silane (2.75 mmol). After 30 min the solution was concentrated in vacuo and acetonitrile (5 mL) and DBN (5 mmol) were then added. The solution was heated to reflux for 12–48 h. The cooled reaction was then worked up as in method A.

2-Cyclohexen-1-ol (8): NMR 5.75–5.50 (m, 2 H), 4.30–3.95 (m, 2 H), 2.18–1.40 (m, 6 H); IR 3400, 1070 cm^{-1}.

2-Phenyl-2-cyclohexen-1-ol (9): NMR 7.60–6.90 (m, 5 H), 6.15–5.90 (m, 1 H), 4.63 (br s, 1 H), 3.50–3.28 (m, 1 H), 2.60–1.40 (m, 6 H); IR 3450, 1060 cm^{-1}.

Ethylene Ketal of 5-Hydroxy-6-methyl-6-hexen-2-one (10): ^1H NMR 4.93 (m, 1 H), 4.8 (m, 1 H), 4.1 (br s, 1 H), 3.92 (s, 4 H), 2.85 (m, 1 H), 1.5–1.9 (m, 7 H), 1.32 (s, 3 H); IR 3460, 1655, 1070 cm^{-1}; ^{13}C NMR 147.324, 110.539, 109.781, 75.218, 64.383, 34.751, 29.115, 23.590, 17.468.

2-Methylenecyclohexanol (11): NMR 4.85 (br s, 1 H), 4.74 (br s, 1 H), 3.97 (m, 2 H), 2.4–1.2 (m, 8 H); IR 3400, 1640, 905 cm^{-1}.

Methyl 1-Hydroxy-2-cyclohexenoate (12): NMR 6.15–5.50 (m, 2 H), 3.79 (s, 3 H), 3.30 (br s, 1 H), 2.25–1.50 (m, 6 H); IR 3480, 1730, 1640, 1240 sm^{-1}; ^{13}C NMR 176.741, 132.372, 126.792, 71.588, 52.735, 33.884, 24.511, 18.281.

Mixture of Methyl 9-Hydroxy-10-heptadecenoate and Methyl 8-Hydroxy-9-heptadecenoate (13): NMR 5.63–5.4 (m, 2 H), 4.10–3.90 (m, 2 H), 3.65 (s, 3 H), 2.50–0.70 (m, 27 H); IR 3400, 1735, 1165 cm^{-1}.

Methyl 2-Hydroxy-1-Methyl-3-cyclohexenoate (14): NMR (one diastereomer) 5.76 (br s, 1 H), 5.65 (br s, 1 H), 4.85 (br s, 1 H), 4.55 (m, 1 H), 3.73 (s, 3 H), 2.25–1.40 (m, 4 H), 1.20 (s, 3 H); (other diastereomer) 5.76 (br s, 1 H), 5.65 (br s, 1 H), 4.85 (m, 1 H), 4.05 (m, 1 H), 3.73 (s, 3 H), 2.25–1.40 (m, 4 H), 1.26 (s, 3 H); IR 3430, 1735, 1115 cm^{-1}.

Oxidation of 9. Alcohol **9** was oxidized by the method of Jones to afford 2-phenylcyclohexenone in 88% yield, mp 91–93 °C (lit.[13] mp 95 °C).

Oxidation of 14. Alcohol **14** was oxidized by the method of Corey[14] to afford methyl 1-methyl-2-oxo-3-cyclohexenoate in 78% yield: NMR 7.08–6.73 (m, 1 H), 6.11–5.85 (m, 1 H, 3.70 (s, 3 H), 2.70–1.60 (m, 4 H), 1.39 (s, 3 H); IR 1735, 1685, 1260, 1115 cm^{-1}; ^{13}C NMR 196.568, 173.003, 149.274, 120.796, 53.331, 52.248, 33.288, 23.536, 20.231.

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Registry No. 1, 286-20-4; 2, 4829-01-0; 3, 39810-29-2; 4, 1713-33-3; 5, 17550-59-3; 6, 73611-70-8; 7, 73611-71-9; 8, 822-67-3; 9, 32363-86-3; 10, 24108-30-3; 11, 4065-80-9; 12, 58547-47-0; 14, isomer 1, 73611-72-0; 14, isomer 2, 73611-73-1; methyl 9-hydroxy-10-heptadecenoate, 73611-74-2; methyl 8-hydroxy-9-heptadecenoate, 73611-75-3; 2-phenylcyclohexenone, 4556-09-6; methyl 1-methyl-2-oxo-3-cyclohexenoate, 73611-76-4.

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Stereochemical Course of the Haworth-Type Synthesis of Optically Active 2-(1-Methylpropyl)naphthalene[1]

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The preparation of (*S*)-2-(1-methylpropyl)naphthalene has been accomplished by starting from (*S*)-(1-methylpropyl)benzene with detectable racemization. The partially unstereospecific steps have been distinguished by evaluating the optical purity of key intermediates through chemical correlations with known optically active compounds.

