action mixture produced carbinol which was crystallized four times from pentane, wt. 1.5 g., $[\alpha]^{22}\text{D}$ −67.8° (*c* 0.28 in $CHCl_3$), m.p. 71.5–72.5°, m.m.p. with (−)-*erythro*-1,2-diphenyl-1-propanol, 71.5–72.5°. The filtrates from the above crystallizations were combined, the solvent was evaporated and the resulting oily carbinol was converted to the *p*-nitrobenzoate. This solid was submitted to fractional crystallization (nine times) from an ether–pentane mixture to give 2.8 mg. of *p*-nitrobenzoate, $[\alpha]^{22}\text{D}$ −89° (*c* 0.28 in $CHCl_3$), m.p. 168.5–170.5°, m.m.p. with *p*-nitrobenzoate of (−)-*threo*-1,2-diphenyl-1-propanol, 169.5–170.5°.

Conversion of (−)-3-Phenyl-1-butene to (−)-*threo*-1,2-Diphenyl-1-propanol.—Ozone was passed through a solution of 1.4 g. of (−)-3-phenyl-1-butene ($[\alpha]^{22}\text{D}$ −6.39°, homog.)[11] in 10 ml. of freshly distilled methylene chloride until no more ozone was absorbed (25 minutes). The solution of the ozonide was added dropwise to a stirred boiling mixture of 20 ml. of water, 0.7 g. of zinc dust and a small crystal of silver nitrate. The reaction mixture was cooled, filtered and extracted with ether. The ether layer was washed with water, dried and evaporated to an oil. This oil was flash-distilled at 20 mm. to give 0.80 g. of 2-phenylpropionaldehyde.

An ether solution of 0.40 g. of the above aldehyde was added dropwise to an ether solution of phenylmagnesium bromide (large excess). The reaction mixture was worked up in the usual way[3] to give an oil which was flash-distilled at 20 mm. This material was dissolved in 2 ml. of pentane and chromatographed on a 1.5 × 5 cm. column of alumina. The column was thoroughly washed with pentane, and the carbinol was eluted with methanol. The methanol eluate was concentrated using a Vigreux column to give about 30 mg. of an oil which was converted to the *p*-nitrobenzoate by the usual method.[3] This material was crystallized six times from an ether–pentane mixture to give 17 mg. of pure ester, $[\alpha]^{21}\text{D}$ −89° (*c* 1.6 in $CHCl_3$), m.p. 167–168.5°, m.m.p. with the *p*-nitrobenzoate of (−)-*threo*-1,2-diphenyl-1-propanol, 168.5–170°.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Studies in Stereochemistry. XIV. Differences in the Reactivity of Diastereomerically Related Alkyl Halides and Sulfonates in the SN2 and E_2 Reactions

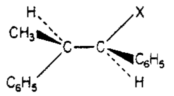
BY DONALD J. CRAM AND FATHY AHMED ABD ELHAFEZ[1]

RECEIVED APRIL 25, 1952

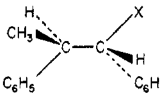
The *p*-bromobenzenesulfonates of D-, L- and racemic *erythro*- and *threo*-1,2-diphenyl-1-propanol were prepared. When treated with lithium chloride, bromide or iodide in acetone, these esters gave the corresponding D-, L- and racemic *threo*- and *erythro*-1,2-diphenyl-1-propyl halides, respectively. In each case, simple Walden inversion occurred at the carbon carrying the *p*-bromobenzenesulfonate group. The differences found in reactivity between diastereomerically related starting materials is correlated with the differences in steric strains in the two types of starting material. The E_2 reactions of these alkyl halides and *p*-bromobenzenesulfonates were studied. Substantial differences in reactivity were observed between the two classes of compounds as well as between diastereomerically related alkyl halides. These differences are interpreted in terms of the effects of the bulks of the departing and remaining groups on the respective starting and transition states of the E_2 reaction. The results of these reactions serve to establish the configurations of all the 1,2-diphenyl-1-propyl halides relative to D-glyceraldehyde. An attempt to carry out an asymmetric degradation as applied to the E_2 reaction of these alkyl halides failed. A novel, lithium–amine catalyzed substitution of chloride by iodide in *threo*-1,2-diphenyl-1-propyl chloride that occurs in benzene and with retention of configuration is reported.

Differences in reactivity between diastereomerically related starting materials in acyclic systems have been noted in the cases of Wagner–Meerwein[2] and pinacol-like rearrangements,[3] the E_1,[4] E_2[5] and pyrolytic elimination reactions,[6] reactions involving neighboring group participation,[7] and reactions involving O- to N-acyl migration.[8]

The present investigation is concerned with the differences in reactivities in the E_2 and SN2 reactions between the *erythro*- and *threo*-isomers of the *p*-bromobenzenesulfonates (brosylates), chlorides, bromides and iodides of the 1,2-diphenyl-1-propyl system.



L-*erythro*-isomer of
1,2-diphenyl-1-propyl-X
(X = *p*-$BrC_6H_4SO_3$, Cl, Br, I)



L-*threo*-isomer of
1,2-diphenyl-1-propyl-X
(X = *p*-$BrC_6H_4SO_3$, Cl, Br, I)

SN2 Reactions of Halide Ions with Brosylates of 1,2-Diphenyl-1-propanol.—The brosylates of the stereoisomeric 1,2-diphenyl-1-propanols[9] were prepared by the method usually employed for the sulfonation of benzylhydroxyl groups.[10] In the case of both the active and racemic forms the *erythro*-esters were stable and could be stored without deterioration whereas the *threo*-esters were unstable and had to be used as soon as prepared. The *p*-toluenesulfonates (tosylates) of racemic and L-*erythro*-1,2-diphenyl-1-propanol were also prepared and found to be equally stable. Although the tosylates of the *threo*-alcohol could be prepared, their extreme instability made them impractical as starting materials. Table I reports the physical properties, the configurations[9] and analyses of these substances.

The displacement reactions of the brosylate

---

[1] Predoctoral Fellow of the Egyptian Government. This paper is abstracted from the thesis of this author presented to the University of California at Los Angeles in partial fulfillment of the requirements for the Ph.D. degree.

[2] (a) D. J. Cram, THIS JOURNAL, **74**, 2149 (1952); (b) **74**, 2152 (1952).

[3] (a) D. Y. Curtin and P. I. Pollak, *ibid.*, **72**, 961 (1950); (b) **73**, 992 (1951).

[4] D. J. Cram, *ibid.*, **74**, 2137 (1952).

[5] P. T. Dillon, W. G. Young and H. J. Lucas, *ibid.*, **52**, 1953 (1930); W. G. Young, D. Pressman and C. D. Coryell, *ibid.*, **61**, 1640 (1939).

[6] (a) D. J. Cram, *ibid.*, **70**, 3883 (1948); (b) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **74**, 5828 (1952).

[7] S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *ibid.*, **74**, 1118 (1952). Other pertinent references are listed here.

[8] G. Fodor, V. Bruckner, J. Kiss and G. Ohegyi, *J. Org. Chem.*, **14**, 337 (1949).

[9] F. A. Abd Elhafez and D. J. Cram, THIS JOURNAL, **74**, 5846 (1952).

[10] S. Winstein and B. K. Morse, *ibid.*, **74**, 1133 (1952).

