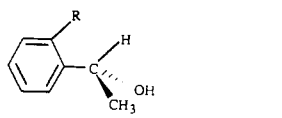
Application of the Benzene Sector and the Benzene Chirality Rules to Perhydrobenzocycloalkenes and Related Compounds[1]

Ronald J. Lorentzen,[2a] James H. Brewster,*[,2a] and Howard E. Smith*[,2b]

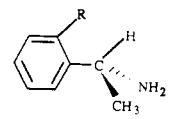
Contribution from the Departments of Chemistry, Purdue University, West Lafayette, Indiana 47907, and Vanderbilt University, Nashville, Tennessee 37235.
Received October 22, 1990

Abstract: Enantioenriched 1-substituted indans were prepared from (*R*)-1-indancarboxylic acid and (*R*)-1-indanylacetic acid as model compounds for the correlation of their absolute configurations with the sign of the ^1L_b Cotton effects (CEs) from about 250 to 270 nm in their circular dichroism spectra. The CEs are the result of vibronic and induced contributions to the rotational strength, and their sign is in agreement with that predicted on the basis of the benzene sector and the benzene chirality rules. The application of these rules to other, nonplanar perhydrobenzocycloalkenes evolves into sector sign projections suggested earlier to correlate the sign of ^1L_b CEs of enantiopure 1,2,3,4-tetrahydronaphthalenes and 1,2,3,4-tetrahydroisoquinolines with their absolute configurations.

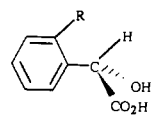
The benzene sector[3] and the benzene chirality rules[4,5] were used previously to correlate the sign of the ^1L_b Cotton effects (CEs) from about 250 to 270 nm in the circular dichroism (CD) spectra of enantiopure (100% ee) phenylalkylcarbinols[4] (**1**), phenylalkylcarbinamines[4] (**2**), and mandelic acids[5] (**3**) with their absolute configurations. For such compounds without additional ring substituents, the ^1L_b CEs are the result of vibronic borrowing from transitions at shorter wavelengths, and their sign depends only on the configuration of the chiral center contiguous to the benzene ring.[3-5]



(*R*)-**1a**, R = H
b, R = CH_3



(*R*)-**2a**, R = H
b, R = CH_3



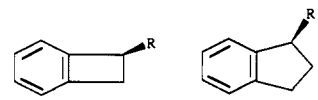
(*S*)-**3a**, R = H
b, R = CH_3

On further ring substitution, an additional contribution to the ^1L_b CEs is induced, and the induced contribution may have the same sign or the opposite sign from that of the vibronic contribution. The sign of the ^1L_b CEs may be the same or different from that of the unsubstituted parent,[4-6] and a change in sign for an additional substituent may be predicted on the basis of the benzene chirality rule[4] and depends on the ring position and spectroscopic moment[7] of the additional substituent.[4-6]

The benzene sector and the benzene chirality rules can also be used for the correlation of the sign of the ^1L_b CEs of enantiopure substituted perhydrobenzocycloalkenes. As a demonstration of this, we now report the synthesis and the electron absorption (EA) and CD spectra of a series of enantioenriched (0% < ee < 100%) 1-substituted indans (**5**, Table I) and compare these spectra with those of some related compounds reported earlier.

One aspect of this application is that the correlation of the sign of the ^1L_b CEs using the benzene sector and the benzene chirality rules for these compounds evolves into sector sign projections

Table I. Electronic Absorption (EA) and Circular Dichroism (CD) Data for the ^1L_b Band Origin Maxima of Enantiopure Perhydrobenzocycloalkenes[a]



4 **5**

code	R	EA λ, nm (ϵ^b)	CD λ, nm ($\Delta\epsilon^c$)
		(*S*)-**4**	
a	NH_2[d]	273 (1300)[e]	274[e,f]
		(*S*)-**5**	
a	NH_2[d]	273 (800)[e]	268 (−0.11)[e]
b	NH_3Cl[g]	272 (1000)	271 (−0.39)
c	$N(CH_3)_3I$	274 (1300)	274 (−1.3)
d	OH	272 (920)	271 (−0.44)[h]
e	CH_3[i]	273 (1300)	274 (−0.33)
f	CH_2OH	271 (1300)	272 (−0.49)
g	CH_2OCOCH_3	271 (1200)	271 (−0.49)
h	CO_2H	273 (850)	273 (−0.044)[h]
i	CO_2K[j]	274 (1200)	276 (+0.21)[h]
j	CF_3	272 (840)	272 (−0.11)[h]
k	$C(CH_3)_2NH_2$	272 (1100)	274 (−1.2)
l	$C(CH_3)_2NH_3Cl$[j]	272 (1100)	273 (−1.0)
m	$C(CH_3)_2CH_2Br$	272 (1400)	274 (−1.1)
n	$C(CH_3)_2CH_2OH$	272 (1100)	273 (−0.94)
o	$C(CH_3)_2CO_2H$	272 (1300)	273 (−0.34)
p	$C(CH_3)_2CO_2K$[j]	272 (1300)	272 (−0.25)
		(*R*)-**5**	
q	CH_2CO_2H	271 (1200)	272 (−0.53)
r	CH_2CO_2K[j]	271 (1200)	272 (−0.31)
s	CH_2COCH_3	271 (1100)	272 (−0.45)
t	$C(CH_3)_3$	272 (1300)	274 (−1.2)

[a] Methanol as solvent or as otherwise noted. [b] Molar absorptivity. [c] Molar dichroic absorption adjusted to 100% ee. $\Delta\epsilon = [\theta]/3300$ where $[\theta]$ is the molecular ellipticity. [d] Data from ref 8. [e] Cyclohexane as solvent. [f] Inflection. Cotton effect is negative on a strongly positive background curve. [g] Data from ref 9. [h] Enantiomer used. [i] Data from ref 10. [j] Formed in situ from the corresponding carboxylic acid or amine.

(1) Taken in part from the Ph.D. Thesis of J.R.L., Purdue University, West Lafayette, IN, January 1971. This report is also Part 37 in the Vanderbilt University series Optically Active Amines. Part 36 is ref 5.
(2) (a) Purdue University. (b) Vanderbilt University.
(3) Smith, H. E.; Fontana, L. P. *J. Org. Chem.* **1991**, *56*, 432-435.
(4) Pickard, S. T.; Smith, H. E. *J. Am. Chem. Soc.* **1990**, *112*, 5741-5747.
(5) Colon, D. F.; Pickard, S. T.; Smith, H. E. *J. Org. Chem.* **1991**, *56*, 2322-2326.
(6) Smith, H. E.; Burrows, E. P.; Chen, F.-M. *J. Am. Chem. Soc.* **1978**, *100*, 3714-3720.
(7) Platt, J. R. *J. Chem. Phys.* **1951**, *19*, 263-271.
(8) Ghislandi, V.; La Manna, A.; Vercesi, D. *Farmaco, Ed. Sci.* **1976**, *31*, 561-571.
(9) Smith, H. E.; Willis, T. C. *J. Am. Chem. Soc.* **1971**, *93*, 2282-2290.
(10) Smith, H. E.; Padilla, B. G.; Neergaard, J. R.; Chen, F.-M. *J. Am. Chem. Soc.* **1978**, *100*, 6035-6039.

0002-7863/92/1514-2181$03.00/0

Table II. Enantioenriched 1-Substituted Indans

compd	name	$[\alpha]^{24-26}_D$, deg (solvent)[a]	% ee[b]
(*S*)-**5c**	(*S*)-*N*,*N*,*N*-trimethyl-*N*-(1-indanyl)ammonium iodide	*c*	35
(*R*)-**5d**	(*R*)-1-indanol	−34.7 (chloroform)	89
(*S*)-**5f**	(*S*)-1-indanylmethanol	−9.8 (isooctane) −11.6 (benzene)	68
(*S*)-**5g**	(*S*)-1-indanylmethyl acetate	−17.3 (acetone)	68
(*R*)-**5h**	(*R*)-1-indancarboxylic acid	+41.6 (benzene)	96
(*R*)-**5j**	(*R*)-1-(trifluoromethyl)indan	−1.7 (isooctane)	96
(*S*)-**5k**	(*S*)-2-amino-2-(1-indanyl)propane	+6.2 (isooctane)	68
(*S*)-**5m**	(*S*)-1-bromo-2-methyl-2-(1-indanyl)propane	−26.8 (acetone)	68
(*S*)-**5n**	(*S*)-2-methyl-2-(1-indanyl)-1-propanol	−1.4 (acetone)	68
(*S*)-**5o**	(*S*)-2-methyl-2-(1-indanyl)propanoic acid	+1.2 (acetone) −4.1 (benzene)	68
(*R*)-**5q**	(*R*)-1-indanylacetic acid	+6.9 (acetone) +7.7 (methanol) −6.8 (benzene)	90[d]
(*R*)-**5s**	(*R*)-1-indanylacetone	+24.9 (acetone)	68
(*R*)-**5t**	(*R*)-1-*tert*-butylindan	+5.1 (acetone)	68

[a] Concentration: 0.369–2.57 g/100 mL of solvent. [b] Enantiomeric excess; see Experimental Section. [c] Not observed. [d] Enantioenriched (*R*)-**5q** of 68% ee was used for the CD measurements and for the syntheses shown in Scheme I.

