6.20 (bs, 2H),

7.13-7.34 (m, 7H), 7.45 (d, $J = 8.6$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 14.1, 39.9, 45.3, 46.5, 59.3, 72.3, 94.8, 125.9, 126.5, 127.2, 128.6, 128.9, 133.5, 145.1, 148.9, 154.4, 170.2. Anal. Calcd for $\text{C}_{21}\text{H}_{22}\text{ClNO}_3$: C, 67.83; H, 5.96; N, 3.77. Found: C, 67.61; H, 5.92; N, 3.91.

2-Amino-4-hydroxy-4,6-diphenylcyclohex-1-enecarboxylic acid *t*-butyl ester (9c). Mp 163-164 °C. IR (KBr) 3366.9, 3321.5, 2969.8, 2928.8, 1664.9, 1614.5, 1539.2, 1448.1, 1364.1, 1246.5, 1166.6 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 1.11 (s, 9H), 1.96 (dd, $J = 13.6, 11.5$ Hz, 1H), 2.25-2.34 (m, 2H), 2.38 (dd, $J = 16.9, 3.0$ Hz, 1H), 2.99 (dd, $J = 16.9, 1.9$ Hz, 1H), 4.02 (dd, $J = 10.9, 6.6$ Hz, 1H), 6.30 (bs, 2H), 7.13-7.40 (m, 8H), 7.52 (dd, $J = 8.0, 1.1$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 28.4, 40.3, 45.4, 46.7, 72.5, 79.5, 96.3, 124.9, 125.8, 127.4, 127.7, 128.6, 128.8, 146.7, 149.6, 153.9, 170.0. Anal. Calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_3$: C, 75.59; H, 7.45; N, 3.83. Found: C, 75.31; H, 7.28; N, 3.78.

2-Amino-4-(4-chlorophenyl)-4-hydroxy-6-phenylcyclohex-1-enecarboxylic acid *t*-butyl ester (9d). Mp 185-186 °C. IR (KBr) 3530.7, 3461.7, 3312.6, 2976.3, 2920.0, 1658.1, 1613.3, 1540.0, 1367.9, 1276.7, 1164.2 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 1.10 (s, 9H), 1.92 (dd, $J = 13.7, 11.4$ Hz, 1H), 2.20-2.39 (m, 3H), 2.94 (dd, $J = 16.9, 1.8$ Hz, 1H), 4.00 (dd, $J = 11.1, 6.7$ Hz, 1H), 6.10 (bs, 2H), 7.14-7.34 (m, 7H), 7.45 (d, $J = 8.6$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 28.3, 40.2, 45.4, 46.6, 72.2, 79.6, 96.2, 125.9, 126.5, 127.3, 128.6, 128.9, 133.5, 145.1, 149.2, 153.5, 169.9. Anal. Calcd for $\text{C}_{23}\text{H}_{26}\text{ClNO}_3$: C, 69.08; H, 6.55; N, 3.50. Found: C, 68.80; H, 6.49; N, 3.79.

General procedure for the reduction of compounds (5) or (9) to (10)

A solution of sodium triacetoxyborohydride ($\text{NaBH}(\text{OAc})_3$) was prepared by adding sodium borohydride (6 mmol) to glacial acetic acid (3 mL) while the temperature was kept between 15 to 20 °C. After hydrogen evolution ceased (30 min), the enamino ester **5** or **9** (1 mmol) was added in

one portion and the reaction mixture was stirred for 2 h at room temperature. After completion of the reaction, the mixture was diluted with water, neutralized with saturated sodium bicarbonate solution, and extracted twice with CH₂Cl₂ (30 mL). This solution was washed with saturated sodium bicarbonate solution, dried (anhyd. Na₂SO₄), and evaporated under reduced pressure. The products were separated by silica gel column chromatography using petroleum ether- ethyl acetate (96:4, v/v) as eluent.

