6-CH_3), 3.79/0.58 (3, s, 9-OCH_3), 6.64/0.06 (1, dd, J_o = 8 Hz, J_m = 2 Hz, 8-H), 6.90–7.48 (4, m, Ar H), 7.68/0.10 (1, d, J_o = 8 Hz, 4-H), 8.79/–0.64 (1, d, J_o = 9 Hz, 1-H); mass spectrum, *m/e* (relative intensity) 288 (100), 273 (18), 245 (5); calcd for M^+ 288.11502, found 288.1144. Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.44; H, 5.60.

Thermolysis of Benzo[*c*]fluorenone 13a. A solution of 0.17 mmol of **13a**, dissolved in 20 mL of diphenyl ether, was thermolyzed at 250 °C in the dark during 18 h. Preparative TLC on silica gel with benzene–hexane (4:1), after removal of the diphenyl ether as usual, yielded besides **13a**, a red product; recrystallization from heptane afforded 0.13 mmol of the benzo[c]fluorenone **16** (77%): mp 193 °C; IR 1690 cm^{-1} ($\nu_{C=O}$); ^1H NMR ($CDCl_3/\Delta$) δ 2.53/0.35 (3, s, 5-CH_3), 2.72/–0.03 (3, s, 6-CH_3), 3.86/0.66 (3, s, 9-OCH_3), 6.87/0.15 (1, dd, J_o = 8 Hz, J_m = 3 Hz, 10-H), 7.10–7.56 (3, m, Ar H), 7.73/0.25 (1, d, J_o = 8 Hz, 11-H), 7.9/0.18 (1, m, 4-H), 8.26/0.04 (1, m, 1-H); mass spectrum, *m/e* (relative intensity) 288 (100), 273 (40), 245 (17); calcd for M^+ 288.11502, found 288.1151. Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 82.92; H, 5.69.

Trapping the *o*-Quinodimethane with Tetracyanoethylene. A solution of 1.00 mmol of **9a**, 0.5 mmol of hydroquinone, and 5.96 mmol of tetracyanoethylene dissolved in 15 mL of diphenyl ether was degassed and thermolyzed in the dark at 250 °C during 5 h. Preparative TLC on silica gel with benzene, after removal of the diphenyl ether as usual, yielded 0.74 mmol (74%) of the *o*-quinodimethane–tetracyanoethylene adduct and 0.07 mmol (7%) of the indenone **5a**; no other products were isolated. Identification of the *o*-quinodimethane–tetracyanoethylene adduct: mp 253–256 °C dec; IR 2240 cm^{-1} ($\nu_{C\equiv N}$), 1705 ($\nu_{C=O}$); ^1H NMR ($CDCl_3/\Delta$) δ 1.60/0.30 (3, s, 11a-CH_3), 1.96/0.36 (3, s, 6a-CH_3), 2.36/0.22 (3, s, 1-CH_3), 3.66/0.76 (3, s, 9-OCH_3), 4.00/0.50 (1, s, 6-H), 6.63–7.4 (7, m, Ar H); mass spectrum, *m/e* (relative intensity) 432 (28), 304 (100), 289 (51), 276 (11), 188 (33); calcd for M^+ 432.1586, found 432.1586. Anal. Calcd for $C_{27}H_{20}N_4O_2$: C, 74.99; H, 4.66; N, 12.95. Found: C, 75.36; H, 5.01; N, 12.60.

Acknowledgment. We are indebted to the Instituut tot Aanmoediging van Wetenschappelijk Onderzoek in Nijverheid en Landbouw (IWONL) for predoctoral fellowships (to D.V. and R.C.) and to the FKFO and the Ministry of Scientific Programming for financial support. We are also grateful to R. De Boer and P. Valvekens for technical assistance.

Registry No. *exo*-**3**, 85749-62-8; *endo*-**3**, 85798-63-6; **4**, 85798-64-7; **5a**, 55288-46-5; **5b**, 85749-63-9; **5c**, 85762-04-5; **5d**, 55288-49-8; **7**, 85749-64-0; **9a**, 85749-65-1; **9b**, 85749-66-2; **9c**, 85749-67-3; **9d**, 85749-68-4; **10a**, 85798-65-8; **11a**, 85749-70-8; **12a**, 85749-70-8; **12b**, 85749-71-9; **12d**, 85749-72-0; **13a**, 85749-73-1; **13a** dihydro derivative, 85749-74-2; **13b**, 85749-75-3; **13c**, 85749-76-4; **13d**, 85749-77-5; **14a**, 85749-78-6; **14d**, 85749-79-7; **15**, 85749-80-0; **16**, 85749-81-1; *o*-acetylphenylacetic acid, 36073-90-2; tetracyanoethylene, 670-54-2; *o*-quinodimethane–tetracyanoethylene adduct, 85749-82-2; cuneane, 20656-23-9.

