CHEMISTRY LETTERS, pp. 1371-1374, 1988.

Efficient Optical Resolution of 2,2'-Dihydroxy-1,1'-binaphthyl and 10,10'-Dihydroxy-9,9'-biphenanthryl by Complex Formation with Novel Chiral Host Compounds Derived from Tartaric Acid

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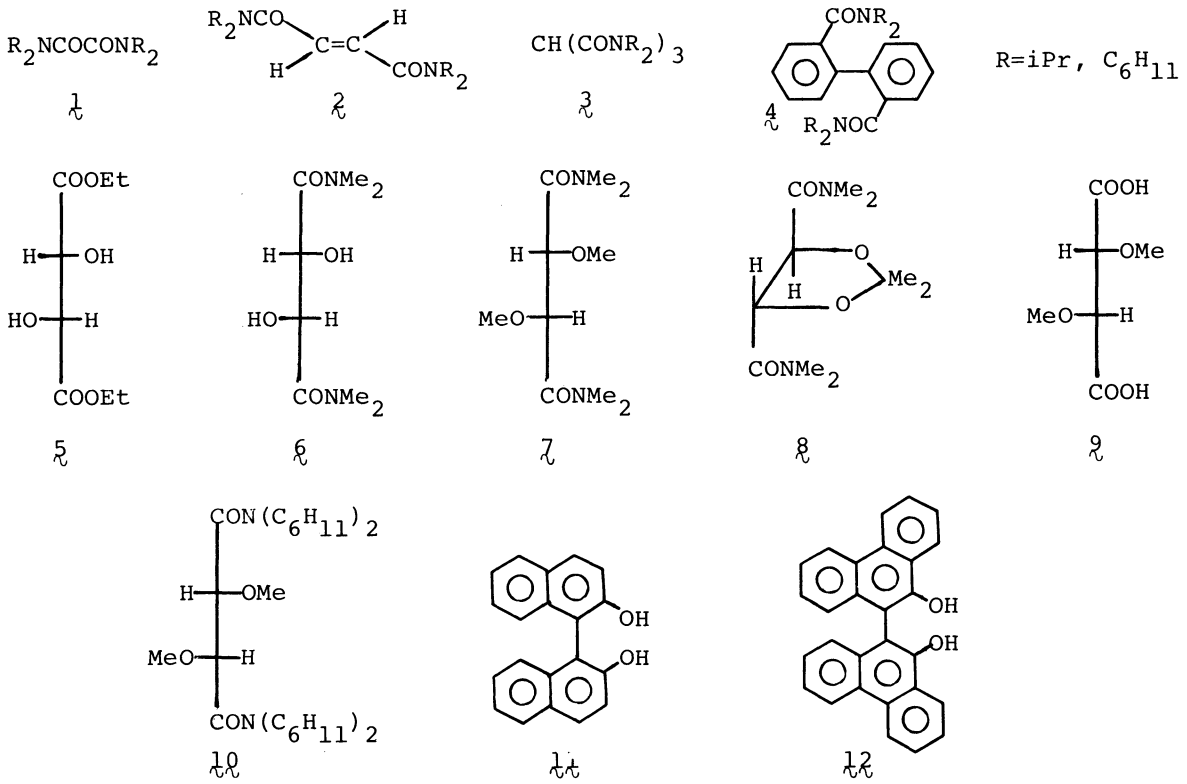
2,2'-Dihydroxy-1,1'-binaphthyl and 10,10'-dihydroxy-9,9'-biphenanthryl were resolved efficiently by complex formation with novel chiral host compounds derived from tartaric acid, (*R*,*R*)-(+)-2,3-dimethoxy-N,N,N',N'-tetramethylsuccinamide and (*R*,*R*)-(+)-N,N,N',N'-tetramethyl-2,2-dimethyl-1,3-dioxolane-*trans*-4,5-dicarboxamide, respectively. X-Ray crystal structure of these complexes was studied.

