December, 1985] © 1985 The Chemical Society of Japan NOTES Bull. Chem. Soc. Jpn., 58, 3631—3632 (1985) 3631

Optical Resolution of 3a,4,7,7a-Tetrahydro-4,7-methano-1*H*-indene Derivatives

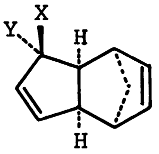
Toshio Ito, Yoshio Okamoto,† and Takeshi Matsumoto*
Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo, 060
†*Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka 560*

(Received July 10, 1985)

Synopsis. (1*RS*,3a*RS*,4*RS*,7*SR*,7a*SR*)-3a,4,7,7a-Tetrahydro-4,7-methano-1*H*-inden-1-ol was resolved kinetically and its C-1 epimer was resolved chromatographically. Absolute configurations of these resolved compounds were determined.

Optically active 3a,4,7,7a-tetrahydro-4,7-methano-1*H*-indene(dicyclopentadiene) and allied compounds seem useful chiral synthons for syntheses of optically active natural products,[1] because they contain at least four asymmetric centers and a variety of reactive sites. We report here optical resolution of (1*RS*,3a*RS*,4*RS*,7*SR*,7a*SR*)-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-inden-1-ol-[(±)-**1**] and its C-1 epimer (±)-**2** (Fig. 1).[2]

Titanium(IV) tartrate-catalyzed asymmetric epoxidation developed by Sharpless *et al.*[3] was adopted for kinetic resolution of (±)-**1**. Allylic alcohol (±)-**1** (50 mmol) was treated with 0.6 mol eq of *t*-butyl hydroperoxide in the presence of diisopropyl tartrate and Ti(*i*-PrO)$_4$ as catalyst to afford epoxy compound (−)-**6** and starting material enriched in (+)-**1** in 38 and 34% isolated yields, respectively (Fig. 2). Specific rotation of the resolved **1** was +78°(*c* 1.00, CHCl$_3$). A portion of this sample was esterified with (*S*)-2-methoxy-2-trifluoromethylphenylacetyl chloride ((*S*)-MTPACl)[4] to yield (*S*)-MTPA ester **5**, which was found to be a mixture of diastereomers by the 400 MHz ^{1}H NMR spectrum. The diasteromeric excess was 68.2%. Optically pure (+)-**1** was readily obtained by recrystallization in 63% yield, from the 68.2% e. e. **1**.



1 X=H, Y=OH
3 X=H, Y=OBz
5 X=H, $Y=OCOC(CF_3)(C_6H_5)OCH_3$
2 X=OH, Y=H
4 X=OBz, Y=H

Fig. 1.

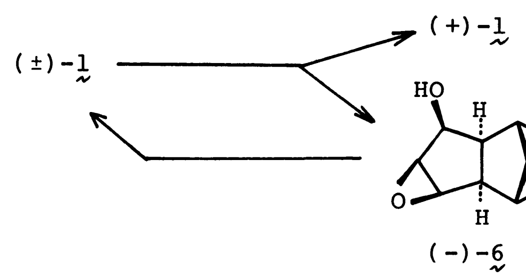


Fig. 2.

Next, the absolute configuration of the above optically active alcohol was determined by the allyl benzoate rule.[5] Alcohol (+)-**1** (68.2% e.e.) was converted to its benzoate **3**, whose CD spectrum exhibited a positive first Cotton effect peak at 222 nm. Therefore the absolute configuration of (+)-**1** was determined to be as shown in Fig. 3.

Produced epoxy alcohol (−)-**6** had low optical purity (39% e.e., by ^{1}H NMR of (*S*)-MTPA ester), and was not synthetically useful. Therefore (−)-**6** was reverted to **1**. Epoxy alcohol (−)-**6** was reduced with TiCl$_3$–LiAlH$_4$[6] to give (±)-**1** in 65% yield (Fig. 2).

The above kinetic resolution is practical for preparing a large quantity of optically active (+)-**1**. However, the method is operationally not so simple. On the other hand, the resolution by chromatography developed by one of us (Y. O.)[7] is simple. Although this method is at present not so practical for large scale preparation, resolution of dicyclopentadiene derivatives by means of the (+)-PTrMA-coated silicagel column[7] was next attempted. Dicyclopentadiene, (±)-**1** and (±)-**2**, and acetates of (±)- **1** and (±)-**2** were not resolved. Since it was reported that aryl groups strongly interacted with (+)-PTrMA,[7] (±)-**1** and (±)-**2** were

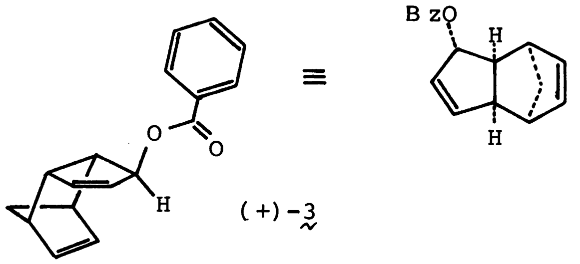


Fig. 3.

