tracted with methylene chloride, and the combined organic layers were dried, evaporated and the residual oil was distilled through a short path still to give 1.61 g. (74%) of colorless ketol, b.p. 120° at 11 mm., $n^{25}D$ 1.4883. This crude ketol gave a 67% yield of the 2,4-dinitrophenylhydrazone of *cis*-ketol, m.p. 151–153° (undepressed by admixture with an authentic sample).

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

Studies in Stereochemistry. XXIX. Neighboring Hydrogen Participation in Ionization to Give Ethylene Protonium Ions as Intermediates in the Wagner–Meerwein Rearrangement[1]

BY DONALD J. CRAM AND JACK TADANIER

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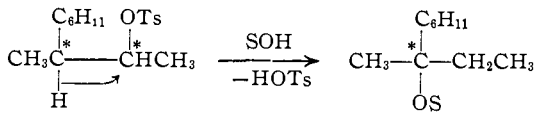
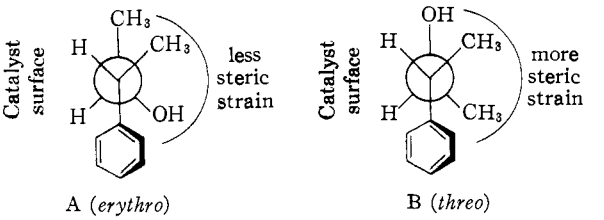
The optically pure diastereomeric *p*-toluenesulfonate esters of 3-cyclohexyl-2-butanol have been prepared, and the rates and solvolysis products have been examined. The yields of solvolysis products varied between 12 and 29% depending on the nucleophilicity of the solvent. The other product was olefin. In 20% water–80% dioxane, 2-cyclohexyl-2-butanol was the major and 3-cyclohexyl-2-butanol the minor solvolysis product. Starting material of the *threo* configuration gave tertiary alcohol (product of hydrogen migration) which was 59% optically pure, and secondary alcohol (simple solvolysis product) 90% inverted. Starting material of the *erythro* configuration gave tertiary alcohol 44% optically pure, and secondary alcohol 72% inverted. The relative configurations of starting material and rearranged tertiary alcohol were demonstrated in independent experiments, and thus the predominant steric course of hydrogen migration with respect to the migration origin could be determined. *Solvent was found to react at the tertiary carbon atom from the side originally occupied by hydrogen.* The rates of solvolysis of the diastereomeric 3-cyclohexyl-2-butyl *p*-toluenesulfonates differed by factors of 2.38 to 2.97 depending on solvent and temperature, with the *erythro* isomer the faster. These rates are greater than those of 2-butyl tosylate by factors of from 6 to 31 depending on solvent and diastereomer. The diastereomeric 3-cyclohexyl-2-butyl-3-*d* *p*-toluenesulfonates were prepared, and their rates of acetolysis were compared with those of the undeuterated compounds. For the *erythro* isomer, k_H/k_D = 1.85, and for the *threo* isomer, k_H/k_D = 1.72. The only satisfactory interpretation of the data is as follows. (1) Neighboring hydrogen participates in ionization of the starting esters to form a bridged protonium ion. (2) This bridged ion partitions between secondary and tertiary carbonium ions, which in turn give secondary and tertiary alcohol, respectively, and olefin. (3) Solvent hydrogen-bonds with the bridged ion (conjugate acid of a weak base) and is therefore, well oriented to attack carbon from the side of the bridge, which offers little steric resistance to such a process.

Extensive studies have been made of the Wagner–Meerwein rearrangement with phenyl or methylene as the migrating group, but relatively little has been done with hydrogen migration, particularly with respect to stereochemistry. Cope[2] and Prelog[3] have studied transannular hydrogen migration in the medium sized rings in solvolysis reactions, whereas hydrogen migration in bicyclic systems has been examined by Roberts,[4] and in six-membered rings by Winstein,[5] Rearrangements involving hydrogen migration have been observed in open-chain systems in deamination reactions,[6,7] in *p*-toluenesulfonate ester solvolysis,[8] and in reactions of alkyl halides with silver acetate.[9]

This paper is concerned with the mechanism of hydrogen migration which occurs during the solvolysis of the *p*-toluenesulfonates of the diastereomeric 3-cyclohexyl-2-butanols. In the starting material both the migration origin and terminus are asymmetric, whereas the migration origin is asymmetric in the product. These relationships allow the steric course of reaction at the migration origin to be examined, and the behavior of the diastereomers to be compared. Both the kinetics and reaction products of solvolyses of this system have been examined, the former with both hydrogen and deuterium as the migrating group.



Preparation and Relative Configurations of the 3-Cyclohexyl-2-butanols, and of 2-Cyclohexyl-2-butanol.—Both optically pure and racemic *threo*- and *erythro*-3-phenyl-2-butanol were prepared[10] and reduced catalytically to the corresponding *threo*- and *erythro*-3-cyclohexyl-2-butanols[11] (I), which were characterized as their crystalline *p*-toluenesulfonates. In all cases, the *erythro* reduced about twice as fast as the *threo* isomer. This rate difference correlates with the configurations of the diastereomers. Conformations A and B present the least hindered face of the benzene ring to the catalyst surface, and since CH_3 is larger than OH,



(1) This work was sponsored by the Office of Ordnance Research, U. S. Army.

(2) A. C. Cope, S. W. Fenton and C. F. Spencer, THIS JOURNAL, **74**, 5884 (1952), and subsequent papers.

(3) V. Prelog and K. Schenker, *Helv. Chim. Acta*, **35**, 2044 (1952), and subsequent papers.

(4) J. D. Roberts, C. C. Lee and W. H. Saunders, THIS JOURNAL, **76**, 4501 (1954).

(5) S. Winstein and N. J. Holness, *ibid.*, **77**, 5562 (1955).

(6) J. D. Roberts and J. A. Yancey, *ibid.*, **74**, 5943 (1952).

(7) D. J. Cram, J. E. McCarty, *ibid.*, **79**, 2866 (1957).

(8) D. J. Cram, *ibid.*, **74**, 2137 (1952).

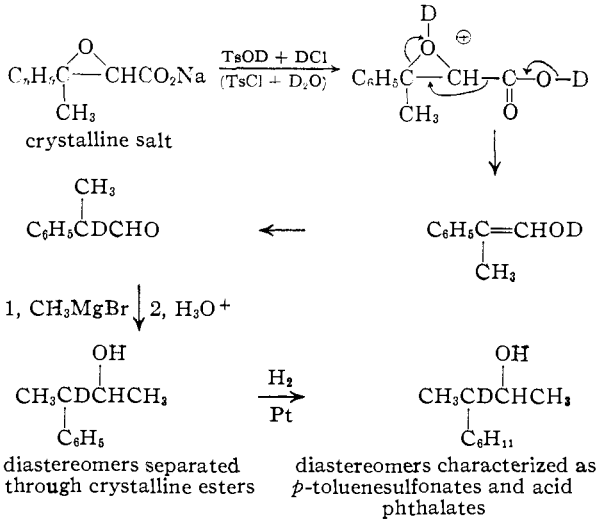
(9) E. Linnemann, *Ann.*, **162**, 12 (1872).

