and spectroscopic analysis; R_f 0.23 (1:4 ether–hexanes); IR ($CHCl_3$) 3011, 2947, 2887, 2858, 2829, 1776, 1728, 1457, 1368, 1363, 1335, 1305, 1246, 1186, 1161, 1138, 1112, 1090, 1058, 1035, 1004, 966, 935, 905, 857, 838 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.39 (br s, 1 H), 4.68 (ddd, 1 H, J = 13.2, 8.0, 4.9 Hz), 4.21 (m, 2 H), 3.13 (dd, 1 H, J = 11.2, 8.3 Hz), 2.84 (br m, 1 H), 2.67 (dd, 1 H, J = 14.6, 11.2 Hz), 2.14 (br m, 1 H), 2.03 (m, 2 H), 1.79 (dd, 1 H, J = 14.2, 4.9 Hz), 1.37 (dd, 1 H, J = 14.2, 13.2 Hz), 1.31 (t, 3 H, J = 7.1 Hz), 1.08 (s, 3 H), 1.02 (s, 3 H), 0.09 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 173.76 (s), 172.79 (s), 136.34 (s), 121.87 (d), 75.98 (d), 60.78 (t), 42.77 (t), 42.10 (d), 41.60 (d), 41.50 (d), 38.75 (t), 32.09 (s), 31.52 (d), 31.52 (q), 29.96 (q), 13.79 (q), -1.54 (q).

Anal. Calcd for $C_{19}H_{30}O_4Si$: C, 65.10; H, 8.63. Found: C, 65.17; H, 8.60.

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Registry No. **3a**, 16807-60-6; **3b**, 4683-45-8; **4a**, 84132-55-8; **4b**, 76999-36-5; **5a**, 84132-56-9; **5b**, 76999-38-7; **6a**, 84132-57-0; **6b**, 84132-61-6; **7a**, 84132-58-1; **7b**, 84142-96-1; **8a**, 84132-59-2; **8b**, 84132-62-7; **9a**, 84132-60-5; **9b**, 84132-63-8; **10a**, 84192-49-4; **10b**, 84132-64-9; **11a**, 84132-69-4; **12**, 21634-43-5; **13**, 84132-65-0; **14**, 84132-66-1; **15**, 84132-67-2; **19a**, 84132-70-7; **19b**, 84132-68-3; **20a**, 84132-71-8; **20b**, 84143-12-4; *trans*-β-(trimethylsilyl)vinyllithium, 55339-31-6; methallyl chloride, 563-47-3; prenyl bromide, 870-63-3; vinylmagnesium bromide, 593-60-2; *trans*-β-carbethoxyacryloyl chloride, 26367-48-6.

On the Relation between Elution Order and Absolute Stereochemistry of Alkylarylcarbinols from a Pirkle Column

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A study of the relation between the absolute stereochemistry of a series of alkylarylcarbinols and two groups of benzocycloalkenols with their elution order from an HPLC column containing a chiral stationary phase has shown that the enantiomer more strongly retained by the column in each group of compounds has the same absolute stereochemistry except for benzoin and its *p*-methyl derivative. The enantiomer more strongly retained in the acyclic series does *not* have the same absolute stereochemistry as that retained in the two cyclic series examined. Better separations were observed in the acyclic series for the acetate esters than the free alcohols, while the reverse situation occurred for the benzocycloalkenols. In each series of compounds the enantiomer of the alcohols and corresponding acetates more strongly retained on the column differs in absolute stereochemistry. These results are *not* in accord with the current model for "chiral recognition" on the chiral phase employed. The reliability of using elution order to assign the absolute stereochemistry of previously unassigned compounds is compared with other methods currently in use.

While many theoretical and empirical relations between chiroptical data and absolute stereochemistry are known, it is impossible to assign the absolute stereochemistry of many compounds from circular dichroism or optical rotatory dispersion measurements. The traditional solution of this dilemma is to transform the compound in question chemically into one that can be analyzed. However, alternative approaches have explored the uses of other physical properties that can be related to the absolute stereochemistry of an enantiomer. One measurement that has been used with some success is the elution order of diastereomers from a chromatographic column. The approach has been used with satisfactory results for amino acids[2a] and terpenoid acids.[2b] However, a significant number of exceptions to such correlations exist in the literature;[3] for example, Schooley and his associates[3a,b] have shown that the elution order differs for the amides from 1-(1-naphthyl)ethylamine and 3-methyl- and 3-ethyl-3-hydroxyglutaric acid, of the same absolute stereochemistry. Thus, an assignment made for the ethyl derivative based on the elution order of the methyl analogue would be in error. Despite these reports the approach is very attractive as the measurement is nondestructive and can be used to characterize nanogram quantities of material. Recently some theoretical rationalizations for the interactions between the substrate and the chiral phase have been proposed[4] that may improve the reliability of the method.

