Substituent Effects on Suspected Phenonium Ion Reactions

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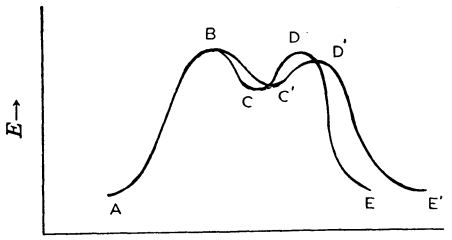
The stereochemistry of the various conversions in the 1,2-diphenyl-1-propyl system was measured as a function of aromatic substituent. For β-anisyl groups the reaction occurred with retention of configuration. For compounds with indifferent electron donating aryl groups, the conversions were stereoselective forming mostly *threo* product. For β-*p*-nitrophenyl groups the stereochemical course of the reaction was "racemization." The latter reactions were associated with the presence of open ions. In certain reactions, acetate products were formed in low yield with retention of configuration, irrespective of substituent. The kinetics of ethanolysis were consistent with (partial) bridged ion formation for the *threo* isomers and with extensive open ion formation for the *erythro* species.

The problem of the intermediacy of a phenonium ion species has occupied the attention of chemists for a considerable period.[1,2] In a sense, the question of whether or not a phenonium ion can exist has been answered by the direct spectral observation of Olah, Pittman, Namenworth, and Comisarow,[3] and in a related system, by Winstein and Baird.[4] The question remains whether the type of ion thus observed is similar to a solvolysis reaction intermediate.

The nature of the solvolysis intermediate has been inferred from stereochemical[5] and in other cases from kinetic data.[6] The inferences from stereochemical data are in actuality concerned with the relative rates of processes that give retention of configuration, (*e.g.* C→D→E of Scheme 1) and processes that give other stereochemical results (*e.g.* C′→D′→E′). These processes are sensitive not only to the nature of the intermediate (or intermediates) but also to the energy levels of the various possible transition states leading to products.[1c] Thus, product of a certain stereochemistry (*e.g.* E′) may not reflect the nature of the most stable intermediate (*e.g.* C), but merely the lowest energy pathway for conversion to products.

On the other hand, inferences from kinetic data depend on the relative energy levels A and B, and do not directly involve the intermediate C. The hope is that the energy level of B will parallel that of the first-formed intermediate C or C′. This expectation is perhaps reasonable if anchimeric assistance is present, that is where the β-aryl group pushes off the leaving group. Brown and co-workers[6,7] have advanced the existence of a large rate enhancement (over a standard compound) as the criterion for the presence of a phenonium ion intermediate. This criterion is not met in the solvolysis of 3-phenyl-2-butyl compounds, although certain β-anisyl substrates appear to fulfill this criterion.[6,7] However, in non-nucleophilic solvents such as trifluoroacetic acid, Nordlander and Deadman[8] have shown that ordinary β-phenyl substrates are indeed characterized by large rate enhancements. On the other hand, Lancelot and Schleyer believe that even a small rate enhancement may reflect the intermediacy of a bridged ion.[9]



Scheme 1.

The compounds of interest to this study are shown in Scheme 2. In these studies various of the groups Z were interposed. The question of interest is whether any evidence for participation by a β-aryl group can be detected, if the cationic center is stabilized by the effect of an α-aryl group. In a bicyclic system, Brown and co-workers have suggested that additional stabilization of a quite stable tertiary cation by participation would be unnecessary.[10] Winstein has questioned this conclusion.[11] The elegant tracer studies of Collins and Benjamin were discouraging in this regard, as there was no evidence for the existence of a bridged ion of the σ variety in the 1,2,2-triphenylethyl cation.[12] This work also showed that one must be cognizant of the fact that one of the prime pieces of evidence for participation, namely retention stereochemistry, may arise by other means. In this work, steric interference with the inversion pathway by a β-aryl group was

1) (a) H. Tanida, *Accounts Chem. Res.*, **1**, 239 (1968). (b) B. Capon, *Quart. Rev.* (London), **12**, 173 (1958). (c) B. Capon, M. Perkins, and C. Rees, "Organic Reaction Mechanisms, 1966," Interscience Publishers, New York, N. Y., (1965).

2) J. L. Coke, F. McFarlane, M. Mourning, and M. Jones, *J. Amer. Chem. Soc.*, **91**, 1154 (1969) and references cited therein.

3) G. Olah, C. Pittman, E. Namenworth, and M. Comisarow, *ibid.*, **88**, 5571 (1966); **89**, 711 (1967).

4) R. Baird, and S. Winstein, *ibid.*, **85**, 567 (1963); see also M. Brookhart, F. Anet, D. J. Cram, and S. Winstein, *ibid.*, **88**, 5659 (1966).

5) D. J. Cram, *ibid.*, **86**, 3767 (1964). This work presents the case for the phenonium ion.

6) H. C. Brown, K. Morgan, and F. Chloupek, *ibid.*, **87**, 2137 (1965). This work presents the opposing case.

7) H. C. Brown and C. Kim, *ibid.*, **90**, 2082 (1968); *ibid.*, **91**, 4289 (1969).

8) J. E. Nordlander and W. Deadman, *ibid.*, **90**, 1590 (1968).