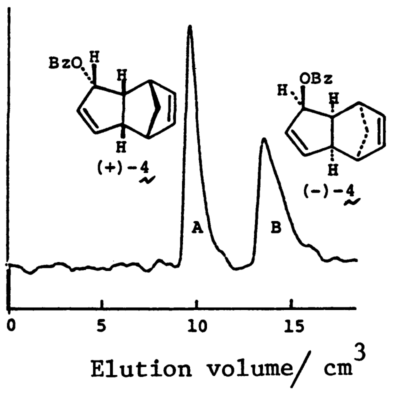


Fig. 4. Resolution of (±)-**4**(0.4 mg). (+)-PTrMA column, 25×0.46 (i.d.); eluent, MeOH; flow rate 0.76 cm^3 min^{-1}; temperature 25 °C.

benzoylated. While benzoate (±)-**3** was not separated (R_s=0.5), its C-1 epimer (±)-**4** was cleanly resolved (R_s=2.02, Fig. 4). The eluents A and B contained respectively enantiomers (+)-**4** and (−)-**4** with the absolute configuration shown in Fig. 4, which was proved as follows. Alcohol (+)-**1** (68.2% e.e.) with known configuration was converted to (−)-**2**,[2] which in turn was benzoylated and passed through the (+)-PTrMA column. The main peak coincided in retention volume with that of the eluent B (Fig. 4).

Experimental

Measurements. Melting points were uncorrected. IR spectra were measured with a JASCO model IR-S spectrophotometer. Unless otherwise noted, ^{1}H NMR spectra were recorded at 60 MHz (HITACHI R-20B). ^{1}H NMR spectra at 400 MHz were taken on a JEOL JNM FX-400. Low resolution mass spectra were obtained with a HITACHI model RMS-6U instrument. Optical rotations and CD spectra were measured by means of a JASCO model DIP-SL automatic polarimeter and a JASCO J-20 automatic recording spectropolarimeter respectively. The high-performance liquid chromatography was accomplished on a Waters associates model 6000A chromatograph equipped with a Waters associates R-401 RI detector.

Kinetic Resolution of (±)-1 and Absolute Configuration of (+)-1. A mixture of (±)-**1** (7.1 g, 50.0 mmol), diisopropyl (2*R*,3*R*)-tartrate (13.5 g, 57.7 mmol) and Ti(*i*-PrO)$_4$ (14.9 cm^3, 50.0 mmol) in dry CH_2Cl_2 (500 cm^3) was stirred at −20 °C. Anhydrous *t*-BuOOH (11.3 g, 30.0 mmol) in dry CH_2Cl_2 (about 24 w/w%) was then added, and the resulting mixture was maintained at −20 °C in a freezer. After 4 d, the cold reaction mixture was poured into a precooled (−20 °C) solution of 1000 cm^3 of acetone containing 14 cm^3 of water. The resulting mixture was stirred for 1 h at −20 °C and for 30 min at room temperature. After *ca.* 400 cm^3 of the acetone was evaporated, the residue was diluted with ether (400 cm^3) and filtered. The filtrate was concentrated and diluted again with 430 cm^3 of ether, and then 1 M NaOH soution (170 cm^3) (1 M=1 mol dm^{-3}) was added to the ether solution. The resulting homogeneous mixture was stirred for 1 h at 0 °C. After hydrolysis of the tartrate was complete, the ether layer was separated and the aqueous layer was extracted with ether (3×100 cm^3). The combined ether extracts were washed with water and NaCl solution. After drying (Na_2SO_4), the solvent was evaporated to give 5.8 g of an oily residue, which was chromatographed on silica gel (200 g) with 30% AcOEt in hexane. The elution gave 2.4 g (34%) of (+)-**1** and 3.0 g (38%) of (−)-**6**. (+)-**1**: $[\alpha]_D$=+78° (*c* 1.00, $CHCl_3$); mp 50—52 °C. (−)-**6**: $[\alpha]_D$=−32.6 (*c* 4.05, $CHCl_3$); mp 35—38 °C; IR($CHCl_3$) 3560, 1255 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=6.06 (2H, t, *J*=1.0 Hz), 3.78 (1H, t, *J*=1.5 Hz), 3.41 (1H, t, *J*=2 Hz), 3.27 (1H, d, *J*=2 Hz), 3.2—2.8 (2H, m), 1.49 and 1.30 (ABq, *J*=8 Hz); *m/z* 148 ($M-H_2O$). Found: C, 73.03; H, 7.39. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37%. E. e. was 68.2% for (+)-**1**; two kinds of peaks due to C-7a-H of (+)-**1** (*S*)-MTPA ester were observed at 2.70 (84%) and 2.60 (16%) in the 400 MHz ^{1}H NMR spectrum. For (−)-**6**, e. e. was 39%; two kinds of peaks due to C-6-H of (−)-**6** (*S*)-MTPA ester appeared at 4.85 (69.5%) and 4.82 (30.5%) in the 400 MHz ^{1}H NMR spectrum.

