

Chiral Hydantoin; A New Dienophile for Diels–Alder Reaction

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Synopsis. A chiral hydantoin derivative, 5-methylene-1,3-bis[(*S*)-1-phenylethyl]-2,4-imidazolidinedione, was synthesized and the scope of this compound in Diels–Alder reaction was investigated.

Hydantoin ring systems are structural units frequently encountered in naturally occurring substances. They are well-known as anticonvulsants,¹⁾ antimicrobial reagents,²⁾ and also effect neurotransmission.³⁾ One more important utility of hydration skeleton is that it has been used as an α -amino acid intermediate,⁴⁾ but yet its application as chiral synthon in asymmetric reaction remains almost unexplored.⁵⁾

Herein, we report the first Diels–Alder cyclization of chiral 5-methylene hydantoin bearing *S*-(1)-phenylethyl groups at N1 and N3 as a chiral source. This new synthetic method proved to be an efficient route to various new enantiomerically pure hydantions, and therefore, to optically pure cyclic α -amino acids.

Chiral 5-methylene hydantoin (**4**) was easily prepared in a reasonable yield (45%) by treatment of pyruvic acid (**2**) with bis[(*S*)-1-phenylethyl]carbodiimide⁶⁾ (**1**) at room temperature in dry CH₃CN for 2 d (Scheme 1).

Thermal cyclization of **4** with cyclopentadiene upto 110°C yielded no product. However, the reaction with cyclopentadiene catalyzed by Lewis acid (Me₂AlCl, 1.2 equiv) proceeded smoothly at 0°C to produce four cyclized products in 93% isolated yield (Scheme 1). These four diastereomers were separated by high-performance liquid chromatography (HPLC) to give $\geq 99\%$ ee of each stereoisomer (determined by 500 MHz ¹H NMR spectral data). The absolute configuration of major adduct (**5a**) was confirmed by X-ray crystallographic analysis⁷⁾ (Fig. 1) and the absolute configu-

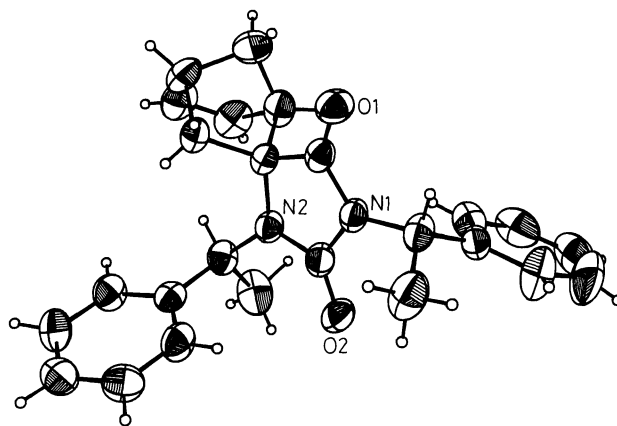


Fig. 1. ORTEP drawing of **5a**.

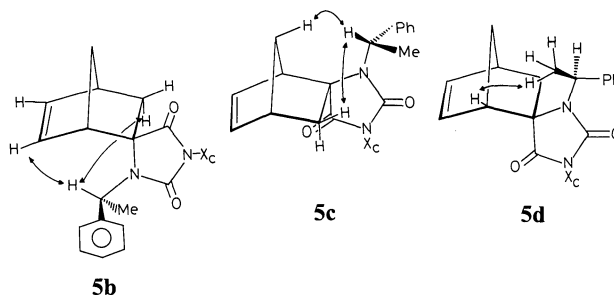
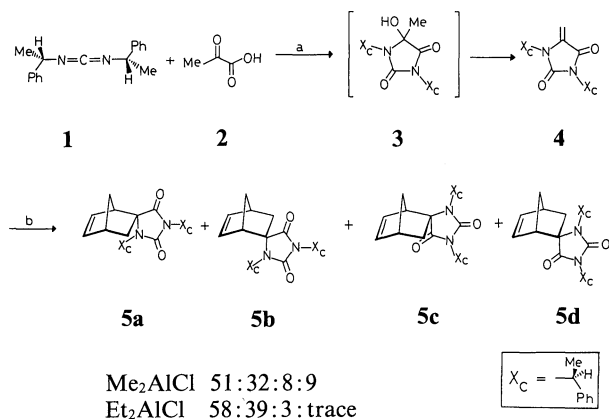