2-Butylamino-4-hydroxy-4,6-diphenylcyclohexanecarboxylic acid ethyl ester (10a). Mp 146-147 °C. IR (neat) 3316.1, 2925.3, 2831.5, 1706.4, 1454.7, 1372.0, 1174.2, 1025.3 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.88-0.99 (m, 6H), 1.34-1.45 (m, 2H), 1.48-1.59 (m, 2H), 1.85 (dd, *J* = 14.2, 2.6 Hz, 1H), 2.02 (dd, *J* = 13.5, 12.1 Hz, 1H), 2.14 (ddd, *J* = 13.6, 4.0, 2.1 Hz, 1H), 2.27 (dt, *J* = 14.2, 2.6 Hz, 1H), 2.45-2.55 (m, 1H), 2.84-2.94 (m, 1H), 3.03 (dd, *J* = 12.3, 2.9 Hz, 1H), 3.44 (q, *J* = 2.7 Hz, 1H), 3.76 (td, *J* = 12.1, 4.0 Hz, 1H), 3.85-3.98 (m, 2H), 7.18-7.39 (m, 8H), 7.55 (dd, *J* = 7.5, 1.4 Hz, 2H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.2, 14.4, 20.8, 32.2, 37.6, 38.2, 47.8, 48.6, 52.7, 56.4, 60.9, 74.3, 124.8, 126.9, 127.1, 128.1, 128.5, 128.8, 143.2, 148.6, 174.6. Anal. Calcd for C₂₅H₃₃NO₃: C, 75.91; H, 8.41; N, 3.54. Found: C, 75.90; H, 8.35; N, 3.79.

2-Butylamino-4-(4-chlorophenyl)-4-hydroxy-6-phenylcyclohexanecarboxylic acid ethyl ester (10b). Mp 121-122 °C. IR (neat) 3316.1, 2931.8, 2861.3, 1714.8, 1454.0, 1375.7, 1177.2, 1093.0 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.93 (t, *J* = 7.2 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H), 1.34-1.43 (m, 2H), 1.45-1.60 (m, 2H), 1.78 (dd, *J* = 14.2, 2.7 Hz, 1H), 1.98 (dd, *J* = 13.5, 12.1 Hz, 1H), 2.09 (ddd, *J* = 13.5, 4.1, 2.1 Hz, 1H), 2.22 (dt, *J* = 14.1, 2.6 Hz, 1H), 2.45-2.55 (m, 1H), 2.82-2.92 (m, 1H), 3.02 (dd, *J* = 12.4, 2.9 Hz, 1H), 3.43 (q, *J* = 2.8 Hz, 1H), 3.74 (td, *J* = 12.2, 4.1 Hz, 1H), 3.84-3.99 (m, 2H), 7.17-7.34 (m, 7H), 7.48 (d, *J* = 8.7 Hz, 2H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.2, 14.4, 20.8, 32.2, 37.6, 38.2, 47.8, 48.5, 52.6, 56.4, 60.9, 74.1, 126.4, 127.2, 128.0, 128.6, 128.9, 132.6, 143.0, 147.2, 174.5. Anal. Calcd for C₂₅H₃₂ClNO₃: C, 69.83; H, 7.50; N, 3.26. Found: C, 69.62; H, 7.50; N, 3.52.

2-Butylamino-4-hydroxy-4,6-diphenylcyclohexanecarboxylic acid *t*-butyl ester (10c). Mp 124-125 °C. IR (neat) 3308.6, 2931.0, 2861.3, 1710.9, 1601.7, 1454.1, 1367.7, 1150.3 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.96 (t, *J* = 7.1 Hz, 3H), 1.17 (s, 9H), 1.35-1.48 (m, 2H), 1.49-1.63 (m, 2H), 1.84 (dd, *J* = 14.2, 2.7 Hz, 1H), 1.98 (dd, *J* = 13.5, 12.2 Hz, 1H), 2.12 (ddd, *J* = 13.6, 4.0, 2.3 Hz, 1H), 2.26 (dt, *J* = 14.2, 2.5 Hz, 1H), 2.47-2.57 (m, 1H), 2.84-2.92 (m, 1H), 2.96 (dd, *J* = 12.3, 2.9 Hz, 1H), 3.45 (q, *J* = 2.8 Hz, 1H), 3.71 (td, *J* = 12.3, 4.0 Hz, 1H), 7.20-7.39 (m, 8H), 7.54 (dd, *J* = 8.7, 1.5 Hz, 2H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.4, 20.8, 28.0, 32.2, 37.7, 38.3, 47.8, 48.9, 53.4, 56.5, 74.4, 81.6, 124.8, 126.9, 127.0, 128.3, 128.5, 128.7, 143.4, 148.7, 173.9. Anal. Calcd for C₂₇H₃₇NO₃: C, 76.56; H, 8.80; N, 3.31. Found: C, 76.33; H, 8.63; N, 3.47.