9) C. J. Lancelot and P. Schleyer, *ibid.*, **91**, 4294 (1969).

10) H. C. Brown, F. Chloupek, and M.-H. Rei, *ibid.*, **86**, 1246 (1964).

11) S. Winstein, *ibid.*, **87**, 381 (1965).

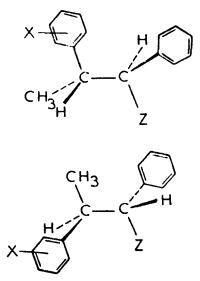
12) C. V. Collins and B. M. Benjamin, "Advances in Physical-Organic Chemistry," Vol. 2, Academic Press, London, England, 1964, p. 1, and references cited therein. See also W. B. Smith and M. Schowalter, *J. Amer. Chem. Soc.*, **86**, 4136 (1964).

Table 1. Activation parameters and first order rate constants for the solvolysis of **1**, in 80% aqueous[a] ethanol

	k, sec^{-1} ($\times 10^4$)								
Temp.	34.9°C	45.0°C	55.0°C	62.5°C	70.0°C	75.0°C	k_{rel}[b]	ΔH^* (kcal)[c]	ΔS^* (e.u.)[d]
Threo **1**									
a *p*-CH_3O	4.06±0.04	10.5±0.4	25.6±0.4	52.4±0.9			390	18[e]	−15
b *o*-CH_3O	6.50±0.01	18.6±0.1	52±4				780	20	− 8
c H			2.05±0.12	4.19±0.01	8.34±0.2	11.8±0.05	31	21	−11
d *p*-NO_2			0.194±0.007	0.416±0.004	0.88±0.04	1.39±0.01	2.9	22	−14
Erythro **1**									
a *p*-CH_3O			0.926±0.013	2.01±0.07	4.34±0.01	7.11±0.04	14	22	− 9
c H			0.313±0.004	0.69±0.013	1.41±0.03	2.24±0.01	4.7	22[e]	−14
d *p*-Cl			0.159±0.006	0.362±0.001	0.805±0.068	1.20±0.07	2.4	22[e]	−12
e *p*-NO_2			0.0664±0.0003	0.167±0.006	0.352±0.007	0.541±0.004	1	21[e]	−19

a) Actual composition 79.6% by weight.
b) At 55°C.
c) The activation enthalpies are considered good to ±1 kcal.
d) The activation entropies are considered good to 4 ±e.u.
e) Taken from the most linear portion of a curved Arrhenius plot.

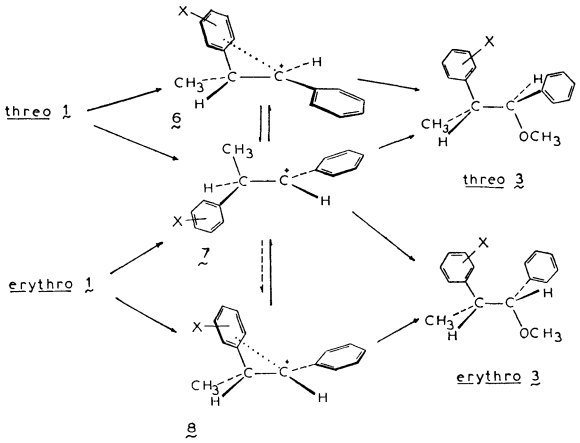
postulated.[13] On the other hand, the early work of Cram and Elhafez[14] on the 1,2-diphenyl-1-propyl system was interpreted in terms of β-aryl participation, although the nature of the intermediates perhaps needs to be recast in more modern terms.[14,15] In still other work, retention has been observed in solvolyses forming several types of α-aryl cations, in which no possibility of participation exists.[16-19] The leaving group may lead in the attacking solvent fragment producing retention, but, generally speaking, the mechanism of these processes requires further elaboration.



Z	X
1 Br	**a** *p*-CH_3O
2 OH	**b** *o*-CH_3O
3 OCH_3	**c** H
4 OAc	**d** *p*-Cl
5 Cl	**e** *p*-NO_2

Scheme 2.

The solvolysis data are listed in Table 1. These data will be discussed in terms of the mechanism shown in Scheme 3, which is similar to that originally proposed by Cram and Elhafez.[14] The greater reactivity of the *threo* compounds could be explained by the greater stability of the bridged intermediate **6** than the analogous intermediate, **8**, which results from *erythro* **1**. The latter intermediate would be destabilized



Scheme 3.

by an unfavorable phenyl-methyl interaction. However, Cram and Elhafez also showed that the *threo* **1c** is more reactive than *erythro* **1c** in S_N2 reactions.[14,20] Thus, a sizable *threo*/*erythro* rate ratio would be expected for both β-aryl participation (k_Δ) and direct solvent attack (k_s).[2,9] Of more significance is the fact that a large *threo*/*erythro* ratio is observed for the *p*-methoxy compounds (*ca.* 28). Participation, if any, should be facilitated by this substituent.[9] Conversely, the *threo*/*erythro* ratio is minimum for the *p*-nitro compounds (2.9), which, most likely, form open ions.[21] The rate differences between *erythro* and *threo* isomers cannot be ascribed to differences in ground state energies. Equilibration of either pure *threo* or pure *erythro* **1c** produced 52±5% *erythro* and 48±5% *threo* **1c**, indicative of very similar stabilities.[20]