Fig. 2. NOESY spectral data of **5b**, **5c**, and **5d**.

ration of minor adducts (**5b**, **5c**, and **5d**) were ascertained from NOESY spectra (Fig. 2). The *endo* and *exo* product ratio was improved upto $>30:1$ in the reaction with Et₂AlCl as Lewis acid (1.2 equiv, 0°C, 3 h, 84% yield, Scheme 1).

While the reaction with *trans*-1,3-pentadiene and cyclohexadiene did not exhibit any selectivity, the cyclization with isoprene gave four isomers in the ratio of 14:2:1:trace in 71% yield and in the case of 2,3-dimethyl-1,3-butadiene two cyclized adducts were obtained in the ratio of 5:1 in 79% yield.⁸⁾ These results showed that the substitution at 2- and 3-positions of the diene increased the selectivity of the reactions.

The trial to convert Diels–Alder product to an α -amino acid derivative was done with **5a**.⁹⁾ Initially, **5a** was hydrogenated in a quantitative yield with H₂–Pd/C in EtOH to give **6a**, which was subsequently hydrolyzed with a large excess of saturated NaOH methanol–water (2:1) solution at 170°C for 8 h in a sealed tube to give N-protected α -amino acid. Without purification, exposure of this acid to diazomethane afforded N-protected



Scheme 1. a) CH₃CN, rt, 2 days. b) Lewis acid, –70°C, 1 h then cyclopentadiene, 0°C, 3 h, CH₂Cl₂.

α -amino acid methyl ester **7a** in 82% overall yield. Similar treatment of **5b** gave a comparable yield of **7b**.

Experimental

Preparation of 5-Methylene-2,4-imidazolidinedione (**4**).

To a solution of pyruvic acid **2** (0.440 g, 4.50 mmol) in 5 ml dry acetonitrile at 0°C was added 0.07 ml (0.1 equiv) of triethylamine and stirring was continued for 10 min under nitrogen before the solution of bis[(*S*)-1-phenylethyl]carbodiimide (1.249 g, 4.50 mmol) in 5 ml dry acetonitrile was added dropwise for 10 min. An ice-water bath was then removed and the mixture was allowed to react at ambient temperature for 2 d. After the reaction was completed the solid residue was filtered off and the filtrate was evaporated to give brown oil. Flash chromatography (ethyl acetate–hexane) gave yellow oil **4** (0.448 g, 45%); $[\alpha]_D^{23} = -62.6^\circ$ (*c* 1.07, CHCl₃); IR (CHCl₃) 3049, 2995, 2950, 1770, 1720, 1649, 1408, 1378, 1195, 1175, and 710 cm⁻¹; ¹H NMR (270 MHz, CDCl₃) $\delta = 1.74$ (d, *J* = 7.3 Hz, 3H), 1.90 (d, *J* = 7.3 Hz, 3H), 4.42 (d, *J* = 1.9 Hz, 1H), 5.21 (d, *J* = 1.9 Hz, 1H), 5.42 (q, *J* = 7.3 Hz, 1H), 5.59 (q, *J* = 7.3 Hz, 1H), 7.2–7.6 (m, 10H); ¹³C NMR (22.4 MHz, CDCl₃) $\delta = 16.1$ (CH₃), 17.3 (CH₃), 50.0 (CH), 50.6 (CH), 96.1 (CH₂), 126.4 (CH), 127.2 (CH), 127.5 (CH), 127.7 (CH), 128.4 (CH), 128.5 (CH), 133.4 (C), 138.5 (C), 139.9 (C), 153.8 (C=O), 162.1 (C=O). HRMS Found: *m/z* 320.1535. Calcd for C₂₀H₂₀N₂O₂: *M*, 320.1526.