Pirkle and co-workers[5] have prepared a series of chiral phases bonded ionically to a silanized silica column that can separate a racemate without the necessity of converting the latter into a mixture of diastereomers. Their reports suggest that this approach may avoid the limitations observed with the elution order of diastereomers. These investigators also proposed a theoretical model that was employed in designing these columns. So that the "chiral recognition" needed for separation could be achieved, the

[†] This paper is dedicated to Dr. Ulrich Weiss on the occasion of his 75th birthday.

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(4) G. Helmchen, H. Völter, and W. Schühle, *Tetrahedron* Lett., 1417–1420 (1977).

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Table I. Elution Order and Absolute Stereochemistry of Acyclic Alkylarylcarbinols and Their Acetates[a]

compd	X = H		enantiomer retained	X = Ac		enantiomer retained
	α	k'		α	k'	
1a	1.03	8.0	*R*	1.11	1.1	*S*
1b	1.04	7.0	*R*	1.16	1.1	*S*
1c	1.04	5.4	*R*	1.16	0.94	*S*
1d	1.05	4.1	*R*	1.20	0.98	*S*
1e	1.07	2.2	*R*	1.35	1.1	*S*
1f	1.02	13	*S*	1.00	0.63	
1g	1.07	24	*S*	1.00	3.3	
1h	1.02	9.9	*R*	1.08	1.9	*S*
1i	1.03	26	*R*	1.07	7.3	*S*
1j	1.05	44	*R*	1.08	9.9	*S*
1k	1.00	19		1.00	3.5	
2a	1.03	9.1	*R*	1.14	1.3	*S*
2b	1.00	47		1.05	5.0	
2c	1.02	21		1.12	2.8	
2d	1.06	7.1	*R*	1.18	0.99	*S*
3	1.07	7.5	*S*	1.00	2.6	
4	1.03	23	*R*	1.32	2.9	*S*
5	1.08	28	*R*	1.30	3.3	*S*
6	1.08	75	*R*	1.20	9.6	*S*
7	1.00	12		1.00	2.9	
8	1.00	11		1.04	1.0	*S*

[a] The solvent mixture was 0.5% isopropyl alcohol in hexane. α is defined as retention volume of the second peak less the dead volume divided by the retention volume of the first peak less the dead volume. k' = (retention volume of the first peak)/(column volume).

chiral phase was designed to interact with the substrate via three different interactions, i.e., a π-donor–acceptor interaction, a hydrogen bond, and a less-well-defined van der Waals interaction. Therefore, the observation that these columns do resolve a variety of racemic compounds was taken as supporting Pirkle's analysis. In our studies of the microbial reduction of aromatic ketones[6] and of enantioselective microbially mediated hydrolyses[7] we wished to utilize the ability of an enzyme to produce chiral products and to facilitate enantioselective reactions. The compounds employed in our studies were acyclic and cyclic substituted benzylic alcohols, the configurations of many of which had been assigned previously. The separation of some substituted benzylic alcohols had been reported by Pirkle et al.; however, the absolute stereochemistry of the enantiomer more strongly retained on the column had been established in only a few cases.

The most direct and critical test of the validity of using elution orders to assign absolute stereochemistry is to examine a variety of related compounds of defined configuration and to compare predictions with observations. Since Pirkle et al.[5a] had proposed some bonding schemes and/or a theoretical model to account for the observed separation, we have also examined the logical consequences of these models. An unfortunate typographical error that specified H for both H and OH in Pirkle et al.'s tabulation[5a] left some doubt as to the configuration of the enantiomer most rapidly eluted (first peak). The column used in this study was (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine ionically bonded to a γ-aminopropyl-silanized silica column, as described by Pirkle et al.;[5a] it is commercially available from the Regis Chemical Co.

Results and Discussion

The chromatographic behavior of a series of substituted benzylic alcohols and their corresponding acetates is summarized in Table I. Inspection of this table shows that the configuration of the enantiomer (alcohol) eluted as the second peak (i.e., more strongly retained by the column than its antipode) is as shown for **14a**. Where the alcohols listed in Table I are identical with those described by Pirkle et al., the data agree with only small differences in the α values. The α value, or separation factor, is defined as the retention volume of the second peak less the dead volume divided by retention volume of the first peak less the dead volume.