2-Butylamino-4-(4-chlorophenyl)-4-hydroxy-6-phenylcyclohexanecarboxylic acid *t*-butyl ester (10d). Mp 95-96 °C. IR (neat) 3313.4, 2930.7, 2861.3, 1712.9, 1601.4, 1455.0, 1368.4, 1151.4 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.97 (t, *J* = 7.2 Hz, 3H), 1.17 (s, 9H), 1.35-1.46 (m, 2H), 1.49-1.65 (m, 2H), 1.78 (dd, *J* = 14.1, 2.6 Hz, 1H), 1.94 (dd, *J* = 13.4, 12.2 Hz, 1H), 2.08 (ddd, *J* = 13.4, 3.9, 2.2 Hz, 1H), 2.20 (dt, *J* = 14.1, 2.6 Hz, 1H), 2.47-2.59 (m, 1H), 2.82-2.90 (m, 1H), 2.94 (dd, *J* = 12.3, 2.9 Hz, 1H), 3.44 (q, *J* = 2.8 Hz, 1H), 3.69 (td, *J* = 12.2, 4.0 Hz, 1H), 7.20-7.34 (m, 7H), 7.47 (d, *J* = 8.6 Hz, 2H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.3, 20.7, 28.0, 32.2, 37.8, 38.2, 47.7, 48.7, 53.2, 56.4, 74.1, 81.7, 126.4, 127.1, 128.2, 128.6, 128.7, 132.6, 143.2, 147.2, 173.7. Anal. Calcd for C₂₇H₃₆ClNO₃: C, 70.80; H, 7.92; N, 3.06. Found: C, 70.74; H, 7.81; N, 3.24.

2-Hexylamino-4-hydroxy-4,6-diphenylcyclohexanecarboxylic acid ethyl ester (10e). Mp 113-114 °C IR (neat) 3323.6, 2922.3, 1708.8, 1603.1, 1455.7, 1376.4, 1175.8 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.89-0.96 (m, 6H), 1.28-1.43 (m, 6H), 1.51-1.60 (m, 2H), 1.85 (dd, *J* = 14.2, 2.6 Hz, 1H), 2.01 (dd, *J* = 13.5, 12.1 Hz, 1H), 2.14 (ddd, *J* = 13.4, 4.0, 2.0 Hz, 1H), 2.27 (dt, *J* = 14.2, 2.6 Hz, 1H), 2.48-2.52 (m, 1H), 2.83-2.93

(m, 1H), 3.03 (dd, $J = 12.4, 2.9$ Hz, 1H), 3.45 (q, $J = 2.8$ Hz, 1H), 3.76 (td, $J = 12.2, 4.0$ Hz, 1H), 3.85-3.98 (m, 2H), 7.16-7.39 (m, 8H), 7.55 (dd, $J = 7.8, 1.4$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 14.2, 14.5, 23.0, 27.3, 30.1, 32.1, 37.6, 38.2, 48.1, 48.6, 52.8, 56.4, 60.9, 74.3, 124.8, 126.9, 127.1, 128.0, 128.5, 128.8, 143.2, 148.6, 174.5. Anal. Calcd for $\text{C}_{27}\text{H}_{37}\text{NO}_3$: C, 76.56; H, 8.80; N, 3.31. Found: C, 76.56; H, 8.60; N, 3.54.