General Procedure for the Diels–Alder Reaction of 4. To a solution of **4** in dry dichloromethane (about 0.2 M, 1M = 1 mol dm⁻³) under nitrogen at -70°C was added Me₂AlCl (1.01 M in hexane, 1.1–1.2 equiv). Stirring was continued for 1 h and freshly distilled diene (1.5 equiv) was added dropwise. The mixture was then allowed to react at 0°C. After quenching with 1 M HCl aqueous solution, an organic layer was separated and the aqueous layer was extracted with dichloromethane for two times. The combined organic phase was dried (MgSO₄) and evaporated to give crude product which was purified by flash column chromatography.

5a. White solid; mp 129.0–131.0°C; $[\alpha]_D^{23} = +69.4^\circ$ (*c* 1.26, CHCl₃); IR (CHCl₃) 2980, 1760, 1701, 1422, 1375, 1359, and 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) $\delta = 1.33$ –1.40 (m, visible with *J* = 8.8, 12.6 Hz, 2H), 1.81 (d, *J* = 7.1 Hz, 3H), 1.86 (d, *J* = 7.3 Hz, 3H), 2.14 (dd, *J* = 3.7, 12.6 Hz, 1H), 2.54 (d, *J* = 8.8 Hz, 1H), 2.93 (br m, 1H, COSY spectra show couplings with proton at $\delta = 2.14$ and 6.31), 2.98 (br m, 1H, COSY spectra show coupling with proton at $\delta = 6.31$), 4.50 (q, *J* = 7.1 Hz, 1H), 5.38 (q, *J* = 7.3 Hz, 1H), 6.31 (dd, *J* = 2.9, 5.5 Hz, 1H), 6.52 (dd, *J* = 3.2, 5.5 Hz, 1H), 7.0–7.4 (m, 10H); ¹³C NMR (125.6 MHz, CDCl₃) $\delta = 16.8$ (CH₃), 19.6 (CH₃), 33.8 (CH₂), 42.2 (CH), 47.6 (CH₂), 49.9 (CH), 52.5 (CH), 54.9 (CH), 69.2 (C), 125.7 (CH), 126.8 (CH), 127.3 (CH), 127.5 (CH), 128.4 (CH), 128.5 (CH), 132.9 (CH), 140.3 (C), 141.7 (CH), 141.9 (C), 155.5 (C=O), 176.8 (C=O). MS *m/z* (rel intensity, %) 386 (M⁺, 43), 320 (26), 216 (29), 105 (100), 77 (57), 66 (45), 51 (11), 39 (13), 27 (14). Found: C, 77.81; H, 6.80; N, 7.25%. Calcd for C₂₅H₂₆N₂O₂: C, 77.69; H, 6.78; N, 7.25%.

5b. White solid; mp 145.0–147.0°C; $[\alpha]_D^{23} = -68.8^\circ$ (*c* 1.26, CHCl₃); IR (CHCl₃) 3001, 2990, 1760, 1701, 1422, 1360, and 699 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) $\delta = 1.30$ (m, visible with *J* = 3.4, 8.8 Hz, 1H), 1.51 (dd, *J* = 3.4, 12.6 Hz, 1H), 1.66 (d, *J* = 7.4 Hz, 3H), 1.88 (d, *J* = 7.4 Hz, 3H), 2.29 (dd, *J* = 3.6, 12.6 Hz, 1H), 2.54 (d, *J* = 8.8 Hz, 1H), 2.82 (br m, 1H, COSY spectra show coupling with proton at $\delta = 5.57$), 2.97 (br m, 1H, COSY spectra show couplings with proton at $\delta = 2.29$ and 6.37), 4.40 (q, *J* = 7.4 Hz, 1H), 5.42 (q, *J* = 7.4 Hz, 1H), 5.57 (dd, *J* = 2.9, 5.6 Hz, 1H), 6.37 (dd, *J* = 3.2, 5.6 Hz, 1H), 7.2–7.5 (m, 10H); ¹³C NMR (125.6 MHz, CDCl₃) $\delta = 17.4$ (CH₃), 20.1 (CH₃), 34.7 (CH₂), 41.9 (CH), 47.8 (CH₂), 50.2 (CH), 53.1 (CH), 54.0 (CH), 68.9 (C), 125.9 (CH), 126.5 (CH), 127.1 (CH), 127.4 (CH), 128.4