TABLE I

THE PROPERTIES AND ANALYSES OF THE BROSYLATES, TOSYLATES AND HALIDES OF THE 1,2-DIPHENYL-1-PROPYL SYSTEM

Compound $C_6H_5-\overset{\overset{CH_3}{\vert}}{C}H-\underset{\vert}{C}H-C_6H_5$	Prepd.[a] in run no.	M.p.,[b] °C.	$\alpha^{21-23}D$[c]	Formula	Analyses, %			
					Carbon		Hydrogen	
					Calcd.	Found	Calcd.	Found
			Chlorides					
d,l-erythro	2	139.5–140.5	......	$C_{15}H_{15}Cl$	78.06	77.85	6.55	6.52
d,l-threo	1	54–55	......	$C_{15}H_{15}Cl$	78.06	78.12	6.55	6.76
L-*erythro*	[d]	141.5–142.5	+97.0	$C_{15}H_{15}Cl$	78.06	77.88	6.55	6.54
D-*erythro*	8	141.5–142.5	−96.9	$C_{15}H_{15}Cl$	78.06	77.84	6.55	6.69
L-*threo*	7	42.8–43.6	+7.1	$C_{15}H_{15}Cl$	78.06	77.88	6.55	6.67
D-*threo*	[d]	42.8–43.8	−6.1[e]	$C_{15}H_{15}Cl$	78.06	77.95	6.55	6.48
			Bromides					
d,l-erythro	4	159–160	......	$C_{15}H_{15}Br$	65.46	65.53	5.49	5.56
d,l-threo	3	60–61	......	$C_{15}H_{15}Br$	65.46	65.48	5.49	5.72
L-*erythro*	13	159–160	+135.8	$C_{15}H_{15}Br$	65.46	65.50	5.49	5.53
D-*erythro*	12	159–160	−136.1	$C_{15}H_{15}Br$	65.46	65.49	5.49	5.67
L-*threo*	[d]	60–61	−54.8	$C_{15}H_{15}Br$	65.46	65.71	5.49	5.58
D-*threo*	11	60–61	+53.7	$C_{15}H_{15}Br$	65.46	65.25	5.49	5.52
			Iodides					
d,l-erythro	6	124–125[f]	......	$C_{15}H_{15}I$	55.91	55.87	4.69	4.83
d,l-threo	5	130–131[f]	......	$C_{15}H_{15}I$	55.91	56.39	4.69	4.86
			Brosylates					
	Prep. Proc.							
d,l-erythro	A	80–81[f]	......	$C_{21}H_{19}O_3SBr$	58.47	58.34	4.44	4.53
d,l-threo	A	46–47[f]	......	$C_{21}H_{19}O_3SBr$	58.47	58.36	4.44	4.74
L-*erythro*	A	83–84[f]	+81.0	$C_{21}H_{19}O_3SBr$	58.47	58.48	4.44	4.46
D-*erythro*	A	83–84[f]	−82.1	$C_{21}H_{19}O_3SBr$	58.47	58.21	4.44	4.41
L-*threo*	A	67–68[f]	+33.4	$C_{21}H_{19}O_3SBr$	58.47	58.79	4.44	4.70
D-*threo*	A	67–68[f]	−32.7	$C_{21}H_{19}O_3SBr$	58.47	58.75	4.44	4.68
			Tosylates					
d,l-erythro	A	84–85[f]	......	$C_{22}H_{22}O_3S$	72.10	72.03	6.05	6.08
L-*erythro*	A	89–90[f]	......[g]	$C_{22}H_{22}O_3S$	72.10	71.95	6.05	5.92

[a] See Table II for the identification of these runs. [b] Melting points reported for 3°/min. Many of these melting points varied with the rate and total length of time of heating. [c] *c*, 5% in $CHCl_3$. [d] These compounds were prepared by procedures that will be reported in paper XVII of this series. Their properties and analyses are included here for comparative purposes. [e] *c* 15% in $CHCl_3$. [f] Melted with decomposition. [g] Rotation not taken.

group by halide ions were in all cases carried out in acetone, the lithium salt of the halide being employed. Higher yields were usually obtained when barium carbonate was present as a second phase (see Table II). The halide products were in all cases crystalline compounds which could be readily purified. The chlorides[11] and *erythro*-bromides[11] were stable and could be crystallized and stored under ordinary conditions, but the *threo*-bromides and both diastereomeric iodides required careful solvent selection for crystallization, and low temperatures for preservation. In every case, the brosylates, tosylates, chlorides, bromides and iodides of *erythro*-isomers[11] were more stable than the corresponding *threo*-isomers.[11] In every case except that of the iodides, the *erythro*- melt higher than the *threo*-materials; and in the cases of the brosylates, bromides and chlorides, the rotations of the diastereomerically related isomers differ widely (see Table I).

An examination of the relative configurations of starting brosylate esters and the halide products (Table II) reveals that the substitution reaction occurred with inversion of configuration at the carbon atom originally carrying the brosylate group. The yields of inverted product ranged from 50–75%, and in two cases trace amounts of halide were isolated whose configuration was the same as that of the starting material[12] (runs 3 and 11). The remainder of the starting material was in each case accounted for as an oily mixture of brosylate ester, olefin and halide. Thus the preponderance of product seems to have arisen by an S_N2 mechanism in which brosylate was displaced by halide ion.

Although kinetic studies were not made,[13] it was very obvious from the times that passed before lithium brosylate started to precipitate from the reaction mixture (see Table II) as well as from the times required to produce substantial yields of product (preliminary experiments) that with each of the three halide ions, the brosylate of *threo*-alcohol reacted much faster than the brosylate of the *erythro*-isomer. This observation is particularly interesting because these differences in rates must

---

[11] The configurations of these halides were demonstrated through the use of the E_2 reaction (see next section).

[12] In each case, the diastereomerically related halides can be easily separated by fractional crystallization. These trace amounts probably arose by epimerization of the inverted halide once it had formed. That such a reaction occurs under the conditions of the experiment has been demonstrated (unpublished results).

[13] A study of the rates of these and analogous reactions is in progress.

TABLE II

RESULTS OF S$_N$2 REACTIONS OF THE STEREOISOMERS OF 1,2-DIPHENYL-1-PROPYL BROSYLATES AND TOSYLATES WITH LITHIUM HALIDES IN ACETONE[a]

Run no.	Starting material[b]		Lithium halide[c]		Base[d] pres.	Temp., °C.	Times (hr.)[e]		Product[f]	Yield, %
	Structure	Concn. mole/l.	Kind	Concn. mole/l.			Ppt. to form	Total react.	Structure	
1	*d,l-erythro*-Bros.	0.050	Chloride	0.471	BaCO$_3$	57	15	144	*d,l-threo*-chloride	75
2	*d,l-threo*-Bros.	.050	Chloride	.471	BaCO$_3$	57	0.3	18	*d,l-erythro*-chloride	60
3	*d,l-erythro*-Bros.	.133	Bromide	.769	BaCO$_3$	57	.8	11	*d,l-threo*-bromide[g]	49
4	*d,l-threo*-Bros.	.133	Bromide	.769	BaCO$_3$	57	.08	7	*d,l-erythro*-bromide	62
5	*d,l-erythro*-Tos.	.200	Iodide	1.120	None	25	None	300	*d,l-threo*-iodide	15
6	*d,l-threo*-Tos.	.200	Iodide	1.120	None	25	1.0	72	*d,l-erythro*-iodide	60
7	L-*erythro*-Bros.	.050	Chloride	0.471	BaCO$_3$	57	15	144	L-*threo*-chloride	67
8	D-*threo*-Bros.	.050	Chloride	.471	BaCO$_3$	57	0.2	8	D-*erythro*-chloride	57
9	*d,l-threo*-Bros.	.050	Chloride	.741	None	25	10	144	*d,l-erythro*-chloride	55
10	*d,l-erythro*-Tos.	.057	Chloride	.471	None	57	16	144	*d,l-threo*-chloride	60
11	D-*erythro*-Bros.	.133	Bromide	.769	BaCO$_3$	57	0.8	13	D-*threo*-bromide[h]	63
12	D-*threo*-Bros.	.133	Bromide	.769	BaCO$_3$	57	.08	3	D-*erythro*-bromide	60
13	L-*threo*-Bros.	.133	Bromide	.769	BaCO$_3$	57	.08	2	L-*erythro*-bromide	66
14	*d,l-erythro*-Bros.	.133	Bromide	.769	None	57	.7	24	*d,l-threo*-bromide	50
15	*d,l-threo*-Bros.	.133	Bromide	.769	None	25	3	72	*d,l-erythro*-bromide	45
16	*d,l-erythro*-Bros.	.200	Iodide	1.120	Pyridine[i]	57	...	24	*trans*-α-methylstilbene	68
17	*d,l-threo*-Bros.	.200	Iodide	1.120	Pyridine[i]	57	...	3	*cis*-α-methylstilbene	67
18	*d,l-erythro*-Bros.	.200	Iodide	1.120	None	57	...	24	*d,l-threo*-iodide	38
19	*d,l-threo*-Bros.	.200	Iodide	1.120	None	57	...	3	*d,l-erythro*-iodide	45