As an extension of our studies on the synthetic and stereochemical aspects connected with obtaining optically active aromatic hydrocarbons,[1,2] we were interested in evaluating the limits and the applicability of the Haworth-type synthesis[3] in the preparation of optically active polysubstituted naphthalene derivatives as well as of more complex chiral polynuclear substrates.

To test the stereochemical course of this type of sequence we chose to synthesize (*S*)-2-(1-methylpropyl)-naphthalene (**1**) by starting from (*S*)-(1-methylpropyl)-benzene (**2**), since the maximum rotatory powers of **1** and **2** were known.[2c,h]

Our preliminary results[3e] showed that in the sequence **2** → **1** (Scheme I) a rather high degree of racemization had occurred. In the present work we report the results of our investigation where special effort was made to follow the relationship between the optical purity of the starting material and of the final product.

Results and Discussion

Since it is known that optically active **2** racemizes even at 0 °C in the presence of aluminum chloride,[4] the conversion of samples of optically active **2** into the methyl 3-[4-(1-methylpropyl)benzoyl]propionate (**3**) was accomplished in 75–82% yields by following the Perrier modi-

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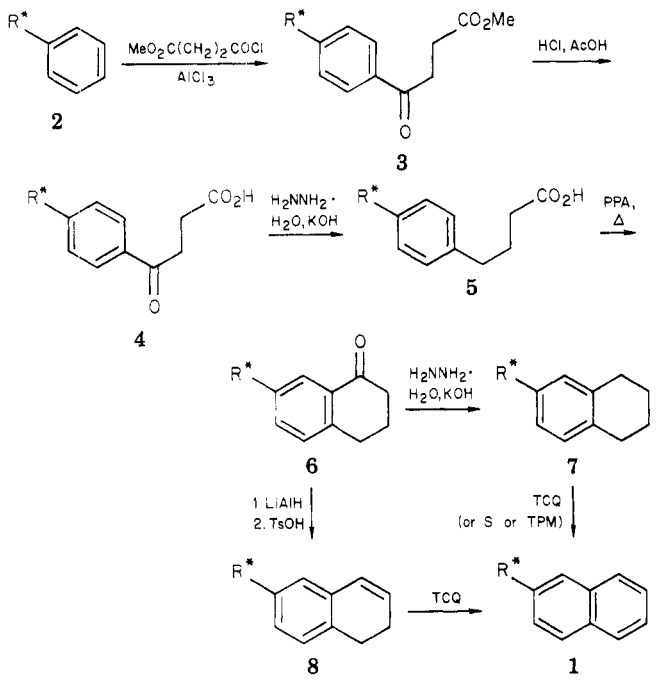
Table I

compd	$[\alpha]^{25}_D$,[a] deg (optical purity, %) run 1	run 2	run 3	run 4
2	+28.32[b] (96.8)[c]	+27.08[b] (92.5)[c]	−19.03[b] (65.0)[c]	−21.24[b] (72.6)[c]
	+26.54[b,d] (90.7)[c]	+16.39[b,d] (56.0)[c]	−18.08[b,d] (61.8)[c]	−15.91[b,d] (54.4)[c]
3	+28.86[b,e]	+26.37[b,e]	−18.98[b,e]	−19.94[b,e]
4		+23.13	−16.05	−17.79
5	+19.43	+17.57	−12.60	−13.46
6	+19.38	+18.16		−8.02
7	+20.28	+19.18		
8		+21.74		
1	0.00[h]	+14.35[b,f] (47.5)[g]		
		+19.64[b,i] (65.0)[g]		
		+19.70[b,j] (65.2)[g]		

[a] In benzene. [b] Neat. [c] See ref 2c. [d] Sample recovered from the Perrier reaction. [e] α^{25}_D (l = 1). [f] Obtained by reacting 7 with TPM in TFA. [g] See ref 2h. [h] Obtained by reacting 7 with sulfur. [i] Obtained by reacting 7 with TCQ. [j] Obtained by reacting 8 with TCQ.