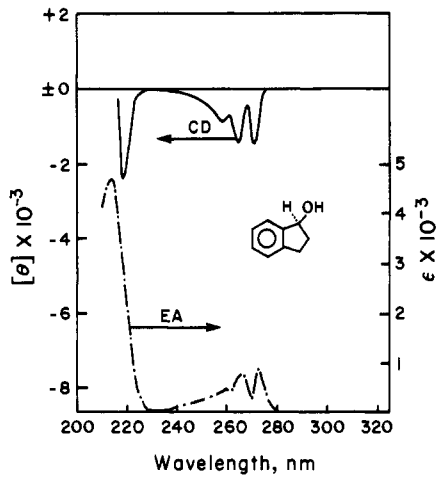


Figure 1. Electronic absorption (EA) and circular dichroism (CD) spectra of (*S*)-1-indanol [(*S*)-**5d**] in methanol.

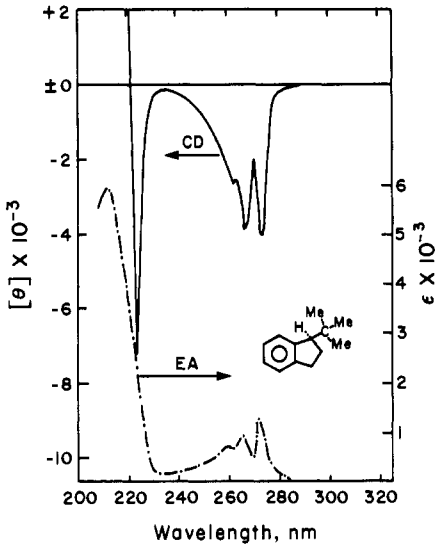


Figure 2. Electronic absorption (EA) and circular dichroism (CD) spectra of (*R*)-1-*tert*-butylindan [(*R*)-**5t**] in methanol.

suggested some time ago by Snatzke, Kajtar, and Werner-Zamojska[11] to correlate the sign of the ^1L_b CEs of enantiopure 1,2,3,4-tetrahydronaphthalenes and 1,2,3,4-tetrahydroisoquinolines.

Results and Discussion

Synthesis. The 1-substituted indans prepared in connection with this work are shown in Table II. The quaternary salt (*S*)-**5c** was prepared earlier in a reaction series from (*S*)-1-indancarboxylic acid[12] [(*S*)-**5h**], and on the basis of the absolute configuration of this acid[13] and Fredga's values for the rotatory power of (*S*)-**5h**,[14] (*S*)-**5c** and (*R*)-**5h** are assigned the absolute configuration and percent enantiomeric excess (% ee) shown in Table II. (*R*)-1-Indanol [(*R*)-**5d**] was also prepared earlier from (*R*)-**5h**,[12] but the sample shown in Table II was obtained by resolution.[15] Treatment of racemic 1-indancarboxylic acid [(±)-**5h**] and (*R*)-**5h** with sulfur tetrafluoride at 70–75 °C for 6 h gave, respectively, (±)-1-(trifluoromethyl)indan [(±)-**5j**] and (*R*)-**5j**; the % ee of the latter was assumed to be the same as that of (*R*)-**5h** used in the preparation of (*R*)-**5j**.

The other racemic and enantioenriched 1-substituted indans in Table II (**5f,g,k,m–o,s,t**) were prepared from (±)- and (*R*)-1-indanylacetic acid [(±)- and (*R*)-**5q**] by way of familiar reactions (Scheme I), and thus those in Table II have the same generic configuration and % ee as the (*R*)-**5q** used for the preparations. The absolute configuration and maximum rotatory power of (*R*)-**5q** were assigned by its conversion to (*S*)-1-indanylmethanol [(*S*)-**5f**] (Scheme I). The enantiomer of this alcohol was obtained earlier from (*R*)-1-indancarboxylic acid [(*R*)-**5h**] via lithium aluminum hydride reduction of its methyl ester.[16] Thus the sample of (*S*)-**5f** used here and the other enantioenriched substances prepared from (*S*)-**5q** as shown in Scheme I have ee's of 68% (Table II).

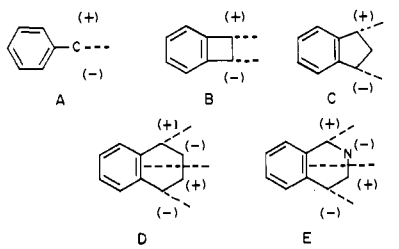
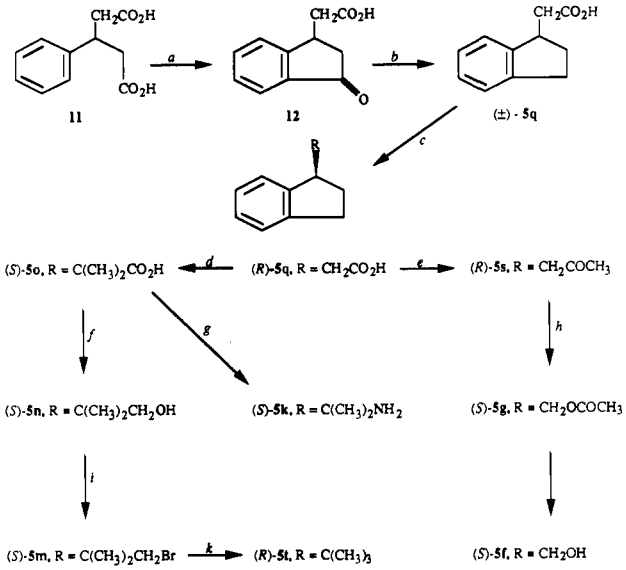


Figure 3. Near sector signs giving the vibronic contribution to the ^1L_b Cotton effects for atoms or groups at contiguous chiral centers for various substituted benzene chromophores. For far sectors, the signs are reversed.

Spectral Data. Table I shows the electronic absorption (EA) and circular dichroism (CD) maxima for the ^1L_b band origin for (*S*)-1-amino-1,2-dihydrobenzocyclobutene [(*S*)-**4a**] and for the

(11) Snatzke, G.; Kajtár, M.; Werner-Zamojska, F. *Tetrahedron* **1972**, *28*, 281–288.
(12) Brewster, J. H.; Buta, J. G. *J. Am. Chem. Soc.* **1966**, *88*, 2233–2240.
(13) Brewster, J. H. *Helv. Chim. Acta* **1982**, *65*, 317–324.
(14) Fredga, A. *Chem. Ber.* **1956**, *89*, 322–327.
(15) Prudence, R. T. Ph.D. Thesis, Purdue University, West Lafayette, IN, 1971.
(16) Battail-Robert, D.; Gagnaire, D. *Bull. Chim. Soc. Fr.* **1966**, 208–210.

Scheme I



[a] Reagent (yield): *a*, polyphosphoric acid (73%); *b*, $Zn(Hg)_x$, HCl (80%); *c*, resolution with (+)-α-phenylethylamine; *d*, lithium diisopropylamide, methyl iodide (67%); *e*, methyllithium (89%); *f*, lithium aluminum hydride (88%); *g*, thionyl chloride and then sodium azide (70%); *h*, hydrogen peroxide, trifluoroacetic anhydride (61%); *i*, phosphorus tribromide, quinoline, bromobenzene (55%); *j*, aqueous sodium hydroxide (90%); *k*, lithium aluminum hydride (85%).

enantiopure 1-substituted indans (**5**) with the configurations as shown at the top of Table I, regardless of the enantiomer used in the spectral measurements. Figures 1 and 2 show the complete EA and CD spectra for (*S*)-1-indanol [(*S*)-**5d**] and (*R*)-1-*tert*-butylindan [(*R*)-**5t**], and as noted in Table I, complete EA and CD data are given in other reports[8-10] or in the Experimental Section below for the enantiomer actually used. The CD spectra of other enantiopure compounds are also discussed for a particular configuration, but the CD spectra with reversed signs may have been reported for the enantiomer. The actual reports of these spectra are also given in appropriate references.