[a] Dry, C.P. acetone was used. [b] Dry, C.P. lithium halides were employed. [c] The solutions of lithium bromide and iodide were homogeneous, but lithium chloride was not soluble enough in acetone to give a homogeneous solution. The solution was therefore saturated with lithium chloride throughout the reaction. [d] The BaCO$_3$ was present as a second phase. When no base was present, the solution slowly became acid, due to a competing but relatively insignificant E$_1$ reaction. [e] Although in some cases BaCO$_3$ or LiCl was present as a second phase, this material remained in the bottom of the flask and did not obscure the very easily recognized precipitation of the lithium sulfonate. [f] In every run in which the same product was isolated, m.m.p.'s were taken for identification purposes. [g] A 4% yield of *d,l-erythro*-bromide was also isolated. [h] A 3% yield of D-*erythro*-bromide was also isolated. [i] These reaction mixtures were 0.063 molar in pyridine.

originate in steric effects since the same groups are attached to the asymmetric atoms in the two starting materials, and only sterically induced electronic differences should exist in two diastereomers. Therefore this type of system permits an isolation of steric effects in a manner not possible in the study of different molecular systems.

In the development of the "Rule of Steric Control of Asymmetric Induction"[6b] it was found that the relative bulks of substituents on an asymmetric carbon atom determined the stereochemical direction of addition of a reagent to a double bond attached to an adjacent carbon atom which was becoming asymmetric. It has also been observed that in the esterification of 1,2-diphenyl-1-propanol with 3-nitrophthalic anhydride, the proportion of α- to β-ester (anhydride ring opens to give the more or less hindered ester, respectively) in the product changed in passing from *erythro* to *threo* starting material.[9] This phenomenon was interpreted in terms of the relative steric stabilities of the two starting materials and of the four transition states involved. The same general principles provide an explanation for the differences in reactivities of the diastereomeric brosylates in their reactions with halide ion.

Molecular models of the brosylate esters suggest that the effective bulks of the phenyl and brosylate groups are probably approximately the same, and therefore the thermodynamic stability of the two diastereomeric esters are probably close together. The widely differing rates of reaction of each isomer with halide ion must then be due mainly to differences in stabilities of the diasteromerically related transition states. In these transition states five groups are dispersed about the carbon undergoing displacement, and the phenyl group can best stabilize the system (distribute charge) in only that rotational conformation shown in the formulation. Since the geometric requirements for the reaction are so specialized, it is not surprising that large steric differences exist in the diastereomeric transition states. The question now arises as to which of the two diasteromeric esters would be predicted on the basis of steric principles to give the least strained transition state.

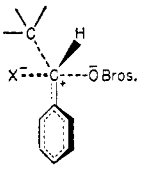


Chart I outlines a series of representative conformational relationships for the starting and transition states for the S$_N$2 reaction of the *threo*- and *erythro*-brosylate esters of 1,2-diphenyl-1-propanol. The models are end on projections[14] in which L, M and S (large, medium and small groups) represent the phenyl, methyl and hydrogen, respectively, attached to the rear asymmetric carbon, and L, L′ and S represent the phenyl, the brosylate and hydrogen, respectively, attached to the front asymmetric carbon. Of these models, (a), (c) and (e) of the *threo* series and (g), (i) and (k) of the *erythro* series have non-eclipsed conformations in the starting states, and these sequences would in

---

(14) The authors are indebted to M. Newman for suggesting the use of these projection formulas.

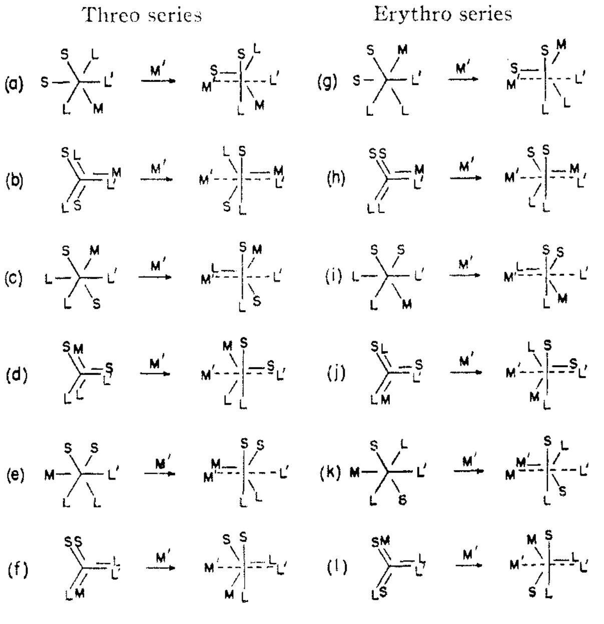
TABLE III

RESULTS OF THE E_2 REACTIONS OF THE STEREOISOMERS OF THE 1,2-DIPHENYL-1-PROPYL HALIDES

Run[a] no.	Starting material: Structure	Starting material: Concn. mole/l.	Reaction solvent: Base	Reaction solvent: Solvent	Concn. mole/l.	Temp. °C.	Time, hr.	Product[b]: Structure	Product[b]: Yield, %
20	*dl-erythro*-Chloride	0.4	KOH	EtOH	1	78	12–14	*cis*-α-Methylstilbene	84
21	*dl-threo*-Chloride	.4	KOH	EtOH	1	78	12–14	*trans*-α-Methylstilbene	85
22	L-*erythro*-Chloride	.4	KOH	EtOH	1	78	12–14	*cis*-α-Methylstilbene	87
23	L-*threo*-Chloride	.4	KOH	EtOH	1	78	12–14	*trans*-α-Methylstilbene	84
24	*dl-erythro*-Bromide	.4	KOH	EtOH	1	78	8–10	*cis*-α-Methylstilbene	86
25	*dl-threo*-Bromide	.4	KOH	EtOH	1	78	8–10	*trans*-α-Methylstilbene	90
26	L-*erythro*-Bromide	.4	KOH	EtOH	1	78	8–10	*cis*-α-Methylstilbene	87
27	L-*threo*-Bromide	.4	KOH	EtOH	1	78	8–10	*trans*-α-Methylstilbene	92
28	*dl-erythro*-Iodide	.4	KOH	EtOH	1	78	6–8	*cis*-α-Methylstilbene	85
29	*dl-threo*-Iodide	.4	KOH	EtOH	1	78	6–8	*trans*-α-Methylstilbene	87
30	*dl-erythro*-Chloride	0.2	*dl*-K-2-Octylate	C_6H_6	0.5	80	16–18	*dl-erythro*-Chloride	92
31	*dl-threo*-Chloride	.2	*dl*-K-2-Octylate	C_6H_6	.5	80	16–18	*trans*-α-Methylstilbene	91
32	*dl-erythro*-Bromide	.2	*dl*-K-2-Octylate	C_6H_6	.5	80	12–14	*cis*-α-Methylstilbene	84
33	*dl-threo*-Bromide	.2	*dl*-K-2-Octylate	C_6H_6	.5	80	12–14	*trans*-α-Methylstilbene	87
34	*dl-erythro*-Iodide	.2	*dl*-K-2-Octylate	C_6H_6	.5	80	8–10	*cis*-α-Methylstilbene	88
35	*dl-threo*-Iodide	.2	*dl*-K-2-Octylate	C_6H_6	.5	80	8–10	*trans*-α-Methylstilbene	85
36	*dl-erythro*-Chloride	.2	*dl*-K-2-Octylate	C_6H_6	.5[c]	80	16–18	*dl-erythro*-Chloride	90
37	*dl-threo*-Chloride	.2	*dl*-K-2-Octylate	C_6H_6	.5[c]	80	16–18	*trans*-α-Methylstilbene	90
38	*dl-erythro*-Chloride	.2	*dl-threo*-K-1,2-Diphenyl-1-propylate	C_6H_6	.5	80	18–20	*dl-erythro*-Chloride	84
39	*dl-threo*-Chloride	.2	*dl-threo*-K-1,2-Diphenyl-1-propylate	C_6H_6	.5	80	18–20	*trans*-α-Methylstilbene	86
40	*dl-erythro*-Chloride	.2	*dl-threo*-K-1 2-Diphenyl-1-propylate	C_6H_6	.5[d]	80	18–20	*dl-erythro*-Chloride	86
41	*dl-threo*-Chloride	.2	*dl-threo*-K-1,2-Diphenyl-1-propylate	C_6H_6	.5[d]	80	18–20	*trans*-α-Methylstilbene	82
42	*dl-erythro*-Chloride	..[e]	N,N-Dimethyl-α-phenylmethylamine		..[e]	190	15–17	Polymer	..
43	*dl-threo*-Chloride	..[e]	N,N-Dimethyl-α-phenylethylamine		..[e]	190	15–17	*trans*-α-Methylstilbene and polymer	14
44	*dl-threo*-Chloride	1.04	(+)-K-2-Octylate	C_6H_6	.6	80	14–16	*trans*-α-Methylstilbene *dl-threo*-chloride and oil	32 47
45	*dl-erythro*-Bromide	1.04	(+)-K-2-Octylate	C_6H_6	.6	80	14–16	*cis*-α-Methylstilbene *dl-erythro*-bromide	45 30
46	*dl-erythro*-Chloride	0.62	L-N-Li-N-Neopentyl-α-phenylethylamine	C_6H_6	.49	80	22	*dl-erythro*-Chloride	97
47	*dl-threo*-Chloride	0.35	L-N-Li-N-Neopentyl-α-phenylethylamine	C_6H_6	.28	80	22	*dl-threo*-Iodide and oil	61