(CH), 133.4 (CH), 140.4 (CH), 140.6 (C), 141.9 (C), 155.3 (C=O), 176.8 (C=O). HRMS Found: *m/z* 386.1997. Calcd for C₂₅H₂₆N₂O₂: *M*, 386.1996. Found: C, 77.69; H, 6.80; N, 7.25%. Calcd for C₂₅H₂₆N₂O₂: C, 77.69; H, 6.78; N, 7.25%.

5c. Colorless oil; IR (neat) 2976, 1760, 1708, 1498, 1450, 1416, 1376, 1336, 1312, 1182, 1168, 1030, 754, 718, 698, and 666 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) $\delta = 1.63$ (ddd, *J* = 1.1, 1.1, 11.7 Hz, 1H, COSY spectra show couplings with proton at $\delta = 1.72$ and 1.96), 1.72 (dd, *J* = 2.6, 11.7 Hz, 1H, COSY spectra show couplings with proton at $\delta = 1.63$ and 1.96), 1.77 (d, *J* = 7.3 Hz, 3H), 1.90 (d, *J* = 7.1 Hz, 3H), 1.96 (m, 2H), 2.87 (br m, 1H), 3.07 (br m, 1H), 4.74 (q, *J* = 7.1 Hz, 1H), 5.28 (q, *J* = 7.3 Hz, 1H), 6.15 (dd, *J* = 3.1, 5.7 Hz, 1H, COSY spectra show coupling with proton at $\delta = 2.87$), 6.4 (dd, *J* = 3.1, 5.7 Hz, 1H, COSY spectra show coupling with proton at $\delta = 3.07$), 7.2–7.4 (m, 10 H); ¹³C NMR (22.4 MHz, CDCl₃) $\delta = 16.7$ (CH₃), 18.8 (CH₃), 34.6 (CH₂), 43.1 (CH), 48.2 (CH₂), 49.8 (CH), 51.9 (CH), 54.4 (CH), 70.5 (C), 125.8 (CH), 126.9 (CH), 127.3 (CH), 127.4 (CH), 128.2 (CH), 128.4 (CH), 134.0 (CH), 140.0 (CH), 140.3 (C), 141.3 (C), 154.7 (C=O), 174.9 (C=O). HRMS Found: *m/z* 386.1986. Calcd for C₂₅H₂₆N₂O₂: *M*, 386.1996.