Vibronic Contribution to the ^1L_b Cotton Effects. Figure 3A gives the sign of the vibronic contribution to the ^1L_b CEs of a monosubstituted benzene chromophore by atoms or groups attached to a contiguous chiral center and lying in sectors in front of the benzene ring plane (near sectors), the sector boundaries being defined by the attachment bond of the chiral center and the benzene ring plane. For atoms or groups in sectors behind the plane of the benzene ring (far sectors) in Figure 3A, the signs of the contributions are reversed, and for those lying in sector boundaries, there is no contribution to the CEs. The sum of the contributions gives the sign to the observed CEs of the ^1L_b band, since for benzene compounds with only a single substituent, the CEs are the result only of vibronic borrowing.[4]

The signs for the sectors follow from the observed negative ^1L_b (CEs for (*R*)-1-phenylethanol [(*R*)-**1a**], the preferred conformation of (*R*)-**1a** in which the hydrogen atom at the chiral center eclipses the benzene ring plane, and the assumption of a larger rotatory contribution for a methyl group than for a hydroxyl group.[3] This latter assumption is based on a larger bond transition moment for a carbon–carbon bond than for a carbon–oxygen bond.[17] Since both (*R*)-α-phenylethylamine [(*R*)-**2a**] and (*S*)-mandelic acid [(*S*)-**3a**] show negative ^1L_b CEs and in each the preferred conformation is such that the hydrogen atom at the chiral center is essentially in the benzene ring plane,[3] a methyl group makes a greater vibronic contribution to the ^1L_b CEs than does an amino group, and a carboxyl group makes a greater contribution than does a hydroxyl group. Using the CD data for similar enantiopure compounds in which one substituent at the contiguous chiral center is a hydrogen atom and for which the absolute configurations are known, a sequence for the summation of vibronic contributions to the ^1L_b CEs has been established.[3,18] This sequence and sector diagram A (Figure 3A) may be used to correlate the sign of the CEs of its ^1L_b band with the absolute configuration of an enantiopure benzene compound in which one substituent at the contiguous chiral center is a hydrogen atom.[3]

The sector diagrams for the vibronic contributions to the ^1L_b CEs for various other benzene chromophores are also shown in Figure 3. These diagrams follows from that deduced for monosubstituted benzene compounds (Figure 3A). In sector diagrams B–E, the sector boundaries correspond to the attachment bonds of the cycloalkene or tetrahydropyridine moiety and the benzene ring plane. Again, the sum of the contributions of groups in the sectors gives the vibronic contribution to the ^1L_b CEs. When a hydrogen atom is at a contiguous chiral center and lies in one sector or another, it is assumed, on the basis of a very small bond transition moment for a carbon–hydrogen bond,[17] that it makes no significant vibronic contribution to the sign of the ^1L_b CEs.

Induced Contributions to the ^1L_b Cotton Effects. When enantiopure phenylalkylcarbinols and carbinamines are ring-substituted, an additional contribution to the ^1L_b CEs is induced. For a methyl group in the ortho position, the induced contribution is of opposite sign from that of the vibronic contribution. Thus the negative vibronic contribution to the ^1L_b CEs of (*R*)-α-(*o*-methylphenyl)ethyl alcohol [(*R*)-**1b**] and α-(*o*-methylphenyl)ethylamine [(*R*)-**2b**] is overshadowed by a positive induced contribution, and these ortho methyl derivatives show positive ^1L_b CEs,[4] opposite in sign from that of the unsubstituted parents, (*R*)-**1a** and (*R*)-**2a**. For the compounds in Tables I and III, the respective attachment bonds of the cycloalkene and tetrahydropyridine groups are equivalent to the attachment of an alkyl group ortho to the attachment bond of a contiguous chiral center in a noncondensed benzene system. Since an alkyl group has a spectroscopic moment of the same sign as a methyl group,[7] the presence of an alkyl group in an ortho position also induces a contribution to the ^1L_b CEs opposite from that of the vibronic contribution.[4]

For the enantiopure compounds in Table I, all with the same generic configuration and a planar cycloalkene ring, the substituents at C-1 all make a positive vibronic contribution to the ^1L_b CEs (Figure 1B,C), while the contribution of the attached hydrogen atom is insignificant. This positive vibronic contribution, however, is in general overshadowed by a negative induced contribution arising from the cycloalkene attachment ortho to the attachment bond of the chiral group. The single exception is observed with potassium (*S*)-1-indancarboxylate [(*S*)-**5i**]. The positive ^1L_b CEs for (*S*)-**5i** as compare to the negative ones for (*S*)-1-indancarboxylic acid [(*S*)-**5h**] are similar to the CD observations with (*S*)-mandelic acid [(*S*)-**3a**], (*S*)-*o*-methylmandelic acid [(*S*)-**3b**], and their potassium salts.[5]

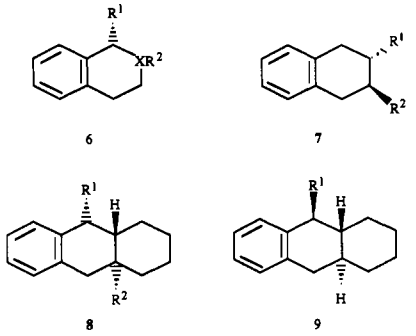
For (*S*)-mandelic acid [(*S*)-**3a**], the preferred conformation is such that the hydrogen atom at the chiral center eclipses or nearly eclipses the benzene ring plane.[5] Since the rotatory contribution by a carboxyl group is greater than that by a hydroxyl group,[18] the sum of the vibronic contributions to the ^1L_b CEs is negative (Figure 3A), and the ^1L_b CEs are negative. For (*S*)-*o*-methylmandelic acid [(*S*)-**3b**], the ortho methyl group induces a positive contribution to the ^1L_b CEs, which overshadows the negative vibronic contribution and results in positive ^1L_b CEs.[5] Treatment of the (*S*)-*o*-methylmandelic acid [(*S*)-**3b**] in situ with potassium hydroxide gives the potassium salt, and the sign of the ^1L_b CEs is now positive, reversed from that of (*S*)-**3b**, the vibronic contribution to the ^1L_b CEs no longer overshadowed by the induced contribution.[5]

The CD observations with (*S*)-*o*-methylmandelic acid [(*S*)-**3b**] and (*S*)-1-indancarboxylic acid [(*S*)-**5h**] and their potassium salts underscore the point made earlier[4] that, when the vibronic and

(17) Inskeep, W. H.; Miles, D. W.; Eyring, H. *J. Am. Chem. Soc.* **1970**, *92*, 3866–3872.

(18) Sequences for the summation of the vibronic contributions to the ^1L_b CEs are as follows: SH, CO_2^-, $C(CH_3)_3$ > CH_3 > NH_2, $^+NH_3$, $^+N(CH_3)_3$, OH, OCH_3, Cl; CH_3 > CO_2H > $^+NH_3$, OH, OCH_3.

Table III. Electronic Absorption (EA) and Circular Dichroism (CD) Data for the ^1L_b Band Origin Maxima of Enantiopure 1,2,3,4-Tetrahydronaphthalenes, 1,2,3,4-Tetrahydroisoquinolines, and Related Compounds



code	R^1	R^2	EA λ, nm (ε[a])	CD λ, nm (Δε[b])	ref[c]
			(*R*)-**6**, X = CH		
a	NH_2	H	274 (320)[d]	274 (+0.14)[d,e]	8
b	$N(CH_3)_2$	H	*f*	242[g] (+0.24)[h,i]	22
c	OH	H	*f*	264 (+0.15)[h,i]	22
d	CH_3	H	273 (289)[j]	273 (+0.23)[j]	23
e	CO_2CH_3	H	*f*	274 (+0.04)[h,i]	22
f	CO_2H	H	*f*	274 (+0.05)[h,i]	22
			(*S*)-**6**, X = N		
g	CH_3	H	*f*	273 (+0.24)[k]	24
h	CH_3	H_2Cl	271 (450)[k]	272 (+0.11)[k]	24
i	CH_3	CH_3	*f*	273 (+0.30)[k]	24
j	CH_3	HCH_3Cl	271 (280)[k]	272 (+0.10)[k]	24
k	CH_3	$(CH_3)_2I$	*f*	269 (+0.06)[k]	24
			7		
a	CH_3	CH_3	274 (703)[j]	272 (+0.19)[j]	23
b	CH_3	H	274 (746)[j]	272 (+0.16)[e,j]	23
c	NH_2	H	273 (417)[d]	270 (+0.13)[d,e]	8
			8		
a	H	H	274 (746)[l]	273 (+0.27)[l]	23
b	CH_3	H	273 (735)[j]	273 (+0.57)[j]	23
c	CH_2OH	H	273 (619)[l]	272 (+0.41)[l]	23
d	H	CH_3	274 (859)[l]	273 (+0.30)[l]	23
			9		
a	CH_3		273 (578)[j]	273 (−0.06)[j]	23
b	CH_2OH		273 (536)[l]	270 (+0.04)[l]	23

[a] Molar absorptivity. [b] Molar dichroic absorption. $\Delta\epsilon = [\theta]/3300$ where $[\theta]$ is the molecular ellipticity. [c] Original report of EA and CD data. [d] Cyclohexane as solvent. [e] Enantiomer used. [f] Not reported. [g] Probably a misprint and should be 272 nm. [h] Only one maximum reported. [i] Isooctane as solvent. [j] Hexane as solvent. [k] 95% ethanol as solvent. [l] Methanol as solvent.