Resolution and Absolute Configuration of Bicyclo[3.3.0]octa-2,6-diene-2-carboxylic Acid

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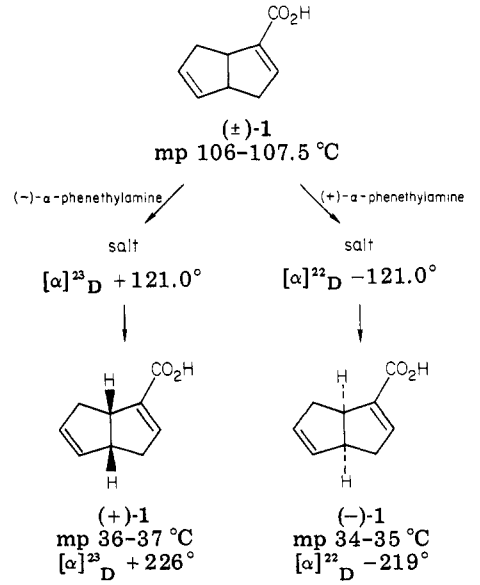
An efficient resolution of the title acid (1) by using (+)- and (–)-α-phenethylamine is described. The (+) acid was determined to be 1*S* by chemical correlation through (+)-*cis*-bicyclo[3.3.0]octan-2-one (3) with (+)-*cis*-bicyclo[3.3.0]oct-7-en-*endo*-2-ol (4) where the absolute configuration is known to be 1*R*. The 1*R* configuration for (–)-3 was consistent with the negative Cotton effect observed for this ketone.

We have been involved for some time in exploiting the bicyclo[3.3.0]octane framework for the synthesis of terpenoid and other natural products.[1] Recently[2] we detailed convenient syntheses for two, isomeric diene acids with this framework which have been particularly useful to us in our synthetic studies. For one of these, bicyclo[3.3.0]octa-2,6-diene-2-carboxylic acid (1), we have been able to effect an exceptionally efficient resolution and to correlate one of the enantiomers with known chirality in order to establish the absolute configuration in this series (see Scheme I).

Resolution of the acid was effected through the salts formed with the enantiomers of α-phenethylamine. Progress of the separation of the diastereomeric salts thus formed could not be followed by melting point determinations since the salts melted with decomposition. However, optical rotation was found to be quite sensitive to the degree of separation as the diastereomeric salts had nearly equal magnitude but opposite rotations (+121° for the (+) acid and (–) amine and –131° for the (–) acid and (–) amine). The degree of resolution could also be followed, though less conveniently, by conversion of the salt to the acid and then to the methyl ester by using diazomethane. The methyl group absorptions of the enantiomers in the

Scheme I



(1) See for example: Whitesell, J. K.; Matthews, R. S.; Minton, M. A.; Helbling, A. M. *J. Am. Chem. Soc.* **1981**, *103*, 3468–3472.
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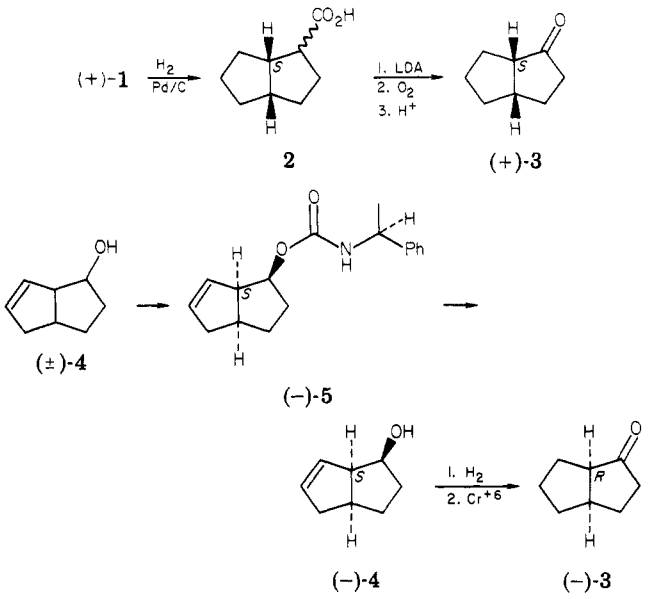
Scheme II