(10) (a) D. J. Cram, THIS JOURNAL, **71**, 3863 (1949); (b) **74**, 2129 (1952).

(11) D. J. Cram and F. D. Greene, *ibid.*, **75**, 6005 (1953).

conformation B of the *threo* isomer is expected to be of higher energy and hence least subject to absorption on the catalyst. Complete reduction of each sample was demonstrated by the absence of absorption in the ultraviolet in the region of 210 to 300 mμ.

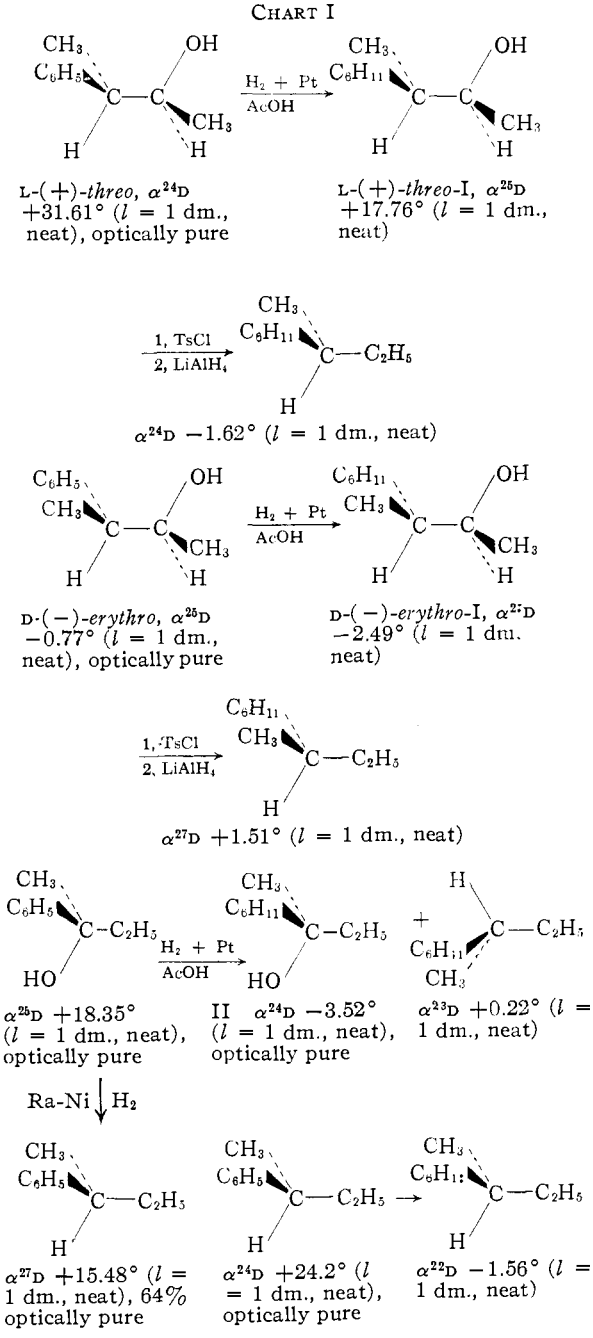
Racemic *threo*-and *erythro*-3-cyclohexyl-2-butanol-3-*d* were prepared by the sequence shown.



To establish the rotation of optically pure 2-cyclohexyl-2-butanol (II), optically pure 2-phenyl-2-butanol[12] was reduced to II with a platinum catalyst in glacial acetic acid. Racemic II was also prepared for comparison of physical properties by addition of methylmagnesium iodide to ethyl cyclohexyl ketone. Similarly, optically pure phenylisopropylcarbinol was reduced to cyclohexylisopropylcarbinol (potential product of methyl migration during solvolysis of *p*-toluenesulfonate esters of I).

The absolute configurations of the isomeric 3-cyclohexyl-2-butanols (I) are known because the absolute configurations of the isomeric 3-phenyl-2-butanols have been established.[13] The conversion of 2-phenyl-2-butanol to 2-cyclohexyl-2-butanol establishes the configurational relationships between these two compounds. The configuration of 2-phenyl-2-butanol was provisionally assigned[12b] on the basis of the conversion with Raney nickel of optically active (+)-material to (+)-2-phenylbutane, whose absolute configuration is known.[13] The stereochemistry of such hydrogenolyses has been established to go with predominating retention in systems of known configuration.[14] In the conversion of (+)-2-phenyl-2-butanol to (−)-2-cyclohexyl-2-butanol with hydrogen and platinum in acetic acid (52% yield), a 28% yield of (+)-2-cyclohexylbutane was obtained. Reduction of (+)-2-phenylbutane under the same conditions gave (−)-2-cyclohexylbutane.[15] Thus the hydrogenolysis of 2-phenyl-2-butanol with platinum and acetic acid must have occurred with predominating inversion of configuration. Unequivocal evidence for the configurational assignment given to (−)-2-cyclohexyl-2-butanol will be published shortly in connection with other studies. Chart I summarizes the configurational relationships discussed above.

CHART I



The possibility exists that during the reduction of the isomeric 3-phenyl-2-butanols to the corresponding isomeric 3-cyclohexyl-2-butanols some epimerization at the benzyl carbon atom occurred. Since the latter compounds were converted to sharp-melting cyrstalline *p*-toluenesulfonates before use, any diastereomeric impurity would be lost.

(12) (a) H. H. Zeiss, THIS JOURNAL, **73**, 2391 (1951); (b) D. J. Cram and J. Allinger, *ibid.*, **76**, 4516 (1954).

(13) D. J. Cram, *ibid.*, **74**, 2149 (1952).

(14) W. A. Bonner, J. A. Zderic and G. A. Casalleto, *ibid.*, **74**, 5086 (1952).

(15) We are indebted to K. Kopecky for carrying out this reaction. These two configurational relationships are in harmony with the earlier findings of P. A. Levene and S. A. Harris, [*J. Biol. Chem.*, **112**, 195 (1935)] and P. A. Levene and R. E. Marker, [*ibid.*, **100**, 685 (1933)].

