# Improved Optical Resolution of (±)-1,2-Diphenylethylenediamine

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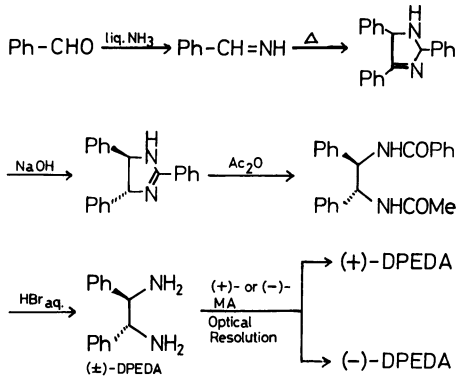
**Synopsis.** (±)-1,2-Diphenylethylenediamine (DPEDA) was efficiently resolved by the fractional crystallization of its diastereomeric salts with optically active mandelic acid. $^1$H-NMR spectrum of *N*-monoacylated DPEDA with an optically active derivatizing agent showed that DPEDA thus obtained was optically pure.

(±)-Diphenylethylenediamine (DPEDA) having an interesing structure of $C_2$ symmetry has been frequently used as a unique ligand of several metal complexes.[1] Moreover, it can be an auxiliary in asymmetric induction and an optically active component for the synthesis of optically active polyamides. From the viewpoint of synthetic utilization of optically active DPEDA, it is very important to develop a highly efficient method for the optical resolution of (±)-DPEDA. For its optical resolution there has been reported only one method using optically active tartaric acid as a resolving agent.[2] However, this seems to have some operational problems since it is very hard to recrystallize the diastereomeric salt deposited from the reaction mixture of (±)-DPEDA with optically active tartaric acid. Additionally, (+)-DPEDA is difficult to obtain in pure state because nonnatural type (−)-tartaric acid is too expensive to obtain in a large quantity.

In the present paper, we describe an efficient optical resolution of (±)-DPEDA by fractional crystallization using optically active mandelic acid (MA) as a resolving agent, of which both enantiomers are industrially available. We also confirmed the specific rotation of optically pure DPEDA, for which various values have been reported previously.[2]

(±)-DPEDA was prepared from benzaldehyde via isoamarine according to the methods in the literatures,[1a,3] as shown in the following scheme. The




reaction of (±)-DPEDA with two molar amounts of (+)-MA gave a mixture of diastereomeric salts. Recrystallization of the mixture for two times from ethanol yielded (+)-DPEDA·(+)-MA (1:2) salt in 82% yield. (−)-Enriched DPEDA, recovered from the mother solution and the filtrates, was allowed to react with two molar amounts of (−)-MA, and the resulting salt was similarly recrystallized twice from ethanol to give (−)-DPEDA·(−)-MA (1:2) salt in 82% yield. Decomposition of each salt with aqueous sodium hydroxide solution gave (+)- and (−)-DPEDA in 72 and 79% total yields, respectively.

To determine the optical purity, (+)-DPEDA ($[\alpha]_D^{22}$ +106.5° (*c* 1.07, MeOH)) was acylated with (−)-(benzylmethylphenylsilyl)acetic acid (BMPSA),[4] giving monoacylated (+)-DPEDA. Its $^1$H-NMR spectrum was compared with that of *N*-monoacylated (±)-DPEDA. On the basis of the area ratio of methyl protons of the (−)-BMPSA resudue in two diastereomeric monoamides, the optical purity of (+)-DPEDA was found to be 99.6%. Consequently, the specific rotations of optically pure DPEDA were determined as follows.

Table 1. The Specific Rotations of Optically Pure DPEDA

| Solvent | [α] 589 | 577 | 546 | 435 | 405 |
|---|---|---|---|---|---|
| MeOH[a] | 106.9 | 109.8 | 126.3 | 243.7 | 290.5 |
| $Et_2O$[b] | 82.6 | 85.4 | 99.8 | 191.3 | 243.0 |

a) *c* 1.07 at 22 °C. b) *c* 0.97 at 18 °C.

## Experimental

Melting points were measured by a laboratory devices MEL-TEMP apparatus and are uncorrected. IR spectra were recorded on a JASCO IR-810 Spectrophotometer. Optical rotations were masured by a JASCO DIP-360 Digital Polarimeter. $^1$H-NMR spectra were recorded on a JEOL JMR GX 400 Spectrometer.

(±)-DPEDA was prepared by the methods reported in the literature,[1a,3] mp 76—77 °C (lit,[3] 83 °C).