In probing the scope and limitations of the relation of elution order and absolute stereochemistry utilizing this chiral phase, we have varied the structures of the carbinols: first, the size and nature of the aromatic moiety, then the size and electronegativity of the R group, and finally the importance of hydrogen-bonding sites. The effect of variations in the size and nature of the aromatic ring can be seen from a comparison of α values for **1a**, **2a**, **2d**, and **4–8** (Chart I). It is apparent that larger separations occur for polycyclic aromatics in comparison with monocyclic aromatics. Simple heterocyclics (**7** and **8**) form weaker complexes and are not resolved. Similar comparisons can be made from Pirkle's data,[5d] which also show that α values for **1f**, **15a**, **15b**, and **15c** (1.06, 1.08, 1.33, and 1.43) increase in an analogous manner. The data therefore demonstrate that π-donor–acceptor interactions are important in any bonding scheme meant to account for the observed separations. This is entirely consistent with the Pirkle chiral recognition model. Examination of the second variable, the size and electronegativity of the R group, showed that changes in R produced smaller changes in the α values (1.02–1.07). The relative insensitivity of the elution order and α values to these changes is consistent with the small differences that would be associated with their van der Waals interactions with the chiral phase. The consistency of the elution order is critical, as it establishes the reliability of the method. The variation in R from CH_3 to $C(CH_3)_3$, CF_3, or CO_2Me constitutes a more severe test than that employed in relating the elution order of a series of diastereomeric amides of isoprenoic acids and α-methyl-*p*-nitrobenzylamine.[4] Regardless of the nature of the aromatic substituent or the R group, with the exception of **1i** and **1j**, the absolute stereochemistry of the enan-

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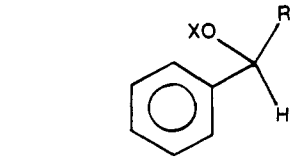
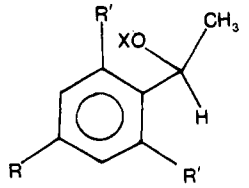
(7) K. Kawai, M. Imuta, and H. Ziffer, *Tetrahedron Lett.*, **22**, 2527–2530 (1981).

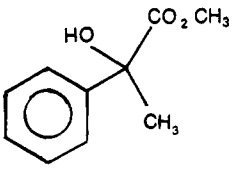
Chart I



1a, R = CH_3
b, R = C_2H_5
c, R = n-C_3H_7
d, R = i-C_3H_7
e, R = t-C_4H_9
f, R = CF_3
g, R = CO_2CH_3
h, R = $CH_2(C_6H_5)$
i, R = $CO(C_6H_5)$
j, R = CO-p-$CH_3C_6H_4$
k, R = $C{\equiv}CCH_3$



2a, R = CH_3; R′ = H
b, R = NO_2; R′ = H
c, R = OCH_3; R′ = H
d, R = R′ = CH_3



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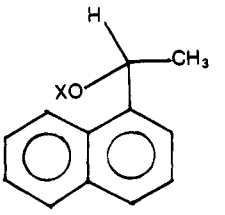

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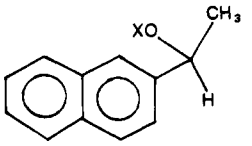

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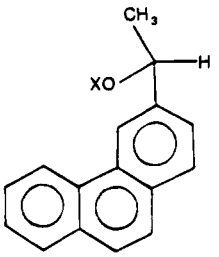

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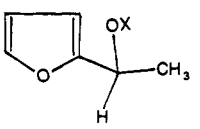

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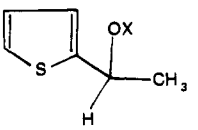

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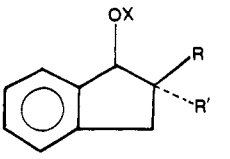
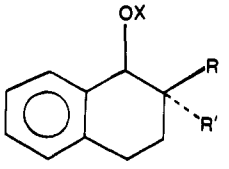
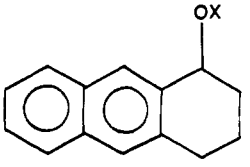


9a, R = R′ = H
b, R = CH_3; R′ = H
c, R = H; R′ = CH_3
d, R = R′ = CH_3
e, R = Br; R′ = H
f, R = H; R′ = Br
g, R = Cl; R′ = H
h, R = H; R′ = Cl