induced contributions to the ^1L_b CEs are of opposite sign, a prediction as to the sign of the ^1L_b CEs shown by a particular enantiomer is somewhat ambiguous. In the case of (*S*)-**3b**, the reversal in the sign of the ^1L_b CEs on formation of its potassium salt might possibly be ascribed to a change in the preferred conformation of the chiral group about its attachment bond to the benzene ring. For (*S*)-**5h** and its potassium salt (*S*)-**5i**, no such conformational change is possible, and the reversal in sign of the ^1L_b CEs on going from (*S*)-**5h** to (*S*)-**5i** must be electronic in nature. However, for all of the enantiopure α-phenylethyl alcohols[4] (**1a**), α-phenylethylamines[4] (**2a**), mandelic acids[5,19,20] (**3a**), methyl mandelates,[19] and β-hydroxy-β-phenylpropionic acids,[21] which are ortho-substituted with an atom or group with a positive spectroscopic moment (CH_3, F, Cl, Br, OCH_3), show ^1L_b CEs with a sign opposite from that of their unsubstituted parent. For ortho-substituted mandelic acid salts, however, only the CD of the *o*-methyl derivative has been reported,[5] and it is not known if the sign of the ^1L_b CEs is reversed on formation of the corresponding potassium salts of other ortho-substituted mandelic acids.

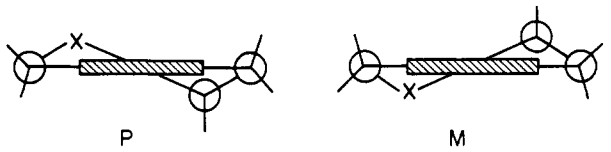


Figure 4. Conformational helicities of substituted 1,2,3,4-tetrahydronaphthalenes (X = CH_2) and 1,2,3,4-tetrahydroisoquinolines (X = NH).

When both the vibronic and induced contribution to the ^1L_b CEs have the same sign, there is no ambiguity in the prediction of the sign of the ^1L_b CEs for a particular enantiomer. Since the trifluoromethyl group has a negative spectroscopic moment,[7] both the vibronic and induced contributions to the ^1L_b CEs for the *o*-trifluoromethyl derivatives of (*R*)-α-phenylethyl alcohol [(*R*)-**1a**] and (*R*)-α-phenylethylamine [(*R*)-**2a**] show ^1L_b CEs with the same negative sign as the unsubstituted parent.[4]

Applications to Nonplanar Condensed Systems. The signs of the ^1L_b CEs in the CD spectra of a number of 1- and 2-substituted 1,2,3,4-tetrahydronaphthalenes[8,22,23] [(*R*)-**6a–f** and **7a–c**] and 1-methyl-1,2,3,4-tetrahydroisoquinolines[24,25] [(*S*)-**6g–k**] (Table III) may also be correlated with their absolute configurations using the benzene sector and the benzene chirality rules.

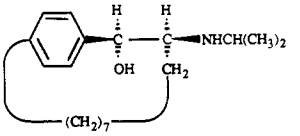
As suggested earlier by Ho and Snatzke,[26] the cyclohexene and tetrahydropyridine moieties in **6–7** are not planar, and this nonplanarity must be considered in the prediction of the sign of their ^1L_b CEs, the helicity of the cyclohexene and tetrahydropyridine moieties being determined by the absolute configurations of the groups attached at chiral centers. Using the enantiomer of the enantiopure, conformationally rigid tricyclic compound **8a**, Ho and Snatzke[26] were able to show that P helicity (Figure 4) of the ring attached to the benzene ring led to positive ^1L_b CEs, while M helicity resulted in negative ^1L_b CEs. It is further suggested that the sign of the ^1L_b CEs for **8a** and the more conformationally mobile systems **6** and **7** depends only on the preferred helicity of the cyclohexene and tetrahydropyridine groups (chirality of the second sphere[26]) and can be predicted using a sector rule with signs opposite those shown in Figure 3D,E.

Application of the benzene sector and the benzene chirality rules to the same systems also leads to the same prediction for the sign of the ^1L_b CEs. In compounds **8a–d**, the P helicity and the R^1 group in **8b,c** give a negative vibronic contribution to the ^1L_b CEs (Figure 3D). The induced positive contribution, however, overshadows the vibronic contribution, and the observed CEs for **8a–d** are positive. The positive ^1L_b CEs shown by the 1-methyl-1,2,3,4-tetrahydronaphthalenes [(*R*)-**6a–f**] and the 1-methyl-1,2,3,4-tetrahydroisoquinolines [(*S*)-**6g–k**] may be interpreted in a similar way. For (*R*)-1-methyl-1,2,3,4-tetrahydronaphthalene [(*R*)-**6d**], it has been shown that the methyl group has preferably a quasiaxial conformation[23] and the helicity of the cyclohexene group is P. With this helicity, the sign of the vibrational contribution to the ^1L_b CEs is negative (Figure 3D), but the induced contribution to the ^1L_b CEs is positive. Since the latter in general overshadows the former, the sign of the ^1L_b CEs, as predicted, is positive. The other substituents at C-1 in (*R*)-**6a–c,e,f** also cause the cycloalkene group to have P helicity, and their observed ^1L_b CEs are positive. On the basis of the equatorial conformation for the substituents in **7a–c**, the cyclohexene group also has P helicity, and the observed ^1L_b CEs are correctly predicted to be

(19) Korver, O. *Tetrahedron* **1970**, *26*, 5507–5518.
(20) Korver, O.; De Jong, S.; van Soest, T. C. *Tetrahedron* **1976**, *32*, 1225–1229.
(21) Collet, A.; Jacques, J. *Bull. Chim. Soc. Fr.* **1972**, 3857–3862.
(22) Weidmann, R.; Guettè, J.-P. *C. R. Acad. Sci. Paris C* **1969**, *268*, 2225–2227.
(23) Hagishita, S.; Kuriyama, K. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3216–3224.
(24) Craig, J. C.; Lee, S.-Y. C.; Chan, R. P. K.; Wang, I. Y.-F. *J. Am. Chem. Soc.* **1977**, *99*, 7996–8002.
(25) Potapov, V. M.; Dem'yanovich, V. M.; Skvortsova, T. V. *Khim. Geterotsikl. Soedin.* **1987**, 1238–1240.
(26) Snatzke, G.; Ho, P. C. *Tetrahedron* **1971**, *27*, 3645–3653.

positive. For the (*S*)-1-methyl-1,2,3,4-tetrahydroisoquinolines [(*S*)-**6g,i**], a similar analysis for the free bases also predicts positive ^1L_b CEs. When the nitrogen atom has a positive charge [(*S*)-**6h,j,k**], the C-1 chiral group will have a negative spectroscopic moment,[27] and the sign of its induced contribution to the ^1L_b CEs will be negative while the induced contribution of the C-4 group is still positive. Thus, the overall prediction as to the sign of the induced contribution to the CEs is ambiguous. The ^1L_b CEs for the salts, however, are still positive, but their intensities as compared to those of the free bases are reduced. It should also be noted that any additional substitution of the benzene ring causes a change in the induced contribution to the CEs, depending on the ring position and spectroscopic moment of the additional substituent, and a prediction as to the sign of the ^1L_b CEs in these cases is at present not possible. For **9a** and **9b**, the ring substituent R^1, with positive contribution to the ^1L_b CEs and opposite in sign from the P helicity of the attached cyclohexene ring, also makes a prediction as to the sign of the ^1L_b CEs uncertain, and in fact **9a** shows a negative ^1L_b band origin while that of **9b** is positive.[23]

For very flexible condensed systems, a preferred helicity of the cycloalkene attachment need not be important. The relative configuration of (+)-*threo*-1-hydroxy-2-(isopropylamino)[10]-paracyclophane [(+)-**10**] was established on the basis of its ^1H NMR spectrum,[28] and although (+)-**10** showed positive ^1L_b CEs in its CD spectrum,[28] the 1*S*,2*S* absolute configuration was assigned on the basis of a comparison of the CD spectrum of the complex formed in situ from (+)-**10** and copper(II)(succinimido)$_2$(isopropylamine)$_2$ [Cu(su)$_2$(ip)$_2$] with Cu(su)$_2$(ip)$_2$ complexes of model enantiopure amines of known absolute configuration. The same absolute configuration can be assigned to (+)-**10**



(1*S*,2*S*)-10

using the benzene sector and the benzene chirality rules. Thus, a preferred conformation of (1*S*,2*S*)-**10** in which the hydrogen atom at C-1 eclipses the benzene ring plane[3] predicts positive ^1L_b CEs for (1*S*,2*S*)-**10**, since a negative vibronic contribution (Figure 3A) is predicted to be overshadowed by a positive contribution as the result of the para substitution by a group with a positive spectroscopic moment,[4] there being no preferred helicity to the alicyclic system.