[a] Runs 20–29, procedure B; runs 30–41, procedure C; runs 42–43, procedure D (see Experimental). [b] In each case mixed melting points taken with authentic samples prepared by other means showed no depression. The *cis*- and *trans*-α-methylstilbenes were reported previously (ref. 6b). [c] In these runs, the solution was 0.2 *M* in *dl*-2-octanol. [d] In these runs, the solution was 0.2 *M* in *dl-threo*-1,2-diphenyl-1-propanol. [e] No solvent was used; 0.01 mole of starting material was heated with 0.05 mole of amine.

Chart 1



general appear to be more favorable than the other six in which the starting states are eclipsed.[15] Of the six sequences involving non-eclipsed starting states, (a) and (g) probably have the most stable transition states since the two eclipsed groups (S and M′) are of lower bulk than those found eclipsed in (c), (e), (i) and (k). Since the same groups are eclipsed in the two diastereomerically related transition states of (a) and (g), the relative stabilities of these two species can be judged on the basis of the respective differences in steric repulsions between the substituents distributed in staggered conformations. The only differences are that transition state (a) has one L>–< M and one L >–< S steric repulsion whereas transition state (g) has one L>–< L and one M>–< S steric repulsion. Clearly sequence (a) should have a lower activation energy than (g). Since (a) represents the reactions of *threo* starting materials and (g) those of *erythro* starting materials, the argument based on steric

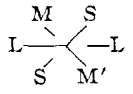
---

(15) Of the six sequences involving eclipsed starting states, sequences (d) and (j) would have the most stable transition states since the eclipsing of S and L should cost the least energy. These two transition states should be less stable than those of (a) and (g), however, where S and M, are eclipsed.

grounds is compatible with the experimental observation that the *threo* materials react faster than the *erythro* materials in the S_N2 reaction. Although only six cases are reported here, the phenomena might be general, provided an unambiguous selection of models is possible.

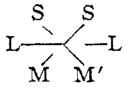
E_2 Reaction of Different Bases with the Isomeric 1,2-Diphenyl-1-propyl Halides.—Although the tosylates of the diastereomeric 3-phenyl-2-butanols underwent the E_2 reaction readily when treated with sodium ethylate in ethanol,[16] neither the tosylates nor brosylates of the isomers of 1,2-diphenyl-1-propanol underwent the E_2 reaction when submitted to a variety of reaction conditions. In every case the competing S_N2 reaction dissipated the starting material. In contrast to the sulfonate esters, when the chlorides, bromides and iodides of the 1,2-diphenyl-1-propyl system (both diastereomers) were submitted to the action of alcoholic potassium hydroxide, an E_2 reaction occurred almost to the exclusion of the S_N2 reaction (see Table III). These differences in behavior of the halides and brosylates will be discussed in a later paper.

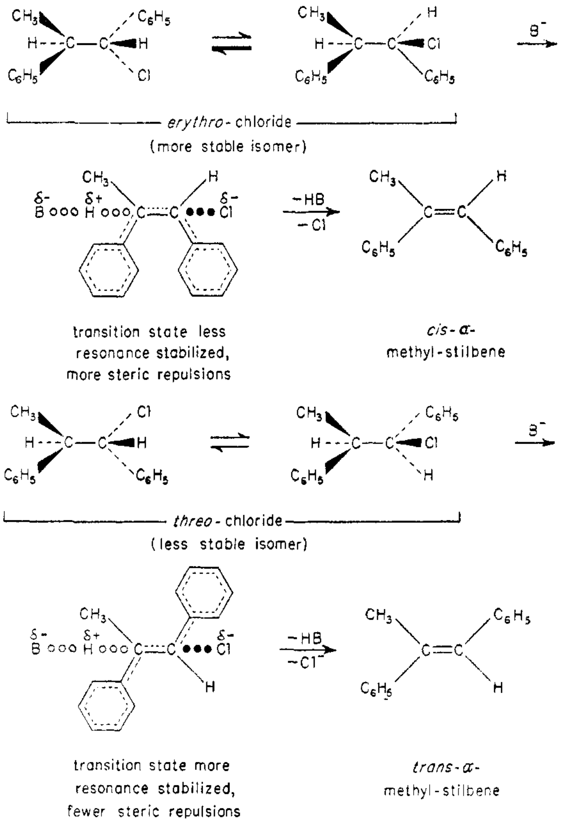
As indicated in Table III, with alcoholic potassium hydroxide at reflux temperature, the *erythro*-chlorides, bromides and iodides readily undergo the E_2 reaction (runs 20, 22, 24, 26 and 28) to give yields from 85–87% of *cis*-α-methylstilbene, and the *threo*-chlorides, bromides and iodides similarly went to *trans*-α-methylstilbene (runs 21, 23, 25, 27 and 29). When *d,l*-potassium 2-octylate dissolved in refluxing benzene (both in the presence and absence of excess alcohol) was employed as the reaction medium (runs 30 to 37), the bromides and iodides of both diasteromers underwent the E_2 reaction readily, but although the *threo*-chloride reacted to give a 91% yield of *trans*-olefin, the *erythro*-chloride when submitted to the same reaction conditions remained unchanged (run 30). The potassium salt of 1,2-diphenyl-1-propanol when similarly applied to the two chlorides (runs 38 and 39) gave the same results obtained with the *d,l*-potassium 2-octylate. This striking difference in reactivities of these two chlorides is attributed to three effects. (1) The starting *erythro*-chloride should be more thermodynamically stable than the *threo*-chloride because lower order steric repulsions exist in the most stable conformation of the former isomer. This supposition is demonstrated in models I and II in which L, M, M′ and S represent phenyl, methyl, halide and hydrogen groups, respectively, and where the most stable conformation is drawn for each isomer. The difference between the isomers is that I has one M >–< S and one M′ >–< S steric repulsion whereas II has one M >–< M′ and one S >–< S steric repulsion. (2) The transition state for the E_2 reaction of the *threo*-isomer should be more resonance stabilized than that of the *erythro*-isomer. (3) The steric repulsions between the two phenyl groups found in the transition state of the *erythro*-isomer are replaced in the transition state of the *threo*-isomer by the less important repulsions between a methyl and a phenyl group. All three of these effects should promote the observed differences in reactivity between the two chlorides. These same effects undoubtedly also operate in the cases of the bromides and iodides, but went undetected because the reaction conditions were drastic enough to drive even the slower reactions to completion. The observation that the iodides > bromides > chloride in ease (rate) of undergoing the E_2 reaction (Table III) is in harmony with previous work.[17] The diagram illustrates the points made in the above argument.



model I (*erythro*)

model II (*threo*)





The results of these reactions serve to establish the configurations of all the 1,2-diphenyl-1-propyl halides relative to D-glyceraldehyde.