TABLE I

KINETICS OF SOLVOLYSES OF THE *p*-TOLUENESULFONATES OF *threo*- AND *erythro*-3-CYCLOHEXYL-2-BUTANOLS (*threo*- AND *erythro*-I)

Run	*p*-Toluenesulfonate of	Solvent[a]	Base	ROTs, mole/liter	Base, mole/liter	*T*, °C. (±0.02°)	*k*, sec.$^{-1}$ × 10^5
1	*threo*-I	AcOH	AcOK	0.02903	0.03221	50.01	2.58 ± 0.02
2	*threo*-I	AcOH	AcOK	.02966	.03144	50.01	2.60 ± .04
3	*threo*-I	AcOH	AcOK	.02891	.03200	75.00	46.8 ± .4
4	*threo*-I	AcOH	AcOK	.02912	.03310	75.00	46.3 ± .6
5	*threo*-I	HCO_2H	HCO_2Na	.03396	.04007	25.00	59.5 ± 1.2
6	*erythro*-I	AcOH	AcOK	.02911	.03270	50.01	6.14 ± 0.09
7	*erythro*-I	AcOH	AcOK	.02900	.03070	50.01	6.20 ± 0.05
8	*erythro*-I	AcOH	AcOK	.02901	.03200	75.00	102.7 ± 1.5
9	*erythro*-I	AcOH	AcOK	.02905	.03310	75.00	102.4 ± 2.0
10	*eruthro*-I	HCO_2H	HCO_2Na	.03391	.04007	25.00	159 ± 2.3
11	*threo*-I-3-d[b]	AcOH	AcOK	.02982	.03375	49.94	1.597 ± 0.16
12	*threo*-I-3-d[b]	AcOH	AcOK	.02960	.03415	75.00	29.96 ± .19
13	*threo*-I-3-d[c]	AcOH	AcOK	.02916	.03403	74.94	29.58 ± .20
14	*threo*-I-3-d[b]	HCO_2H	HCO_2Na	.03609	.04023	25.00	40.89 ± .94
15	*erythro*-I-3-d[b]	AcOH	AcOK	.02964	.03453	49.94	3.315 ± .012
16	*erythro*-I-3-d[b]	AcOH	AcOK	.02962	03376	75.00	57.3 ± .7
17	*erythro*-I-3-d[c]	AcOH	AcOK	.02930	03403	74.94	55.6 ± 1.4
18	*erythro*-I-3-d[b]	HCO_2H	HCO_2Na	.03689	04023	25.00	92.0 ± 1.6

[a] Solvents were free of water. [b] These solid esters were made diastereomerically pure by repeated recrystallization. [c] The alcohols from which these esters were made were first purified by conversion to their acid phthalates, which were repeatedly recrystallized. The alcohols were regenerated, and converted to their *p*-toluenesulfonates.

Confirmation of configurational homogeneity at the carbon carrying the cyclohexyl group was demonstrated through reduction of these *p*-toluenesulfonates to optically pure 2-cyclohexylbutane.

The deuterium contents of *threo*-and *erythro*-3-phenyl-2-butanol-3-*d* were found to be 0.95 and 0.94 gram atom per mole, respectively.[16] These values are in substantial agreement with those obtained from nuclear magnetic resonance spectra measurements. The spectra of deuterated and non-deuterated isomeric 3-phenyl-2-butanols were compared. Bands associated with benzyl hydrogen were well resolved and readily identified by their virtual absence in the spectra of the deuterated compounds. The amount of deuterium in the benzyl position was determined by comparing the area under the residual benzyl hydrogen peaks in the spectra of the deuterated materials with the area under the overlapping peaks of the hydroxyl hydrogen and the hydrogen attached to the carbon bonded to the hydroxyl group. The relative areas beneath these peaks in undeuterated materials was essentially 1 to 2, respectively, but was 1 to 31 and 1 to 43 in the deuterated *threo*- and *erythro*-isomers, respectively. Clearly the *threo* isomer contains agout 6% hydrogen on the benzyl carbon, and the *erythro* isomer about 5%.[17] These facts indicate that all the deuterium in these isomers is on the benzyl carbon atom.

The deuterium content of the 3-cyclohexyl-2-butanols dropped during hydrogenation to 0.82 and 0.88 gram atom of deuterium per mole for the *threo* and *erythro* isomers, respectively. Apparently a small amount of hydrogen–deuterium exchange occurred before or during hydrogenation. The greater exchange for the *threo* isomer correlates with the greater time required for hydrogenation of this isomer. The above deuterium analysis applies to samples before they were converted to crystalline derivatives. After each reduction mixture was purified through a crystalline acid phthalate derivative to get rid of any diastereomeric impurity introduced during the reduction, deuterium analysis showed 0.89 and 0.99 gram atom of deuterium per mole for the regenerated *threo*-and *erythro*-alcohols, respectively. These data are interpreted as follows. For the *threo*-isomer, 13% exchange of deuterium for hydrogen at the benzyl carbon occurred during hydrogenation, 7% of which was accompanied by epimerization. In the *erythro* isomer, 6% exchange of deuterium for hydrogen occurred, most of which was accompanied by epimerization. In addition, some deuterium enrichment of the *erythro* isomer occurred by epimerization of some of the non-labeled material. The rate of epimerization of the non-labeled compound might have been greater than that of the deuterated material, due to the usual isotope effect. Exchange reactions at benzyl carbon during catalytic reductions have been observed before.[18]

Kinetics of Solvolysis.—The rates of acetolysis and formolysis of the *p*-toluenesulfonates of *threo*- and *erythro*-3-cyclohexyl-2-butanols were followed titrimetrically by the procedures described by Winstein.[19] The rate constants were calculated from the integrated first-order rate equation, and the rates were found to be clearly first order. In all runs a mole of base was added to neutralize the *p*-toluenesulfonic acid formed. About ten points were taken in each run. Table I reports the rate data obtained on both deuterated and non-deuterated material.

(16) The deuterium analyses were kindly carried out by Dr. Nelson Trenner of Merck Sharp and Dohme, by combustion and analysis of the water produced.

(17) The nuclear magnetic resonance spectra of these diastereomers will be discussed in a future paper of this series.

(18) (a) D. J. Cram, THIS JOURNAL, **74**, 5518 (1952); (b) W. A. Bonner and J. A. Zderic, *ibid.*, **78**, 4369 (1956).

(19) (a) S. Winstein and K. Schreiber, *ibid.*, **74**, 2165 (1952); (b) S. Winstein and H. Marshall, *ibid.*, **74**, 1120 (1952).

Within experimental error, the rate constants for runs 12 and 13 on the one hand and 16 and 17 on the other are the same. This fact indicates that about the same degree of diastereomeric, and therefore isotopic purity, was attained by purification of *threo*-and *erythro*-I through either the *p*-toluenesulfonate derivatives alone, or through both the acid phthalate and *p*-toluenesulfonate derivatives.