The absolute rates of reaction are also largest for the *p*-methoxy compounds and minimum for the *p*-nitro compounds. For the *threo* isomers, a linear ρ—σ^+ dependence is observed, in which ρ is −1.3. This value is rather low compared to certain model compounds which solvolyze by anchimerically assisted

13) B. Murr and C. Santiago, *J. Amer. Chem. Soc.*, **88**, 1127 (1966).
14) D. J. Cram and F. Abd Elhafez, *ibid.*, **76**, 30 (1954); *ibid.*, **75**, 339 (1953); **74**, 5828 (1952); **74**, 5825 (1952).
15) H. C. Brown, R. Bernheimer, C. Kim, and S. Schepelle, *ibid.*, **89**, 370 (1967).
16) H. L. Goering and S. Change, *Tetrahedron Lett.*, **1965**, 3107.
17) P. A. Levene, and A. Rothen, *Science*, **87**, 510 (1938).
18) K. M. Okamoto, M. Hayashi, and H. Shingu, This Bulletin, **39**, 408 (1966).
19) See however, W. Doering, and H. Zeiss, *J. Amer. Chem. Soc.*, **75**, 4733 (1953).
20) D. J. Cram, C. DePuy, and F. Greene, *ibid.*, **78**, 790 (1956).
21) D. J. Cram and J. Thompson, *ibid.*, **89**, 6762 (1967).

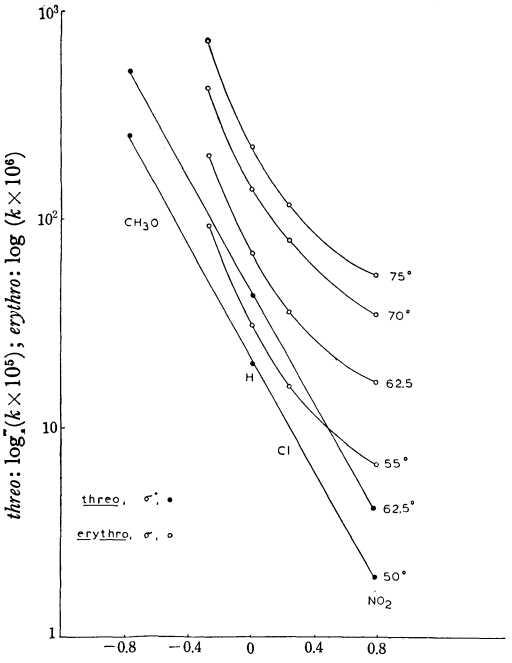


Fig. 1. Plots of log k *vs.* Hammett σ parameters for the *erythro* isomers, and Okamoto-Brown σ^+ parameters for the *threo* isomers.

paths (ρ near -3).[9,22,23]

For the *erythro* isomers, curved ρ—σ plots are observed (Fig. 1), which, in other cases, have been ascribed to a change in mechanism from the k_s route to the k_Δ route as the electron donating character of the substituent progressively improves.[9] However, for the *p*-nitro and *p*-chloro compounds, the ΔS^* values are generally higher than the value given by Winstein as indicative of nucleophilic assistance to ionization by solvent (-18 e.u.).[24] The cation, which is stabilized by the α-aryl group, requires less solvent stabilization.

Table 2. PER CENT *threo* OF AN *erythro*/*threo* MIXTURE IN THE REACTION **1**→**3** AT 56±3°C IN 90% AQUEOUS METHANOL

			% *Threo* **3**[e]
Thero	**1 a**	*p*-CH_3O	(89)[a]
	1 b	*o*-CH_3O	*ca.* 100[b]
	1 c	H	73
	1 e	*p*-NO_2[c]	43
Erythro	**1 a**	*p*-CH_3O	35
	1 c	H	76[d]
	1 d	*p*-Cl	62
	1 e	*p*-NO_2	55

a) Total *threo* product (80% ether **3** plus 20% alcohol **2**).
b) No *erythro* product was observable.
c) Uncorrected for *ca.* 10% *erythro* inpurity.
d) At 75°C, 68% *threo* **3c** was observed.
e) The overall yield is 80±5% ethers **3** and 20% alcohols **2**.

The product ratios in ethanol were difficult to establish by NMR due to overlapping of peaks. The stereochemistry of the solvolysis in 90% aqueous methanol was therefore determined, and the results are recorded in Table 2. The stereochemistry in methanol and in ethanol was qualitatively similar, however. The data shown in Table 2 were somewhat temperature dependent with lower stereoselectivity observed at higher temperatures.

The data in Tables 1 and 2 indicate a fairly good correlation between solvolysis rate and stereochemistry. For the anisyl compounds, which solvolyze the most rapidly, a high degree of retention is observed for the *threo* isomers, and somewhat less retention is observed for the *erythro* compound. In the latter case, formation of the open ion **7** is quite important due to steric strains present in the bridged ion **8**. We agree with Brown that π bridged intermediates,[15,24b] such as **6** and **8**, deserve serious consideration due to the absence of strong rate accelerations and the absence of high stereospecificity.