Scheme I[a]



[a] R* = MeC*H(Et).

fication[4,5] of the Friedel–Crafts acylation. In every run 5–40% racemized precursor was also recovered. Huang-Minlon[6] reduction of 3-[4-(1-methylpropyl)benzoyl]-propionic acid (4), in turn prepared from 3 by acidic hydrolysis, gave (80–85%) 4-[4-(1-methylpropyl)phenyl]butanoic acid (5). Cyclization of 5 in polyphosphoric acid[3c,7] (PPA) provided (85–92%) 7-(1-methylpropyl)-1-tetralone (6) (Scheme I). Reduction of the ketone carbonyl group[6] then furnished (83–94%) 1,2,3,4-tetrahydro-6-(1-methylpropyl)naphthalene (7). Aromatization of 7 was attempted by several different ways:[8] (i) sulfur[9] at 250 °C afforded (23%) completely racemized 1; (ii) triphenylmethanol (TPM) in boiling trifluoroacetic acid[10] (TFA) yielded (40%) chemically pure and optically active 1; (iii) 3,4,5,6-tetrachloro-1,2-benzoquinone[11] (TCQ) in refluxing benzene for 4 h gave a 2.2:1 mixture of 1 and 7. However, after preparative GLC separation, pure 1 was obtained, showing a rotatory power higher than that previously determined (reaction ii), and, moreover, unreacted 7 was recovered without racemization.

In the context of optimizing the conversion of 6 into 1 (Scheme I), as well as of verifying the optical yield of the last reaction, an alternative method was also employed. Lithium aluminum hydride reduction of 6 followed by acid-catalyzed dehydration provided (93% overall yield) a pure sample of 3,4-dihydro-7-(1-methylpropyl)-naphthalene (8). The aromatization of this substance was once more carried out with TCQ in benzene. In this case, after 2.5 h of refluxing, pure 1 was recovered (78%), and its rotatory power was in a very good agreement with the value obtained by reaction iii. The experimental rotatory powers of the compounds prepared in repeated runs (1–4) as well as the optical purities of the starting material and final product are given in Table I.

To remove any possible doubt about a possible racemization in the acid-catalyzed conversion of 3 into 4, a sample of this last compound was reacted with diazomethane, and no loss of optical activity was observed in the recovered 3. Moreover, since Huang-Minlon reduction does not appreciably affect the chiral center in analogous substrates[2d,12] and since the aromatization of 7 and 8 with TCQ gave samples of 1 having the same optical rotation, within the limit of experimental error (Table I), we have excluded detectable racemization in these two reactions. From these observations, the racemization in the conversion of 2 into 1 (Table I) should be caused by the Perrier acylation and/or by the PPA cyclization. The evaluation of the optical purity of a sample of the key intermediate 3 should enable us to elucidate the stereochemical course of both the above-reported reactions.

Our initial correlation sequence involved the conversion of the keto ester 3 into 4-(1-methylpropyl)benzoic acid (11) (Scheme II, path a) because its maximum rotatory power has been reported.[5c] Although Amberlist-15 is claimed to be suitable to convert a carbonyl group into the corresponding enol ether,[13] a sample of 3, α^{25}_D (l = 1) −18.98°

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(8) Metal-catalyzed aromatization[3c] was rejected because we have a number of examples of optically active aromatic substrates, in which the chiral center is bound to the aromatic nucleus, that racemize in the presence of a hydrogenation catalyst also at room temperature.

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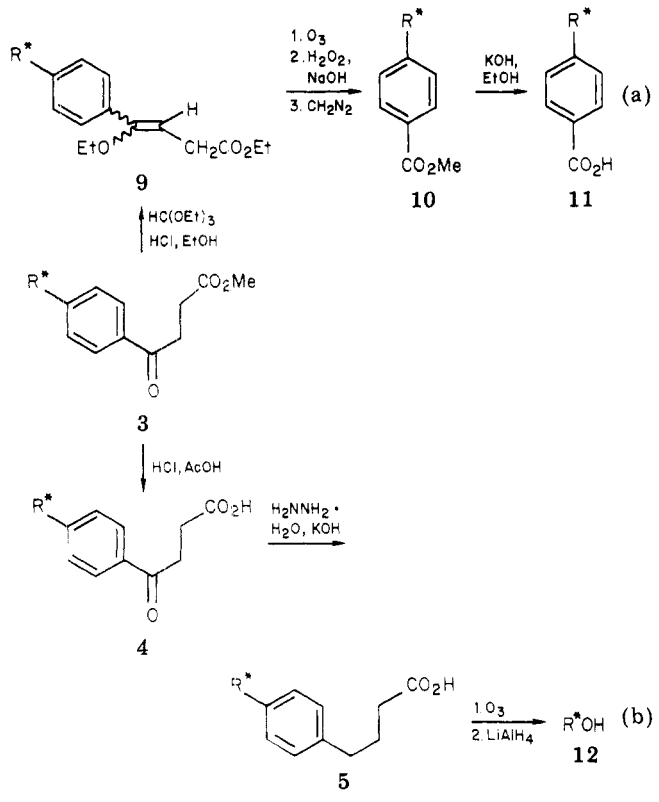
Scheme II[a]



[a] R* = MeC*H(Et)