10a, R = R′ = H
b, R = CH_3; R′ = H
c, R = H; R′ = CH_3
d, R = R′ = CH_3
e, R = Br; R′ = H
f, R = H; R′ = Br
g, R = Cl; R′ = H
h, R = H; R′ = Cl



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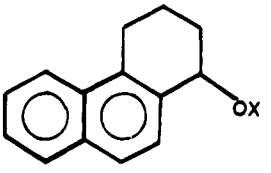

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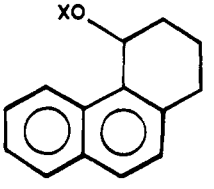

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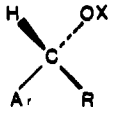
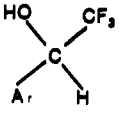
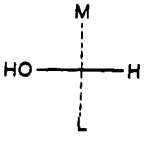


14a, X = H
b, X = $COCH_3$



15a, Ar = 1-naphthyl
b, Ar = 9-anthranyl
c, Ar = 9-(10-CH_3)-anthranyl



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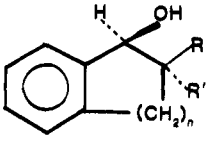

17, n = 1 or 2

tiomer preferentially retained (second peak) by the column was that given by **14a**.

The configurations of the enantiomers of **1i** and **1j** preferentially retained on this colum are not the same as that of **1a** and the other substituted benzylic alcohols. The observation that both benzoins and their acetates show different elution orders suggests that the relative importance of some unknown factors has changed. The factor(s) is unknown and perplexing since these compounds are remarkably similar to **1g** or **1h**, which behave like the other alkylarylcarbinols. The factors may be related to the presence of a second aromatic ring capable of complexing with the π acid of the chiral phase. However, compound **1h** also has a second aromatic ring, and its presence does not alter the standard elution order.

Two hydrogen bonds were shown in Pirkle's model and assumed to be important for "chiral recognition",[5] one between the OH of the substrate and the carboxylate of the chiral phase and the second between the methine hydrogen of the substrate and the amide carbonyl of the chiral phase. The simplest and most direct test of the importance of these bonds was effected by preventing their formation. For assessment of the role, if any, of the first type of H bond, the alcohols were converted to acetates, and their chromatographic behavior was examined (see Table I), while the importance of the carbinyl hydrogen bond was evaluated by examining compound **3**, where the critical hydrogen has been replaced by a methyl group. Much to our surprise, the racemic acetates were more completely resolved, i.e., larger α values were obtained than those for the corresponding alcohols. The elution pattern *differed* from that of the alcohols; the enantiomer shown in **14b** was now the first peak eluted from the column. One important consequence of this observation is that in at least one case, compound **8**, it was possible to resolve the acetate, whereas the alcohol was eluted as a single peak. Thus, if one wanted to use this chiral phase to separate useful quantities of these compounds, it would be best to work with the acetates instead of the alcohols. We also examined the elution order of one benzoate **1a** (X = Bz),

Table II. Elution Order and Absolute Stereochemistry of Substituted 1-Indanols, 1-Tetralols, and Their Acetates[a]

compd	X = H		config at carbinol C of enantiomer retained	X = OAc		config at carbinol C of enantiomer retained
	α	k'		α	k'	
9a	1.00	5.3		1.00	1.9	
9b	1.03	7.2	*S*	1.00	0.96	
9c	1.00	10		1.00	1.0	
9d	1.02	6.5	*S*	1.00	0.77	
9e	1.00	6.1		1.00	1.5	
9f	1.00	17		1.00	1.5	
9g	1.00	6.2		1.00	1.5	
9h	1.00	17		1.00	1.5	
10a	1.00	12		1.00	1.9	
10b	1.03	5.6	*S*	1.00	1.9	
10c	1.00	7.8		1.00	1.2	
10d	1.02	4.4	*S*	1.00	1.6	
10e	1.03	7.8	*R*	1.00	1.7	
10f	1.03	9.7	*R*	1.00	1.7	
10g	1.03	8.3	*R*	1.00	1.7	
10h	1.02	9.3	*R*	1.00	1.8	
11	1.00	50		1.00	5.3	
12	1.00	44		1.00	5.2	
13	1.15	20	*S*	1.02	3.4	*R*

[a] The solvent system was 0.5% isopropyl alcohol in hexane. α is defined as retention volume of the second peak less the dead volume divided by the retention volume of the first peak less the dead volume. k' = (retention volume of the first peak)/(column volume).

and found that the α value (α = 1.10, k' = 1.3) was, within experimental error, equal to that of the acetate and the elution order was also the same as that for the acetate.