Previously, we reported that amide host compounds such as oxoamide (1),[1,2] fumaramide (2),[3,4] methanetricarboxamide (3),[5] and 2,2'-biphenyldicarboxamide derivatives (4)[6] include a wide variety of organic compounds and form crystalline complexes of a stoichiometric host:guest ratio. Optical resolution of a guest compound by enantioselective inclusion is expected when an optically active amide host compound is used. We designed chiral amide host compounds, succinamide derivatives (7, 10) and dioxolane-4,5-dicarboxamide (8), starting from the naturally occurring cheap chiral compound, (+)-tartaric acid.

Treatment of (*R*,*R*)-(+)-2,3-dihydroxy-N,N,N',N'-tetramethylsuccinamide (6), which can easily be prepared from (*R*,*R*)-(+)-diethyl tartarate (5) and dimethylamine,[7] with dimethyl sulfate and 2,2-dimethoxypropane gave (*R*,*R*)-(+)-dimethoxy-N,N,N',N'-tetramethylsuccinamide (7) and (*R*,*R*)-(+)-N,N,N',N'-tetramethyl-2,2-dimethyl-1,3-dioxolane-*trans*-4,5-dicarboxamide (8), respectively, in yields of more than 90%. Although (+)-7 (mp 61-62 °C, $[\alpha]_D$ +115° (*c* 1.2, $CHCl_3$)) is a known compound,[7] its inclusion ability for organic compounds has never been reported. (+)-8 has the following physical properties: mp 86-88 °C, $[\alpha]_D$ +2.5° (*c* 1.4, $CHCl_3$)). Treatment of (*R*,*R*)-(+)-2,3-dimethoxysuccinic acid (9)[8] with PCl_5 followed by dicyclohexylamine gave the tetracyclohexyl derivatives of (+)-7 ((*R*,*R*)-(+)-10) (mp 135-140 °C, $[\alpha]_D$ +57.7° (*c* 0.4, $CHCl_3$)) in 53% yield. By the same method, (*S*,*S*)-(-)-7, (*S*,*S*)-(-)-8, and (*S*,*S*)-(-)-10 were prepared from nonnaturally occurring (-)-tartaric acid.

The chiral host compounds prepared were found to form inclusion complexes with C_2 symmetrical chiral guest compounds such as 2,2'-dihydroxy-1,1'-binaphthyl (11) and 10,10'-dihydroxy-9,9'-biphenanthryl (12). It was also found that the complex formation occurs enantioselectively and optical resolution of 11 and 12 was achieved



very efficiently. For example, when a solution of (+)-7 (4.06 g, 17.5 mmol) and (±)-11 (5.0 g, 17.5 mmol) in benzene (20 ml) and hexane (5 ml) was kept at room temperature for 12 h, a 1:1 complex of (+)-7 and (-)-11 was formed as colorless prisms (4.1 g). The crude crystals were recrystallized from benzene and then chromatographed on silica gel using benzene as a solvent to give (*S*)-(-)-11 of 100% ee[9] (1.8 g, 72%,[10] $[\alpha]_D$ -33.2° (*c* 1.1, THF)). The filtrate left after the separation of a 1:1 complex of (+)-7 and (-)-11 was chromatographed on silica gel to give crude (+)-11 (2.7 g, $[\alpha]_D$ +21° (*c* 1.1, THF)). Treatment of the crude (+)-11 (2.7 g) with (-)-7 finally gave (*R*)-(+)-11 of 100% ee (1.48 g, 59%, $[\alpha]_D$ +33.3° (*c*, 1.1, THF). These complexes of 7 and 11 can also be decomposed to the components by treatment with aq. NH_2NH_2. For example, when a MeOH solution of the complex was treated with 64% aq. NH_2NH_2 at room temperature under stirring for 5 min, a 1:1 complex of (+)-11 and NH_2NH_2 was formed as colorless needles (1.78 g) which upon acidification with dil HCl gave (+)-11 (1.7 g, 98%). From the filtrate left after the separation of the NH_2NH_2 complex of (+)-11, (-)-7 (1.4 g, 97%) was recovered.

The best method for the preparation of optically active 11 which has been reported so far is the optical resolution with cinchonine of the cyclic binaphthylphosphoric acid derived from 11 by reaction with $POCl_3$ followed by hydrolysis.[11,12] In comparison with the diastereomeric method, the present complexation method, which does not involve any synthetic step on the racemic guest, is much simpler and gives both (+)- and (-)-11 easily.