(Table I, run 3), reacted with ethyl orthoformate in the presence of this catalyst and gave, in 60 days of reaction time, only a small amount (31%) of a mixture of the stereoisomers of ethyl 4-ethoxy-4-[4-(1-methylpropyl)-phenyl]-3-butenoate (**9**) in a ratio of 1:10. The same mixture was best achieved (16 days reaction time, 90% yield) by using catalytic amounts of ethanolic hydrogen chloride.[14] Oxidative ozonolysis of **9** afforded a complex acid mixture from which, after diazomethane esterification and preparative GLC purification, a sample of chemically pure methyl 4-(1-methylpropyl)benzoate (**10**) was recovered (15%) and then saponified to pure **11**, $[\alpha]^{25}_D$ −20.30° (methanol). On the basis of its maximum rotatory power, $[\alpha]^{25}_D$ +31.3° (methanol),[5c] an ~65% enantiomeric purity is to be evaluated for the recovered acid. For verification of the reliability of this result, which suggests no racemization in the Perrier acylation (Table I), a further correlation was carried out to relate **3** to optically active 2-methylbutan-1-ol (**12**) (Scheme II, path b). A sample of **5**, $[\alpha]^{25}_D$ −12.60° (benzene) (Table I, run 3), prepared as usual from **3**, was ozonized and the ozonide reduced with lithium aluminum hydride.[2h] The alcohol **12**, recovered by preparative GLC, was 59% optically pure on the basis of its maximum rotatory power, $[\alpha]^{25}_D$ +6.66° (*n*-heptane).[15]

Such evidence indicates that racemization occurs in the Perrier reaction as previously reported.[5c] By assuming as more correct the last result, it is possible to attribute to optically pure **3** a value of α^{25}_D (l = 1) 32.17° and then to obtain a value of 7–15% racemization in the Perrier acylation (Table I). Moreover, as the optical purity of **1** is closely related to that of **6** (Table I, run 2), a 21–23%

Table II

compd	$[\alpha]^{25}_D$, deg	exptl condit	$[\alpha]^{25}_D$,[a] deg	% racemization
1	+13.49	$AlCl_3$[b]	0.00	100
		PPA[c]	+13.40	<1
2	+1.53[d,e]	$AlCl_3$[e,f]	0.00[e]	100[e]
	+27.08	PPA[c]	+26.29	3
3	−18.98[d]	$AlCl_3$[b]	−19.15[d]	0
5	−12.60 (benzene)	$AlCl_3$[b]	0.00	100
6	+19.38 (benzene)	PPA[c]	+17.50 (benzene)	10
7	+19.18 (benzene)	PPA[c]	+18.17 (benzene)	5

[a] Referred to the recovered product. [b] Temperature 0 °C, CH_2Cl_2, 1 h. [c] Temperature 90–100 °C, 2 h. [d] α^{25}_D (l = 1). [e] See ref 4. [f] Temperature 0 °C, 2 h.

racemization in the PPA cyclization (Table I, run 1, 2) can be calculated. In run 4 (Table I) a 55% racemization was found even if the PPA cyclization had been carried out apparently under the usual experimental conditions.

The overall results seemed to suggest that the racemizations observed in the preparation of **3** and **6** may be related to the carbonyl group present in these compounds. This was tested by treating **3** and **6** with $AlCl_3$ and PPA, respectively, under the same experimental conditions adopted to convert **2** into **3** and **5** into **6**. To gain further general information about eventual racemization of asymmetric centers adjacent to aromatic moieties, in the presence of Lewis or protic acid, we have also treated compounds **1**, **2**, **5**, and **7** with $AlCl_3$ and/or PPA under the conditions of Table II.

When $AlCl_3$ was used, the following results were obtained: (i) quantitatively recovered **3** was unracemized; (ii) optically inactive **1** was obtained from a 1:3.5:1.4 (GLC) mixture of naphthalene, **1**, and a bis(1-methylpropyl)-naphthalene compound;[16] (iii) optically inactive **5** was obtained from a 1.8:1.6:2.8:1 (GLC) mixture of 4-phenylbutanoic acid, a positional isomer of **5**, **5**, and a bis(1-methylpropyl)-4-phenylbutanoic acid.[17]

With PPA chemically pure products were almost quantitatively recovered (no isomerization or disproportionation products have been detected), and while definite racemizations were observed for **6** (10%) and **7** (5%), **1** and **2** showed optical rotations close to those of the starting material (Table II).