The lack of isotopic purity in runs 11 and 15 (Table I) can be easily corrected for with equation 1. In these two runs, at $t = 0$ (time at which the first point was determined) only 0.8 to 1.3% of

$$k_D = \frac{2.303}{t} \log \frac{x_0}{z - y_0 e^{-k_H t}} \quad (1)$$

x_0 = initial concn. of deuterated material
y_0 = initial concn. of non-deuterated material
z = concn. of total unreacted *p*-toluenesulfonate ester

ester had reacted, and therefore, the relative amounts of deuterated and non-deuterated materials were essentially the same as in the starting material. Table II gives the results of these corrections for each point in the two runs, as well as the isotope effect at each point. Table III records the activation energies and entropies for the acetolyses of the diastereomeric *p*-toluenesulfonate esters.

TABLE II

CORRECTION FOR DEUTERIUM CONTENT OF THE RATE CONSTANTS FOR THE ACETOLYSIS OF THE *p*-TOLUENESULFONATES OF *threo*-I-3-*d* AND *erythro*-I-3-*d* AT 50°

Run 11, ester of *threo*-I-3-*d*, 0.89 gram atom of deuterium per mole, $k_H = (2.58 \pm 0.02) \times 10^{-5}$ sec.$^{-1}$, $z_0 = 3.135c$, $x_0 = 2.790c$ and $y_0 = 0.345c$, z/c = (volume of titrant used at time t) − (volume of titrant used at $t\alpha$)

Point	z/c	$k_D \times 10^{-5}$, sec.$^{-1}$	Time, sec.	k_H/k_D
1	2.503	1.454	14,340	1.77
2	2.083	1.522	25,140	1.70
3	1.892	1.521	31,140	1.70
4	1.755	1.515	35,940	1.70
5	1.606	1.497	41,940	1.72
6	1.441	1.508	48,540	1.72
7	1.247	1.512	57,540	1.70
8	1.086	1.507	66,540	1.72
9	0.952	1.494	75,540	1.73
10	0.800	1.502	86,340	1.72
11	0.637	1.508	100,740	1.72

$k_D = (1.504 \pm 0.12) \times 10^{-5}$ sec.$^{-1}$; $k_H/k_D = 1.715 \pm 0.025$)

Run 15, ester of *erythro*-I-3-*d*, 0.99 gram atom of deuterium per mole, $k_H = (6.20 \pm 0.05) \times 10^{-5}$ sec.$^{-1}$, $z_0 = 3.120c$, $x_0 = 3.089c$ and $y_0 = 0.0312c$

1	2.435	3.448	7,140	1.80
2	2.192	3.357	10,440	1.85
3	2.082	3.366	11,940	1.84
4	1.922	3.357	14,340	1.85
5	1.705	3.345	17,940	1.85
6	1.520	3.318	21,540	1.87
7	1.345	3.325	25,140	1.86
8	1.122	3.332	30,540	1.86
9	0.957	3.325	35,340	1.86
10	0.834	3.321	39,540	1.87
11	0.665	3.297	46,680	1.88

$k_D = (3.345 \pm 0.027) \times 10^{-5}$ sec.$^{-1}$; $k_H/k_D = 1.845 \pm 0.025$

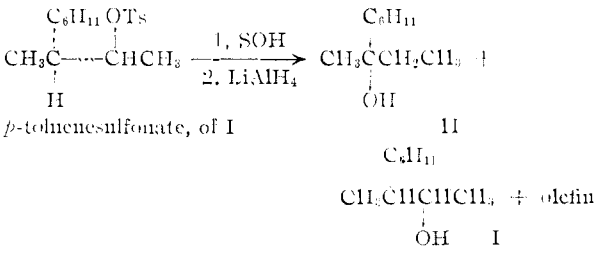
TABLE III

ACTIVATION ENERGIES AND ENTROPIES FOR THE ACETOLYSES OF THE *p*-TOLUENESULFONATES OF *threo*- AND *erythro*-3-CYCLOHEXYL-2-BUTANOLS (I)

p-Toluenesulfonate of	E_a, kcal./mole	$\Delta H^{\ddagger}$, kcal./mole	$\Delta S^{\ddagger}$, kcal./deg. mole
threo-I	25.8	25.8	−1.9
erythro-I	25.1	25.2	−2.2
threo-I-3-*d*	26.2	26.1	−1.4
erythro-I-3-*d*	25.5	25.6	−2.3

Products of Solvolyses.—Formolyses of the *p*-toluenesulfonates of *threo*- and *erythro*-I led exclusively to olefinic products. The lack of substitution products is probably due to the instability of the expected product, 2-cyclohexyl-2-butyl formate under the reaction conditions. Acetolysis of both optically pure and racemic diastereomeric *p*-toluenesulfonates in the presence of one mole of sodium acetate gave a mixture of olefin and acetate which was converted to a mixture of olefin and alcohol with lithium aluminum hydride. Olefin and alcohol were separated by chromatography, and the composition of the alcohol fraction was determined through use of infrared analysis and separation procedures involving crystalline derivatives (see Experimental). Hydrolysis of optically pure diastereomeric *p*-toluenesulfonates of I were carried out in 80% aqueous dioxane at 50° in the presence of sodium acetate to neutralize the *p*-toluenesulfonic acid liberated. The products were separated and analyzed as in the acetolysis runs.

The alcohol fraction in all cases consisted mainly of 2-cyclohexyl-2-butanol (II), the product of hydrogen migration. Small amounts of 3-cyclohexyl-2-butanol were also present (product of simple substitution), and 1-cyclohexyl-2-methyl-1-propanol (product of methyl migration) was demonstrated to be absent in other than trace amounts. Compounds I and II were separated through use of derivatives, and their configurations determined. The results of these analyses are recorded in Table IV.



The olefinic products were not examined in detail. Treatment of the olefinic products from the acetolysis of each diastereomeric sulfonate ester with 2,4-dinitrobenzenesulfenyl chloride gave in each case about a 25% yield of crude adduct. When purified, this derivative of olefin produced from each diastereomer proved to be the same compound. Since 2,4-dinitrobenzenesulfenyl chloride has been demonstrated to add stereospecifically to *cis*-and *trans*-olefins,[20] this experiment demonstrates that some of the same olefin was produced from each diastereomer.

(20) D. J. Cram, THIS JOURNAL, **71**, 3883 (1949).