2-Heptylamino-4-hydroxy-4,6-diphenylcyclohexanecarboxylic acid ethyl ester (10f). Mp 107-108 °C. IR (neat) 3319.4, 2925.6, 2853.1, 1708.1, 1455.6, 1376.6, 1175.7 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 0.89-0.97 (m, 6H), 1.24-1.40 (m, 8H), 1.54-1.61 (m, 2H), 1.85 (dd, $J = 14.2, 2.6$ Hz, 1H), 2.02 (dd, $J = 13.5, 12.1$ Hz, 1H), 2.14 (ddd, $J = 13.4, 4.0, 2.1$ Hz, 1H), 2.28 (dt, $J = 14.2, 2.6$ Hz, 1H), 2.45-2.55 (m, 1H), 2.83-2.93 (m, 1H), 3.04 (dd, $J = 12.3, 2.9$ Hz, 1H), 3.45 (q, $J = 2.9$ Hz, 1H), 3.77 (td, $J = 12.2, 4.1$ Hz, 1H), 3.86-3.99 (m, 2H), 7.17-7.39 (m, 8H), 7.56 (dd, $J = 7.8, 1.4$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 14.2, 14.6, 23.1, 27.6, 29.6, 30.2, 32.2, 37.6, 38.2, 48.1, 48.6, 52.8, 56.4, 60.9, 74.3, 124.8, 126.9, 127.1, 128.1, 128.5, 128.8, 143.2, 148.6, 174.5. Anal. Calcd for $\text{C}_{28}\text{H}_{39}\text{NO}_3$: C, 76.85; H, 8.98; N, 3.20. Found: C, 76.65; H, 8.74; N, 3.41.

4-(4-Chlorophenyl)-2-hexylamino-4-hydroxy-6-phenylcyclohexanecarboxylic acid ethyl ester (10g). Mp 122-123 °C. IR (neat) 3316.1, 2924.3, 2846.4, 1708.1, 1455.1, 1327.2, 1175.9 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 0.89-0.96 (m, 6H), 1.29-1.43 (m, 6H), 1.53-1.62 (m, 2H), 1.78 (dd, $J = 14.2, 2.6$ Hz, 1H), 1.97 (dd, $J = 13.5, 12.1$ Hz, 1H), 2.09 (ddd, $J = 13.4, 4.0, 2.0$ Hz, 1H), 2.22 (dt, $J = 14.2, 2.4$ Hz, 1H), 2.45-2.54 (m, 1H), 2.81-2.91 (m, 1H), 3.02 (dd, $J = 12.4, 2.9$ Hz, 1H), 3.43 (q, $J = 2.8$ Hz, 1H), 3.74 (td, $J = 12.2, 4.1$ Hz, 1H), 3.85-3.98 (m, 2H), 7.17-7.34 (m, 7H), 7.48 (d, $J = 8.6$ Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 14.2, 14.5, 23.0, 27.2, 30.1, 32.1, 37.6, 38.1, 48.1, 48.4, 52.6, 56.3, 60.9, 74.0, 126.4, 127.2, 128.0, 128.6, 128.8, 131.4, 143.0, 147.1, 174.4. Anal. Calcd for $\text{C}_{27}\text{H}_{36}\text{ClNO}_3$: C, 70.80; H, 7.92; N, 3.06. Found: C, 70.56; H, 7.76; N, 3.28.

4-(4-Chlorophenyl)-2-heptylamino-4-hydroxy-6-phenylcyclohexanecarboxylic acid ethyl ester (10h). Mp 99-100 °C. IR (neat) 3316.1, 2926.4, 2855.3, 1709.9, 1454.0, 1376.0, 1176.8 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.89-0.96 (m, 6H), 1.24-1.40 (m, 8H), 1.50-1.65 (m, 2H), 1.78 (dd, *J* = 14.2, 2.6 Hz, 1H), 1.98 (dd, *J* = 13.4, 12.1 Hz, 1H), 2.11 (ddd, *J* = 13.4, 4.0, 2.0 Hz, 1H), 2.22 (dt, *J* = 14.2, 2.5 Hz, 1H), 2.44-2.54 (m, 1H), 2.81-2.86 (m, 1H), 3.02 (dd, *J* = 12.4, 2.9 Hz, 1H), 3.42 (q, *J* = 2.6 Hz, 1H), 3.74 (td, *J* = 12.2, 4.1 Hz, 1H), 3.85-3.98 (m, 2H), 7.17-7.33 (m, 7H), 7.48 (d, *J* = 8.6 Hz, 2H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.2, 14.5, 23.1, 27.5, 29.6, 30.1, 32.2, 37.6, 38.1, 48.1, 48.4, 52.6, 56.3, 60.9, 74.0, 126.4, 127.2, 128.0, 128.6, 128.8, 132.7, 143.0, 147.1, 174.4. Anal. Calcd for C₂₈H₃₈ClNO₃: C, 71.24; H, 8.11; N, 2.97. Found: C, 70.99; H, 7.83; N, 3.10.