Inspection of the α values of **1a** and its para-substituted derivatives **2a–c** shows that the α values cluster between 1.02 and 1.03; α for **2b** is 1.00 (i.e., no resolution). The α values of the acetates, however, vary over a greater range (1.05–1.14); the values for **2a** and **2c** are larger than that for **1a**, while **2b**, which now is resolved, has a smaller α value than **1a**. The results indicate that π-donor–acceptor bonding is also important in the interaction of the ester with the chiral phase.

An unexpected result was obtained for **3**, in that the α value was essentially identical with that observed for its analogue **1g**. These observations suggest that the groups required to form the hydrogen bonds believed necessary for chiral recognition actually reduced the separation of enantiomers. While the strategy employed in designing the column was effective in producing one that separates a variety of alkylarylcarbinols or their acetates in a consistent manner, the mechanism or theoretical rationalization of these results lies elsewhere. However, the relative retention times of enantiomers can be used to assign absolute stereochemistries by analogy (bearing in mind the results from **1i** and **1j**) in much the same way as other empirical observations are, and continue to be, made from chiroptical data.

In addition to the substituted benzylic alcohols in Table I we have examined two series of substituted benzocycloalkenols: the first group consists of 1-indanol, 2-substituted 1-indanols, and the corresponding acetates, while the second group consists of 1-tetralol, some 2-substituted 1-tetralols, and the corresponding acetates. The results from these studies are summarized in Table II. Inspection of this table shows that a greater number of the 2-substituted 1-tetralols were resolved than the corresponding 1-indanol derivatives. In each series the absolute stereochemistry of the enantiomer more strongly retained (second peak) on the column is that shown for **17**. Note that the absolute stereochemistry of the enantiomer preferentially retained in the cyclic series is *not* the same as that retained in the acyclic series. In contrast to the acetates in Table I, the α values of the acetates in Table II were smaller than those of the corresponding alcohols. Thus, the factors dominating the relative retention volumes are consistent within each series, but the molecular interactions that determine the elution order within a series are not obvious.

Since we encountered two examples (substituted benzylic alcohols) in which the enantiomer shown in **14a** was not eluted as the first peak (not preferentially retained) and some benzocycloalkenols were not resolved on the column, it appeared important to compare the usefulness and reliability of employing elution order for assigning absolute stereochemistry with the most commonly used general chemical method, that by Horeau.[8,9] For the acyclic carbinols listed in Table I only compound **1i** and **1j** violate the usual relation between elution order and absolute stereochemistry. Unfortunately, we have no information as to whether the absolute stereochemistry of these compounds can be correctly assigned by using Horeau's method. We have examined the ability of the chiral phase to resolve one tertiary alcohol, **3**. The configuration of the enantiomer more strongly retained is that shown. Horeau's method has not been used for tertiary alcohols, and therefore the HPLC method may be the only one available for this group of compounds. While it is possible to compare the absolute stereochemistry of the enantiomer of **3** that is preferentially retained on the column with that for **1a** and **1g** and come to a conclusion as to the effect of replacing a hydrogen with an alkyl group, we believe it is premature to do so now.

The absolute stereochemistry of the benzocycloalkenols resolved by the chiral phase are all correctly assigned from their elution order. Information on the sign of the specific rotation of 2-phenylbutyric acid formed in Horeau's method is available in the literature for a number of cyclic carbinols. In order to use this information to assign absolute stereochemistry, it is necessary to assign the relative

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(9) For a review of a number of methods of assigning absolute stereochemistry see J. C. Fiaud and H. B. Kagan in "Stereochemistry, Fundamentals and Methods", Vol. 2, pp 2–126, George Thieme, Stuttgart, 1977.

sizes of the two substituents on the carbinol carbon. In the case of the acyclic compounds an aromatic moiety is *always* larger than an alkyl group.[9] However, for the cyclic carbinols the situation is more complex.[11] While a fused aromatic ring is larger than a methylene group for most benzocycloalkenols,[10] there are exceptions, e.g., the configuration of **13** has been incorrectly assigned[13,6a] by assuming that the methylene is effectively smaller than the fused naphtho moiety. The presence of one or more substituents on the methylene group flanking the carbinol carbon (compounds **9b–d** and **10b–d**) requires that the substituted methylene should be treated as the larger substituent.[12] While this comparison of the use of elution order and Horeau's method does not prove the superiority of either method, each procedure clearly has some advantages. It therefore appears reasonable that if one utilizes data from both methods to assign the absolute stereochemistry of an alcohol, the reliability of the assignment is greatly increased.