On the basis of the above-reported results, the racemization, evaluated for the Perrier acylation, may be due to a very rapid loss of optical activity of **2** before the acylation occurs (such a racemization should be determined by free or complexed aluminum chloride) and/or to a reversible process affecting the chiral center of the σ complex. It is more difficult to establish when racemizing processes occur in the synthesis of **6** because this compound is optically unstable in the presence of PPA (Table II). Since under the same experimental conditions the chiral center of **7** is also partially affected (Table II), we tentatively say that the conjugate acid of carbonyl is not necessary to promote racemization. To support this opinion, we remember that the acid-catalyzed conversion of **3** into **4** is a stereospecific process and that, on the contrary, the aromatization of **7** into **1** by TPM in TFA caused an ~

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(16) Mass spectrum, m/e (relative intensity) 211 (100), 240 (35, M^+).
(17) Mass spectra of the corresponding methyl esters [m/e (relative intensity)]: 103 (100), 73 (95), 90 (80), 178 (51, M^+); 173 (100), 117 (35), 160 (29), 131 (29), 234 (24, M^+); 205 (100), 131 (85), 117 (34), 234 (28, M^+); 173 (100), 229 (32), 290 (31, M^+), 261 (23).

27% racemization (Table I). Hence, it is clear that some peculiar acid systems promote, in suitable intermediates, the reversible loss of the hydrogen ion from a carbon atom adjacent to an aromatic moiety.

In conclusion, our results underline the fact that PPA cyclization of optically active compounds is not stereospecific, in contrast to what is generally accepted,[18] and they suggest that the stereochemical course of many acid-catalyzed reactions involving chiral aromatic substrates[19] should be reinvestigated. Moreover, this work points out that even if the optical purity of new substrates, obtained through the Haworth-type route, must always be evaluated, the synthetic potentiality of this reaction sequence is not to be disregarded.

Experimental Section

Melting and boiling points are uncorrected. GLC analyses [2 m × 0.29 cm columns packed with 2.5% silicone gum rubber on 80–100-mesh AW-DMCS Chromosorb G (SE 301) and 15% butanediol succinate on 90–100-mesh Chromosorb W (BDS)] were performed on a Perkin-Elmer F 30 instrument with flame-ionization detectors and N_2 as carrier gas. Preparative GLC was carried out on a Perkin-Elmer F 21 chromatograph using 2 or 3 m × 0.95 cm columns packed with 20% butanediol succinate on 45–60-mesh Chromosorb A (BDS) and 8% Carbowax 20M plus 2% KOH on 80–100-mesh Chromosorb W (CW 20M). NMR spectra were recorded with a JEOL PS 100 instrument using Me_4Si as internal standard. Mass spectra were obtained with a Varian Mat CH 7 mass spectrometer operating at 70 eV. Optical rotations were taken with a Perkin-Elmer 142 polarimeter and refer to pure liquid unless otherwise stated. Microanalyses were carried out in the Microanalysis Laboratory of the Faculty of Pharmacy of the Pisa University. Solvents and commercial reagents were purified by conventional methods before use. Only one of the sequences we have carried out is fully described.

Methyl 3-[4-(1-Methylpropyl)benzoyl]propionate (3). To the filtered solution prepared from 35.6 g (0.266 mol) of $AlCl_3$ and 27.2 g (0.180 mol) of 3-(carbomethoxy)propionyl chloride[20] in 150 mL of dry CH_2Cl_2 was added 27.5 g (0.205 mol) of (*S*)-**2**, $[\alpha]^{25}_D$ +27.08° (lit.[2c] d^{25}_4 0.858, $[\alpha]^{25}_{D,max}$ 29.26°), in 70 mL of dry CH_2Cl_2 at 0 °C. The mixture was stirred at 0 °C (1 h), hydrolyzed with ice and 10% HCl, and then worked up as usual. By distillation 36.6 g of 99% pure (SE 301, 190 °C) (*S*)-**3** [82% with respect to the acyl chloride; bp 146 °C (0.5 mm); α^{25}_D (l = 1) +26.37°] was obtained.

Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.40; H, 8.40.

A 4.1-g sample of 99% pure (SE 301, 100 °C) (*S*)-**2**, $[\alpha]^{25}_D$ + 16.39°, was also recovered.

3-[4-(1-Methylpropyl)benzoyl]propionic Acid (4). A sample of 36.5 g (0.147 mol) of (*S*)-**3**, α^{25}_D (l = 1) +26.37°, dissolved in 600 mL of glacial acetic acid and 725 mL of 36% HCl, was heated at 70 °C (8 h). After the mixture cooled, 10 L of water was added; the organic product was extracted in ether and worked up by a standard procedure to give 33.6 g of (*S*)-**4**: 97%; mp 94–95 °C; $[\alpha]^{25}_D$ +23.13° (*c* 1.729, benzene).

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.57; H, 7.88.

A sample of (*S*)-**4** reacted with diazomethane gave (*S*)-**3**, α^{25}_D (l = 1) +26.33°.