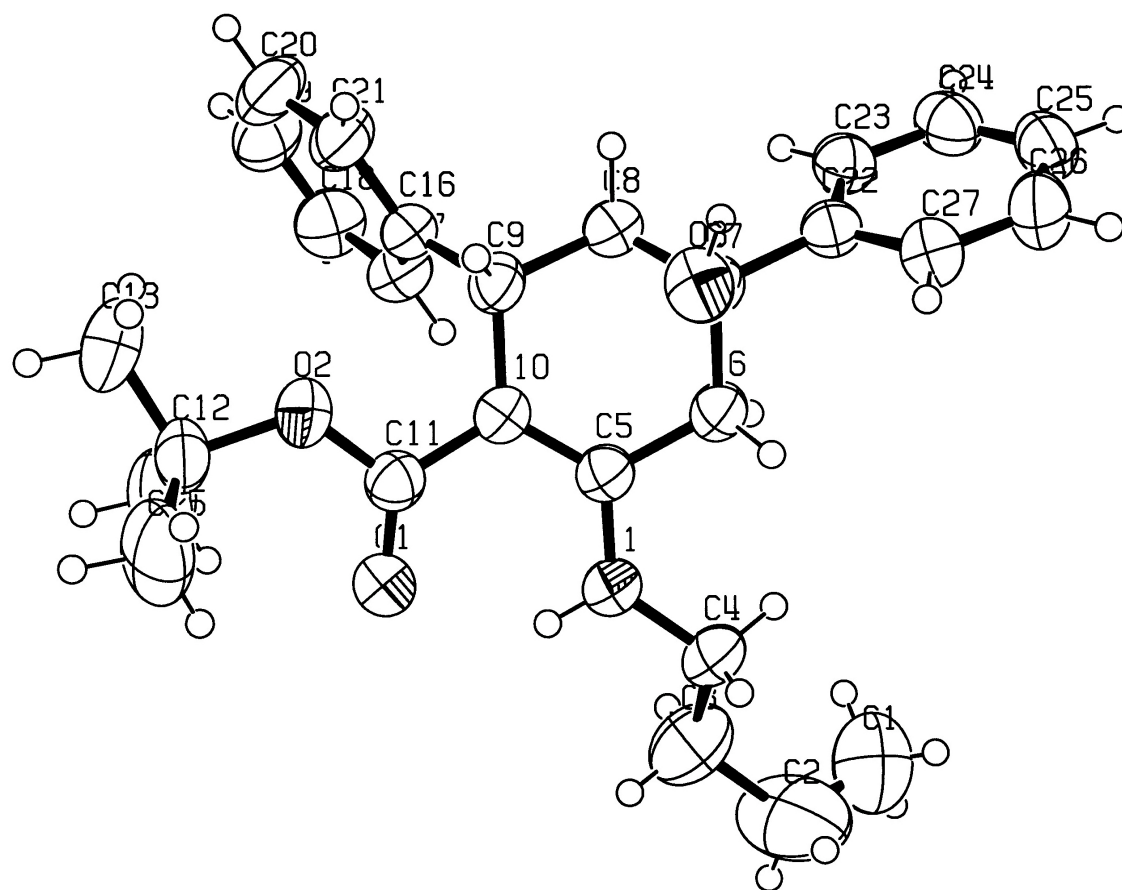
2-Amino-4-hydroxy-4,6-diphenylcyclohexanecarboxylic acid ethyl ester (10i). Mp 174-175 °C. IR (KBr) 3353.9, 3288.6, 3027.8, 2936.9, 1724.1, 1600.0, 1492.2, 1395.8, 1254.7, 1064.9 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.94 (t, *J* = 7.2 Hz, 3H), 2.01-2.17 (m, 4H), 3.01 (dd, *J* = 12.3, 2.9 Hz, 1H), 3.79-3.99 (m, 4H), 7.19-7.39 (m, 8H), 7.55 (dd, *J* = 8.0, 1.5 Hz, 2H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.2, 37.1, 42.6, 48.7, 49.1, 52.8, 60.9, 74.3, 124.8, 127.0, 127.1, 128.1, 128.5, 128.8, 143.3, 148.3, 174.5. Anal. Calcd for C₂₁H₂₅NO₃: C, 74.31; H, 7.42; N, 4.13. Found: C, 74.05; H, 7.31; N, 4.23.

