Convenient Optical Resolution of Axially Chiral 1,1′-Binaphthyl-2,2′-dicarboxylic Acid

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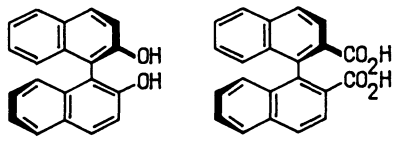
Synopsis. Axially chiral 1,1′-binaphthyl-2,2′-dicarboxylic acid was conveniently resolved through its brucine salts in satisfactory yields. The resolved diacids were confirmed to be optically pure from high-performance liquid chromatographic analyses of the dimethyl esters derived from them on an optically active poly(diphenyl-2-pyridylmethyl methacrylate) column.

In the last decade, much attention has been drawn to a variety of asymmetric reactions assisted by chirally hinged biaryl compounds.[1] For example, 2,2′-dihydroxy-1,1′-binaphthyl (**1**) has been well-known to bring about great success in complexation with chiral crown ethers[2] and asymmetric reductions of carbonyl compounds.[3] Besides the diol **1**, 1,1′-binaphthyl-2,2′-dicarboxylic acid (**2**) has been successfully utilized to the construction of chirality-recognizing units, as well.[4] Concerning the design of such chiral auxiliaries, the carboxylic substituents are advantageous for easy transformations into various functionalities.[5]



(R)-1 (R)-2

Regardless of the above excellent results, the enantiomers of **2** have been prepared by means of a conventional resolution through its quinine salt.[5b] The procedure seemed to be quite tedious, and the efficiency of resolution was rather low. As pointed out by Hall and Turner,[5b] the salt, which gave a higher optical rotation, was not always composed of optically pure **2**.[6] Moreover, the chiroptical property of the resolved salt was complicated by the fact that the salt formed clathrates with solvents used for recrystallization.[5b]

On the other hand, there is a direct synthetic route to homochiral **2** by Miyano et al.[7] via an intramolecular Ullmann coupling of the bis(bromonaphthoic) ester derived from optically active **1**. However, this route required a stoichiometric amount of axially chiral **1**, and the yield of the cyclic diester was not so high.[7]

Herein we wish to describe the improved optical resolution of (*RS*)-**2**. We found that brucine formed a nicely crystallizable salt with an equimolar amount of **2**. In order to effectively separate a mixture of the diastereomeric salts by recrystallization, solvents and the requisite quantities of solvent were screened. Consequently, it was found that a dextrorotatory salt with a relatively high optical purity was obtained under rather high dilution conditions in acetone. Recrystallization of the less soluble salt from acetone/methanol and work-up of the mother liquor led to pure (+)-brucine salt of (*R*)-**2** in a total 41% yield based on racemic **2**. This salt was identified as an acetone clathrate in a 1:1:1 (**2**:brucine:acetone) stoichiometry. In contrast to the case of the previous quinine salt, both the stoichiometric composition of the clathrate and its stability toward vacuum drying under ambient temperature facilitated the unambiguous estimation of the optical purity of each crop. Decomposition of the (+)-salt with diluted hydrochloric acid gave (*R*)-**2** in a 40% yield; the absolute configuration of the diacid was known.[8]

Similar decomposition of the salt in the mother liquor after removal of the (+)-salt gave (*S*)-enriched **2**. A small amount of the opposite (*R*)-**2** could be removed by a simple filtration, because the minor enantiomer formed a *racemic compound* which was sparingly soluble in diethyl ether. Thus, optically active (*S*)-**2** was obtained in a 45% yield. Any recrystallization process of the more soluble (−)-salt[9] was not needed for the acquisition of optically pure (*S*)-**2**; this is another merit of our method.

The diacids resolved thus may be recrystallized from diethyl ether. The rotation values of the purified enantiomers compare favorably with the earlier records.[5b,8] Of course, most of the resolving agent was reusable.

The optical purity of the resolved **2** was determined

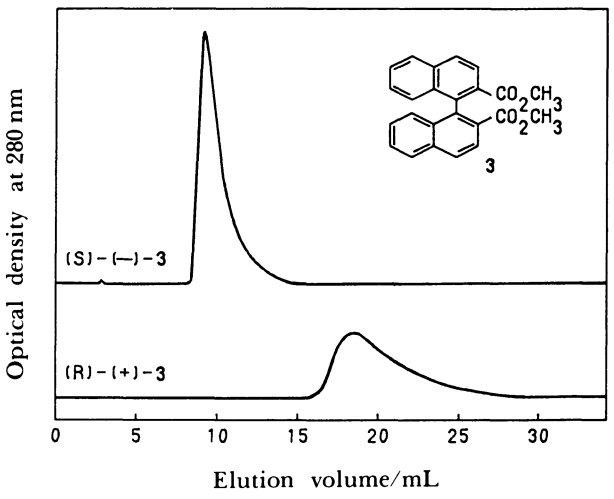


Fig. 1. Chromatograms of the dimethyl ester (**3**) derived from optically resolved **2**. Column: (−)-poly(D2PyMA), 25×0.46 (i.d.) cm; eluent: methanol; flow rate: 1.0 cm^3 min^{-1}; temperature, 25 °C.