Experimental Section

Melting and boiling points are uncorrected. Rotatory powers at the sodium D-line were determined with a visual Zeiss polarimeter using a 1-dm tube. Infrared spectra were recorded on Perkin-Elmer Models 221 and 421 and Infracord spectrophotometers. Nuclear magnetic resonance (NMR) spectra were recorded on Varian Associates Models A-60, A-60A, T-60, HR-60, and HR-100 spectrometers, and chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane as the internal standard. The mass spectra were done on a Hitachi RMU-6A spectrometer by the Purdue University Spectral Service Department. Electronic absorption (EA) spectra were obtained using a Bausch and Lomb Model 505 spectrometer. Optical rotatory dispersion (ORD) and circular dichroism (CD) spectra were recorded using a Cary Model 60 spectropolarimeter with a CD attachment and a 1-cm cell by W. Carl and D. Wilson, Purdue University. Precautions were taken to eliminate artifacts by checking the spectra of corresponding racemates and using them as baselines when it seemed necessary. Although all of the EA, ORD, and CD data are recorded elsewhere in extenso for methanol and isooctane as solvents,[1] only the EA and CD data observed in methanol are given below. The CD data in Table I, however, are adjusted to that for 100% optical purity (100% ee). Combustion analyses were done by Dr. S. Yeh and associates, Purdue University.

(*S*)-*N,N,N*-Trimethyl-*N*-(1-indanyl)ammonium iodide [(*S*)-5c] was prepared earlier[12] in a reaction series from (*S*)-indancarboxylic acid [(*S*)-**5h**] with $[\alpha]^{27}_D$ −15.2° (benzene) [lit.[14] $[\alpha]^{25}_D$ +43.3° (*c* 2.6, benzene)[29] for the enantiomer, 100% ee]: EA max 274 (ϵ 1300), 267 (1200), 261 (860), 217 nm (13 000); CD (*c* 0.0210) $[\theta]_{290}$ ±0, $[\theta]_{274}$ −1500, $[\theta]_{272}$ −840, $[\theta]_{267}$ −1500, $[\theta]_{262}$ −940, $[\theta]_{260}$ −970, $[\theta]_{240}$ −30.

(*R*)-1-Indanol [(*R*)-5d] was prepared eariler by resolution:[15] $[\alpha]^{25}_D$ −34.7° (*c* 0.369, $CHCl_3$) [lit.[30] $[\alpha]^{20}_D$ +38.9° (*c* 1.23, $CHCl_3$),[29] 100% ee]; UV max 272 (ϵ 920), 266 (820), 259 (490), 214 nm (4700); CD (*c* 0.0210) $[\theta]_{280}$ ±0, $[\theta]_{271}$ +1300, $[\theta]_{268}$ +330, $[\theta]_{265}$ +1300, $[\theta]_{261}$ +600, $[\theta]_{259}$ +790, $[\theta]_{233}$ +20, $[\theta]_{219}$ +2300, $[\theta]_{217}$ +390.

(±)-1-Indanylmethanol [(±)-5f]. A mixture of (±)-1-indanylmethyl acetate [(±)-**5g**] (1.00 g, 5.26 mmol) and 25% aqueous sodium hydroxide (25 mL) was boiled for 4 h. The cooled mixture was extracted with ether, and the dried ($MgSO_4$) ether extract was evaporated. The residue of (±)-**5f** (0.70 g, 90%) was purified by VPC: IR (film) 3400 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.6–2.6 (m, 2, C(2)H), 2.40 (s, 1, OH), 2.86 (t, 2, *J* = 7 Hz, downfield signal is a doublet with *J* = 2 Hz, C(3)H), 3.26 (quintet, 1, *J* = 6 Hz, C(1)H), 3.71 (d, 2, *J* = 6 Hz, downfield signal is a doublet with *J* = 2 Hz, CH_2O), 7.15 (s, 4, aromatic H).

(*S*)-1-Indanylmethanol [(*S*)-5f] was prepared (90%) from (*S*)-1-indanylmethyl acetate [(*S*)-**5g**], 68% ee, as outlined above for the preparation of (±)-**5f** from (±)-**5g** and was purified by VPC: $[\alpha]^{25}_D$ −9.8° (*c* 2.04, isooctane), $[\alpha]^{25}_D$ −11.6° (*c* 0.71, benzene) [lit.[16] $[\alpha]^{20}_D$ +17° (*c* 0.41, benzene)[31] for the enantiomer]; EA max 271 (ϵ 1300), 264 (1200), 257 (990), 243 (1100), 211 nm (6300); CD (*c* 0.0134) $[\theta]_{280}$ ±0, $[\theta]_{272}$ −1100, $[\theta]_{269}$ −390, $[\theta]_{265}$ −970, $[\theta]_{260}$ −630, $[\theta]_{258}$ −730, $[\theta]_{230}$ −130, $[\theta]_{221}$ −4900, $[\theta]_{219}$ −1600.

(±)-1-Indanylmethyl Acetate [(±)-5g]. Anhydrous peroxytrifluoroacetic acid was prepared by the dropwise addition of trifluoroacetic anhydride (10.0 g, 47.6 mmol) over a period of 45 min to a stirred mixture of 90% hydrogen peroxide (1.00 mL) and dry methylene chloride (10 mL), keeping the temperature between −10 and −20 °C. The solution was allowed to warm to room temperature and then cooled to −20 °C before being added dropwise over 25 min to a mixture of (±)-1-indanylacetone [(±)-**5s**] (2.61 g, 15.0 mmol), anhydrous disodium hydrogen phosphate (17 g, 0.12 mol), and dry methylene chloride (40 mL). This mixture was then boiled for 4 h. The salts were separated from the solution and washed with methylene chloride. The combined methylene chloride solutions were washed with 10% sodium carbonate, dried ($MgSO_4$), and evaporated. The brown residue was shown by VPC and ^1H NMR analysis to be contaminated with (±)-**5s** (10%). The brown oil was treated with methanol (12 mL), glacial acetic acid (1.5 mL), and Girard's reagent T ((trimethylamino)acetohydrazide chloride) (2.5 g, 0.015 mol). The mixture was boiled for 5 h and poured into ice water (50 mL). Partial neutralization with sodium bicarbonate (1.9 g) in water (10 mL), extraction into methylene chloride, drying ($MgSO_4$), evaporation of the solvent, and distillation gave (±)-**5g** (1.97 g, 69%), bp 87–92 °C (1 mmHg). After VPC, (±)-**5g** had the following spectral data: IR (film) 1750, 1230 cm^{-1}; ^1H NMR (CCl_4) δ 1.5–2.5 (m, 2, C(2)H), 1.95 (s, 3, OCH_3), 2.87 (t, 2, *J* = 7 Hz, C(3)H), 3.38 (quintet, 1, *J* = 7 Hz, C(1)H), 4.13 (d, 2, *J* = 7 Hz, each signal a doublet with *J* = 1 Hz, CH_2O), 7.10 (s, 4, aromatic H); mass spectrum (75 eV) *m/z* (relative intensity) 91 (9), 115 (24), 116 (10), 117 (64), 118 (8), 128 (9), 129 (17), 130 (100), 131 (15). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.47; H, 7.71.

(*S*)-1-Indanylmethyl acetate [(*S*)-5g] was prepared (61%) from (*R*)-1-indanylacetone [(*R*)-**5s**], 68% ee, as outlined above for the preparation of (±)-**5g** from (±)-**5s** and was purified by VPC: $[\alpha]^{25}_D$ −17.3° (*c* 2.25, acetone); EA max 271 (ϵ 1200), 264 (1100), 258 (800), 250 (600) (sh), 212 nm (5700); CD (*c* 0.0190) $[\theta]_{280}$ ±0, $[\theta]_{271}$ −1100, $[\theta]_{269}$ −370, $[\theta]_{264}$ −1000, $[\theta]_{260}$ −520, $[\theta]_{258}$ −670, $[\theta]_{235}$ −80, $[\theta]_{220}$ −4900, $[\theta]_{218}$ −940.

(*R*)-1-Indancarboxylic acid [(*R*)-5h] was prepared earlier by resolution.[12] It was repurified by sublimation (2×) and recrystallization from hexane (2×): $[\alpha]^{25}_D$ +41.6° (*c* 2.1, benzene) [lit.[14] $[\alpha]^{25}_D$ +43.3° (*c* 2.6, benzene)[29] 100‰ ee]; EA max 273 (ϵ 850), 266 (800), 260 (490), 213 nm (5100); CD (*c* 0.0424) $[\theta]_{280}$ ±0, $[\theta]_{273}$ +140, $[\theta]_{272}$ +120, $[\theta]_{269}$ +220, $[\theta]_{267}$ +60, $[\theta]_{264}$ +130, $[\theta]_{259}$ +42, $[\theta]_{242}$ +340, $[\theta]_{241}$ +310, $[\theta]_{227}$ +5400, $[\theta]_{223}$ +340.