2-Amino-4-(4-chlorophenyl)-4-hydroxy-6-phenylcyclohexanecarboxylic acid ethyl ester (10j). Mp 145-146 °C. IR (KBr) 3374.7, 3030.9, 2919.6, 1711.4, 1573.1, 1490.8, 1378.7, 1175.4, 1097.8 cm⁻¹. ¹H-NMR (CDCl₃, 250 MHz) δ 0.94 (t, *J* = 7.1 Hz, 3H), 1.98-2.13 (m, 4H), 3.00 (dd, *J* = 12.2, 2.6 Hz, 1H), 3.65 (bs, 3H), 3.76-3.98 (m, 4H), 7.19-7.33 (m, 7H), 7.48 (d, *J* = 8.4 Hz, 2H). ¹³C-NMR (CDCl₃, 62.9 MHz) δ 14.2, 37.1, 42.6, 48.5, 49.0, 52.7, 60.9, 74.1, 126.4, 127.2, 128.1, 128.6, 128.9, 132.7, 143.0, 146.9, 174.4. Anal. Calcd for C₂₁H₂₄ClNO₃: C, 67.46; H, 6.47; N, 3.75. Found: C, 67.21; H, 6.41; N, 3.90.

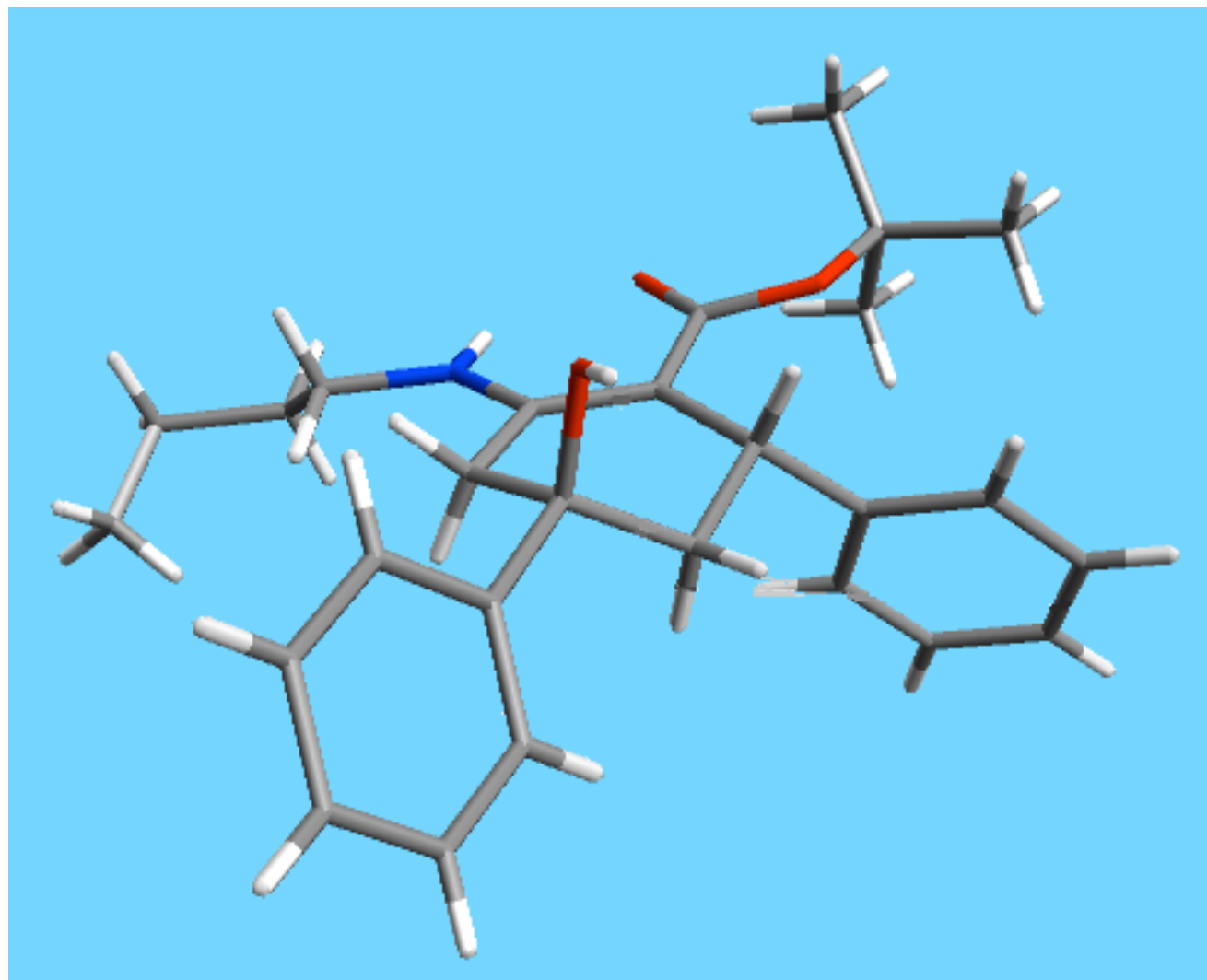
2-Amino-4-hydroxy-4,6-diphenylcyclohexanecarboxylic acid *t*-butyl ester (10k). Mp 119-120 °C. IR (KBr) 3374.9, 3026.1, 2944.1, 1728.8, 1600.4, 1492.4, 1367.5, 1251.1, 1135.6, 1064.0 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 1.16 (s, 9H), 1.98-2.17 (m, 4H), 2.93 (dd, J = 12.2, 2.6 Hz, 1H), 3.70 (bs, 3H), 3.79 (td, J = 12.1, 4.3 Hz, 1H), 3.97 (bq, J = 2.3 Hz, 1H), 7.21-7.39 (m, 8H), 7.54 (d, J = 8.1 Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 28.1, 37.3, 42.7, 48.9, 49.1, 53.3, 74.4, 81.5, 124.8, 126.9, 127.0, 128.4, 128.5, 128.7, 143.4, 148.4, 173.9. Anal. Calcd for $\text{C}_{23}\text{H}_{29}\text{NO}_3$: C, 75.17; H, 7.95; N, 3.81. Found: C, 74.87; H, 7.85; N, 3.95.

2-Amino-4-(4-chlorophenyl)-4-hydroxy-6-phenylcyclohexanecarboxylic acid *t*-butyl ester (10l). Mp 113-114 °C. IR (KBr) 3440.1, 3378.1, 2978.5, 2931.9, 1708.7, 1575.8, 1490.0, 1367.4, 1250.9, 1150.6, 1007.4 cm^{-1} . ^1H -NMR (CDCl_3 , 250 MHz) δ 1.15 (s, 9H), 1.93-2.13 (m, 4H), 2.91 (dd, J = 12.3, 2.0 Hz, 1H), 3.77 (td, J = 12.1, 4.1 Hz, 1H), 3.96 (q, J = 2.7 Hz, 1H), 7.19-7.32 (m, 7H), 7.47 (d, J = 8.6 Hz, 2H). ^{13}C -NMR (CDCl_3 , 62.9 MHz) δ 28.0, 37.3, 42.7, 48.8, 49.0, 53.2, 74.2, 81.6, 126.4, 127.1, 128.3, 128.6, 128.7, 132.6, 143.2, 147.0, 173.8. Anal. Calcd for $\text{C}_{23}\text{H}_{28}\text{ClNO}_3$: C, 68.73; H, 7.02; N, 3.48. Found: C, 68.73; H, 7.01; N, 3.70.

X-Ray data of compound 5c



ORTEP drawing (thermal ellipsoids drawn at 50% probability)



Stick drawing

Spectra of compounds (5), (9) and (10)