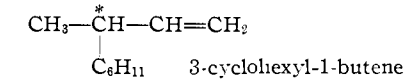
TABLE IV

PRODUCTS OF SOLVOLYSES OF THE *p*-TOLUENESULFONATES OF *threo*- AND *erythro*-3-CYCLOHEXYL-2-BUTANOL (I)

Run	*p*-Toluenesulfonate of	Solvent	*T*, °C.	Concn., mole/liter: Base	Concn., mole/liter: ROTs	% yld. olefin	% yld. ROH	α^{d}_{D} ROH	Composition (ROH = 100%): % I	% II	Composition (I = 100%): % *threo*	% *erythro*	Composition of I: α^{d}_{D}	Composition of I: % opt. purity[b]
19	(±)-*threo*-I	AcOH	35	KOAc 0.181	0.161	40	10	.....	..	.....	.....	.....	.....	..
20	(±)-*erythro*-I	AcOH	35	KOAc .181	.161	58	13	.....	..	.....	.....	.....	.....	..
21	L-(+)-*threo*-I	AcOH	35	KOAc .174	.155	54	12	−1.19°	0–5	95–100[c]	.....		−1.23°[d]	35[e]
22	D-(−)-*erythro*-I	AcOH	35	KOAc .174	.155	61	13	+0.45	0–5	95–100[c]	.....	.....	+1.07°[d]	30[e]
23	L-(+)-*threo*-I	80% diox.	50	NaOAc .0885	.0772	45	29	−1.33	..	.....	.....	.....	−2.06°[d]	59[e]
24	D-(−)-*erythro*-I	80% diox.	50	NaOAc .0885	.0772	53	23	+0.47	..	.....	.....	.....	+1.53°[d]	44[e]
25	(±)-*threo*-I	80% diox.	50	NaOAc .0879	.0772	..	27	.....	15	85[f]	10 ± 5	90 ± 5[g]	.....	..
26	(±)-*erythro*-I	80% diox.	50	NaOAc .0879	.0769	..	22	.....	7	93[f]	77 ± 8	23 ± 8[g]	.....	..

[a] Temperature 23–27°, l = 1 dm., neat. [b] Based on rotation of optically pure II, α^{24}_{D} −3.52° (l = 1 dm., neat). [c] Based on infrared measurements of ROH. [d] Secondary alcohol I was removed by phthalic anhydride procedure, leaving tertiary alcohol behind (see Experimental). [e] These values are in agreement with those obtained by analysis with melting point–composition experiments of solid derivatives (see Experimental). [f] Based on actual separation of alcohols by the phthalic anhydride method. [g] Based on infrared analysis (see Experimental).

The only olefin which may be formed with preservation of an asymmetric center is 3-cyclohexyl-1-butene. The observed difference in the magnitude of rotation of the olefinic mixtures recovered from the acetolyses of optically pure *threo*-and *erythro*-3-cyclohexyl-2-butyl *p*-toluenesulfonates indicates that the olefin from *threo*-ester contains approximately three times as much 3-cyclohexyl-1-butene as that from the *erythro*-ester. Unfortunately the rotation of optically pure olefin is not known.



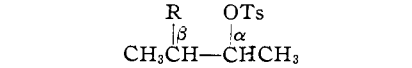
3-cyclohexyl-1-butene

Discussion

Neighboring Hydrogen Participation in Ionization.—In Table V, the rates of acetolysis and formolysis of a number of butyl *p*-toluenesulfonate systems are compared. Clearly a rate increase is evident as methyl is substituted for hydrogen and cyclohexyl for methyl in the β-position. This rate enhancement is probably due largely to the effect of neighboring hydrogen participation in ionization, and to a lesser extent to steric acceleration in ionization.[21] The parent 2-butyl *p*-toluenesulfonate shows only a slight tendency for hydrogen migration during solvolysis,[22] while in the 3-cyclohexyl-2-butyl *p*-toluenesulfonate, the substitution product is almost completely rearranged. Thus the system with the greater rate shows the greater tendency to rearrange. The fact that the rate enhancement is greater in formic than in acetic acid correlates with the greater nucleophilicity of acetic acid, which is better able to compete with neighboring hydrogen in aiding ionization.

TABLE V

RELATIVE RATES OF SOLVOLYSIS OF A NUMBER OF 2-BUTYL *p*-TOLUENESULFONATES



Solvent	*T*°, C.	R = H[a]	R = CH_3[a]	R = C_6H_{11} (*threo*)	R = C_6H_{11} (*erythro*)
AcOH	50	1	3	6	14
HCO_2H	25	1	6	12	31

[a] Taken from the data of S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, THIS JOURNAL, 74, 1113 (1952). The rate constants of the *p*-bromobenzenesulfonate solvolyses were divided by three to get the rates of the corresponding *p*-toluenesulfonates.

TABLE VI

RELATIVE SOLVOLYSIS RATES OF THE *p*-TOLUENESULFONATES OF *threo*- AND *erythro*-3-CYCLOHEXYL-2-BUTANOL

Solvent	AcOH[a]	AcOH	AcOH	HCO_2H
T, °C.	25	50	75	25
k erythro/*k threo*	2.97	2.38	2.21	2.67

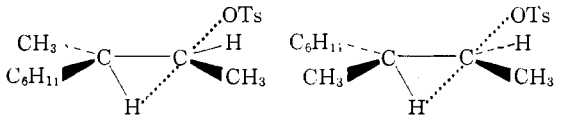
[a] Extrapolated from rate data obtained at 50 and 75°.

In Table VI, the rates of solvolysis of the *p*-toluenesulfonates of *threo*- and *erythro*-I are compared as a function of temperature and solvent.

(21) H. C. Brown and R. S. Fletcher, THIS JOURNAL, **72**, 1223 (1950), and subsequent papers.

(22) J. D. Roberts, R. E. McMahan and E. W. Holroyd, *ibid.*, **74**, 4283 (1952).

In both formic and acetic acids, the *erythro* isomer solvolyzes between 2.2 and 3.0 times as fast as the *threo* isomer, and formic and acetic acid give about the same factors when compared at the same temperature. The rate difference between diastereomers is probably due to differences in both ground state and transition state energies. The group OTs is smaller than CH_3[5] and larger than H just as is the OH group. Since *threo*-I has been shown to be more thermodynamically stable than *erythro*-I,[11] the same relationship should apply to the *p*-toluenesulfonates. Comparison of eclipsing effects in the transition states for hydrogen participation indicates that IV is more stable than III. Both effects probably contribute to the rate differences. As expected, the differences in rate between diastereomers decrease with increasing temperature. It is interesting that the differences depend only a little on the character of the solvent (see Table VI).