Attempted Asymmetric Degradation of Racemic 1,2-Diphenyl-1-propyl Halides.—A number of attempts were made to convert one enantiomer of both the *erythro-* and *threo*-racemic halides (bromides or chlorides) to olefin faster than the other enantiomer through the agency of an optically active base (E_2 reaction).[18] A difference in rate should result from the fact that although the starting materials are enantiomorphically related, the transition states would be diastereomerically re-

---

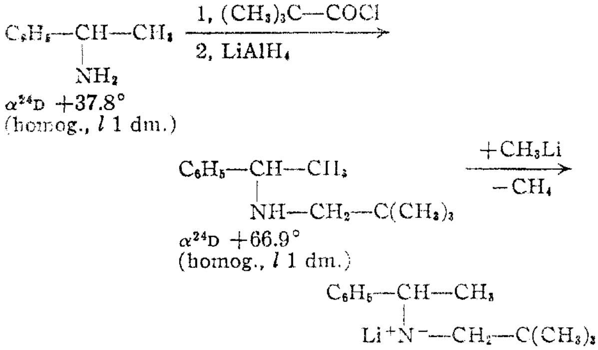
[16] D. J. Cram, THIS JOURNAL, **74**, 2143 (1952).

[17] See series of papers by E. D. Hughes and C. K. Ingold, *et al.*, *J. Chem. Soc.*, 2038 (1948). References to earlier work are summarized here.

[18] H. J. Lucas and C. W. Gould [THIS JOURNAL, **64**, 601 (1942)] stereospecifically destroyed *d,l*-2,3-dibromobutane with brucine to form (at different rates) the diastereomerically related alkylated brucines. S. J. Cristol [*ibid.*, **71**, 1894 (1949)] demonstrated that α-*d,l*-benzene hexachloride could be stereospecifically destroyed by brucine, and that partial resolution could be effected by interrupting the reaction before all the starting material was destroyed.

lated, and one of the two transition states should be more sterically feasible and hence more stable than the other. In the systems used the actual stereochemical relationships between the asymmetric bases and the two asymmetric carbon atoms involved in the E_2 reaction are known, and it was hoped that *a priori* predictions based on molecular models could be made as to which of the two transition states would be the more stable. The two bases employed were optically pure (+)-potassium-2-octylate and L-N-lithium-N-neopentyl-α-phenylethylamine (both in refluxing benzene). The reactions were all run with less than one mole of base per mole of halide, and the remaining halide was then recovered and examined for optical activity.

The L-N-lithium-N-neopentyl-α-phenylethylamine was prepared from optically pure (+)-L-α-phenylethylamine[19] as shown in the reaction sequence.



$$C_6H_5\text{—}\underset{\displaystyle NH_2}{\underset{|}{CH}}\text{—}CH_3 \xrightarrow[\text{2, LiAlH}_4]{\text{1, (CH}_3\text{)}_3\text{C—COCl}}$$

$\alpha^{24}\text{D}$ +37.8°
(homog., l 1 dm.)

$$C_6H_5\text{—}\underset{\displaystyle NH\text{—}CH_2\text{—}C(CH_3)_3}{\underset{|}{CH}}\text{—}CH_3 \xrightarrow[-CH_4]{+CH_3Li}$$

$\alpha^{24}\text{D}$ +66.9°
(homog., l 1 dm.)

$$C_6H_5\text{—}\underset{\displaystyle Li^+N^-\text{—}CH_2\text{—}C(CH_3)_3}{\underset{|}{CH}}\text{—}CH_3$$

With (+)-potassium 2-octylate and *threo*-1,2-diphenyl-1-propyl chloride (run 44), a 32% yield of *trans*-α-methylstilbene and a 47% recovery of completely racemic chloride was obtained. With the same base and *erythro*-1,2-diphenyl-1-propyl bromide, *cis*-olefin and completely racemic bromide were isolated from the reaction mixture (run 45). The failure to get asymmetric degradation in the last two experiments is attributed to the fact that the asymmetric carbon atom of the base and that carrying the proton being lost are too far from one another to produce any asymmetric induction. Therefore the much more bulky L-N-lithium-N-neopentyl-α-phenylethylamine was tried with both the *erythro*- and *threo*-racemic chlorides. No reaction occurred with the *erythro* material and 97% of the starting halide was recovered (run 46). In the case of the *threo*-chloride the following novel reaction occurred (run 47).

The lithium salt of the amine was prepared in each case by allowing the secondary amine dissolved in dry benzene under nitrogen to react with an equivalent of methyl lithium dissolved in ether. Since the methyl lithium was prepared by the action of lithium on methyl iodide, the ether contained lithium iodide which was carried into the benzene solution. From the reaction of the lithium iodide (0.8 equivalent per equivalent of alkyl chloride) with the *d,l-threo*-1,2-diphenyl-1-propyl chloride was obtained a 61% yield of *threo*-1,2-diphenyl-1-propyl iodide, identified by analysis and through its E_2 reaction to give *trans*-α-methylstilbene. The remainder of the starting material was accounted for as an oil from which nothing could be crystallized. A control experiment carried out under the same conditions in which the lithium–amine salt was left out of the reaction mixture gave only recovered starting material.

The above experiment demonstrates that a *substitution reaction of iodide for chloride has occurred in a benzene solution with retention of configuration at the point of substitution,* and *that the presence of the amine salt is necessary for a reaction to occur.* Furthermore, the reaction did not occur when *erythro*-chloride was the starting material. The following explanation for these results is suggested. Since concerted frontside displacement reactions are unknown in systems analogous to the one at hand, the present reaction probably involves *at least* two stages, the first consisting of an ionization of the C–Cl bond, the second the formation of a new C–I bond. Since the reaction occurred with over-all retention of configuration, both the first and second stages probably occurred with inversion. Thus a second group must have been involved at the rear of the carbon atom bearing the chlorine during the breaking of the C–Cl bond. This group could either have been the phenyl of the adjacent asymmetric carbon atom or the highly hindered anion of the amine salt. Had the latter group become involved at all, tertiary amine would probably have resulted. On the other hand, that phenyl participates in substitution reactions to form phenonium ions has been established in similar systems[2,20] and probably occurred in the above reaction. The three-membered ring of the phenonium ion was then probably opened at the most positive carbon by an iodide ion. Two questions remain unanswered. What was the role of the amine in the reaction? Why did the reaction occur with *threo* and not with *erythro* starting materials. The amine salt probably exists as an ion-pair in benzene, and the lithium cation probably acted as a "puller," for the chlorine at the same time that the phenyl group acted as a "pusher" at the rear of the carbon atom involved in the reaction. Thus the amine salt would have the same promoting effect on the ionization of this alkyl halide as *p*-toluenesulfonic acid was found to have on the ionization of 3-phenyl 2-butyl tosylate.[2a,21] An explanation for the difference in reactivities of the *threo* and *erythro* starting materials is found in the geometry of the two phenonium ions that would be involved. The phenonium ion (III) from the *threo*-chloride has a phenyl and a methyl group distributed *trans* to one another, whereas the ion from the *erythro* would have these two groups distributed *cis* to one another. The reaction giving *cis*-bridged ion is less likely for three reasons; the *erythro*-chloride is more thermodynamically stable than the *threo*-

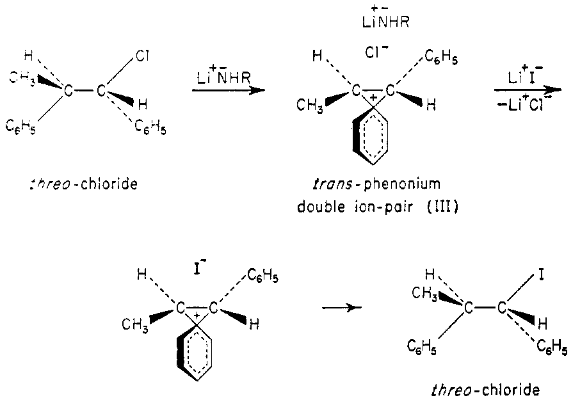
---

[19] A. Campbell and J. Kenyon, *J. Chem. Soc.*, 25 (1946).