from an HPLC analysis of the dimethyl ester (**3**) derived from the diacid. The packing material used for the optically active column was (−)-poly(diphenyl-2-pyridylmethyl methacrylate) [poly(D2PyMA)][10] coated on macroporous silica gel.[11] Base-line resolved separation was accomplished for racemic **3** on this column, using methanol as an eluent.[12] Figure 1 shows chromatograms of (+)- and (−)-**3** under the same conditions as those operated for the racemic material. The enantiomers were eluted at a different retention time to each other, which was in near agreement with that of either of two peaks observed for racemic **3**, and both chromatograms showed the absence of the opposite enantiomer. These results indicate that the diacids resolved in the present method are almost optically pure.

Although the present resolution method relies on a classical recrystallization of the diastereomeric salts, the operational simplicity and high efficiency will help chemists wishing to use the optically pure diacid **2**.

Experimental

General. Melting points are uncorrected. A thermal analysis was carried out with a DAINI SEIKOSHA differential scanning calorimeter SSC/560S, at a heating rate of 5 °C min^{-1}, using an aluminum open sample pan. IR and ^{1}H NMR spectra were recorded on a JASCO A-202 and a JEOL JNM-FX-100S (100 MHz) spectrometer, respectively. Optical rotations were determined on a JASCO DIP-360 digital polarimeter. High-performance liquid chromatograms (HPLC) were run on a 25×0.46 (i.d.)-cm stainless column of (−)-poly(D2PyMA), using a JASCO 880-PU pump equipped with a JASCO UVIDEC-100-II UV detector at 280 nm. Resolution was carried out with methanol at a flow rate of 1.0 cm^3 min^{-1} at 25 °C.

(*RS*)-1,1′-Binaphthyl-2,2′-dicarboxylic Acid (2). The titled compound was prepared by the method reported in the literature.[5b] The racemic diacid (**2**) was recrystallized from acetone to give a 2:1 stoichiometric clathrate of acetone to **2** as transparent prisms, the de-solvation of which converted them gradually into a nontransparent material during storage in an open vessel under ordinary conditions. The clathrate released the acetone molecules at 68 °C, and then melted at 276 °C under atmospheric pressure (from a differential scanning calorimetric analysis). Acetone clathrate of **2**; IR (KBr) 3500—2500, 1725, 1690, 1615, 1595, 1240, 1210, 1195, 1150, 1140 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=2.09 (s, acetone, 12H), 6.8—8.2 (m, ArH, 12H), 12.2 (br s, -COOH). Found: C, 73.34; H, 5.46%. Calcd for $C_{22}H_{14}O_4 \cdot 2C_3H_6O$: C, 73.35; H, 5.72%. A sample was dried at 90 °C under vacuum to give the de-solvated diacid; mp 272—274 °C (lit,[5b] mp 272—274 °C); IR (KBr) 3500—2500, 1680, 1615, 1595, 1280, 1250, 1165, 1140 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=3.3 (br s, -COOH, 2H), 6.8—8.2 (m, ArH, 12H).

Optical Resolution of (*RS*)-1,1′-Binaphthyl-2,2′-dicarboxylic Acid (2). All yields were based on (*RS*)-**2** used. A solution of 30.0 g (87.6 mmol) of de-solvated (*RS*)-**2** in 450 cm^3 of acetone was added to a refluxing solution of 34.6 g (87.7 mmol) of anhydrous brucine (*caution: highly poisonous*[13]) in 1.0 dm^3 of acetone. Colorless needles soon began to deposit from the resulting solution and the mixture was cooled in a refrigerator overnight. The separated crystals were filtered and washed with acetone to give 38.7 g of the less soluble salt after air-drying: $[\alpha]_D^{25}$ +125° (*c* 0.5, chloroform). The crude (+)-salt was dissolved in 1 dm^3 of methanol under refluxing, and then the hot solution was diluted with 500 cm^3 of hot acetone. Cooling the solution gave colorless needles, drying of which for 3 h at room temperature under vacuum gave 24.9 g (36%) of brucine salt of (*R*)-**2** as a 1:1 stoichiometric acetone clathrate: mp 211—214 °C; $[\alpha]_D^{25}$ +200° (*c* 0.5, chloroform). The filtrate was concentrated to about 150 cm^3 to give an additional (+)-salt. This work-up was repeated until (−)-brucine salt crystallized, and a small amount of a nearly inactive salt was discarded. The total yield of the pure (+)-salt was 41% (28.8 g). Found: C, 72.48; H, 5.71; N, 3.62%. Calcd for $C_{45}H_{40}N_2O_8 \cdot C_3H_6O$: C, 72.53; H, 5.83; N, 3.52%.