For the *p*-nitro compounds, which are unreactive, a slight overall inversion of configuration is noted, but the product ratios are close to the equilibrium *threo*/*erythro* ratio. The *erythro* unsubstituted and *p*-chloro compounds give predominately *threo* products. The bridged ion **8** (which would yield *erythro* product) is unimportant because the weak stabilizing character of the β-aryl group is not able to overcome steric repulsions. The predominate pathway is thought to be the formation of the open ion **7**, which forms products of mixed stereochemistry. Internal rotation may also occur in **7**, with concurrent formation of **6**, which yields *threo* products.

Table 3 lists the bromide **1** to methyl ether **3**, and the bromide to acetate **4** conversions catalyzed by silver acetate. These conversions contrast the effects of acetic acid and the more nucleophilic solvent, methanol. Compared to the data in Table 2, a greater tendency for inversion is noted for these silver catalyzed reactions in methanol, particularly for electron withdrawing substituents. The effect of temperature for these conversions is quite pronounced. For example, *erythro* **1c** gave 86% *threo* methyl ether **3c** at room temperature, and 78% at 55°C. On the other hand, *erythro* **1a** gave 33% *threo* **3a** at 3°C, 40% at 34°C, and 54% at 55°C. Thus, the stereochemistry changed from retention to slight inversion.[17]

The loss of stereoselectivity[17] with increasing temperature is interpreted in terms of the greater importance of the open ion **7** (and possibly also of **6**). In acetic acid the **8**→**7**⇌**6** equilibration sequence also has a greater chance of becoming established, due to lower solvent nucleophilicity, and indeed *erythro* **1a** forms predominately *threo* products.

22) R. Heck and S. Winstein, *J. Amer. Chem. Soc.*, **79**, 3432 (1957).
23) See also V. J. Shiner, Jr., W. Buddenbaum, B. Murr, and G. Lamaty, *ibid.*, **90**, 418 (1968).
24) (a) E. F. Jenny and S. Winstein, *Helv. Chim. Acta*, **41**, 897 (1958). (b) S. Winstein, C. Lindegren, H. Marshall, and L. Ingraham, *ibid.*, **75**, 147 (1953). (c) See also R. Heppolette, and R. F. Robinson, *Can. J. Chem.*, **44**, 677 (1966).
25) The activation entropies seem more variable than originally found by Winstein and co-workers, although the k_Δ route uniformly gives higher ΔS^* values than the k_s route. See Ref. 9 and M. G. Jones, and J. L. Coke, *ibid.*, **91**, 4285 (1969).
26) G. Frisone and E. Thornton, *ibid.*, **90**, 1211 (1968) and references cited therein.

Table 3. Overall yield and stereochemical purity of silver acetate catalyzed conversions 1→3 and 1→4 in methanol and acetic acid at 34±4°C

	X		Methanol solvent: % Ether 3 (% *Threo* 3)[a]	Methanol solvent: % Acetate 4 (% *Threo* 4)[a]	Acetic acid solvent (% *Threo* acetate 4)[a]
Thero	**1a**	*p*-CH_3O	92 (91)	8 (>90)	(92)
	1c	H	91 (52)	9 (>90)	(74)
	1e	*p*-NO_2	89 (36)	11 (74)	(52)
Erythro	**1a**	*p*-CH_3O	92 (40)	8 (10)	(62)
	1c	H	91 (86)	9 (43)	(70)
	1d	*p*-Cl	87 (84)	13 (30)	(63)
	1e	*p*-NO_2	93 (70)	7 (30)	(48)

a) % *Threo* of an *erythro/threo* mixture.

In methanol, small amounts of acetates **4** are also formed in addition to the ethers **3**. Although the stereochemistry of **4** is difficult to measure accurately by NMR, predominate retention stereochemistry is evident. The acetates **4** formed from reactions in methanol may result from a four-center type of mechanism.[18]

In order to show the generality of the stereochemical changes, the conversions of the alcohols **2** to the chlorides **5** were studied. The reaction mixture was 4:1 acetic acid and concentrated hydrochloric acid. The products were not stable under the reaction conditions. Epimerization and olefin formation were evident upon long reaction times. The data listed in Table 4 were determined by trial and error variation of reaction times, in an attempt to achieve minimum olefin formation and maximum stereoselectivity. The stereochemistry of the chlorides is rather similar to that of the acetates in Table 3 and the ethers in Table 2. No conclusion is drawn from the acetate data in Table 4 due to the possibilities for Fischer esterification of the parent alcohol.

In conclusion, the stereochemical results are a function of the intrinsic characteristics of the molecules, and not functions of the reaction conditions except for certain minor variations as discussed above. We feel there is definite evidence for participation by β-anisyl groups (rapid solvolysis and generally retention stereochemistry). Participation by the β-phenyl group may be of importance through an ion such as **6**, but no evidence exists for the presence of the less stable ion **8**. While it is true that the α-aryl group reduces the demand for β-aryl participation, the necessity for solvent stabilization is also reduced, which gives the phenonium ion more of a chance.