III (*threo*-transition state) IV (*erythro*-transition state)

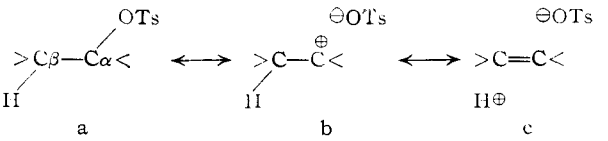
The above rate factors which compare the acetolysis of the diastereomeric *p*-toluenesulfonates are much less than the factor of 170 by which neomenthyl *p*-toluenesulfonate acetolysis exceeds that of the menthyl ester.[23] In the latter isomer, neighboring hydrogen does not occupy a position on C_β *trans* to the leaving group, and thus neighboring group assistance to ionization is impossible for this isomer. In the neomenthyl system, however, the geometry is ideal for such assistance. Hence, the diastereomers solvolyze by different mechanisms. In the open-chain 3-cyclohexyl-2-butyl system, both diastereomers solvolyze by essentially the same mechanism, and the conformations of the system adapt to the reaction path of the lowest energy.

The magnitudes of the isotope effects for the solvolytic reactions are recorded in Table VII. These isotope effects are well outside the range of those which have been observed in solvolysis for substitution of a single hydrogen for deuterium.[24]

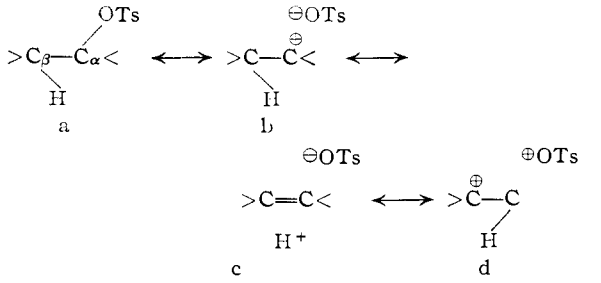
k_H/k_D = 1.28 80% ethanol (ref. 24a)

k_H/k_D = 1.22 (*cis*), 1.17 (*trans*), AcOH, 50° (ref. 24b)

Therefore, it is clear that the enhanced isotope effect observed in the 3-cyclohexyl-2-butyl system is associated with hydrogen participation in ionization. The transition states for *simple ionization* and *ionization* assisted by C_β–H can perhaps be best differentiated by comparison of models V and VI. Thus in V (transition state for simple ionization), the position of the hydrogen is close to that



V (hyperconjugation in simple ionization)



VI (hyperconjugation plus assistance to ionization by neighboring hydrogen)

of the starting state, and Vc probably makes a minor contribution to the hybrid. In VI (transition state for hydrogen-assisted ionization), hydrogen has moved toward C_α, and structures VIc and VId make important contributions to the hybrid. Certainly VI would exhibit a larger isotope effect than V, since the C_β–H bond is more broken in VI than in V.

TABLE VII

ISOTOPE EFFECT IN SOLVOLYSES OF *threo*- AND *erythro*-3-CYCLOHEXYL-2-BUTYL *p*-TOLUENESULFONATES

Run numbers[a]	Solvent	T, °C.	Diastereomer	k_H/k_D
3 and 12	AcOH	75	*threo*	1.56[b]
4 and 13[c]	AcOH	75	*threo*	1.56[b]
1 and 11	AcOH	50	*threo*	1.62[b]
Extrapolated[d]	AcOH	25	*threo*	1.87[b]
5 and 14	HCO_2H	25	*threo*	1.45[b]
8 and 16	AcOH	75	*erythro*	1.79[b]
9 and 17[c]	AcOH	75	*erythro*	1.84[b]
7 and 15	AcOH	50	*erythro*	1.87[b]
Extrapolated[e]	AcOH	25	*erythro*	2.10[b]
10 and 18	HCO_2H	25	*erythro*	1.73[b]
1 and 11	AcOH	50	*threo*	1.72[f]
7 and 15	AcOH	50	*erythro*	1.85[f]

[a] Run numbers refer to Table I. [b] Rate ratios uncorrected for small amount of β-hydrogen in labeled starting material. [c] Starting material made diastereomerically pure by purification of both acid phthalate and *p*-toluenesulfonate. In all other runs, purified only through *p*-toluenesulfonate. [d] Calculated rate at 25°, $k_H = 5.97 \times 10^{-9}$ sec.$^{-1}$, $k_D = 3.19 \times 10^{-9}$ sec.$^{-1}$. [e] Calculated rate at 25°, $k_H = 1.77 \times 10^{-8}$ sec.$^{-1}$, $k_D = 8.39 \times 10^{-9}$ sec.$^{-1}$. [f] Rate ratios corrected for small amount of β-hydrogen in labeled starting material (see Table II).

The relatively small isotope effects of 1.5 to 2.0 observed in the 3-cyclohexyl-2-butyl system is probably associated with C–H wagging rather than the more usual C–H stretching, which can perhaps provide the larger isotope effects found in oxidation[25] and base-catalyzed elimination reactions.[26,27] Isotope factors of 1.85 to 2.26 were obtained[28] in solvolyses of 3-methyl-2-butyl and

(23) S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan and H. Marshall, THIS JOURNAL, **74**, 1127 (1952).

(24) (a) V. J. Shiner, Jr., *ibid.*, **76**, 1603 (1954); (b) A. Streitwieser, Jr., R. H. Jagow and S. Suzuki, *ibid.*, **77**, 6713 (1955).

(25) F. Westheimer and N. Nicolaides, *ibid.*, **71**, 25 (1949).

(26) V. J. Shiner, *ibid.*, **74**, 5285 (1952).

(27) This possibility was suggested by S. Winstein, private communication.

(28) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958).

3 - methyl - 2 - butyl - 3 - *d p* - bromobenzenesulfonates. In this system, eclipsing effects are less important, and structures VIc and VId probably make a greater contribution to the transition state for ionization than in the 3-cyclohexyl-2-butyl system.