^{1}HMR were cleanly split into signals at δ 4.52 ((−) acid) and δ 4.56 ((+) acid) in the presence of 0.2 equiv of tris-[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium (Eu(HFC)$_3$). Multiple cycling between the enantiomers of the amine afforded an 80% yield and 87% conversion to fully resolved acids.

The absolute configuration assignment for **1** was made by correlation through the ketone **3** with alcohol **4**. Catalytic reduction of (+)-**1** followed by oxidative decarboxylation[3] of the resulting mixture of *endo* and *exo* acids afforded (+)-**3** (Scheme II). Alternately, (−)-**4**, obtained by resolution through the α-phenethyl carbamate, was converted by catalytic reduction followed by oxidation to (−)-**3**. Since it has been established[4] that (+)-**4** has the 1*R* configuration, then (+)-**3** and (+)-**1** must be 1*S*. Alternately, the 1*R* configuration for (−)-**3** could inferred from the negative Cotton effect observed for this ketone.

Experimental Section

Materials. Ether and tetrahydrofuran (THF) were distilled prior to use from benzophenone ketyl. Phenethylamine and phenethyl isocyanate were obtained from Norse Laboratories, Newbury Park, Ca.

Procedures. Reactions were routinely effected under a dry nitrogen atmosphere with magnetic stirring. Nuclear magnetic resonance sectra were obtained by using a Varian HA-100 or EM-390 for ^{1}H NMR and a Varian FT-80 spectrometer for ^{13}C NMR. Optical rotations were obtained by using a Perkin-Elmer 141 polarimeter, and all samples reported were homogeneous by ^{13}C spectral and HPLC (μ-Porasil) analyses. Elemental analysis was performed by Chemalytics, Tempe, Az.

Resolution of *cis*-Bicyclo[3.3.0]octa-2,6-diene-2-carboxylic Acid (1). A solution of 34.3 g (0.228 mol) of racemic acid **1** in 200 mL of hot 2-propanol was treated with 14.7 mL (0.114 mol, 0.5 equiv) of (−)-α-phenethylamine. After having cooled slowly to room temperature, the brown-black solution was placed in the refrigerator overnight. The resulting crystals were collected and washed well with cold 2-propanol and then recrystallized twice from the same solvent to afford 14.9 g (50%) of fine white needles: mp 165–167 °C dec; $[\alpha]^{23}_D$ +121.2° (*c* 1.01, absolute EtOH). The optical rotation was unchanged after a third recrystallization. A sample of this salt was converted to the acid and then to the methyl ester with excess diazomethane. The 90-MHz proton NMR of this ester in the presence of 0.2 equiv of the chiral shift reagent Eu(HFC)$_3$ showed no detectable amount of the enantiomer as evidenced by a single, sharp methyl resonance at δ 4.56. In a separate experiment, less than 10% of the enantiomer could be clearly distinguished as a completely resoved singlet at δ 4.52.

The combined supernatant from the above crystallizations was concentrated, and the residue was partitioned between 2 *N* Na_2CO_3(aq) and ether. The combined aqueous layers were washed with ether. The (−) amine was recovered nearly quantitatively from the organic layers. The basic, aqueous layer from above was acidified with concentrated HCl and extracted three times with ether. Concentration afforded 26 g (100%) of acid enriched in the (−) enantiomer. To this material in 200 mL of hot 2-propanol was added 14.7 mL (0.114 mol, 1 equiv, based on the (−) acid present) of (+)-phenethylamine. The resulting crystals were collected and recrystallized as described above affording 16.4 g (55%) of salt, $[\alpha]^{22}_D$ −121.0° (*c* 1.03, absolute EtOH). The process described above was repeated for a total of three cycles, ultimately affording 13.3 g of (+)-**1** [mp 36–37 °C; $[\alpha]^{23}_D$ +226° (*c* 1.00, absolute EtOH)], 14.3 g of (−)-**1** [mp 34–35 °C; $[\alpha]^{23}_D$ −219° (*c* 0.97, absolute EtOH)], and 2.7 g of unresolved material for a total yield of 88%.