Potassium (*R*)-1-indancarboxylate [(*R*)-5c] was formed in methanol by neutralization of (*R*)-1-indancarboxylic acid [(*R*)-**5h**], 96% ee, with a standard solution of potassium hydroxide in methanol: EA max 274 (ϵ 1200), 267 (1200), 261 (880), 214 nm (5400); CD (*c* 0.0395) $[\theta]_{290}$

(27) Smith, H. E.; Neergaard, J. R.; de Paulis, T.; Chen, F.-M. *J. Am. Chem. Soc.* **1983**, *105*, 1578–1584.

(28) Hagishita, S.; Kuriyama, K. *Chem. Pharm. Bull.* **1976**, *24*, 1724–1730.

(29) Maximum rotatory power reported and taken as that for the enantiopure isomer (100% ee).

(30) Hückel, W.; Mössner, F. *Justus Liebigs Ann. Chem.* **1960**, *637*, 57–72.

(31) As described in ref 16, this sample of (*R*)-**5f** was prepared from (*R*)-1-indancarboxylic acid, $[\alpha]^{20}_D$ +43° (*c* 1.7, benzene), which is assumed to have an ee of 100%.

±0, $[\theta]_{276}$ −670, $[\theta]_{273}$ −120, $[\theta]_{269}$ −490, $[\theta]_{265}$ −100, $[\theta]_{263}$ −250, $[\theta]_{228}$ +13 000, $[\theta]_{220}$ +610.

(±)-1-(Trifluoromethyl)indan [(±)-5j]. Sulfur tetrafluoride (3.9 g, 0.036 mol) was added to (±)-1-indancarboxylic acid [(±)-**5h**] (0.250 g, 1.54 mmol) with hexane (3 mL) in a 30-mL Hastalloy bomb at −78 °C. The sealed bomb was then heated to 70–75 °C for 6 h. Periodically the bomb was shaken vigorously. After cooling, the toxic gases were allowed to escape, and the dark residue was extracted with hexane. The hexane solution was washed with aqueous sodium carbonate and dried ($MgSO_4$), and the hexane was removed by evaporation. Purification of the light yellow residual oil by VPC gave (±)-**5j** (0.137 g, 48%) as a colorless oil: IR (film) 1700–1900 cm^{-1} (C–F stretch); ^1H NMR (CCl_4) δ 2.0–2.5 (m, 2, C(2)H), 2.8–3.2 (m, 2, C(3)H, 3.4–4.2 (m, 1, C(1)H), 7.2 (s, 4, aromatic H); ^{19}F NMR (CCl_4) δ 263 Hz upfield from $CF_2ClCOCF_2Cl$; mass spectrum (75 eV) *m/z* (relative intensity) 63 (5), 69 (4), 91 (8), 115 (26), 116 (10), 117 (100), 118 (12), 164 (4), 165 (6), 167 (4), 186 (35), 187 (5). Anal. Calcd for $C_{10}H_9F_3$: C, 64.51; H, 4.78; F, 30.62. Found: C, 64.77; H, 5.14; F, 30.40.

(*R*)-1-(Trifluoromethyl)indan [(*R*)-5j] was prepared (43%) from (*R*)-1-indancarboxylic acid [(*R*)-**5h**], 96% ee, using the same procedure as that outlined above for the preparation of (±)-**5j** from (±)-**5h** and was purified by VPC: $[\alpha]^{25}_D$ −1.7° (*c* 1.11, isooctane); UV max 272 (ε 840), 265 (780), 259 (490), 214 nm (3900); CD (*c* 0.0287) $[\theta]_{280}$ ±0, $[\theta]_{272}$ +350, $[\theta]_{270}$ +50, $[\theta]_{266}$ +360, $[\theta]_{262}$ +140, $[\theta]_{259}$ +230, $[\theta]_{235}$ ±0, $[\theta]_{220}$ +1100.

(±)-2-Amino-2-(1-indanyl)propane [(±)-5k]. The acid chloride of 2-methyl-2-(1-indanyl)propanoic acid [(±)-**5o**] was prepared by heating (±)-**5o** (1.00 g, 4.90 mmol) with thionyl chloride (3 mL) for 4 h. After removal of the excess thionyl chloride by distillation, further distillation of the residue gave the pure acid chloride, bp 90–95 °C (1 mmHg). The latter was dissolved in acetone (10 mL). To this solution, cooled in an ice bath, was added an aqueous solution of sodium azide (1.00 g, 15.4 mmol) in water (3 mL), and the mixture was stirred at 0–5 °C for 4 h. Water (30 mL) was added, the solution was extracted with ether, and the ether solution was dried (Na_2SO_4). Evaporation of the ether gave the impure azide as an oil: IR (film) 2150 cm^{-1} (N≡N stretch). The oil was dissolved in dry benzene (5 mL), and this solution was boiled for 12 h. The benzene was then evaporated, and the residue was identified as the impure isocyanate: IR (film) 2270 cm^{-1} (N=C=O stretch). The latter was redissolved in benzene (5 mL), concentrated hydrochloric acid (10 mL), previously saturated with hydrogen chloride, was added, and the mixture was boiled for 4 h. The aqueous layer was separated from the mixture, made basic with sodium hydroxide, and extracted with ether. The ether extract was dried (KOH), and evaporation gave (±)-**5k** (0.59 g, 69%) as a yellow oil, purified finally by VPC: IR (film) 3400, 1580, 1380, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (s, 3, CH_3), 1.17 (s, 3, CH_3), 1.32 (s, 2 NH_2), 1.6–2.5 (m, 2, C(2)CH_2), 2.6–3.3 (m, 3, C(1)CH and C(3)CH_2), 7.0–7.5 (m, 4, aromatic H); mass spectrum (75 eV) *m/z* (relative intensity) 58 (100), 59 (15), 91 (12), 115 (35), 116 (14), 117 (24), 128 (7), 143 (7), 160 (8). Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.14; H, 9.91; N, 7.95.

(*S*)-2-Amino-2-(1-indanyl)propane [(*S*)-5k] was prepared (70%) from (*S*)-2-methyl-2-(1-indanyl)propanoic acid [(*S*)-**5o**], 68% ee, using the same procedure as that outlined above for the preparation of (±)-**5k** from (±)-**5o** and was purified by VPC: $[\alpha]^{26}_D$ +6.2° (*c* 1.94, isooctane); EA max 272 (ε 1100), 265 (970), 259 (670), 252 (370) (sh), 214 nm (5200); CD (*c* 0.0235) $[\theta]_{290}$ ±0, $[\theta]_{274}$ −2600, $[\theta]_{271}$ −1500, $[\theta]_{267}$ −2700, $[\theta]_{262}$ −1800, $[\theta]_{260}$ −1900, $[\theta]_{235}$ −260, $[\theta]_{224}$ −6400, $[\theta]_{221}$ +220.

(*S*)-2-Amino-2-(1-indanyl)propane hydrochloride [(*S*)-5l] was formed in methanol by neutralization of (*S*)-2-amino-2-(1-indanyl)propane [(*S*)-**5k**], 68% ee, with a standard solution of hydrogen chloride in methanol: EA max 272 (ε 1100), 265 (910), 259 (610), 252 (330) (sh), 215 nm (4500); CD (*c* 0.0384) $[\theta]_{290}$ ±0, $[\theta]_{273}$ −2300, $[\theta]_{269}$ −1240, $[\theta]_{266}$ −2600, $[\theta]_{261}$ −1700, $[\theta]_{259}$ −1800, $[\theta]_{230}$ −90, $[\theta]_{221}$ −3500, $[\theta]_{219}$ +330.

(±)-1-Bromo-2-methyl-2-(1-indanyl)propane [(±)-5m]. To a vigorously stirred solution of (±)-2-methyl-2-(1-indanyl)-1-propanol [(±)-**5n**] (9.50 g, 49.9 mmol) and quinoline (10.0 g, 77.4 mmol) in bromobenzene (40 mL) was added phosphorous tribromide (10.8 g, 39.9 mmol) in bromobenzene (20 mL) dropwise over 2.5 h. The resultant heterogeneous mixture was boiled for 18 h. The cooled liquid was decanted, and the dark residue was broken up and extracted (2×) with bromobenzene (10 mL). The combined bromobenzene solutions were treated with ice, washed with water, and dried (Drierite), and the bromobenzene was removed by distillation. Distillation of the residue gave slightly impure (5% by VPC) (±)-**5m** (7.43 g, 59%) as a light yellow oil, bp 96–100 °C (1 mmHg). The pure sample was obtained by VPC: IR (film) 1385, 1368 cm^{-1}; ^1H NMR (CCl_4) δ 0.95 (s, 3, CH_3), 1.02 (s, 3, CH_3), 1.8–2.3 (m, 2, C(3)H), 3.1–3.4 (m, 1, C(1)H), 3.35 (s, 2, CH_2Br), 7.08 (m, 4, aromatic H); mass spectrum (75 eV) *m/z* (relative intensity) 91 (9), 115 (26), 116 (17), 117 (100), 118 (25), 196 (2), 198 (2), 252 (4), 253 (0.5), 254 (4), 255 (0.5). Anal. Calcd for $C_{13}H_{17}Br$: C, 61.67; H, 6.77; Br, 31.56. Found: C, 61.53; H, 6.80; Br, 31.81.