An examination of molecular models of the cyclic and acyclic esters did not reveal how one can rationalize one elution order in the acyclic series and another one in the cyclic series by using the same interaction between substrate and chiral phase in the two series. It should also be mentioned that preliminary results for the seven-membered ring benzosuberol suggest that the *S* enantiomer is *not* retained more strongly on the column[14] as occurs for the substituted 1-tetralols and 1-indanols described in Table II. Therefore, at present, *the relation that has been observed between elution order and absolute stereochemistry for five- and six-membered benzocycloalkenols should not be used for larger or smaller cycloalkenols.*

Table III. Summary of the Absolute Stereochemistry of the Alcohols Used in This Study

compd	abs stereochem	$[\alpha]^{25}_D$, deg	ref
1a	*S*	−57 (*c* 5.12, $CHCl_3$)	6, 15
1b	*R*	+16.8 (*c* 1.52, $CHCl_3$)	15
1c	*R*	+24.8 (*c* 1.29, $CHCl_3$)	15
1d	*R*	+9.8 (*c* 0.13, $CHCl_3$)	15
1e	*S*	−15.5 (*c* 1.65, $CHCl_3$)	15
1f	*R*	−5.5 (*c* 5.26, EtOH)	16
1g	*S*	+99.1 (*c* 2.25, $CHCl_3$)	17
1h	*S*	+3.7 (*c* 0.58, EtOH)	18
1i	*S*	+48.5 (*c* 0.91, acetone)	19
1j	*S*	+83.1 (*c* 3.08, EtOH)	20
2a	*R*	+42.1 (*c* 2.94, $CHCl_3$)	21
2b			
2c			
2d	*R*	+52.5 (*c* 1.1, $CHCl_3$)	22
3	*S*	+28.5 (*c* 1.2, EtOH)	23
4	*S*	−54.1 (*c* 3.34, $CHCl_3$)	16
5	*R*	+34.9 (*c* 1.29, $CHCl_3$)	22
6	*R*	+27.1 (*c* 2.4, $CHCl_3$)	24
8	*S*	−23.3 (*c* 1.5, $CHCl_3$)	25
9a	*S*	+22.6 (*c* 4.2, $CHCl_3$)	6a
9b	1*R*, 2*R*		26
9c	1*S*, 2*R*	−3.8 (*c* 1.27, $CHCl_3$)	27
9d	*S*	+15.7 (*c* 2.2, $CHCl_3$)	28
9e	1*R*, 2*S*		6b
9f	1*S*, 2*S*	+29.0 (*c* 0.53, EtOH)	29
9g	1*S*, 2*R*		26
9h	1*R*, 2*R*	+18.9 (*c* 3.76, $CHCl_3$)	30
10a	*S*	+26.8 (*c* 2.3, $CHCl_3$)	6a
10b	1*R*, 2*R*	−44 (*c* 1.1, $CHCl_3$)	6a
10c	1*S*, 2*R*	+24 (*c* 2.46, $CHCl_3$)	27
10d	*S*	+24.8 (*c* 1.5, $CHCl_3$)	28
10e	1*S*, 2*R*	−1.0 (*c* 1.9, $CHCl_3$)	31
10f	1*R*, 2*R*	+7.76 (*c* 2.1, $CHCl_3$)	32
10g	1*S*, 2*R*		26
10h	1*R*, 2*R*	+18.9 (*c* 2.4, $CHCl_3$)	33
11	*S*	+138 (*c* 0.8, $CHCl_3$)	6a
12	*S*	−59 (*c* 4.9, acetone)	6a
13	*S*	−19.5 (acetone)	6a

As an interesting aside we compared the average retention times of pairs of cis and trans 2-substituted alcohols in the 1-indanol and 1-tetralol series; the cis isomer in each case is eluted more rapidly than the corresponding trans-substituted compound (see Table II). While this information is not particularly helpful for substituted 1-tetralols, it may be in the 1-indanol series, where it is very difficult to assign stereochemistry solely on the basis of an analysis of coupling constants. Relative retention times of a Pirkle column allow for tentative assignments of geometric isomers. In addition it should be mentioned that it was possible to separate easily some geometric isomers that were very poorly separated on silica columns.