Recrystallization of (+)-**1** (68.2% e.e., 1.0 g) from petroleum ether three times afforded optically pure (+)-**1** (0.63 g, 63%) $[\alpha]_D$=+115.1° (*c* 1.00, $CHCl_3$); mp 69.5—72.0 °C. (*S*)-MTPA ester of (+)-**1**: $[\alpha]_D$=+138° (*c* 1.00, $CHCl_3$); IR (neat) 3120, 1750, 1625, 1460, 1225, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.53 (2H, m), 7.39 (3H, m), 6.06 (1H, dd, *J*=6, 3 Hz), 5.91 (1H, dt, *J*=6, 2 Hz), 5.88 (1H, dd, *J*=6, 3.5 Hz), 5.57 (1H, dt, *J*=6, 2 Hz), 5.18 (1H, q, *J*=2 Hz), 3.56 (3H, q, *J*=1 Hz), 3.54 (1H, m), 3.42 (1H, br s, W_H=10 Hz), 2.84 (1H, br s, W_H=9 Hz), 2.70 (1H, qd, *J*=2, 8 Hz), 1.63 (1H, td, *J*=1.5, 8 Hz), 1.43 (1H, br d, *J*=8 Hz).

$TiCl_3$–$LiAlH_4$ Reduction of (−)-6. To an ice-cooled suspension of $TiCl_3$ (110 mg, 0.71 mmol) in dry THF (3.3 cm^3) was added $LiAlH_4$ (6.8 mg, 0.18 mmol). The resulting mixture was stirred for 20 min at 0 °C, and (−)-**6** (39% e.e., 39 mg, 0.23 mmol) in dry THF (0.5 cm^3) was added. Stirring was continued for 10 min. Celite, anhydrous Na_2SO_4 (each 500 mg), and saturated aq NH_4Cl solution (0.5 cm^3) were then added successively. The resulting mixture was filtered, and the solid material was washed with AcOEt (3×20 cm^3). The combined organic solution was washed with aq NaCl solution and dried (Na_2SO_4). The solvent was evaporated to give an oily residue, which was purified by preparative TLC to afford 22 mg (65%) of (±)-**1**.

References

1) For examples: coriolin; T. Ito, N. Tomiyoshi, K. Nakamura, S. Azuma, M. Izawa, F. Maruyama, M. Yanagiya, H. Shirahama, and T. Matsumoto, *Tetrahedron Lett.*, **23**, 1721 (1982); *Tetrahedron*, **40**, 241 (1984). PGF$_2$; D. Brewster, M. Myers, J. Ormerod, P. Otter, A. C. B. Smith, M. E. Spinner, and S. Turner, *J. Chem. Soc., Perkin Trans. 1*, **1973**, 2796. Vervenalol; T. Sakan and K. Abe, *Tetrahedron Lett.*, **1968**, 2471.

2) Woodward and Katz had prepared (±)-**1** and (±)-**2** and resolved (±)-**1** *via* 3β-acetoxy-Δ^5-etiocholenate, but the absolute configuration of these resolved compounds had not been determined; R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

3) V. S. Martin, S. S. Woodard, T. Katsuki, Y. Yamada, M. Ikeda, and K. B. Sharpless, *J. Am. Chem. Soc.*, **103**, 6237 (1981).

4) J. A. Dale, D. L. Dull, and H. S. Mosher, *J. Org. Chem.*, **34**, 2543 (1969).

5) N. Harada, J. Iwabuchi, Y. Yokota, H. Uda, and K. Nakanishi, *J. Am. Chem. Soc.*, **103**, 5590 (1981).

6) J. E. McMurry and M. P. Fleming. *J. Org. Chem.*, **40**. 2555 (1975).

7) Y. Okamoto, S. Honda, I. Okamoto, and H. Yuki, *J. Am. Chem. Soc.*, **103**, 6971 (1981).