(*S*)-1-Bromo-2-methyl-2-(1-indanyl)propane [(*S*)-5m] was prepared (55%) from (*S*)-2-methyl-2-(1-indanyl)-1-propanol [(*S*)-**5n**], 68% ee, by the same procedure as that above for the preparation of (±)-**5m** from (±)-**5n** and was purified by VPC: $[\alpha]^{25}_D$ −26.8° (*c* 1.89, acetone); EA max 272 (ε 1400), 265 (1200), 259 (950), 212 (7600); CD (*c* 0.0148) $[\theta]_{284}$ ±0, $[\theta]_{274}$ −2400, $[\theta]_{271}$ −1100, $[\theta]_{267}$ −2200, $[\theta]_{262}$ −1460, $[\theta]_{260}$ −1500, $[\theta]_{232}$ −90, $[\theta]_{223}$ −6200, $[\theta]_{220}$ +4200.

(±)-2-Methyl-2-(1-indanyl)-1-propanol [(±)-5n]. A solution of (±)-2-methyl-2-(1-indanyl)propanoic acid [(±)-**5o**] (23.0 g, 0.113 mol) in dry ether (80 mL) was added dropwise over 15 min to a stirred slurry of lithium aluminum hydride (8.0 g, 0.21 mol) in dry ether (50 mL). The mixture was boiled for 4 h, hydrolyzed, and separated, and the aqueous layer was extracted with ether. The combined ether solutions were dried ($MgSO_4$) and evaporated. Distillation of the viscous yellow residue gave (±)-**5n** (17.5 g, 82%) as a colorless oil, bp 108–114 °C (1 mmHg). The analytical sample was obtained by VPC: IR (film) 3400 cm^{-1}; ^1H NMR (CCl_4) δ 0.83 (s, 3, CH_3), 0.88 (s, 3, CH_3), 1.8–2.4 (m, 2, C(2)H), 2.80 (s, 1, OH), 2.84 (t, 2, *J* = 9 Hz, C(3)H), 3.19 (t, 1, *J* = 6 Hz, C(1)H), 3.39 (s, 2, OCH_2), 7.05 (m, 4, aromatic H); mass spectrum (75 eV) *m/z* (relative intensity) 91 (17), 115 (23), 116 (21), 117 (100), 118 (28), 190 (17), 191 (3). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 82.34; H, 9.64.

(*S*)-2-Methyl-2-(1-indanyl)-1-propanol [(*S*)-5n] was prepared (88%) from (*S*)-2-methyl-2-(1-indanyl)propanoic acid [(*S*)-**5o**], 68% ee, by the same procedure as that outlined above for the preparation of (±)-**5n** from (±)-**5o** and was also purified by VPC: $[\alpha]^{25}_D$ −1.4° (*c* 2.29, acetone); EA max 272 (ε 1100), 265 (1000), 259 (610), 252 (400) (sh), 212 nm (6000); CD (*c* 0.0189) $[\theta]_{289}$ ±0, $[\theta]_{276}$ −580 (sh), $[\theta]_{273}$ −2100, $[\theta]_{271}$ −1100, $[\theta]_{266}$ −2000, $[\theta]_{262}$ −1300, $[\theta]_{261}$ −1400, $[\theta]_{232}$ −110, $[\theta]_{222}$ −6600, $[\theta]_{220}$ −830.

(±)-2-Methyl-2-(1-indanyl)propanoic Acid [(±)-5o]. Lithium diisopropylamide (0.43 mol) was prepared by the dropwise addition over 10 min of diisopropylamine (61 mL, 0.43 mol) to a solution of *n*-butyllithium in hexane (270 mL, 1.6 M, 0.43 mol) and dry (distilled from lithium aluminum hydride) tetrahydrofuran (30 mL). (±)-1-Indanylacetic acid [(±)-**5q**] (37.2 g, 0.232 mol) in dry tetrahydrofuran (500 mL) was added dropwise with stirring over 15 min. Stirring was continued for 30 min, and then methyl iodide (14 mL, 0.22 mol) was added by syringe. Stirring was continued for 30 min. A fresh solution of lithium diisopropylamide (0.22 mol) was prepared as before and was added dropwise over 5 min. The entire reaction mixture was boiled for 2 h and cooled to room temperature, and methyl iodide (14 mL, 0.22 mol) was added as before. After 39 min, another portion of lithium diisopropylamide (0.22 mol), also prepared as before, was added to the mixture. The reaction mixture was stirred for 30 min and then treated carefully with dilute hydrochloric acid until the mixture was acidic. The latter was concentrated and extracted with ether. The ether extract was washed with aqueous sodium thiosulfate, dried ($MgSO_4$), and evaporated. Distillation of the residue gave (±)-**5o** as a light yellow oil, bp 140–145 °C (1 mmHg), which solidified on standing. Crystallization from hexane (charcoal) gave (±)-**5o** (31.8 g, 67%) as a colorless solid, mp 97–99 °C. Recrystallization (3×) from hexane gave the analytical sample of (±)-**5o**: mp 101–102 °C; IR (Nujol) 1700 cm^{-1}; ^1H NMR (CCl_4) δ 1.13 (s, 3, CH_3), 1.17 (s, 3, CH_3), 1.6–2.6 (m, 2, C(2)H), 2.86 (t, 2, *J* = 7 Hz, C(3)H), 3.66 (t, 1, *J* = 7 Hz, C(1)H), 7.08 (s, 4, aromatic H), 11.03 (s, 1, CO_2H); mass spectrum (75 eV) *m/z* (relative intensity) 91 (24), 115 (53), 116 (22), 117 (100), 118 (38), 127 (10), 128 (8), 204 (16), 205 (3). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.46; H, 7.92.

(*S*)-2-Methyl-2-(1-indanyl)propanoic acid [(*S*)-5o] was prepared (67%) from (*R*)-1-indanylacetic acid [(*R*)-**5q**], 68% ee, as outlined above for the preparation of (±)-**5o** from (±)-**5q**. A small portion was recrystallized (3×) from hexane: mp 94–96 °C; $[\alpha]^{25}_D$ +1.2° (*c* 2.30, acetone), $[\alpha]^{25}_D$ −4.1° (*c* 2.24, benzene); EA max 272 (ε 1300), 265 (1200), 259 (820), 252 (470) (sh), 212 nm (6500); CD (*c* 0.0175) $[\theta]_{280}$ ±0, $[\theta]_{273}$ −760, $[\theta]_{269}$ −210, $[\theta]_{266}$ −690, $[\theta]_{261}$ −390, $[\theta]_{259}$ −470, $[\theta]_{250}$ −90, $[\theta]_{223}$ −1100, $[\theta]_{220}$ −440.

Potassium (*S*)-2-methyl-2-(1-indanyl)propanoate [(*S*)-5p] was formed in methanol by neutralization of (*S*)-2-methyl-2-(1-indanyl)propanoic acid [(*S*)-**5o**], 68% ee, with a standard solution of potassium hydroxide in methanol: EA max 272 (ε 1300), 265 (1100), 259 (770), 214 nm (5500); CD (*c* 0.0348) $[\theta]_{280}$ ±0, $[\theta]_{272}$ −570, $[\theta]_{269}$ −98, $[\theta]_{265}$ −610, $[\theta]_{261}$ −290, $[\theta]_{258}$ −310, $[\theta]_{233}$ −10, $[\theta]_{224}$ −120, $[\theta]_{223}$ +150.

(±)-1-Indanylacetic Acid [(±)-5q]. Zinc (160 g, 2.45 g-atom) was shaken with mercuric chloride (16 g, 0.059 mol) in water (200 mL) and concentrated hydrochloric acid (16 mL) for 10 min. The liquid was decanted, and water (100 mL), concentrated hydrochloric acid (200 mL), toluene (120 mL), and 1-(3-oxo-1-indanyl)acetic acid (**12**) (57.0 g, 0.300 mol) were added. The mixture was boiled for 6 days with a portion of

concentrated hydrochloric acid (25 mL) being added daily. After cooling, the layers were separated, and the aqueous layer was extracted with ether. The combined organic solutions were extracted with 10% aqueous sodium hydroxide. The basic extract was acidified and extracted with ether. The dried ($MgSO_4$) ether extract was evaporated, and recrystallization of the residue from hexane (charcoal) gave (±)-**5q** (42.1 g, 88%) as a white solid: mp 58–59 °C (lit.[32] mp 60–61 °C); IR (Nujol) 1760 cm^{-1}; ^1H NMR (CCl_4) δ 1.3–3.0 (m, 6, methylene), 3.50 (quintet, 1, J = 7 Hz, C(1)H), 7.03 (s, 4, aromatic H), 12.70 (s, 1, CO_2H).