In summary, these studies have shown that the elution order of alkylaryl alcohols, their acetates, five- and six-membered benzocycloalkenols, and their corresponding acetates is dependent upon their absolute stereochemistry. The dependence differs for each class or group of compounds in a consistent manner (with two exceptions) and therefore can be used to assign tentatively the configuration about the carbinol carbon. These studies also show that the bonding schemes proposed by Pirkle and his associates do not account for the elution order and as more data are accumulated an alternative model may emerge. However, at present this HPLC method appears to be

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(31) Obtained by the sequence described in ref 26.
(32) A sample of the acetate was reduced with $LiAlH_4$ in refluxing THF to (1*S*)-tetralol.
(33) Reaction sequence in ref 32.

sufficiently reliable to provide an additional method that should be used increasingly in conjunction with existing general procedures to assign the configuration of compounds similar to those described here.

Experimental Section

The compounds used in this study were prepared by literature methods. Optically active samples of the alcohols were prepared by resolution (3), reduction of the corresponding ketone using *Cryptococcus macerans*, or by enantioselective hydrolysis of the corresponding acetates using *Rhizopus nigricans*. The ^{1}H NMR spectra (220 MHz) of the optically active samples were identical with authentic racemic materials. Specific rotations were determined by using a Perkin-Elmer 241MC polarimeter. The HPLC measurements were made by using an apparatus constructed from an Altex injector, an Altex pump Model 110A, a Gilson variable-wavelength detector, and a chiral "Pirkle" column (Hi-Chrom reversible column) purchased from the Regis Chemical Co., Morton Grove, IL 60053. The column is (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine ionically bonded to a γ-aminopropyl-silanized silica column.[5a] The alcohols were converted to the corresponding acetates by acetic anhydride/pyridine by using standard techniques.