The salt from pure (−)-**1** and (−) amine was prepared and recrystallized as described above, affording material with $[\alpha]^{23}_D$ −131° (*c* 1.05, absolute EtOH).

(+)-*cis*-Bicyclo[3.3.0]octan-2-one (3). A sample of (+)-**1** obtained above was converted in quantitative yield to a 1:2 *exo* to *endo* mixture of acids **2** by catalytic reduction at atmospheric pressure over 5% palladium on charcoal in methanol. Oxidative decarboxylation was effected by the procedure of Wasserman.[3] Thus, to 0.43 g of saturated acids in 8 mL of the THF at 0 °C was added a solution of 12 mmol of LDA prepared from 12 mmol of 2.25 M *n*-butyllithium in hexane and 12.5 mmol of diisopropylamine in 15 mL of the THF. The solution was stirred for 3 h at 0 °C and then cooled to −78 °C. Dry oxygen was bubbled through the solution for 30 min, and then 2.85 g (15 mmol) of *p*-toluenesulfonic acid monohydrate in 5 mL of THF was added dropwise. The reaction was then warmed slowly and finally heated at reflux for 10 h. The solution was diluted with ether and extraction with 2 *N* HCl(aq). From concentration of the ether layer there was obtained 0.4 g of ketone as an orange oil. Purification was effected by HPLC (10:1 Skelly B–EtOAc, Porasil A) providing 0.13 g (37%, extensive loss due to volatility) of ketone pure by ^{13}C and with $[\alpha]^{23}_D$ +116° (*c* 1.258, absolute EtOH) and $[\alpha]^{23}_D$ +126° (*c* 2.85, $CHCl_3$).

***cis*-Bicyclo[3.3.0]oct-7-en-*endo*-2-yl (1-Phenylethyl)carbamate (5).** A mixture of 4.2 g (34 mmol) of *cis*-bicyclko-[3.3.0]oct-7-en-*endo*-2-ol (**4**)[5] and 5.7 g (39 mmol) of (−)-α-phenethyl isocyanate was heated at 125 °C for 8 h. Purification by column chromatography (silica gel, 5:1) afforded 9.1 g (99%) of a diastereomeric mixture of urethanes, mp 60–80 °C. Three recrystallizations of 7.5 g of this material from ethyl acetate–Skelly B afforded 0.80 g (21%, based on one enantiomer of the alcohol) of a single diastereomer (by ^{1}HMR analysis): mp 97–98 °C; $[\alpha]^{25}_D$ −206.7° (*c* 2.4, $CHCl_3$); ^{1}HMR (C_6D_6) δ 1.18 (d, 3 H, J = 7 Hz), 1.56–1.72 (m, 2 H), 2.2–2.6 (m, 2 H), 3.2–3.54 (m, 1 H), 3.6–4.1 (m, 2 H), 5.22 (q, 1 H), 5.73 (br s, 2 H), 7.12 (br s, 5 H). Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.19; H, 7.88; N, 5.23.

(−)-*cis*-Bicyclo[3.3.0]oct-7-en-*endo*-2-ol (4). A solution of 790 mg (2.9 mmol) of (−) urethane (**5**) and 1.6 g (30 mmol) of sodium methoxide in 15 mL of ethanol was heated at reflux for 24 h. The cooled reaction solution was diluted with 2 N aqueous hydrochloric acid and extracted with three 20-mL portions of methylene chloride. The organic layer was concentrated to afford 510 mg of crude product that was purified by HPLC (2:1) to give 260 mg (72%) of the alcohol. A portion was rechromatographed to obtain a sample for optical rotation; $[\alpha]^{25}_D$ −124° (*c* 6, $CHCl_3$).

(−)-*cis*-Bicyclo[3.3.0]octan-*endo*-2-ol. A solution of 47 mg (0.30 mmol) of (−) alcohol **4** and 50 mg of 5% palladium-on-carbon in 3 mL of ethyl acetate was hydrogenated at atmospheric pressure and 25 °C. After the theoretical amount of hydrogen was absorbed, the solution was filtered and concentrated to give 44 mg

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(92%) of alcohol, pure by ^{1}HMR analysis with $[\alpha]^{25}_D$ −104° (c 4.4, $CHCl_3$).