The (+)-salt was shaken with diethyl ether (200 cm^3) and 6 mol dm^{-3} hydrochloric acid, and the aqueous layer was extracted with ether (50 cm^3×2). The combined ethereal extracts were washed with 1 mol dm^{-3} hydrochloric acid and then brine, dried over Na_2SO_4, and evaporated to dryness. Drying of the amorphous powder at 90 °C under vacuum over P_2O_5 gave 12.1 g (40%) of (*R*)-**2**: $[\alpha]_{546}^{25}$ +123° (*c* 1.0, 0.1 mol dm^{-3} NaOH). An analytical sample was recrystallized from ether to give colorless platelets, that were dried under the same conditions as above: mp 197—199 °C (decomp), reported[5b] decomposition at ca. 120 °C for a 0.5 hydrate; $[\alpha]_{546}^{25}$ +127° (*c* 1.0, 0.1 mol dm^{-3} NaOH) (lit[5b] $[\alpha]_{546}^{20}$ +124.2° (*c* 1.115)). Found: C, 76.90, H, 3.95%. Calcd for $C_{22}H_{14}O_4$: C, 77.18, H, 4.12%.

The mother liquor from the initial salt formation was combined with the (−)-salt and the final filtrate, which were obtained in the above purification of the (+)-salt. The mixture was evaporated to dryness. The residual salt was similarly converted into **2**. The solids of (−)-enriched **2** were mixed with 100 cm^3 of ether, and the suspension was warmed to boiling and then cooled. Insoluble materials were filtered off, and the filtrate was reworked. The final filtrate was evaporated under reduced pressure, and the residue was dried at 90 °C under vacuum over P_2O_5 to give 13.5 g (45%) of (*S*)-**2** as an amorphous powder: $[\alpha]_{546}^{25}$ −125° (*c* 1.0, 0.1 mol dm^{-3} NaOH). Pure (*S*)-**2** was obtained by recrystallization from ether as colorless platelets: mp 199—200 °C (decomp), reported[5b] decomposition at ca. 120 °C for a 0.5 hydrate; $[\alpha]_{546}^{25}$ −127° (*c* 1.0, 0.1 mol dm^{-3} NaOH) (lit,[5b] $[\alpha]_{546}^{22}$ −125.2° (*c* 1.023)). Found: C, 77.17, H. 3.85%. Calcd for $C_{22}H_{14}O_4$: C, 77.18, H, 4.12%.

The acidic layers from the decomposition of the salts were combined, and basified by the addition of aqueous ammonia, and the precipitate was collected. Most of the used brucine was recovered by recrystallization from ethanol.

(*S*)-Methyl 1,1′-Binaphthyl-2,2′-dicarboxylate, (*S*)-3, and (*R*)-3. The resolved diacid (*S*)-**2** was treated with diazomethane, and the evaporated residue was chromatographed with benzene on silica gel to give the diester **3** (96%) as a white powder, which gave $[\alpha]_D^{25}$ −20.5° (*c* 1.0, methanol). A part of the solid was used as an HPLC sample without further purification. The remainder was recrystallized from methanol to give crystalline (*S*)-**3**:[14] mp 157—158 °C (lit,[8] mp 154—155 °C); $[\alpha]_D^{25}$ −21.7° (*c* 1.0, methanol), reported[8] ($[\alpha]_D^{25}$ −18° (*c* 1.2); IR (KBr) 1730, 1240, 1135, 765 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.49 (*s*, -OCH_3, 6H), 7.0—8.2 (m, ArH, 12H).

Similarly (*R*)-**2** was converted into (*R*)-**3**; mp 156.5—157.5 °C; $[\alpha]_D^{25}$ +22.4° (*c* 1.0, methanol).

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poly(D2PyMA) column for HPLC. This work was supported in part by a Grant-in-Aid for Scientific Research No. 61470105 from the Ministry of Education, Science and Culture.

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6) In our trial, optically pure (−)-**2** was obtained not only from the (−)-salt but also, surprisingly, from the (+)-salt, the $[\alpha]_{546}^{25}$ of which were −109°[5b] and +225°, respectively, (*c* 1.0, acetone).

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9) Brucine salt of (*S*)-**2**: colorless needles; mp 190—210 °C with previous softening; $[\alpha]_D^{25}$ −154° (*c* 0.5, chloroform).

10) (−)-Poly(D2PyMA) of $[\alpha]_D^{25}$ −314° (*c* 1.0, $CHCl_3$–10%CF_3CH_2OH) was prepared by the asymmetric polymerization of the achiral monomer with a chiral benzyllithium complex in toluene at −78 °C.[4c]

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12) Results of the chromatographic resolution of (*RS*)-**3**: capacity factors, k_1' (to less retained (*R*)-**3**)=2.61 and k_2'=6.05; separation factor, α=2.32; resolution factor, R_S=2.52; void volume, V_0=2.52 ml (water in methanol).

13) Toxicity of brucine: LD_{50} orally in rats, 1 mg kg^{-1}; "Registry of Toxic Effects of Chemical Substances," ed by R. J. Lewis and R. L. Tatken, Vol. 1, (1979), p. 324.

14) In a preparative scale, **2** was esterified with methanol containing concd H_2SO_4 under refluxing: yield, more than 90%.