Registry No. **1a** (X = H; isomer 1), 1517-69-7; **1a** (X = H; isomer 2), 1445-91-6; **1a** (X = Ac; isomer 1), 16197-92-5; **1a** (X = Ac; isomer 2), 16197-93-6; **1b** (X = H; isomer 1), 1565-74-8; **1b** (X = H; isomer 2), 613-87-6; **1b** (X = Ac; isomer 1), 84275-44-5; **1b** (X = Ac; isomer 2), 83860-48-4; **1c** (X = H; isomer 1), 22144-60-1; **1c** (X = H; isomer 2), 22135-49-5; **1c** (X = Ac; isomer 1), 84194-64-9; **1c** (X = Ac; isomer 2), 84194-65-0; **1d** (X = H; isomer 1), 14898-86-3; **1d** (X = H; isomer 2), 34857-28-8; **1d** (X = Ac; isomer 1), 84194-66-1; **1d** (X = Ac; isomer 2), 84194-67-2; **1e** (X = H; isomer 1), 23439-91-0; **1e** (X = H; isomer 2), 24867-90-1; **1e** (X = Ac; isomer 1), 23439-90-9; **1e** (X = Ac; isomer 2), 84194-68-3; **1f** (X = H; isomer 1), 10531-50-7; **1f** (X = H; isomer 2), 340-06-7; **1f** (X = Ac), 84194-69-4; **1g** (X = H; isomer 1), 20698-91-3; **1g** (X = H; isomer 2), 21210-43-5; **1g** (X = Ac), 947-94-4; **1h** (X = H; isomer 1), 41822-67-7; **1h** (X = H; isomer 2), 5773-56-8; **1h** (X = Ac; isomer 1), 84194-70-7; **1i** (X = H; isomer 1), 5928-66-5; **1i** (X = H; isomer 2), 5928-67-6; **1i** (X = Ac; isomer 1), 84275-45-6; **1i** (X = Ac; isomer 2), 84275-46-7; **1j** (X = H; isomer 1), 84275-47-8; **1j** (X = H; isomer 2), 66768-23-8; **1j** (X = Ac; isomer 1), 84194-72-9; **1j** (X = Ac; isomer 2), 84194-73-0; **1k** (X = H), 4187-87-5; **1k** (X = Ac), 16169-88-3; **2a** (X = H; isomer 1), 42070-92-8; **2a** (X = H; isomer 2), 51154-54-2; **2a** (X = Ac; isomer 1), 84194-74-1; **2a** (X = Ac; isomer 2), 84194-75-2; **2b** (X = H), 6531-13-1; **2b** (X = Ac), 19759-27-4; **2c** (X = H), 3319-15-1; **2c** (X = Ac), 945-89-1; **2d** (X = H; isomer 1), 1517-71-1; **2d** (X = H; isomer 2), 2516-69-0; **2d** (X = Ac; isomer 1), 84194-76-3; **2d** (X = Ac; isomer 2), 84194-77-4; **3** (X = H; isomer 1), 13448-81-2; **3** (X = H; isomer 2), 13448-80-1; **3** (X = Ac), 55012-78-7; **4** (X = H; isomer 1), 42177-25-3; **4** (X = H; isomer 2), 15914-84-8; **4** (X = Ac; isomer 1), 16197-94-7; **4** (X = Ac; isomer 2), 16197-95-8; **5** (X = H; isomer 1), 52193-85-8; **5** (X = H; isomer 2), 27544-18-9; **5** (X = Ac; isomer 1), 84194-78-5; **5** (X = Ac; isomer 2), 84194-79-6; **6** (X = H; isomer 1), 84194-80-9; **6** (X = H; isomer 2), 84194-81-0; **6** (X = Ac; isomer 1), 84194-82-1; **6** (X = Ac; isomer 2), 84194-83-2; **7** (X = H), 4208-64-4; **7** (X = Ac), 22426-24-0; **8** (X = H), 2309-47-9; **8** (X = Ac; isomer 1), 84194-84-3; **8** (X = Ac; isomer 2), 84194-85-4; **9a** (X = H), 6351-10-6; **9a** (X = Ac), 26452-98-2; **9b** (X = H; isomer 1), 84275-48-9; **9b** (X = H; isomer 2), 57089-40-4; **9b/9c** (X = Ac), 58540-44-6; **9c** (X = H), 17496-18-3; **9d** (X = H; isomer 1), 24867-97-8; **9d** (X = H; isomer 2), 57018-62-9; **9d** (X = Ac), 54553-64-9; **9e/9f** (X = H), 5400-80-6; **9e/9f** (X = Ac), 84194-86-5; **9g/9h** (X = H), 67864-28-2; **9g/9h** (X = Ac), 84194-87-6; **10a** (X = H), 529-33-9; **10a** (X = Ac), 21503-12-8; **10b** (X = H; isomer 1), 38157-18-5; **10b** (X = H; isomer 2), 65941-81-3; **10b/10c** (X = Ac), 84194-88-7; **10c** (X = H), 32281-70-2; **10d** (X = H; isomer 1), 24867-99-0; **10d** (X = H; isomer 2), 84275-49-0; **10d** (X = Ac), 84194-89-8; **10e** (X = H; isomer 1), 84275-50-3; **10e** (X = H; isomer 2), 84275-51-4; **10e/10f** (X = Ac), 84194-90-1; **10f** (X = H; isomer 1), 79465-07-9; **10f** (X = H; isomer 2), 84275-52-5; **10g** (X = H; isomer 1), 84194-91-2; **10g** (X = H; isomer 2), 84194-92-3; **10g/10h** (X = Ac), 84194-93-4; **10h** (X = H; isomer 1), 84194-94-5; **10h** (X = H; isomer 2), 84194-95-6; **11** (X = H), 84194-96-7; **11** (X = Ac), 84194-97-8; **12** (X = H), 7508-20-5; **12** (X = Ac), 84194-98-9; **13** (X = H; isomer 1), 79465-08-0; **13** (X = H; isomer 2), 27549-85-5; **13** (X = Ac; isomer 1), 84275-53-6; **13** (X = Ac; isomer 2), 65915-66-4.

Ethylaluminum Dichloride Catalyzed Ene Reactions of Aldehydes with Nonnucleophilic Alkenes

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Ethylaluminum dichloride, which is a strong Lewis acid and a proton scavenger, catalyzes the ene reactions of aliphatic aldehydes with nonnucleophilic alkenes. Higher aldehydes give good yields of ene adducts with terminal alkenes. Formaldehyde gives good yields of adducts with electron-deficient alkenes. This reaction has been used for the synthesis of recifeiolide, ricinelaidic acid, and the insect pheromones (*E*,*E*)-8,10-dodecadienyl acetate and (*E*)-9,11-dodecadienyl acetate.

The ene reaction of carbonyl compounds with alkenes is a potentially valuable route to homoallylic alcohols.[1] With reactive, i.e., electron deficient, aldehydes such as chloral or methyl glyoxylate, these reactions can be carried out thermally at 100–200 °C. Formaldehyde reacts with alkenes at 180 °C, with optimal yields often being obtained when acetic acid–acetic anhydride is the solvent.[2] In the presence of acid, aldehydes and alkenes undergo the Prins reaction.[3] Ene-type adducts have been obtained with Lewis acid catalysis from formaldehyde and alkenes which can give a tertiary carbenium ion.[4]

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