5d. White solid; mp 140.0–141.5°C; IR (KBr) 3004, 2980, 1756, 1702, 1444, 1422, 1378, 1330, 1172, 752, and 700 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) $\delta = 1.34$ (ddd, visible with *J* = 1.2, 9.5 Hz, 1H), 1.76 (m, visible with *J* = 9.5, 12.9 Hz, 2H), 1.83 (d, *J* = 7.1 Hz, 3H), 1.84 (d, *J* = 7.3 Hz, 3H), 2.00 (dd, *J* = 3.6, 12.9 Hz, 1H, COSY spectra show coupling with proton at $\delta = 3.05$), 2.62 (br m, 1H), 3.05 (br m, 1H), 4.67 (q, *J* = 7.1 Hz, 1H), 5.36 (q, *J* = 7.3 Hz, 1H), 5.99 (dd, *J* = 3.3, 5.5 Hz, 1H, COSY spectra show coupling with proton at $\delta = 2.62$), 6.34 (dd, *J* = 2.9, 5.5 Hz, 1H, COSY spectra show coupling with proton at $\delta = 3.05$), 7.2–7.5 (m, 10H); ¹³C NMR (22.4 MHz, CDCl₃) $\delta = 17.5$ (CH₃), 21.3 (CH₃), 35.3 (CH₂), 42.9 (CH), 48.2 (CH₂), 50.2 (CH), 53.4 (CH), 53.9 (CH), 70.5 (C), 126.2 (CH), 126.9 (CH), 127.1 (CH), 127.4 (CH), 128.3 (CH), 128.5 (CH), 134.1 (CH), 139.7 (CH), 140.6 (C), 142.4 (C), 155.3 (C=O), 175.1 (C=O). HRMS Found: *m/z* 386.1997. Calcd for C₂₅H₂₆N₂O₂: *M*, 386.1996. Found: C, 77.77; H, 6.83; N, 7.24%. Calcd for C₂₅H₂₆N₂O₂: C, 77.69; H, 6.78; N, 7.25%.

Major Adduct of the Reaction with Isoprene. Colorless oil; $[\alpha]_D^{20} = -30.9^\circ$ (*c* 1.06, CHCl₃); IR (neat) 3024, 2972, 2932, 1762, 1712, 1498, 1450, 1420, 1368, 1328, 1310, 1266, 1220, 1174, 1068, 1030, 758, and 698 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) $\delta = 1.69$ (s, 3H), 1.7–1.8 (m, 3H), 1.80 (d, *J* = 7.1 Hz, 3H), 1.84 (d, *J* = 7.3 Hz, 3H), 2.2–2.3 (m, 1H), 2.38 (br m, 2H), 4.50 (q, *J* = 7.1 Hz, 1H), 5.35 (q, *J* = 7.3 Hz, 1H), 5.42 (br m, 1H), 7.2–7.5 (m, 10H); ¹³C NMR (22.4 MHz, CDCl₃) $\delta = 17.2$ (CH₃), 21.0 (CH₃), 23.2 (CH₃), 26.6 (CH₂), 29.3 (CH₂), 31.0 (CH₂), 49.8 (CH), 52.6 (CH), 61.9 (C), 116.4 (CH), 126.3 (CH), 126.9 (CH), 127.0 (CH), 127.4 (CH), 128.3 (CH), 128.4 (CH), 134.4 (C), 140.5 (C), 142.7 (C), 154.7 (C=O), 175.3 (C=O). HRMS Found: *m/z* 388.2160. Calcd for C₂₅H₂₈N₂O₂: *M*, 388.2152.

Major Adduct of the Reaction with 2,3-Dimethyl-1,3-butadiene. Colorless oil; $[\alpha]_D^{23} = -26.2^\circ$ (*c* 1.22, CHCl₃); IR (neat) 3020, 2980, 2928, 1760, 1704, 1498, 1450, 1422, 1374, 1314, 1268, 1240, 1220, 1176, 1056, 1028, 756, and 700 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) $\delta = 1.64$ (s, 3H), 1.69 (s, 3H), 1.70–1.72 (m, 2H), 1.80–1.84 (m, 1H), 1.80 (d, *J* = 7.2 Hz, 3H), 1.84 (d, *J* = 7.2 Hz, 3H), 2.24 (br dm, visible with *J* = 17.6 Hz, 2H), 2.36 (br d, *J* = 17.6 Hz, 1H), 4.48 (q, *J* = 7.2 Hz, 1H), 5.34 (q, *J* = 7.2 Hz, 1H), 7.2–7.4 (m, 10 H); ¹³C NMR (22.4 MHz, CDCl₃) $\delta = 17.2$ (CH₃), 18.7 (CH₃), 18.8 (CH₃), 21.0 (CH₃), 28.0 (CH₂), 29.6 (CH₂), 36.6 (CH₂), 49.8 (CH), 52.6 (CH), 63.0 (C), 121.3 (C), 126.0 (C), 126.2 (CH), 126.9 (CH), 127.0 (CH), 127.3 (CH), 128.3 (CH), 128.4 (CH), 140.5 (C), 142.8 (C), 154.7 (C=O), 175.3 (C=O). HRMS Found: *m/z* 402.2296. Calcd for C₂₆H₃₀N₂O₂: *M*, 402.2309.