Some interesting trends in the size of the isotope effects (Table VII) are evident.[29] Thus the isotope effect in acetolysis increases as the temperature decreases, a difference of about 0.3 being associated with a 50° difference in temperature.[30] Also, the more nucleophilic solvent (acetic acid) exhibits a larger isotope effect than formic acid[30] by a factor of about 0.4. Although the difference is not far outside of probable error (see Table II), the two diastereomers do appear to give slightly different values for k_H/k_D. The most accurate data are found in the last two entries of Table VII (acetolysis at 50°), in which k_H/k_D *erythro* − k_H/k_D *threo* = 0.13. This difference is consistent with the greater steric compression which has to be overcome during ionization (with participation of C_β–H) of the *threo* as compared with the *erythro* system (compare structures III and IV). Thus the transition state for *threo* material is expected to be less eclipsed and more like starting material than the *erythro* transition state. As a result, the C_β–H bond is less broken in the *threo* transition state, and the isotope effect is expected to be less. The enhanced isotope effect found in the *erythro* system correlates with the greater solvolytic rate exhibited by this diastereomer. The variation in the character of the transition state as eclipsing effects change has been studied in connection with the E_2 reaction.[31]

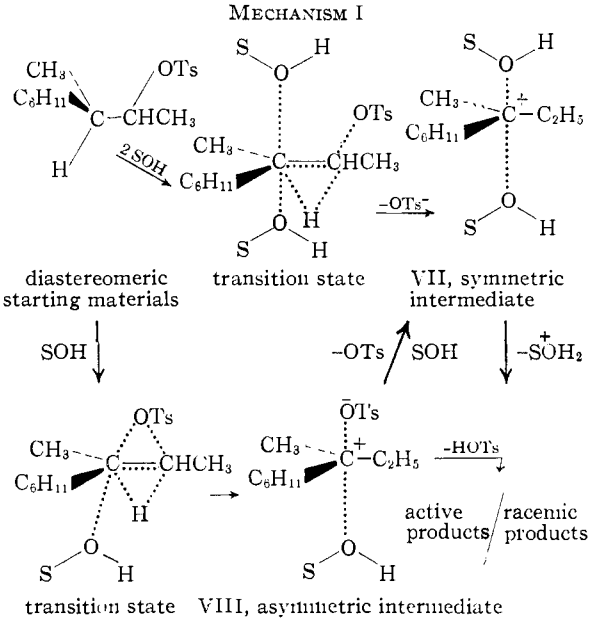
Ethylene Protonium Ions.—The above evidence for neighboring hydrogen participation in ionization provides little information regarding the much discussed question of whether protonium ions intervene as intermediates in solvolysis reactions.[3,5,8,24,32] However, the relatively small isotope and eclipsing effects in the ionization stage of the solvolysis of 3-cyclohexyl-2-butyl *p*-toluenesulfonates suggests that although hydrogen is participating in the ionization, the transition state looks much like starting material in geometry. This condition is more expected if the transition state separates starting material from a bridge ion than if it separates starting material from rearranged open carbonium ion.

The product analysis (Table VI) provides evidence for the existence of a bridged protonium ion in these reactions. In the acetolyses, the ester produced was between 95–100% rearranged (runs 21 and 22) to 2-cyclohexyl-2-butyl acetate. This material was 35% optically pure from *threo* and 30% from *erythro* material. In hydrolysis runs 23 and 24 (80% dioxane–20% water, 50°) rearranged material (2-cyclohexyl-2-butanol or II) accounted for 85% of the alcohol from *threo* and 93% produced from *erythro* satrting material. The *threo* system gave tertiary alcohol II 59% optically pure, and the *erythro* system gave II which was 44% optically pure. *To the extent that the rearrangement was stereospecific solvent attacked tertiary carbon from the side originally occupied by the rearranged hydrogen atom.*

Any reaction mechanisms proposed must accommodate six facts: (1) A process must be involved which can produce racemic, rearranged solvolysis product. (2) A process must be involved which can give optically active, rearranged product. (3) The two diastereomeric starting materials give rearranged product of different optical purity. (4) The rearrangements are more stereospecific in the more nucleophilic solvent (H_2O). (5) In the optically active product, oxygen occupies the same relative position on the tertiary carbon that hydrogen occupied in the starting material. (6) The more ionizing the solvent, the lower the activation energy for these processes.

Two general mechanistic schemes will be considered, each of which involves ionization in their initial stage (to satisfy condition 6). In mechanism I, racemic product arises from symmetric

MECHANISM I



intermediate VII, and optically active product from asymmetric intermediate VIII (conditions 1 and 2). The transition states leading from *threo* and *erythro* materials to VII and VIII are diastereomeric, and hence their energies would depend on the configurations of the starting material (condition 3). It is difficult to predict from such a scheme which of the two transition states would be the more stabilized by an increase in the nucleophilicity of the solvent. Possibly the transition state leading to VII would be favored, since it

(29) The data of Table VII are more accurate for the *erythro* than the *threo* isomer. Only the last two entries have been corrected for the 1% of hydrogen in the labeled *erythro*-ester and the 11% of hydrogen in the labeled *threo*-ester. The correction made little difference for the *erythro* system (0.02) but increased k_H/k_D for the *threo* system by 0.09. Hence the remaining entries for k_H/k_D for the *threo* system are probably low by a somewhat similar amount.

(30) Others have noticed a similar trend in temperature and solvent dependences, *e.g.*, E. S. Lewis and C. E. Boozer, THIS JOURNAL, **76**, 791 (1954).

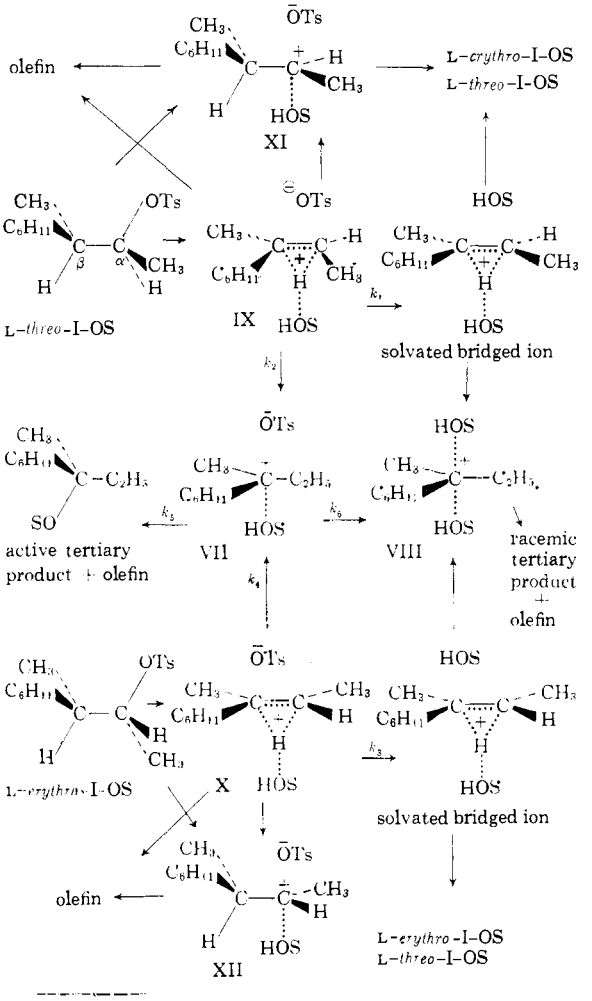
(31) D. J. Cram, F. D. Greene and C. H. Depuy, *ibid.*, **78**, 790 (1956).