4-[4-(1-Methylpropyl)phenyl]butanoic Acid (5). A mixture of 34.5 g (0.147 mol) of (*S*)-**4**, $[\alpha]^{25}_D$ +23.13° (*c* 1.729, benzene), and 30.0 g (0.535 mol) of KOH in 200 mL of diethylene glycol was heated at 50 °C (30 min) and, after cooling, 21.7 g (0.434 mol) of 85% hydrazine hydrate was added. After the mixture was refluxed (15 h), the water and the excess of hydrazine were removed under reduced pressure (18 mm), and the residue was heated at 180 °C (6 h). The reaction mixture was diluted with water (2 L), neutralized with HCl, and extracted with ether. The solvent was removed, and the residue was distilled to give 27.0 g of 99% pure (SE 301, 170 °C, on the corresponding methyl ester) (*S*)-**5**: 83%; bp 138 °C (0.3 mm); $[\alpha]^{25}_D$ +17.57° (*c* 1.679, benzene).

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.15. Found: C, 76.00; H, 9.03.

7-(1-Methylpropyl)-1-tetralone (6). To a hot solution (90–100 °C) of PPA, obtained from 672.5 g (4.75 mol) of P_2O_5 and 727.0 g (7.42 mol) of 85% H_3PO_4, was added 26.0 g (0.118 mol) of (*S*)-**5**, $[\alpha]^{25}_D$ +17.57° (*c* 1.679, benzene). After 2 h the mixture was cooled, diluted with ice water, and extracted with ether. The ethereal extracts were washed with 10% NaOH and water and dried (Na_2SO_4). The solvent was removed, and the residue yielded 21.5 g of 99% pure (SE 301, 155 °C) (*S*)-**6**: 90%; bp 111 °C (0.3 mm); $[\alpha]^{25}_D$ +18.16° (*c* 1.927, benzene).

Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.30; H, 8.97.

1,2,3,4-Tetrahydro-6-(1-methylpropyl)naphthalene (7). To a solution of 16.0 g (79.1 mmol) of (*S*)-**6**, $[\alpha]^{25}_D$ +18.16° (*c* 1.927, benzene), in 40 mL of diethylene glycol was added 11.6 g (0.231 mol) of 85% hydrazine hydrate at 0 °C. After the mixture had been refluxed (1 h), 7.1 g (0.126 mol) of KOH dissolved in 25 mL of diethylene glycol was added, and then the mixture was refluxed again (1 h). The water and the excess of hydrazine were removed under reduced pressure (18 mm), and the residue was heated at 180 °C (4 h). The mixture was worked up as usual to give 14.0 g of 99% pure (SE 301, 155 °C) (*S*)-**7**: 94%; bp 83 °C (0.5 mm); d^{25}_4 0.927; $[\alpha]^{25}_D$ +19.18°.

Anal. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.60; H, 10.45.

3,4-Dihydro-7-(1-methylpropyl)naphthalene (8). By reduction with 0.2 g (5.3 mmol) of $LiAlH_4$ in 50 mL of dry ether, 1.4 g (6.9 mmol) of (*S*)-**6**, $[\alpha]^{25}_D$ +18.16° (*c* 1.927, benzene), afforded, after the usual procedure, a crude product that was dissolved in 150 mL of dry benzene and treated with 0.1 g (0.53 mmol) of $TsOH \cdot H_2O$. The mixture was refluxed (6 h), and the reaction water was removed with a Dean–Stark trap. The solution, diluted with water, washed with 10% NaOH, and dried (Na_2SO_4), gave 1.2 g of pure (SE 301, 160 °C) (*S*)-**8**: 93%; bp 94 °C (0.6 mm); $[\alpha]^{25}_D$ +21.74° (*c* 2.047, benzene).

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.20; H, 9.80.

2-(1-Methylpropyl)naphthalene (1) from 7. (a) Via Aromatization with Sulfur. A mixture of 0.62 g (19.3 mmol) of S and 1.4 g (7.3 mmol) of (*S*)-**7**, $[\alpha]^{25}_D$ +20.28°, was heated at 250 °C for 2 h.[9] By distillation under reduced pressure 0.6 g of 98% pure (SE 301, 155 °C) (*R,S*)-**1** (23%) was recovered.

(b) Via Aromatization with TCQ. To a solution of 12.0 g (51.4 mmol) of TCQ in 25 mL of dry benzene was added at 80 °C 4.0 g (21.2 mmol) of (*S*)-**7**, $[\alpha]^{25}_D$ +19.18°, dissolved in 15 mL of dry benzene.[11] After being refluxed (4 h), the mixture was diluted with water and extracted with pentane. The organic phase was washed with 30% NaOH and water and dried (Na_2SO_4). The solvent was removed, and the crude product was distilled to give 2.7 g of a 2.2:1 mixture (SE 301, 160 °C) of (*S*)-**1** and (*S*)-**7**. By GLC purification (2-m column, BDS; 140 °C) 0.43 g of 98% pure (BDS, 150 °C) (*S*)-**1** was obtained: bp 90 °C (0.8 mm); $[\alpha]^{25}_D$ +19.64° (lit.[2h] bp 93 °C (0.9 mm); d^{25}_4 0.966; $[\alpha]^{25}_{D,max}$ 30.2°). A sample of chemically pure (BDS, 150 °C) (*S*)-**7**, $[\alpha]^{25}_D$ +19.14°, was also recovered.