General Procedure for the Hydrogenation of Diels–Alder

Adducts. The Diels–Alder adduct was dissolved in EtOH (about 0.1 M) and 5% Pd–carbon was added as catalyst. The reaction mixture was subjected to hydrogen atmosphere for 3 h at room temperature under atmospheric pressure. After filtration of Pd–carbon, the solvent was allowed to evaporate under reduced pressure to give a quantitative yield of the adduct. Purification by flash chromatography (hexane:ethyl acetate) gave pure **6a** and **6b**.

6a. White solid; mp 122.5–124.0°C; $[\alpha]_D^{25} = +94.2^\circ$ (*c* 1.46, CHCl₃); IR (neat) 2968, 2944, 1758, 1706, 1498, 1444, 1422, 1376, 1318, 1218, 1170, 1064, 758, 698, and 666 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) $\delta = 1.1$ – 2.1 (m, 8H), 1.84 (d, *J* = 7.4 Hz, 3H), 2.05 (d, *J* = 7.2 Hz, 3H), 2.2–2.6 (m, 2H), 4.37 (q, *J* = 7.2 Hz, 1H), 5.35 (q, *J* = 7.4 Hz, 1H), 7.0–7.5 (m, 10H); ¹³C NMR (22.4 MHz, CDCl₃) $\delta = 16.5$ (CH₃), 21.8 (CH₃), 24.2 (CH₂), 28.3 (CH₂), 34.7 (CH₂), 35.9 (CH), 37.0 (CH₂), 49.7 (CH), 54.5 (CH), 70.6 (C), 125.7 (CH), 126.8 (CH), 127.2 (CH), 127.4 (CH), 128.2 (CH), 128.5 (CH), 140.2 (C), 142.3 (C), 156.4 (C=O), 176.7 (C=O). HRMS Found: *m/z* 388.2143. Calcd for C₂₅H₂₈N₂O₂: M, 388.2152. Found: C, 77.53; H, 7.30; N, 7.25%. Calcd for C₂₅H₂₈N₂O₂: C, 77.29; H, 7.27; N, 7.21%.

6b. White solid; mp 137.0–139.0°C; $[\alpha]_D^{25} = +21.6^\circ$ (*c* 1.02, CHCl₃); IR (neat) 3020, 2944, 1758, 1738, 1706, 1498, 1422, 1370, 1340, 1318, 1174, 1064, 756, 698, and 666 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) $\delta = 1.0$ – 1.7 (m, 6H), 1.72 (d, *J* = 7.0 Hz, 3H), 1.84 (d, *J* = 7.2 Hz, 3H), 2.0–2.7 (m, 4H), 4.42 (q, *J* = 7.0 Hz, 1H), 5.36 (q, *J* = 7.2 Hz, 1H), 7.1–7.6 (m, 10H); ¹³C NMR (22.4 MHz, CDCl₃) $\delta = 17.4$ (CH₃), 20.2 (CH₃), 23.9 (CH₂), 28.3 (CH₂), 48.6 (CH), 50.0 (CH), 54.0 (CH), 70.7 (C), 125.9 (CH), 126.6 (CH), 127.0 (CH), 127.4 (CH), 128.3 (CH), 140.5 (C), 142.0 (C), 155.7 (C=O), 176.9 (C=O). HRMS Found: *m/z* 388.2147. Calcd for C₂₅H₂₈N₂O₂: M, 388.2152. Found: C, 77.18; H, 7.27; N, 7.18%. Calcd for C₂₅H₂₈N₂O₂: C, 77.29; H, 7.27; N, 7.21%.