(−)-*cis*-Bicyclo[3.3.0]octan-2-one (3). The alcohol obtained above was oxidized with Cr^{6+} by using the procedure of Ratcliffe.[6] From 41 mg of alcohol was obtained 36 mg (90%) of the ketone (−)-3, pure by spectral (^{1}HMR) and VPC (25% Carbowax on Chromasorb P, 150 °C) analyses: $[\alpha]^{25}_D$ −105° (c 3, $CHCl_3$); ORD α^{25} (λ, nm) −33.3° (450), −53.3° (400), −100° (350), −227° (318), 0° (291), +40° (280).

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Registry No. (±)-1, 85665-20-9; (+)-1, 85717-55-1; (−)-1, 85717-56-2; (−)-1·(−)-α-phenethylamine, 85760-67-4; (+)-3, 85717-57-3; (−)-3, 85717-59-5; (±)-4, 68317-62-4; (−)-4, 71048-52-7; (−)-4 (dihydro), 85717-58-4; (−)-5, 85665-21-0.

Chiral (β-Aminoalkyl)phosphines. Highly Efficient Phosphine Ligands for Catalytic Asymmetric Grignard Cross-Coupling[1]

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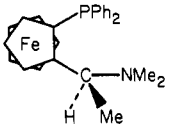
New chiral (β-aminoalkyl)phosphines, $RCH(NMe_2)CH_2PPh_2$ [R = Me (Alaphos), *i*-Bu (Leuphos), $PhCH_2$ (Phephos), *i*-Pr (Valphos), *sec*-Bu (Ilephos), Ph (PhGlyphos), *c*-Hex (ChGlyphos), and *t*-Bu (*t*-Leuphos)], were prepared by starting with optically active amino acids. The phosphines were used as ligands for nickel-catalyzed asymmetric cross-coupling of 1-arylethyl Grignard reagents (ArMeCHMgCl) with vinyl bromide. Coupling products of over 70% enantiomeric excess (ee) were obtained in the reaction with the ligand Phephos, Valphos, Ilephos, PhGlyphos, ChGlyphos, or *t*-Leuphos. A mechanism involving complexation of the magnesium atom in the Grignard reagent with the amino group on the (β-aminoalkyl)phosphine ligand is proposed to account for the high stereoselectivity. The asymmetric cross-coupling was applied to the synthesis of optically active 2-arylpropionic acids.

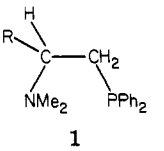
Asymmetric carbon–carbon bond-forming reactions are of great significance for the synthesis of optically active compounds, and the use of chiral transition-metal catalysts for such reactions has recently attracted considerable attention owing to a number of advantages of catalytic asymmetric synthesis.[2] Asymmetric cross-coupling of secondary alkyl Grignard reagents with alkenyl halides[3,4] has been effected by chiral phosphine–nickel or –palladium catalysts and is now recognized to provide an efficient route to the synthesis of optically active olefins, which could hardly be obtained by other methods.

Previously, we have shown[3a,b] that chiral [(aminoalkyl)ferrocenyl]phosphines, represented by (*S*)-*N*,*N*-dimethyl-1-[(*R*)-2-(diphenylphosphino)ferrocenyl]ethylamine [(*S*)-(*R*)-PPFA], are effective ligands for asymmetric



(*S*)-(*R*)-PPFA

cross-coupling. 3-Phenyl-1-butene (68% ee) was produced in the reaction of 1-phenylethylmagnesium chloride with vinyl bromide. Results obtained for the cross-coupling by using various kinds of modified ferrocenylphosphine ligands have proved that the amino group on the phosphine ligand is the first requisite for high stereoselectivity and that the surroundings around the nitrogen atom exert a strong effect on the stereoselectivity. On the basis of these data, we have devoted attention to the design and preparation of new phosphine ligands of higher ability for asymmetric cross-coupling. We have arrived at (β-aminoalkyl)phosphines (1) which seem to fulfull the nec-



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essary conditions mentioned above and could be readily prepared from amino acids. Use of amino acids as optically active starting compounds is convenient because amino acids with various substitutents are readily available in an optically pure form. In this paper, we report the preparation of the (β-aminoalkyl)phosphines and their use for asymmetric Grignard cross-coupling. Application of the

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