(c) Via Aromatization with Triphenylmethanol. A solution of 1.5 g (8.0 mmol) of (*S*)-**7**, $[\alpha]^{25}_D$ +19.18°, and 4.6 g (17.7 mmol) of triphenylmethanol in 20 mL of trifluoroacetic acid was refluxed under nitrogen for 18 h.[10] The reaction mixture was cooled, diluted with ice–water, and extracted with ether. The ethereal solution was washed with 10% NaOH and water and dried (Na_2SO_4). In the crude product no trace of the starting material was detected. After accurate distillation to remove the triphenylmethane, 0.6 g of 99% pure (SE 301, 160 °C) (*S*)-**1** (40%), $[\alpha]^{25}_D$ +14.35°, was recovered.

2-(1-Methylpropyl)naphthalene (1) from 8. Via Aromatization with TCQ. To a solution of 1.7 g (6.9 mmol) of TCQ in 4 mL of dry benzene heated at 80 °C was added 1.2 g (6.4 mmol) of (*S*)-**8**, $[\alpha]^{25}_D$ +21.74° (*c* 2.047, benzene), dissolved in 10 mL of dry benzene. After being refluxed (2.5 h), the mixture was worked

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up as previously described. The crude product was distilled over $LiAlH_4$ to give 0.92 g of pure (SE 301, 160 °C) (*S*)-**1**: 78%; $[\alpha]^{25}_D$ +19.70°.

Methyl 4-(1-Methylpropyl)benzoate (10). A solution of 15.0 g (60.4 mmol) of (*R*)-**3**, α^{25}_D (l = 1) -18.98°, 9.4 g (63.4 mmol) of ethyl orthoformate, and 2 mL of dry HCl-saturated ethanol was stirred at room temperature (16 days) and then concentrated under vacuum (18 mm).[14] The residue was distilled to give 18.0 g of a two-product (A and B) mixture in the ratio 1:10 (SE 301, 190 °C). These products were identified as the stereoisomers of ethyl 4-ethoxy-4-[4-(1-methylpropyl)phenyl]-3-butenoate (**9**) by their mass spectra [m/e (relative intensity)]: A, 133 (100), 161 (95), 217 (65), 55 (54), 57 (35), 290 (30, M^+), 159 (25), 131 (19), 189 (18), 115 (16), 233 (16), 91 (15), 162 (14); B, 161 (100), 133 (58), 217 (40), 55 (28), 57 (17) 290 (16, M^+), 162 (14).

Such a mixture was dissolved in 200 mL of dry CH_2Cl_2, ozonized at 0 °C for 8 h, and concentrated under reduced pressure (18 mm). The residue oil, dissolved in 230 mL of 95% ethanol, was treated with 138 mL of 10% NaOH solution and 92 mL of 35% H_2O_2 and then refluxed (12 h). After the usual procedure a complex mixture of organic acids was recovered, esterified with diazomethane, and purified by preparative GLC (3-m column, CW20M; 150 °C) to give chemically pure (SE 301, 160 °C) (*R*)-**10**, $[\alpha]^{25}_D$ -19.02° (*c* 2.732, ethanol).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.85; H, 8.42.

4-(1-Methylpropyl)benzoic Acid (11). A sample of 1.7 g (8.84 mmol) of (*R*)-**10**, $[\alpha]^{25}_D$ -19.02° (*c* 2.732, ethanol), dissolved in 50 mL of 95% ethanol and 50 mL of 20% NaOH aqueous solution was stirred at reflux (8 h). The cooled mixture was acidified (10% H_2SO_4) and the organic product extracted in ether and dried (Na_2SO_4). The solvent was removed to yield 1.5 g of (*R*)-**11**: 98%; mp 89 °C; $[\alpha]^{25}_D$ -20.30° (*c* 1.867, methanol) [lit.[5b] mp 89-90 °C; $[\alpha]^{25}_{D,max}$ 31.3° (methanol)]; NMR (CCl_4) δ 12.56 (s, 1 H), 8.00-6.80 (2 d, 4 H), 2.80-2.38 (m, 1 H), 1.80-1.40 (m, 2 H), 1.36-1.06 (d, 3 H), 1.00-0.62 (t, 3 H).