Application of optically active 12 for optical resolution has been reported.[13] Although a preparative scale method for obtaining optically active 12 by the enantioselective coupling of 9-hydroxyphenanthrene in the presence of optically active 1,2-diphenylethylamine has been reported,[14] this is not applicable to a large

scale production because of the difficulty in obtaining the resolved amine. We found that 12 is easily resolved by complexation with optically active 8. When a solution of (+)-8 (1.26 g, 5.16 mmol) and (±)-12 (1.0 g, 2.59 mmol) in EtOH (20 ml) was kept at room temperature for 12 h, a 2:1 complex of (+)-8 and (-)-12 was formed as colorless prisms (1.03 g). The crude crystals were recrystallized from EtOH and chromatographed on silica gel using benzene as the solvent to give (*S*)-(-)-12 of 100% ee (0.37 g, 74, $[\alpha]_D$ -64.6° (*c* 1.2, $CHCl_3$)). The filtrate left after the separation of a 2:1 complex of (+)-8 and (-)-12 was concentrated to half the volume to give a 1:1 complex of (+)-8 and (+)-12 as colorless needles (0.8 g). The crude crystals (0.8 g) were recrystallized from EtOH and chromatographed on silica gel to give (*R*)-(+)-12 of 100% ee (0.4 g, 80%, $[\alpha]_D$ +81.1° (*c* 1.0, $CHCl_3$)).

In order to know mechanism of the efficient optical resolution, X-ray crystal structures of a 1:1 complex (13) of (*R*,*R*)-(+)-7 and (*S*)-(-)-11, a 2:1 complex (14) of (*R*,*R*)-(+)-8 and (*S*)-(-)-12, and a 1:1 complex (15) of (*R*,*R*)-(+)-8 and (*S*)-(+)-12 were studied.[15,16] However, structure of complex of (*S*,*S*)-(-)-7 and (*S*)-(-)-11 was not studied, because these two do not form complex. Perspective view of 13, 14, and 15 with their atomic numbering are shown in Figs. 1, 2, and 3, respectively.

The four cyclohexyl rings of (+)-10 in 13 are in the chair conformation. Concerning the (-)-11, the two naphthyl rings are approximately planar (maximum deviation of any one of the plane-defining atoms from the least squares plane less than 0.06 Å), with the dihedral angle between the naphthyls at 101.3(2)°. The host and guest molecules are linked by hydrogen bond of the form O-H···CO to form ribbons parallel to the a axis. In the hydrogen bondings, distances between O2' and H2', and H2' and O4 are 1.1(1) and 1.7(1) Å, respectively. Distance between O2' and O4 is 2.67(1) Å.

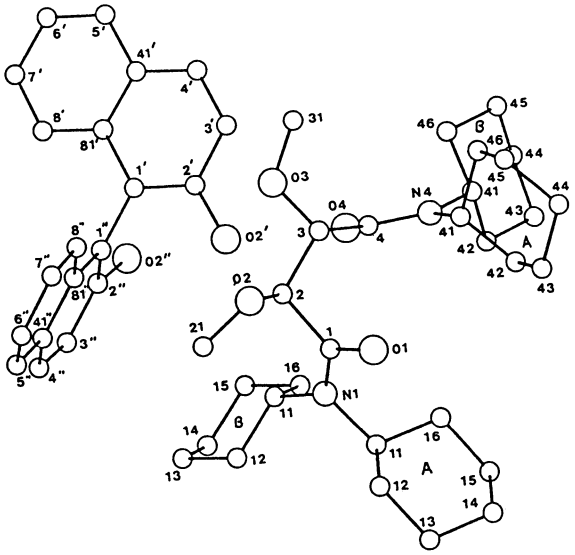


Fig. 1. Perspective view of 13.

Concerning the (+)-8 in 14, the dimethylmethylenedioxy group bridges two carbons to form a five-membered ring in an envelop conformation. The phenanthryl groups of the (-)-12 which are equivalent by symmetry are approximately planar (with the maximum deviation of any one of the plane-defining atoms from the least squares plane less than 0.07 Å) with the torsion angle C10'-C9'-C9''-C10'', (C9'', C10'' symmetry generated) at -84(1)°. In the hydrogen bonding, distance between O10' and H10', and H10' and O4 is 2.66(1) Å. Interestingly, the other possible hydrogen bond acceptor on the host, O1, has no close contacts to any hydrogen donor, which precludes the formation of any polymeric link between the host and guest molecules.