The possibility exists that the predominate *threo* products, which occur from substrates **c** and **d**, result from a simple lower energy pathway from the open ion. However, the trend of the stereochemical data, as substituent progressively becomes more electron donating, is precisely what one would expect on the basis of reaction through a π-phenonium ion. These substituents should not affect the reaction pathways available to an open ion. As discussed in the Introduction, one cannot state that the bridged ion is more stable than the open ion, since relative product yields reflect the relative energies of the intermediate ions and the relative transition state energies leading to products. A second alternate explanation of the data, involving steric interference of groups at the β-carbon upon attack upon one of the two faces of the open ion, would predict predominately *erythro* product,[14] which is not observed. This work and related studies emphasize the importance of *both* open ions and bridged ions in a single reaction sequence,[2,9,14] rather than *either* an open ion[6] *or* a bridged ion mechanism.[5]

Table 4. Overall yield and stereochemical purity of the 2→4 and 2→5 conversion in acetic acid–con. HCl, 4:1 at 26±3°C

	X		%Chloride 5 (% *Threo* 5)[c]	%Acetate 4 (% *Threo* 4)[c]
Threo	**2a**	*p*-CH_3O	94 (>90)	6 (>80)
	2b	*o*-CH_3O	95 (94)	5[a]
	2c	H	87 (68)	9 (37)
Erythro	**2a**	*p*-CH_3O	87 (67)	13 (25)
	2b	*o*-CH_3O	80 (66)	20[b]
	2c	H	89 (66)	11 (27)
	2d	*p*-Cl	67 (48)	33 (11)

a) The product was mostly *threo* **4** but an accurate determination was not possible.

b) Mostly *erythro* **4** but an accurate determination was not possible.

c) % *Threo* product of an *erythro/threo* mixture.

Experimental

The substrates **2** (except **2e**) were prepared by aryl Grignard addition to the appropriate 2-arylpropanals. The latter were usually prepared from the glycidic ester.[23] The following procedure is typical.[27] To 1-(4-chlorophenyl)-1-ethanone (77 g, 0.5 mol) and ethyl chloroacetate (56 g, 0.5 mol) plus 120 m*l* benzene in a 2 *l* three-necked flask, 0.5 mol of potassium *t*-butoxide was added in increments as a solid, and the mixture vigorously stirred for 24 hr. The resulting red solution was poured over ice and extracted with benzene. The organic layers were dried ($MgSO_4$), and the solvent evaporated. The glycidic ester was distilled, the fraction boiling at 121°C/0.75 mmHg was collected. This material was treated with sodium ethoxide (5.8 g sodium in *ca.* 100 m*l* ethanol) and after 2 hr the flask was cooled to 0°C and 8 m*l* of water was added. The sodium salt derived from the glycidic ester

27) A. I. Vogel, "Practical Organic Chemistry," 3rd Edition, Longmans, Green and Co., Ltd., London (1956), p. 907.

separated and was collected by filtration. The mother liquor yielded a second crop when cooled and diluted with ether, total 37 g. This salt was treated with dilute hydrochloric acid (28 m*l* conc. acid plus 150 m*l* water). The mixture was stirred for 2 hr and heated to *ca.* 80°C for 2 hr. The mixture was poured over ice and extracted with ether. The ether layer was washed with water, dil. sodium bicarbonate solution, dried over magnesium sulfate, and distilled; the fraction boiling from 78—80°C/10.7 mmHg was collected, 12.7 g.

The above aldehyde (17.3 g, 0.132 mol) was added dropwise to a solution of phenyl magnesium bromide prepared from 6.5 g magnesium plus 27.4 m*l* bromobenzene. The mixture was poured into ice/ammonium chloride. Hydrochloric acid was added until the aqueous layer was slightly acidic. The ether extract was washed with water, dil. sodium bicarbonate, and distilled, the fraction boiling from 148—150°C/0.7 mmHg (15.7 g) was taken (mixed *erythro* and mostly *threo* diastereomers **2d**).

To 3.14 g (0.0177 mol) of the above alcohol in 70 m*l* pyridine was added 3.5 g *p*-nitrobenzoyl chloride. This mixture was heated on a steam bath for 15 min and stirred for 0.5 hr. The mixture was poured onto ice, and extracted twice with 10% hydrochloric acid, water, twice with dil. sodium hydroxide, and twice with water. The ether layer was dried and evaporated yielding crystals, which were recrystallized from ethanol-water and from pentane-carbon tetrachloride. These were the *threo* **2d** *p*-nitrobenzoate mp 111.6—111.8°C. The *erythro* isomer was elusive in this case but could be prepared by oxidizing the alcohol to the ketone and reducing the ketone with lithium aluminum tri-*t*-butoxy hydride. In general the diastereomerically pure alcohols **2** were prepared by hydrolyzing the purified *p*-nitrobenzoates. Substrates **2c** however were prepared by the method of Cram and Elhafez.[14]

Mixed diastereomers **2e** were prepared from 2-(4-nitrophenyl)-1-phenyl-1-ethanone by the following reactions.[28] To 0.5 g (0.00207 mol) of the above ketone in 50 m*l* dry acetone, 5 g potassium carbonate and 5 m*l* iodomethane were added with rapid stirring. The resulting purple reaction mixture was refluxed 2 hr and poured into ice and extracted with ether. The ether layer was washed with water, dried and the solvent evaporated yielding an oil, whose NMR spectrum indicated predominantly 2-(4-nitrophenyl)-1-phenyl-1-propanone. The material from several runs (9.5 g 0.037 mol) was dissolved in anhydrous tetrahydrofuran and added dropwise to a suspension of 10.0 g (0.0394 mol) of lithium aluminum tri-*t*-butoxy hydride with rapid stirring. After stirring 2 hr the mixture was refluxed 4 hr cooled, treated with saturated potassium carbonate solution and poured onto ice. The mixture was extracted with ether, and the organic layer washed with water, dried solvent evaporated and the product chromatographed on silica gel. The benzene eluant was evaporated to yield yellow crystals, mp 102.8—103.1°C, *erythro* **2e**.