(*R*)-1-Indanylacetic Acid [(*R*)-5q]. (±)-1-Indanylacetic acid [(±)-**5q**] (5.28 g, 33.0 mmol) was dissolved in acetone. (*R*)-α-Phenylethylamine, $[\alpha]^{25}_D$ +38.2° (neat), (3.63 g, 30.0 mmol) was added, and the mixture was diluted to 75 mL with acetone. The crystalline solid which formed after 6 h at room temperature was recrystallized (2×) from acetone. The salt (2.54 g, 54%) had a specific rotation of $[\alpha]^{26}_D$ +39.0° (*c* 1.78, acetone), unchanged by further recrystallization. The acid was obtained by way of treatment of a portion of the salt with 10% aqueous sodium hydroxide, extraction with benzene, acidification with concentrated hydrochloric acid, extraction into ether, drying ($MgSO_4$) of the ether extract, evaporation of the ether, and recrystallization of the residue from hexane gave (*R*)-**5q**: mp 73–75 °C; $[\alpha]^{26}_D$ +6.9° (*c* 2.11, acetone), +7.7° (*c* 1.89, methanol), −6.8° (*c* 2.57, benzene); 90% ee as discussed below. Another larger sample of (*R*)-**5q**, used in all subsequent synthetic operations, had $[\alpha]^{25}_D$ +5.3° (*c* 3.40, acetone), 68% ee based on comparison of the rotatory power of (*S*)-1-indanylmethanol [(*S*)-**5f**] with $[\alpha]^{25}_D$ −11.6° (*c* 0.71, benzene) [lit.[16] $[\alpha]^{20}_D$ +17° (*c* 0.41, benzene)[31] for the enantiomer], to which this sample of (*R*)-**5q** was eventually converted: EA max 271 (ε 1200), 264 (1200), 258 (790), 252 (420) (sh), 212 (5900); CD (*c* 0.0146) $[\theta]_{280}$ ±0, $[\theta]_{272}$ −1200, $[\theta]_{268}$ −250, $[\theta]_{265}$ −930, $[\theta]_{261}$ −470, $[\theta]_{260}$ −560, $[\theta]_{240}$ −130, $[\theta]_{221}$ −5300, $[\theta]_{219}$ −1900.

Potassium (*R*)-1-indanylacetate [(*R*)-5r] was formed in methanol by neutralization of (*R*)-1-indanylacetic acid [(*R*)-**5q**], 68% ee, with a standard solution of potassium hydroxide in methanol: EA max 271 (ε 1200), 265 (1200), 258 (800), 214 nm (5400); CD (*c* 0.0294) $[\theta]_{280}$ ±0, $[\theta]_{272}$ −700, $[\theta]_{269}$ −210, $[\theta]_{264}$ −720, $[\theta]_{261}$ −410, $[\theta]_{258}$ −510, $[\theta]_{240}$ −73, $[\theta]_{223}$ −4100, $[\theta]_{222}$ −1400.

(±)-1-Indanylacetone [(±)-5s]. Methyllithium in ether (70 mL, 2.16 M, 0.151 mol) was added dropwise over a period of 15 min to a cooled solution of (±)-1-indanylacetic acid [(±)-**5q**] (11.2 g, 69.9 mmol) in dry ether (200 mL). The solution was stirred for 105 min and then hydrolyzed by the slow addition of water. The layers were separated, and the aqueous layer was extracted with ether. The combined ether extracts were dried ($MgSO_4$), and the solvent was evaporated. Distillation of the residue gave (±)-**5s** (9.15 g, 75%), bp 90–92 °C (1 mmHg). Final purification was by VPC: IR (film) 1720 cm^{-1}; ^1H NMR (CCl_4) δ 1.2–3.0 (m, 6, CH_2), 2.02 (s, 3, CH_3), 3.51 (quintet, 1, J = 7 Hz, CH), 7.00 (s, 4, aromatic H); mass spectrum (75 eV) m/z (relative intensity) 91 (18), 115 (30), 116 (100), 117 (64), 118 (7), 128 (9), 129 (12), 131 (19), 159 (7), 174 (24), 175 (4). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.87; H, 7.93.

(*R*)-1-Indanylacetone [(*R*)-5s] was prepared (89%) from (*R*)-1-indanylacetic acid [(*R*)-**5q**], 68% ee, using the same procedure as that outlined above for the preparation of (±)-**5s** from (±)-**5q** and was also purified by VPC: $[\alpha]^{26}_D$ +24.9° (*c* 2.13, acetone); EA max 271 (ε 1100), 265 (1000), 259 (710), 252 (430) (sh), 212 nm (5600); CD (*c* 0.0222) $[\theta]_{330}$ ±0, $[\theta]_{305}$ −100, $[\theta]_{275}$ +1400, $[\theta]_{272}$ −1000, $[\theta]_{269}$ −250, $[\theta]_{264}$ −1600, $[\theta]_{260}$ −1100, $[\theta]_{259}$ −1200, $[\theta]_{240}$ −20, $[\theta]_{233}$ −60, $[\theta]_{228}$ −20, $[\theta]_{221}$ −4100, $[\theta]_{220}$ +240.

(±)-1-*tert*-Butylindan [(±)-5t]. A clear solution of lithium aluminum hydride in tetrahydrofuran was prepared by stirring enough of the hydride to make an approximately 1 M solution with dry tetrahydrofuran (distilled from lithium aluminum hydride) and filtering in a dry system through diatomaceous earth on sintered glass. (±)-1-Bromo-2-methyl-2-(1-indanyl)propane [(±)-**5m**] (4.00 g, 15.8 mmol) was added to the lithium aluminum hydride solution (25 mL, 0.025 mol), and the mixture was boiled and stirred for 17 h. Dilute hydrochloric acid was added carefully, and the mixture was concentrated and extracted with ether. The ether extract was dried ($MgSO_4$), and the ether was evaporated. Distillation of the residue gave (±)-**5t** (2.22 g, 81%) as a colorless oil, bp 52–55 °C (1 mmHg). A sample for analysis was obtained by VPC: IR (film) 1395, 1368 cm^{-1}; ^1H NMR (CCl_4) δ 0.93 (s, 9, CH_3), 1.8–2.3 (m, 2, C(2)H), 2.6–3.1 (m, 3, C(3)H and C(1)H), 7.03 (m, 4, aromatic H); mass spectrum (75 eV) m/z (relative intensity) 57 (19), 91 (11), 115 (25), 116 (23), 117 (100), 118 (60), 159 (5), 174 (12), 175 (1.5). Anal. Calcd for $C_{13}H_{18}$: C, 89.59; H, 10.41. Found: C, 89.70; H, 10.56.

(*R*)-1-*tert*-Butylindan [(*R*)-5t] was prepared (85%) from (*S*)-1-bromo-2-methyl-2-(1-indanyl)propane [(*S*)-**5m**], 68% ee, by the same procedure as that outlined above for the preparation of (±)-**5t** from (±)-**5m** and was also purified by VPC: $[\alpha]^{24}_D$ +5.1° (*c* 2.28, acetone); EA max 272 (ε 1300), 265 (970), 259 (760), 252 (430) (sh), 212 nm (5900); CD (*c* 0.0162) $[\theta]_{290}$ ±0, $[\theta]_{274}$ −2700, $[\theta]_{271}$ −1200, $[\theta]_{267}$ −2600, $[\theta]_{263}$ −1700, $[\theta]_{262}$ −1800, $[\theta]_{234}$ −50, $[\theta]_{224}$ −4600, $[\theta]_{221}$ +3100.

(±)-1-(3-Oxo-1-indanyl)acetic Acid (12). Finely divided β-phenylglutaric acid[33] (**11**) (88.0 g, 0.423 mol) was added rapidly to polyphosphoric acid (400 g) at 125 °C. The mixture was stirred at 125 °C for 10 min, quenched with ice, and cooled. The dark yellow precipitate was recrystallized (2×) from benzene (charcoal) to give **12** (58.7 g, 73%) as a light yellow solid: mp 147–149 °C (lit.[34] mp 151 °C); IR (Nujol) 1650, 1720, 2500–2700 cm^{-1}; ^1H NMR (trifluoroacetic acid) δ 1.8–3.0 (m, 4, CH_2), 3.40 (broad s, 1, CH), 6.8–7.5 (m, 4, aromatic H).

(32) v. Braun, J.; Danziger, E.; Koehler, Z. *Chem. Ber.* **1917**, *50*, 56–64.

(33) Meerwein, H. *Justus Liebigs Ann. Chem.* **1908**, *360*, 323–347.

(34) Jackson, J. G.; Kenner, J. *J. Chem. Soc.* **1928**, 573–581.