In 15, the intermolecular close contacts resulting from hydrogen bonding are as follows: O10A···O1 (2.625(4) Å, O-H···O angle 169(3)°), O10B···O4 (2.647(3) Å, O-H···O angle 172(3)°). The hydrogen bonding is such that only pairs of the two

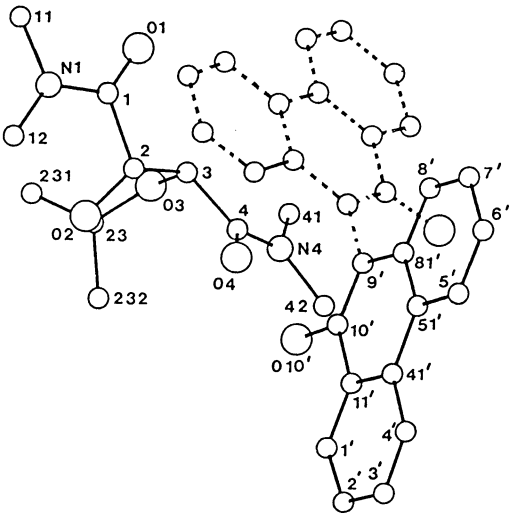


Fig. 2. Perspective view of 14.

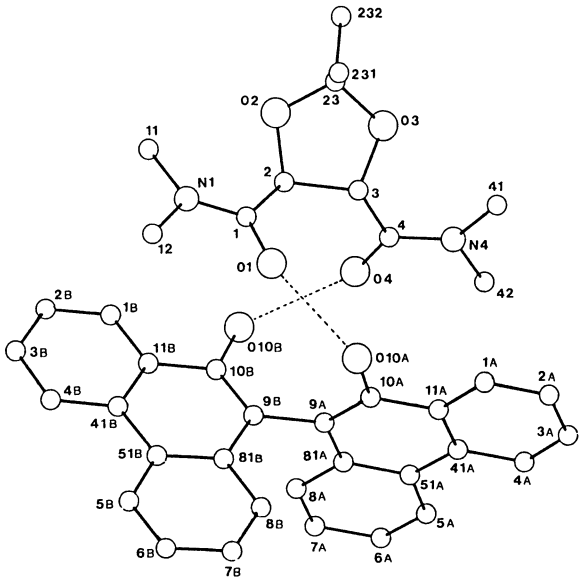


Fig. 3. Perspective view of 15.

molecules are linked and there is no evidence of polymerization throughout the structure. Therefore, 14 which has a polymeric structure is less soluble and crystallizes initially, and 15 which has a cyclic structure is more soluble and crystallizes finally. This would be the reason for the efficient resolution of 12 with 8.

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9) Optical purity was obtained by comparison of the observed $[\alpha]_D$ value with reported one.
10) All yields of the optical resolution were calculated on the basis of the theoretical amount of the optical isomer contained in the initial (±)-compound.
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15) Since a 1:1 complex of 7 and 11 does not form good single crystal for X-ray analysis, crystal of a 1:1 complex of 10 and 11 was used for the analysis. Although 11 is also resolved efficiently by complexation with 10, it is much better to use readily available 7 for the resolution.
16) Crystal data of 13: a=10.52(1), b=20.290(7), c=11.681(2) Å, β=110.58(5), V=2334(2) Å^3, D_c=1.13 g cm^{-3} for Z=2, μ(MoKα)=0.681 cm^{-1}, F(000)=856. Crystal data of 14: a=9.978(3), c=47.203(8) Å, V=4700(2) Å^3. D_c=1.24 g cm^{-3} for Z=4, μ(MoKα)=0.807 cm^{-1}, F(000)=1864. Crystal data of 15: a=11.750(3), b=12.479(6), c=22.844(4) Å, V=3350(2) Å^3, Dc=1.25 g cm^{-3} for Z=4, μ(MoKα)=0.790 cm^{-1}, F(000)=1336.

(Received June 10, 1988)