The bromides **1** were prepared from the alcohols by treatment with HBr. The following procedure is illustrative. To *erythro* **2c** (1.0 g, 0.0047 mol) dissolved in 20 m*l* CCl_4, cooled to 0°C, 50 m*l* of chilled conc. HBr and 39 g LiBr were added to the rapidly stirred mixture and the resulting mixture was stirred 4 hr and then allowed to come to room temperature.

The organic phase was separated, and the diluted aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed several times with distilled water, and then dried ($MgSO_4$). The filtered solution was concentrated by rotary evaporation. The resulting oil was *ca.* 80% *threo* **1c** and 20% *erythro* **1c**. Crystallization was induced by cooling. The isomers were separated by repeated recrystallization making use of the fact that the *erythro* isomer was not soluble in ethanol (for other compounds, **1a**, **b**, **d**, pentane was used). Of the 1.29 g (94% of theoretical) crude product usually about 0.2 g pure *erythro* **1c**, mp 157—159°C, and 0.6 g *threo* **1c**, mp 57—59°C, could be isolated in a pure state.

Threo **2a** (X=*p*-CH_3O), bp 150°C (0.1 mmHg); PNB (*p*-nitrobenzoate), mp 92.8—93.8°C; NMR (CCl_4) δ 1.17 (d, 3, C<u>H</u>$_3$), 2.45 (s, 1, O<u>H</u>), 2.87 (m, 1, C<u>H</u>–CH_3), 3.54 (s, 3, C<u>H</u>$_3$O), 4.48 (d, 1, J=6 Hz, C<u>H</u>–OH), and *ca.* 6.8 (m, 9. Ar).

PNB, Found: C, 70.50; H, 5.52%. Calcd for $C_{23}H_{21}NO_5$: C, 70.57; H, 5.42%.

Threo **2b** (X=*o*-CH_3O), bp 140—144°C (0.05 mmHg); PNB, mp 99.5—100.5°C; NMR (CCl_4) δ 1.11 (d, 3, C<u>H</u>$_3$), 2.65 (s, 1, O<u>H</u>), 2.8 (m, 1, C<u>H</u>–CH_3), 3.5 (s, 3, C<u>H</u>$_3$O), 4.66 (d, 1, J=5 Hz, C<u>H</u>–OH), and 6.5—7.2 (m, 9, Ar).

Found: C, 70.26; H, 5.84%. Calcd for $C_{23}H_{21}NO_5$: C, 70.57; H, 5.42%.

Threo **2c**, (X=H), bp 154—156°C (1.7 mmHg); PNB, mp 143—144°C (lit,[14] 143—144°C); NMR ($CDCl_3$) δ 1.22 (d, 3, J=7 Hz, C<u>H</u>$_3$), 1.82 (s, 1, O<u>H</u>), 2.95 (m, 1, C<u>H</u>–CH_3), 4.6 (d, 1, J=6 Hz C<u>H</u>–OH), and 7.15 (s, 10, Ar).

Threo **2d** (X=*p*-Cl), bp 148—150°C (0.7 mmHg); PNB, mp 111—112°C; NMR (CCl_4) δ 1.18 (d, 3, C<u>H</u>$_3$), 2.35 (s, 1, O<u>H</u>), 2.87 (m, 1, C<u>H</u>–CH_3), 4.75 (d, 1, J=6 Hz, C<u>H</u>–CH_3), and *ca.* 6.8 (m, 9, Ar).

PNB, Found: C, 66.53; H, 4.52%. Calcd for $C_{22}H_{18}ClNO_4$: C, 66.75; H, 4.57%.

Erythro **2a** (X=*p*-CH_3O), mp 86—87°C; NMR ($CDCl_3$) δ 1.05 (d, 3, C<u>H</u>$_3$), 1.95 (s, 1, O<u>H</u>), 2.97 (m, 1, C<u>H</u>–CH_3), 4.58 (d, 1, J=8.4 Hz, C<u>H</u>–OH), 7.04 (d of d, 4, CH_3O–$C_6\underline{H}_4$), and 7.3 (s, 5, $C_6\underline{H}_5$).

Found: C, 79.34; H, 7.60%. Calcd for $C_{10}H_{18}O_2$: C, 79.12; H, 7.50%.

Erythro **2b**, (X=*o*-CH_3O), oil; PNB, oil; 3,5-DNB, oil; NMR (CCl_4) δ 0.98 (d, 3, C<u>H</u>$_3$), 2.3 (s, 1, O<u>H</u>), 3.51 (m, 1, C<u>H</u>–CH_3), 3.58 (s, 3, OC<u>H</u>$_3$), 4.6 (d, 1, J=7.7 Hz, C<u>H</u>–OH), and 6.5—7.2 (m, 9, Ar).