2-Methylbutan-1-ol (12). A sample of 7.0 g (32.0 mmol) of (*R*)-**5**, $[\alpha]^{25}_D$ -12.60° (*c* 1.774, benzene), was dissolved in 80 mL of glacial acetic acid and ozonized at room temperature (30 h). The solvent was removed at reduced pressure (18 mm), and the residue oil was reduced with an ethereal suspension of 12.0 g (0.316 mol) of $LiAlH_4$. The hydrolysis was carried out as usual, and the organic products were extracted in continuum. From the recovered mixture, by preparative GLC purification a sample of pure (*R*)-**12**, $[\alpha]^{25}_D$ +3.93° (*c* 3.738, *n*-heptane), was recovered [lit.[15] $[\alpha]^{25}_{D,max}$ 6.66° (*c* 3.020, *n*-heptane)].

Registry No. (*R,S*)-**1**, 73494-13-0; (*S*)-(+)-**1**, 65419-63-8; (*S*)-(+)-**2**, 5787-28-0; (*S*)-(+)-**3**, 73434-44-3; (*R*)-(-)-**3**, 73434-45-4; (*S*)-(+)-**4**, 73434-46-5; (*R*)-(-)-**4**, 73434-47-6; (±)-**5**, 73434-48-7; (±)-**5** methyl ester, 73453-16-4; (±)-**5** positional isomer methyl ester, 73434-60-3; (*S*)-(+)-**5**, 73494-14-1; (*R*)-(-)-**5**, 73494-15-2; (*S*)-(+)-**6**, 73434-49-8; (*R*)-(-)-**6**, 73434-50-1; (*S*)-(+)-**7**, 73434-51-2; (*S*)-(+)-**8**, 73434-52-3; (*R*)-**9** (*E* isomer), 73434-53-4; (*R*)-**9** (*Z* isomer), 73434-54-5; (*R*)-(-)-**10**, 73434-55-6; (*R*)-(-)-**11**, 73434-56-7; (*R*)-(+)-**12**, 14898-79-4; 3-(carbomethoxy)propionyl chloride, 1490-25-1; (*S*)-(+)-**5** methyl ester, 73434-57-8; naphthalene, 91-20-3; bis(1-methylpropyl)naphthalene, 73434-58-9; methyl 4-phenylbutanoate, 2046-17-5; methyl bis(1-methylpropyl)-4-phenylbutanoate, 73434-59-0.

New Perspectives on the Semmler-Wolff Aromatization Reaction[1]

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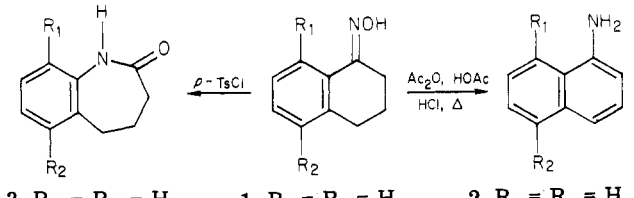
The conversion of 4-methyl-5,6,7,8-tetrahydro-5-(hydroxyimino)-2-hydroxyquinoline (**13a**) to 4-methyl-5-acetamido-2-quinolone (**10**) was carried out in 53% yield under Semmler–Wolff conditions. In the pyridone **13a** the oxime must assume the anti to pyridone configuration; consequently, this transformation provides evidence that the syn to phenyl configuration is not a necessary requirement for the Semmler–Wolff aromatization reaction.

The conversion of cyclohexenone oximes to anilines was first investigated by Semmler.[2] Several years later Wolff conducted a more detailed investigation of this phenomenon[3] while Schroeter expanded the scope of the rearrangement by conversion of tetralone-1-oximes to α-naphthyl amines.[4] In addition, it was determined that these oximes could be made to undergo the Beckmann rearrangement rather than aromatization; for example, tetralone-1-oxime (**1**) gave the aromatic amine **2** (see Scheme I) when treated with Beckmann's mixture; however, the lactam **3** was formed on heating **1** with *p*-toluenesulfonyl chloride (see Scheme I).

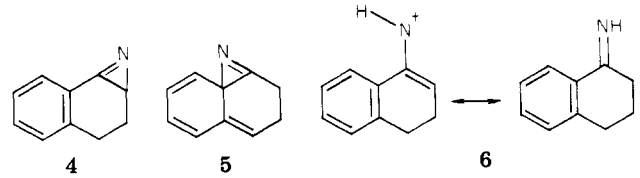
The mechanism of this transformation has been studied principally by five groups,[5a-e] and their work has been reviewed.[6] Although many species have been proposed[6]

Scheme I



3, $R_1 = R_2 = H$ **1**, $R_1 = R_2 = H$ **2**, $R_1 = R_2 = H$
8, $R_1 = R_2 = CH_3$ **7**, $R_1 = R_2 = CH_3$ **9**, $R_1 = R_2 = CH_3$

Scheme II



4 **5** **6**

as the key intermediate for this reaction, those that have received the most attention are represented by structures

(1) This is contribution no. 1572 to the Army Research Program on Malaria (Contract No. DAMD17-78-C-8003).

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