[20] D. J. Cram and J. D. Knight, THIS JOURNAL, **74**, 5839 (1952).

[21] C. G. Swain [*ibid.*, **70**, 1119 (1948), and **72**, 2794 (1950)] has demonstrated that the methanolysis of trityl chloride in benzene–methanol mixtures is third order. This and other observations were interpreted as evidence that methanol (or other hydroxylic substances) solvated the chloride ion as it was formed.

isomer; the transition state leading to *cis*-bridged ion involves a methyl–phenyl steric repulsion absent in the transition state leading to III; the resonance of stabilization due to the distribution of positive charge into the ring of the non-participating phenyl group is sterically inhibited by the methyl group in the transition state leading to the *cis*-phenonium ion-pair, whereas this damping of resonance is absent in the transition state leading to the *trans*-phenonium ion-pair.[22] The formulation summarizes the explanation proposed for these results. In this mechanism, ion-pairs similar to those found to occur in the ionization of 3-phenyl-2-butyl tosylate[2a] probably are the intermediate species.



Experimental

Preparation of the Tosylates and Brosylates of the Stereoisomers of 1,2-Diphenyl-1-propanol (Procedure A).—Procedure is illustrated by the conversion of *d,l-erythro*-1,2-diphenyl-1-propanol to the brosylate ester as follows. A solution of 53.1 g. (0.25 mole) of carbinol in 530 ml. of pure, dry pyridine was cooled to −7° and treated with 68.8 g. (0.27 mole) of pure *p*-bromobenzenesulfonyl chloride in such a way (added in small portions over several hours) as to keep the temperature of the solution below 0°. After the addition was complete, the mixture was allowed to stand at 0° for six days, and was then poured onto a mixture of ice and water. The solid that separated was collected, the filtrate was extracted with benzene, and the solid was dissolved in the benzene extract. The resulting solution was washed with water, ice-cold 1 *N* sulfuric acid solution, again with water, sodium carbonate solution, and was finally dried and evaporated under 20 mm. pressure at room temperature. The residue was treated with pentane to give 68 g. (68% yield) of *d,l-erythro*-brosylate, m.p. 80° (dec., 3° per minute). An analytical sample crystallized from ether gave m.p. 81° (dec., 3° per min.). Large amounts of the brosylate or tosylate esters can be conveniently recrystallized from dry acetone. In each case the m.p. depended greatly on the rate of heating.

In the various attempts to prepare the tosylate of *threo*-1,2-diphenyl-1-propanol by the above procedure, seemingly pure product could be obtained, but within five minutes of the time it was dry it became hot and decomposed. Material prepared by the addition of *p*-toluenesulfonyl chloride to the potassium alcoholate behaved the same way.

If procedure A was carried out at room temperature, the alkyl chloride was the main product of the reaction.

Reaction of Lithium Halides with Brosylates and Tosylates of 1,2-Diphenyl-1-propanol.—C.P. acetone (dried for several days over Drierite and finally fractionally distilled) was used as solvent, and freshly prepared brosylate or tosylate ester and dry, pure lithium halides were used as reactants. The reactions involving lithium bromide and iodide were homogeneous at the beginning; however, the limited solubility of lithium chloride in acetone prohibited homogeneity in those runs involving that salt. In those runs (see Table II) in which barium carbonate was present as a second phase, the yields were slightly higher since the E_1 reaction which competes with the S_N2 reaction appeared to be acid-catalyzed. A sample procedure is outlined below (run 11, Table II).

A mixture of 8.61 g. (0.02 mole) of D-(−)-*erythro*-1,2-diphenyl 1-propyl-brosylate, 10 g. of freshly-fused lithium bromide, 150 ml. of pure, dry acetone and 10 g. of pure, dry barium carbonate was held at reflux temperature. After 50 minutes a flocculent and easily recognized precipitate of lithium brosylate appeared in the body of the solution. After 13 hours the mixture was cooled to room temperature, filtered, and the solvent was evaporated from the filtrate under reduced pressure. The residue was extracted with a pentane–ether–water mixture. The organic layer was washed with dilute sodium carbonate solution, with water and was dried. The solvent was evaporated to a 10-ml. volume (without heating above 50°), and this solution was cooled to −80°. The solid that separated was collected, and the filtrate was further evaporated and cooled to give a second crop. The combined solids were dissolved in 10 ml. of ethanol (40°), cooled to room temperature and filtered to give 0.18 g. (3% yield) of D-(−)-*erythro*-bromide, m.p. 159–160° (3°/min.), $[\alpha]^{23}\text{D}$ −136.1° (*c* 2.5 in $CHCl_3$). The filtrate was concentrated at room temperature to a volume of about 5 ml. during which time solid appeared. The mixture was cooled to 0° and the product was collected to give (including a second crop) a total of 4.0 g. (63% yield) of D-(+)-*threo*-bromide, m.p. 60–61°, $[\alpha]^{23}\text{D}$ +52.6° (*c* 6.8 in $CHCl_3$). Further fractional crystallization (five cycles) of this solid from ethanol gave tail crops, m.p. 60–61°, $[\alpha]^{23}\text{D}$ +54.7 (*c* 5.2 in $CHCl_3$). Further fractional crystallization of this material did not result in a change of either melting point or rotation. The *threo*-bromides decomposed if heated for any length of time in ethanol and must be stored at a low temperature.

Mixtures of diastereomers were encountered only when the *threo*-bromides were being produced. That the *threo*-bromides slowly isomerize to *erythro*-bromide under the conditions of the displacement reaction has been demonstrated in other work (see paper XVII of this series).

In those runs involving lithium chloride, a single diastereomer was produced which was crystallized from absolute ethanol (small volume, particularly in the case of the *threo*-isomer).

In those runs involving lithium iodide, the procedure was modified as follows. At the end of the reaction the mixture was filtered, and the filtrate was concentrated at room temperature under vacuum. The residue was dissolved in an ether–water mixture, the extract was washed successively with sodium thiosulfate solution and water. The ether solution was dried, evaporated under vacuum to give an oil which was dissolved in a small volume of absolute ethanol. The resulting solution was immediately cooled to −78° and the solid that separated was collected and recrystallized from ether–pentane. The material that separated appeared to be homogeneous in each run. The melting points (dec.) of each diastereomer were sharp, and a mixed melting point of the two diastereomers amounted to 107–120° (dec.). These iodides could be stored at low temperatures only for a short time.

The E_2 Reactions of the 1,2-Diphenyl-1-propyl Halides (Procedure B).—This general procedure is illustrated by that used in run 21. A mixture of 4.61 g. (0.02 mole) of *d,l-threo*-1,2-diphenyl-1-propyl chloride and 50 ml. of a 5–7% solution of potassium hydroxide in 95% ethanol (2–3 equivalents of base) was refluxed for 12 hours. At the end of this time the solvent was evaporated using a small Vigreux column, and the residue was shaken with a mixture of ice-water and ether. The organic layer was washed, dried and concentrated to an oil. This oil was dissolved in pentane, and the solution when cooled gave a solid which when recrystallized from absolute ethanol gave 3.4 g. (85% yield) of *trans*-α-methyl-stilbene, m.p. 81–82°, undepressed by admixture with an authentic sample.[6b]

Those runs involving *erythro*-halides were carried out in the same way except that the product was recrystallized from pentane to give *cis*-α-methylstilbene, m.p. 47–48°, undepressed by admixture with an authentic sample.[6b]

---

[22] Curtin and Pollak (ref. 3a) suggested an analogous explanation for the fact that different groups migrate in the semipinacolic deamination reaction of the one as compared to the other racemate of various *d,l*-1,2-diphenyl-1-aryl-2-aminoethanols.