Erythro **2c** (X=H), bp 118—123°C (1.5 mmHg), mp 52—53°C (lit,[14] mp 51—52°C); NMR (CCl_4) δ 1.06 (d, 3, C<u>H</u>$_3$), 1.60 (s, 1, O<u>H</u>), 2.95 (m, 1, C<u>H</u>–CH_3), 4.5 (d, 1, J=8.4 Hz, C<u>H</u>–OH), and 7.12 (s, 10, Ar).

Erythro **2d** (X=*p*-Cl), mp 87—88°C; NMR ($CDCl_3$) δ 1.06 (d, 3, C<u>H</u>$_3$), 1.93 (s, 1, O<u>H</u>), 3.0 (m, 1, C<u>H</u>–CH_3), 4.61 (d, 1, J=8.2 Hz, C<u>H</u>–OH), 7.28 (s, 5, $C_6\underline{H}_5$), and 7.05—7.38 (d of d, 4, Cl–$C_6\underline{H}_4$).

Found: C, 73.12; H, 6.07%. Calcd for $C_{15}H_{15}OCl$: C, 73.02; H, 6.13%.

Erythro **2e** (X=*p*-NO_2), mp 102.8—103.8°C; NMR ($CDCl_3$) δ 1.16 (d, 3, C<u>H</u>$_3$), 1.88 (s, 1, O<u>H</u>), 3.16 (m, 1, C<u>H</u>–CH_3), 4.74 (d, 1, J=7.8Hg, C<u>H</u>–OH), 7.28 (s, 5, $C_6\underline{H}_5$), 7.36 (d, 2, Ar), and 8.13 (d, 2, Ar).

Found: C, 70.00; H, 5.84%. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.87%.

Threo **1a** (X=*p*-CH_3O), oil; NMR (CCl_4) δ 1.51 (d, 3, C<u>H</u>$_3$O),3.3 (doublet of quartets, 1, C<u>H</u>–CH_3), 3.45 (s, 3, C<u>H</u>$_3$O), 4.95 (d, 1, J=9.2 Hz, C<u>H</u>–Br), 6.52 (d, 2, $C_6\underline{H}_4$–OCH_3), 8.82 (d, 2, $C_6\underline{H}_4$–OCH_3), and 6.8—7.3 (m, 5, $C_6\underline{H}_5$). Mass spectrum: molecular ion 304, 306; base peak 135.

Threo **1b** (X=*o*-CH_3O), mp 86—87°C; NMR ($CDCl_3$) δ 1.52 (d, 3, C<u>H</u>$_3$), 3.66 (s, 3, C<u>H</u>$_3$O), 3.83 (doublet of quartets, 1, C<u>H</u>–CH_3), 5.33 (d, 1, J=8.6 Hz, C<u>H</u>–Br), and 6.5—7.4

28) G. Badcock, G. Cavill, A. Robertson, and W. Whailey, *J. Chem. Soc.*, **1950**, 2961.

(m, 9, Ar).

Found: C, 62.76; H, 5.70%. Calcd for $C_{16}H_{17}BrO$: C, 62.91; H, 5.61%.

Threo **1c** (X=H), mp 57—59°C(lit,[14] mp 60—61°C); NMR ($CDCl_3$) δ 1.60 (d, 3, $C\underline{H}_3$), 3.43 (doublet of quartets, 1, $C\underline{H}$–CH_3), 5.06 (d, 1, J=9.5, $C\underline{H}$–Br), 7.02 (s, 5, Ar), and 7.11 (s, 5, Ar).

Threo **1e** (X=*p*-NO_2), mp 70—71°C; NMR ($CDCl_3$) δ 1.60 (d, 3, $C\underline{H}_3$), 3.58 (doublet of quartets, 1, $C\underline{H}$–CH_3), 5.08 (d, 1, J=9.0 Hz, $C\underline{H}$–Br), 7.15 (s, 5, Ar), 7.17 (d, 2, $C_6\underline{H}_4NO_2$), and 8.0 (d, 2, $C_6\underline{H}_4NO_2$).

Found: C, 56.04; H, 4.27%. Calcd for $C_{15}H_{14}BrNO_2$: C, 56.45; H, 4.11%.

Erythro **1a** (X=*p*-CH_3O), mp 132—133°C, NMR ($CDCl_3$) δ 1.13 (d, 3, $C\underline{H}_3$), 3.43 (doublet of quartets, 1, $C\underline{H}$–CH_3), 3.78 (s, 3, $C\underline{H}_3O$), 5.00 (d, 1, J=9.2 Hz, $C\underline{H}$–Br), 6.84 (d, 2, $C_6\underline{H}_4$–OCH_3), 7.15 (d, 2, $C_6\underline{H}_4OCH_3$), 7.30 (s, 5, $C_6\underline{H}_5$).

Found: C, 62.83; H, 5.49%. Calcd for $C_{16}H_{17}BrO$: C, 62.96; H, 5.61%.

Erythro **1c** (X=H), mp 157—159°C, (lit,[14] mp 159—160°C); NMR ($CDCl_3$) δ 1.14 (d, 3, $C\underline{H}_3$), 3.49 (doublet of quartets, 1, $C\underline{H}$–CH_3), 5.07 (d, 1, J=9.7 Hz, $C\underline{H}$–Br), 7.30 (s, 5, Ar), and 7.35 (s, 5, Ar).