General Procedure for the Preparation of N-Protected Amino Acid Methyl Ester. Compound **6a** or **6b** was dissolved in methanol (about 0.1 M) and saturated NaOH methanol: H₂O (2:1) solution was added to the mixture. After heating at 170°C in a sealed tube for 8 h, ethyl acetate was added to the mixture and methanol was evaporated under reduced pressure. The residue was again dissolved in ethyl acetate and diazomethane in ether was added. The reaction mixture was stirred for 1 to 2 h and organic layer was separated. Extraction by ethyl acetate for two times and evaporation of the combined organic layers gave crude oil, which on purification by flash chromatography (hexane:ethyl acetate) gave N-protected amino acid methyl ester in 82% yield.

Methyl (1S,2R,4R)-2-[(S)-1-Phenylethylamino]bicyclo[2.2.1]heptane-2-carboxylate (7a). Colorless oil; $[\alpha]_D^{25} = -50.48^\circ$ (*c* 1.28, CHCl₃); IR (neat) 2948, 2868, 1728, 1456, 1274, 1260, 1238, 1210, 1178, 1156, 1126, 1108, 1082, 760, and 702 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) $\delta = 1.0$ – 1.5 (m, 6H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.7–1.9 (m, 1H), 1.85 (s, 1H), 2.1–2.5 (m, 3H), 3.5 (s, 3H), 3.59 (q, *J* = 6.9 Hz, 1H), 7.25 (s, 5H); ¹³C NMR (22.4 MHz, CDCl₃) $\delta = 21.7$ (CH₂), 25.2 (CH₃), 29.4 (CH₂), 36.3 (CH), 37.8 (CH₂), 41.5 (CH₂), 43.9 (CH), 51.3 (CH₃), 55.4 (CH), 69.4 (C), 126.6 (CH), 126.8 (CH), 128.0 (CH), 146.0 (C), 177.3 (C=O). HRMS Found *m/z* 273.1731. Calcd for C₁₇H₂₃NO₂: M, 273.1737.

Methyl (1R,2S,4S)-2-[(S)-1-Phenylethylamino]bicyclo[2.2.1]heptane-2-carboxylate (7b). Colorless oil; $[\alpha]_D^{25} = +67.0^\circ$ (*c* 0.66, CHCl₃); IR (CHCl₃) 3352, 2952, 1730, 1450, 1206, 1078, 760, and 702 cm⁻¹; ¹H NMR (90 MHz, CDCl₃) $\delta = 0.85$ (dm, 1H), 1.1–1.5 (m, 5H), 1.29 (d, *J* = 7.0 Hz, 3H), 1.81 (s, 1H), 1.9–2.2 (m, 3H), 2.3 (br s, 1H), 3.30 (s, 3H), 3.59 (q, *J* = 7.0 Hz,

1H), 7.22 (s, 5H); ¹³C NMR (125.6 MHz, CDCl₃) $\delta = 22.2$ (CH₂), 26.0 (CH₃), 29.0 (CH₂), 36.4 (CH), 37.9 (CH₂), 41.4 (CH₂), 43.7 (CH), 51.4 (CH₃), 55.4 (CH), 69.1 (C), 126.5 (CH), 126.7 (CH), 128.1 (CH), 146.6 (C), 177.3 (C=O). HRMS Found: *m/z* 273.1729. Calcd for C₁₇H₂₃NO₂: M, 273.1737.