Procedure C.—This general procedure is illustrated by that used in run 31. A mixture of 4.0 g. of potassium metal, 3.0 g. (0.023 mole) of *d,l*-2-octanol and 60 ml. of dry benzene was heated at reflux for eight hours and cooled. The unreacted metal was removed with a wire, and 2.3 g. (0.01 mole) of *d,l-threo*-1,2-diphenyl-1-propyl chloride was added to the heterogeneous mixture. The mixture became homogeneous when heated to reflux, and after 16 hours at this temperature the solvent was evaporated through a Vigreux column to a low volume. This solution was shaken with a mixture of ether and ice-water, the ether extract was washed with water, dried and evaporated to an oil. This oil was dissolved in pentane and passed through a column of activated alumina (10 × 2.5 cm.) with pentane as an eluting agent (the octanol remained on the column). When concentrated, the column eluates gave 1.77 g. (91% yield) of *trans*-α-methylstilbene, m.p. 81–82°, undepressed by admixture with an authentic sample.[6b]

Runs 38 and 39 were carried out utilizing the above procedure except that an equivalent amount of *d,l-threo*-1,2-diphenyl-1-propanol was substituted for the *d,l*-2-octanol. Runs 36, 37, 40 and 41 were carried out by procedure C except that after the excess potassium metal had been removed from the solution, 0.01 mole of the carbinol in question was added to the mixture. In runs 30, 36, 38 and 40 the starting material was isolated from the alumina column filtrates (pentane).

Procedure D.—A mixture of 2.0 g. of *d,l-threo*-1,2-diphenyl-1-propyl chloride (run 42) and 14 g. of *d,l*-N,N-dimethyl-α-phenylethylamine[23] was heated at 195° for 15 hours and cooled. The dark solution was shaken with a mixture of ethyl ether and water, the ether layer was washed with water, dried and evaporated to an oil. The gummy, pentane-insoluble residue was extracted with hot ethanol to give a solution that on concentration gave 0.25 g. (14% yield) of *trans*-α-methylstilbene, m.p. 80–81°, undepressed by admixture with authentic material.[6b] In run 43, no olefin could be isolated. When the above procedures were carried out with either diastereomeric chlorides at temperatures of 100° or under, only starting material was recovered (90–95%).

Attempts to Carry Out E_2 Reaction on Tosylates and Brosylates.—The tosylates and brosylates of both *d,l-erythro*- and *d,l-threo*-1,2-diphenyl-1-propanol when submitted to procedures B or C gave oils which were free of halogen or sulfur, contained only traces of olefin (as shown by bromine uptake), and although not definitely identified, appeared to be ethers. Analogous results were obtained when sodium ethylate in ethanol was employed as the basic medium.

Attempted Asymmetric Degradations of Racemic 1,2-Diphenyl-1-propyl Halides with (+)-Potassium 2-Octylate.—In runs 44 and 45 (Table III) *d,l-threo*-1,2-diphenyl-1-propyl chloride and *d,l-erythro*-1,2-diphenyl-1-propyl bromide, respectively, were submitted to procedure C except for the following modifications. (1) Only 0.58 equivalent of base was used per equivalent of alkyl halide. (2) Optically pure (+)-2-octanol, $[\alpha]^{25}\text{D}$ +9.42° (*c* 5.3 in ethanol)[24] was substituted for racemic alcohol in the preparation of the potassium alcoholate. (3) The reaction was carried out in the presence of 0.15 mole of (+)-2-octanol per mole of alkyl halide. (4) The mixtures of olefin and starting alkyl halide were separated by fractional elution from an alumina chromatographic column with pentane, followed by fractional crystallization of the material in the column eluates. The rotations of all the materials obtained including the oils from the combined filtrates turned out to be 0.00 ± 0.03°.

Preparation of L-(+)-N-Neopentyl-α-phenylethylamine.—To a well-stirred mixture of 24 g. (0.20 mole) of optically pure (+)-α-phenylethylamine ($[\alpha]^{24}\text{D}$ +37.6, homog.)[25] in 300 ml. of dry ether was added 11.2 g. (0.11 mole) of trimethylacetyl chloride (prepared from 11.3 g. of trimethylacetic acid and thionyl chloride) over a period of 30 minutes. The heterogeneous mixture was stirred at room temperature for three hours and was then filtered to give the solid α-phenylethylamine hydrochloride. The filtrate was washed with water, dried and evaporated to a low volume, and when cooled the solution deposited pure (+)-N-trimethylacetyl-α-phenylethylamine, wt. 18 g. (90% yield), m.p. 119–120°, $[\alpha]^{25}\text{D}$ +107° (*c* 5.3 in $CHCl_3$).

Anal. Calcd. for $C_{13}H_{20}ON$: C, 76.05; H, 9.33. Found: C, 75.86; H, 9.48.

A solution of 18.0 g. of the above amine in 50 ml. of dry ether was slowly added to a well-stirred solution of excess lithium aluminum hydride in dry ether. After the addition was complete the mixture was held at reflux for four hours, cooled, decomposed cautiously with ice-water and filtered. The solid was washed with ether, and the combined ether filtrates were washed with water, dried and concentrated to a brown oil. This material when distilled (b.p. 90–91° at 2–3 mm.) gave 16 g. of L-(+)-N-neopentyl-α-phenylethylamine, $n^{25}\text{D}$ 1.5871, $\alpha^{24}\text{D}$ +66.9° (homogen., *l* 1 dm.).

Anal. Calcd. for $C_{13}H_{21}N$: C, 81.18; H, 11.53. Found: C, 81.17; H, 11.50.

The hydrochloride of this amine was prepared by the addition of excess concentrated hydrochloric acid to 0.19 g. of this amine. The solid precipitate was isolated and crystallized from a methanol–ether mixture to give 0.12 g. of the pure salt, m.p. 292–293° (dec.).

Anal. Calcd. for $C_{13}H_{22}NCl$: C, 68.54; H, 9.73. Found: C, 68.45; H, 9.71.

Attempted Asymmetric Degradation of *d,l-erythro*- and *d,l-threo*-1,2-Diphenyl-1-propyl Chlorides with L-(+)-N-Lithium-N-neopentyl-α-phenylethylamine.[26]—The following reactions were carried out in a series of connected flasks in such a way that the reaction mixtures were always kept under an atmosphere of pure dry nitrogen. The procedure will be illustrated as applied to run 47.