**Optical Resolution of (±)-DPEDA.** (±)-DPEDA (1.70 g, 8 mmol) and (+)-MA (2.43 g, 16 mmol) were dissolved in ethanol (20 ml) on heating. After cooling to room temperature, the crystals deposited were collected by filtration and washed with two portions of ethanol (1.5 ml each). Recrystallization of the mixture of the diastereomeric salts for two times from ethanol (25 ml then 20 ml), followed by drying over $P_2O_5$ under reduced pressure, gave almost pure (+)-DPEDA·(+)-MA (1:2) salt (1.69 g, 82% based on the half amount of DPEDA used): Mp 164—165 °C; IR (KBr) 3450 (-OH), 3100 ($-\overset{+}{N}H_3$), and 1530 ($-CO_2^-$) cm$^{-1}$; $[\alpha]_{435}^{16}$ +278.8°, $[\alpha]_D^{16}$ +126.9° (*c* 1.51, MeOH).

Calcd for $C_{30}H_{32}N_2O_6$: C, 69.75; H, 6.24; N, 5.42%. Found: C, 69.49; H, 6.11; N, 5.30%.

The minus enriched DPEDA (0.96 g, 4.5 mmol), recovered from the mother liquor and the filtrates by treating with aqueous sodium hydroxide, was similarly reacted with (−)-MA (1.37 g, 9 mmol) in ethanol (20 ml) on heating.

Cooling the solution at room temperature gave almost pure (−)-DPEDA·(−)-MA (1:2) salt (1.70 g, 82% based on the half amount of DPEDA used) without any recrystallization: Mp 163—164 °C; IR (KBr) 3450 (-OH), 3100 ($-\overset{+}{N}H_3$), and 1530 ($-CO_2^-$) $cm^{-1}$; $[\alpha]_{435}^{20}$ −277.9°, $[\alpha]_D^{20}$ −126.5° (*c* 1.40, MeOH).

Calcd for $C_{30}H_{32}N_2O_6$: C, 69.75; H, 6.24; N, 5.42%. Found: C, 69.78, H, 6.31; N, 5.36%.

(+)-DPEDA·(+)-MA (1:2) salt (1.68 g, 3.3 mmol) was treated with 4 mol $dm^{-3}$ sodium hydroxide solution (36 ml) and extacted with ether (3×40 ml). The extracts were combined, dried over sodium hydroxide pellets, and concentrated under reduced pressure. Recystallization of the remaining residue from hexane gave (+)-DPEDA (0.61 g, 72% based on the half amount of DPEDA used): Mp 85—86.5 °C (lit,[2c] 80 °C); IR (KBr) 3380 ($-NH_2$), 3360 ($-NH_2$), and 705 (-Ar) $cm^{-1}$; $[\alpha]_D^{22}$ +106.5° (*c* 1.09, MeOH).

Calcd for $C_{14}H_{16}N_2$: C, 79.21, H, 7.60, N, 13.20%. Found: C, 79.26; H, 7.40; N, 13.00%.

The enantiomeric excess of (+)-DPEDA thus obtained was determined as follows: The $^1H$-spectrum of the diastereomeric N-monoacylated mixture, prepared from (±)-DPEDA and (−)-BMPSA according to the procedure in the literature,[4] showed two methyl proton signals at δ 0.216 and 0.247 ppm, which correspond to methyl proton signal of the (−)-BMPSA residue in each diastereomeric N-monoacylated DPEDA. The integral ratio of these signals was 1:1. The $^1H$-NMR spectrum also showed two methyl proton signals, of which integral ratio was 249:1. Based on this integral ratio, the enantiomeric excess of (+)-DPEDA was established to be 99.6%.

Using the values of the specific rotation and the enantiomeric excess of (+)-DPEDA, the specific rotation of optically pure DPEDA was calculated as shown in the Table.

A similar alkaline treatment of (−)-DPEDA·(−)-MA (1:2) salt (1.70 g, 3.3 mmol) gave (−)-DPEDA (0.67 g, 79% based on the half amount of DPEDA used): mp 85.5—86 °C (lit,[2c] 85—90 °C); $[\alpha]_D^{16}$ −105.2° (*c*, 1.06, MeOH); 97.5% optical purity.

Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20%. Found: C, 79.25; H, 7.30; N, 13.16%.

Similar satisfactory results were obtained when the optical resolution was carried out in 0.1—0.05 mol scales.

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