X-Ray Crystallographic Analysis of 3a. A colorless rod crystal of C₂₅H₂₆N₂O₂ having approximate dimension of 0.43×0.53×0.15 mm was mounted on a glass fiber in a random orientation. Preliminary examination and data collection were performed with Mo K α radiation on Enraf–Nonius CAD4 computer-controlled kappa axis diffractometer equipped with a graphite, incident beam monochromator. The orthorhombic cell parameters and calculated volume are: *a* = 9.751(1), *b* = 10.048(1), *c* = 21.379(2) Å, *V* = 2094.6 Å³. For *Z* = 4 and *FW* = 386.50 the calculated density is 1.23 g cm⁻³. A total of 1702 unique reflections with *F*(0) > 3 σ (*F*_o) were obtained by using ω – 2θ scan technique with a 2θ scan speed of 4 min⁻¹ to $2\theta = 50^\circ$. The structure was solved by the MOLEN system on the basis of the direct method and refined to a final *R* value of 0.039. Further crystallographic details are deposited as Document No. 8981 at the Office of the Editor of Bull. Chem. Soc. Jpn.

References

- 1) P. T. H. Wong, S. F. Tan, and W. L. Teo, *Asia Pac. J. Pharmacol.*, **4**, 107 (1989); D. Hovevey-Sion, I. J. Kopin, R. W. Stull, and D. S. Goldstein, *Neuropharmacology*, **28**, 791 (1989); P. Wong, H. Tsun, and S. F. Tan, *Jpn. J. Pharmacol.*, **49**, 309 (1989); "Anticonvulsants," ed by J. A. Vida, Academic Press, New York (1977).
- 2) C. V. R. Sastry, B. Ram, M. Jogibhukta, V. S. H. Krishnan, A. N. Singh, J. G. Reddy, S. C. Chaturvedi, P. S. Rao, and D. R. Shridhar, *Indian J. Chem., Sect. B*, **28**, 52 (1989); N. Kujundzic, K. Kovacevic, M. Jakovina, and B. Gluncic, *Croat. Chem. Acta*, **61**, 121 (1988); Y. Miura, S. Tahara, and J. Mizutani, *J. Pesticide Sci.*, **4**, 25 (1979).
- 3) G. Guella, I. Mancini, H. Zibrowius, and F. Pietra, *Helv. Chim. Acta*, **71**, 773 (1988).
- 4) C. Syltatk, G. Dombach, C. Gross, R. Mueller, and F. Wagner, *Ann. N. Y. Acad. Sci.*, **1988**, 542 (Enzyme Eng. 9), 323; M. Battilotti and U. Barberini, *J. Mol. Catal.*, **43**, 343 (1988); J. F. Klebe and H. Finhbeiner, *J. Am. Chem. Soc.*, **90**, 7255 (1968), etc.
- 5) Alkylation of chiral hydantoin: D. Mostowics, W. Abramski, and C. Belzecki, *Pol. J. Chem.*, **55**, 1387 (1981).
- 6) The utility of bis[(S)-1-phenylethyl]carbodiimide in asymmetric reaction: K. Kishikawa, M. Yamamoto, S. Kohmoto, and K. Yamada, *Chem. Lett.*, **1989**, 787; K. Kishikawa, K. Horie, M. Yamamoto, S. Kohmoto, and K. Yamada, *Chem. Lett.*, **1990**, 1009; K. Kishikawa, M. Yamamoto, S. Kohmoto, and K. Yamada, *Chem. Lett.*, **1988**, 1623; *idem*, *J. Org. Chem.*, **54**, 2428 (1989).
- 7) C. K. Johnson, "ORTEP-II, Report ORNL-5138," Oak Ridge National Laboratory, Tennessee (1974).
- 8) We did not try to determine the absolute configuration of these adducts.
- 9) An asymmetric synthesis of 2-aminonorbornane-2-carboxylic acid: C. Cativiela, P. Lopez, and J. A. Mayoral, *Tetrahedron: Asymmetry*, **1**, 61 (1990); **1**, 379 (1990); **2**, 449 (1991).