To a mixture of 100 ml. of dry ether and excess lithium ribbon was added 9.94 g. (0.070 mole) of methyl iodide over a period of 30 minutes. The mixture was heated at reflux for three hours and filtered directly (the floor of the flask was a sintered glass plate) into a dry flask. To the clear solution of methyl lithium and lithium iodide was added a solution of 15 g. of L-(+)-N-neopentyl-α-phenylethylamine in 100 ml. of dry benzene. Methane was evolved during this addition. Pure, dry *d,l-threo*-1,2-diphenyl-1-propyl chloride (21 g. or 0.0913 mole) dissolved in 75 ml. of benzene was then added to the above solution. The resulting clear solution was warmed to reflux temperature and the mixture was concentrated by allowing ether to escape through the top of an attached condenser. The residual benzene solution (150–160 ml.) was held at reflux temperature for 20 hours (lithium chloride started to separate in about five minutes), and cooled to room temperature. The mixture was shaken with ether and ice-water, the ether layer was washed with ice-cold 2 *N* sulfuric acid solution, water, sodium carbonate solution and again with water and dried. The initial water washings were analyzed for chloride ion (Volhard method) and were found to contain 0.060 equivalents. The ether was evaporated under vacuum, and the residual oil solidified upon addition of ice cold absolute ethanol, wt. 4.05 g., m.p. 129–131° (dec. to deep red liquid), $[\alpha]^{21}\text{D}$ 0.00 ± 0.01° (*c* 5.9 in $CHCl_3$). The filtrate when cooled at 0° for a few hours gave 5.10 g. of the same material, m.p. 130–131° (dec.), $\alpha^{21}\text{D}$ 0.00 ± 0.01° (*c* 6.1 in $CHCl_3$). The second filtrate when cooled at −15° gave 5.90 g. of the same material, m.p. 130–131° (dec.), $\alpha^{21}\text{D}$ 0.00 ± 0.01° (*c* 4.6 in $CHCl_3$). The last filtrate when evaporated to a low volume at 20 mm. pressure (below room temperature) gave an additional 3.01 g. of the same material, m.p. 130–131° (dec.). Mixed melting points of each crop with each other crop showed no depression. The final filtrate was evaporated under reduced pressure to give 6.84 g. of a light brown oil, $\alpha^{21}\text{D}$ 0.00 ± 0.01 (homog., *l* 0.5 dm.). Attempts to crystallize this oil failed.

A representative sample of the above crystalline fractions was found to give a 20° melting point depression when mixed with *d,l-erythro*-1,2-diphenyl-1-propyl iodide. Other representative samples were submitted to the E_2 reaction by both procedures B and C to give 87% and 85% yields of *trans*-α-methylstilbene, respectively. The chemical and physical properties of the compound correspond to those of *d,l-threo*-1,2-diphenyl-1-propyl iodide.

---

[23] H. T. Clark, H. B. Gillespie and S. T. Weisshaus, THIS JOURNAL, **55**, 4571 (1933).

[24] J. Kenyon, "Organic Syntheses," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, pp. 418.

[25] A. W. Ingersoll, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1947, pp. 506.

[26] The configuration of α-phenylethylamine has been related to 2-phenylpropionic acid [H. I. Bernstein and F. C. Whitmore, THIS JOURNAL, **61**, 1324 (1939)] which in turn has been related to D-glyceraldehyde (see ref. 6b for a summary of the references).

When 24.0 g. of *d,l-erythro*-1,2-diphenyl-1-propyl chloride was submitted to the above procedure, 96% of the starting material was recovered, m.p. 139–140°, undepressed by admixture with an authentic sample.

When a mixture of 5.0 g. of *d,l-threo*-1,2-diphenyl-1-propyl chloride, 10 g. of lithium iodide and 75 ml. of benzene was held at reflux for 48 hours, a 94% recovery of starting material was realized, m.p. 53–54° (undepressed by admixture with an authentic sample).

Acknowledgment.—The authors wish to acknowledge the value of conversations about portions of this paper with Dr. R. L. Scott.

LOS ANGELES, CALIFORNIA

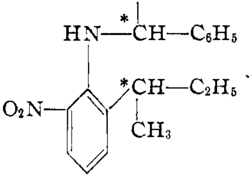
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Studies in Stereochemistry. XV. Effect of Configuration on Steric Inhibition of Resonance in Diastereomerically Related Compounds

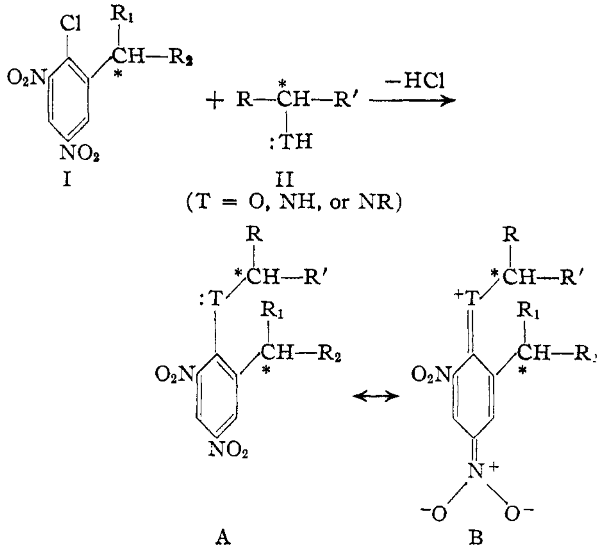
BY FRED HAWTHORNE[1] AND DONALD J. CRAM[2]

RECEIVED MAY 3, 1952

This investigation has demonstrated the feasibility of using differences between the ultraviolet absorption spectra of certain diastereomerically related compounds to determine the relative configurations of the asymmetric carbon atoms involved. The four stereoisomers of Compound VIII have been prepared, and the configurations of the two asymmetric carbon atoms in each have been related to D-glyceraldehyde by chemical transformations. Comparisons of the spectra of the diastereomers of VIII, and of model compounds and VIII indicate that different degrees of steric inhibition of resonance exist in the diastereomers. The direction of this difference is in agreement with the direction predicted from a comparison of molecular models of the diastereomers. The relative rates of the reaction of the enantiomers of 2-*s*-butyl-4,6-dinitrochlorobenzene with (+)-α-phenylethylamine to form diastereomers of VIII have been determined. The qualitative relationship between these rates has been correlated with the differences in spectra in the products, and the differences in the steric situations found in hypothetical models for the diastereomerically related transition states for the two reactions.



Correlations between the signs of rotations of optically active molecules and the configurations about the asymmetric centers responsible for the activity have been of great value in making configurational assignments to substances whose stereochemical structures are unknown. The use of other physical properties in relating the configurations about two or more asymmetric carbon atoms within the same molecule has occasionally been of value,[3] but has never received widespread attention. This investigation was undertaken to explore the possibility of determining the configurations of optically active amines and alcohols relative to D-glyceraldehyde through the use of ultraviolet absorption spectral techniques.



(T = O, NH, or NR)

III (resonance hybrid)

If an optically active reagent of structure I is allowed to react with an optically active amine or alcohol such as II, then compound III is capable of existing in either of two diastereomeric forms. It has long been recognized that the damping of resonance through steric effects in systems similar to III decreases the intensity and usually the wave length of the major absorption peak in the ultraviolet absorption spectrum.[4] Therefore that diastereomer of III in which the two asymmetric carbon atoms come closest to becoming coplanar with the benzene ring should absorb light at the longer wave length and higher intensity. Since the way in which R_1, R_2, R and R′ fit together sterically is a function of the configurations about the two asymmetric carbon atoms, then differences in molecular models of the two diastereomers of III should correlate in an *a priori* predictable fashion with the

---

[1] Atomic Energy Commission Predoctoral Fellow, 1950–1951.

[2] Requests for reprints should be sent to this author.

[3] Differences in dipole moments [A. Weissberger, THIS JOURNAL, **67**, 778 (1945)], and dielectric constants [S. Winstein and R. E. Wood, *ibid.*, **62**, 548 (1940)] between diastereomerically related compounds have been found, and might in some cases prove useful in making configurational assignments. The use of X-ray diffraction techniques has been of great value in a few cases in assigning configurations in such complicated molecules as cholesteryl iodide [C. H. Carlisle and D. Crowfoot, *Proc. Roy. Soc. (London)*, **A184**, 64 (1945)] and penicillin [D. Crowfoot, C. W. Bunn, B. W. Rogers-Low and A. Turner-Jones, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 310]. Recently N. H. Cromwell, *et al.*, [THIS JOURNAL, **73**, 1044 (1951)] made provisional assignments of configuration to two diastereomerically related iminoketones based on differences in ultraviolet absorption spectra due to differences in steric inhibition of resonance in the two diastereomers.

[4] (a) G. Wheland, "Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 160 (numerous references); (b) W. R. Remington, THIS JOURNAL, **67**, 1838 (1945); (c) N. J. Leonard, *et al.*, *ibid.*, **72**, 484, 5388 (1950); (d) R. T. Arnold and P. N. Craig, *ibid.*, **72**, 2728 (1950).