Erythro **1d** (X=*p*-Cl), mp 115—116°C; NMR ($CDCl_3$) δ 1.10 (d, 3, $C\underline{H}_3$), 3.45 (doublet of quartets, 1, $C\underline{H}$–CH_3), 4.98 (d, 1, J=9.6 Hz, $C\underline{H}$–Br), 7.20 (d, 2, $C_6\underline{H}_4Cl$), 7.30 (d, 2, $C_6\underline{H}_4Cl$), and 7.30 (s, 5, Ar).

Found: C, 58.18; H, 4.41%. Calcd for $C_{15}H_{14}ClBr$: C, 58.18; H, 4.56%.

Erythro **1e** (X=*p*-NO_2), mp 139—140°C; NMR ($CDCl_3$) δ 1.16 (d, 3, $C\underline{H}_3$), 3.62 (doublet of quartets, 1, $C\underline{H}$–CH_3), 5.03 (d, 1, J=9.7 Hz, $C\underline{H}$–Br), 7.35 (s, 5, Ar), 7.40 (d, 2, $C_6\underline{H}_4NO_2$), and 8.20 (d, 2, $C_6\underline{H}_4NO_2$).

Found: C, 56.30; H, 4.11%. Calcd for $C_{15}H_{14}BrNO_2$: C, 56.45; H, 4.11%.

Product Runs. A typical run is given (silver acetate catalyzed reaction of *threo* **2e** in methanol, Table 2). Approximately 150 mg of substrate was dissolved in 30 m*l* absolute methanol, and 150 mg silver acetate was added. The mixture was stirred at *ca.* 35°C for 6 hr. The mixture was filtered, and the liquid added to a separatory funnel containing ether and water. The aqueous layer was extracted with ether several times. The combined organic layers were extracted with water twice, and dried ($MgSO_4$). The solvent was removed by rotary evaporation and the product analyzed by NMR (Fig. 2).

Product Analyses. *Erythro* and *threo*-1,2-diphenyl-1-propyl bromides, chlorides, methyl ethers, and acetates were prepared which showed the literature physical constants in each case. Since the NMR resonances were only slightly affected by aromatic substituent, the above compounds sufficed as models for all compounds. The NMR analyses were possible because the methyl resonances of the *threo* isomers uniformly fell in the region δ 1.2—1.5, whereas the resonances of the *erythro* isomers fell upfield (δ 1.0—1.2).

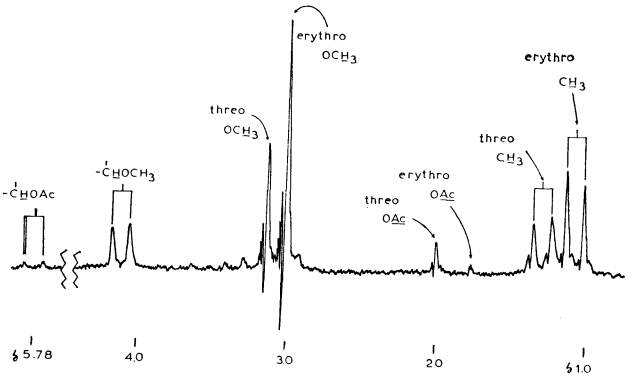


Fig. 2. Silver acetate catalyzed reaction product (**1e**→**3e**, **4e**).

The percentage of each isomer was determined from an average of 3—5 integrations. The methyl ethers also showed separate resonances for the *erythro* and *threo* isomers, an integration over the CH_3O peaks was always in good agreement with integration over the methyl resonances. The various conversions were very clean, with no apparent rearrangement, and little or no olefin formation (olefin formation was only apparent in the alcohol to chloride conversions, Table 4). The possible rearrangement products 2-methoxy-1,2-diphenylpropane and 3,3-diphenyl-2-propanol were synthesized. The distinctive resonances of these materials were never observed. Similarly *erythro*-1,2-diphenyl-1-deuterio-1-propanol was subjected to the **2**→**5** conversion. No deuterium scrambling was evident. Only in the case of the *o*-methoxy were small peaks observed, not associated with the normal products.

Kinetics. The rates of reaction were followed conductometrically. By making up known standards, it was proved that conductance was linear with hydrogen bromide concentration. Two cells were used, one with platinized electrodes, the other with plain platinum electrodes. These gave the same rates at low temperature although some divergence occurred at the higher temperatures. At the lower temperatures, due to the difference in surface area of the two cells, it is unlikely that the platinum surface was catalyzing the reaction. At higher temperatures the lower rates found with the plain cell were considered the most reliable. From sixteen to fifty-five points were taken. The rate plots were always linear over three and usually over four to five half-lives, with little scatter evident except in the latest stages of the reaction. The rates were determined graphically. The data given in Table 1 are the average of two to four runs. In one case **1c**, four-fold variation of concentration of the substrate produced very similar rate constants indicative of true first-order kinetics. Substrate concentration normally was *ca.* 10^{-4} to 10^{-5}M. The solvent (ρ=0.8403 at 25°C; 79.6% ethanol by weight) was prepared by mixing weighed amounts of redistilled ethanol with redistilled water. Activation parameters were obtained from least squares analysis of log rate *vs.* inverse temperature plots.