(32) (a) R. W. Taft, Jr., *ibid.*, **74**, 5372 (1952); (b) J. B. Levy, R. W. Taft, Jr., and L. P. Hammett, *ibid.*, **75**, 1253 (1953); (c) R. W. Taft, Jr., E. L. Purlee, P. Riesz and C. A. De Fazio, *ibid.*, **77**, 1586 (1955); (d) L. G. Cannall and R. W. Taft, Jr., *ibid.*, **78**, 5812 (1956).

involves two molecules of solvent as compared to the one molecule utilized by the transition state leading to VIII. This conclusion is in conflict with condition 4. Intermediate VIII should give active product of the observed configuration (condition 5).

The most objectionable feature in mechanism I is that six groups are bound to the migration origin in both of the transition states leading to the two intermediates. Since carbonium ions normally have a coördination number of 4 or 5, the above mechanism seems highly improbable. Also eliminated are any mechanisms which require all rearranged product to funnel through VIII. Should VIII be produced from both diastereomers, both would give equal amounts of active rearranged material, in violation of condition 3. The remote possibility exists that VIII can exist in two diastereomeric forms depending on the conformation of the ethyl group, and that these rotomers do not equilibrate faster than they partition to give other species.[33] The latter condition

MECHANISM II



seems highly improbable since the carbonium ion is tertiary, relatively long lived, and is solvated.

In contrast to mechanism I and its variants, mechanism II is entirely consistent with all the facts.[34] In this scheme, a bridged protonium *p*-toluenesulfonate ion-pair intermediate (IX or X) is formed in the primary step. A small amount of open, unrearranged ion-pair (XI or XII) is also formed in a primary step. The bridged cation (protonium ion) is a conjugate acid of a very weak base (olefin), and hydrogen-bonds strongly with solvent. The bridged ion-pair (IX or X) partitions between olefin, rearranged open ion-pair VII, unrearranged open ion-pair XI or XII, and solvated bridged ion. Solvated bridged ion partitions between symmetrical ion VIII, and retained, unrearranged solvolysis product. Rearranged open ion-pair VII partitions between active, rearranged solvolysis product, and symmetrically solvated ion VIII. This carbonium ion gives racemic rearranged solvolysis product and olefin. Unrearranged ion pair XI or XII partitions between olefin and predominantly inverted, unrearranged solvolysis product (unrearranged solvolysis product in runs 25 and 26 of Table IV are largely inverted).

In this scheme, different amounts of active and racemic rearranged solvolysis products are produced because bridged ion-pairs IX and X are diastereomeric, and therefore, $k_1/k_2 \neq k_3/k_4$. Bridge IX is more compressed and less stable than X, and there, $k_2/k_1 > k_4/k_3$. As SOH grows more nucleophilic, k_5/k_6 increases, and as a consequence optically active rearranged solvolysis product increases. Thus the mechanism is in full accord with all the facts.

Perhaps the most striking feature of the results is the fact that the migration origin retains its configuration in the over-all rearrangement process. With all other migrating groups in 1,2-rearrangements, this center is inverted, or racemizes. This unique property of hydrogen is attributed to its small size and to its acidity when bridging an olefin. Solvent hydrogen-bonds with the protonium ion, and as a result is well oriented to react at the face of the protonated olefin that bears hydrogen. To the extent that the ion-pair maintains its integrity, the opposite side is blocked by the leaving group, and must undergo anion-solvent, exchange before reaction can occur from that direction. It also seems probable that the hydrogen bridged ion-pair can react at C_α to give XI and XII and this provides a route for the unexpectedly large amount of over-all inversion that occurred at C_α. The system is hindered enough so that simple solvolysis would be expected to give less than the 85–93% inversion observed.

A few other cases of *cis* opening of three-membered rings have been reported, most of which involve reactions of ethylene oxide rings with acids.[35,36] The mechanism proposed[35] is not dissimilar to that proposed in the present investigation

(33) Both D. J. Cram and J. E. McCarty [THIS JOURNAL, **79**, 2866 (1957)] and B. M. Benjamin, H. J. Schaeffer and C. J. Collins [*ibid.*, **79**, 6160 (1957)] have demonstrated that in deaminations to give "hot" secondary carbonium ions, these unsolvated ions partition between several products faster than they undergo conformational equilibration.

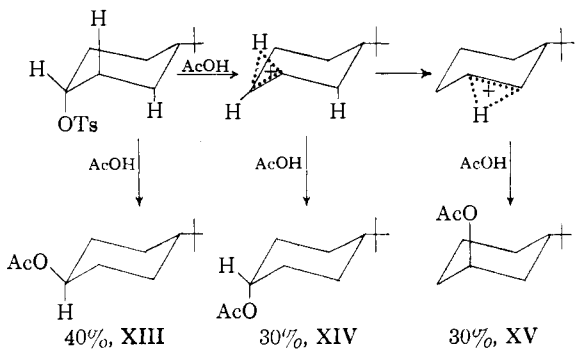
(34) For purposes of simplicity, L-*threo* and L-*erythro* are written in this scheme as the configurations of the starting materials, rather than the L-*threo* and D-*erythro* which were actually employed. The argument is independent of which enantiomers were actually used.

(35) J. H. Brewster, *ibid.*, **78**, 4061 (1956).

(36) D. Y. Curtin, A. Bradley and Y. G. Hendrickson, *ibid.*, **78**, 4064 (1956).

for the *cis* opening of an ethylene protonium ion. Both mechanisms postulate that the attacking nucleophile is oriented by the bridging atom, and that the carbonium ion when formed reacts with this oriented species faster than with randomly oriented solvent at the back of the bridge. These mechanisms are similar to those proposed for the SNi reaction.[37]

It is interesting to compare the above results with those obtained in other systems in which hydrogen is a migrating group. In acetolysis of 3-phenyl-2-butyl *p*-toluenesulfonate, hydrogen migrates to give completely racemic 2-phenyl-2-butyl acetate.[8] In this system, the tertiary benzyl carbonium ion appears to be stable and long enough lived to become symmetrically solvated. In the acetolysis of *cis*-4-*t*-butylcyclohexyl *p*-toluenesulfonate, Winstein and Holness[5] observed that the acetate produced had the composition: 40% *trans*-4-*t*-butylcyclohexyl acetate (XIII), 30% *cis*-4-*t*-butylcyclohexyl acetate (XIV) and 30% *trans*-3-*t*-butylcyclohexyl acetate (XV). In the last product, hydrogen has rearranged,and the migration origin has *retained its configuration*. The authors assumed that the three-membered ring (protonium ion) only underwent *trans* opening, and explained the stereochemical result through intervention of two bridged ions XVI and XVII. In view of the results obtained in the present



investigation, it seems more likely that bridged ion XVI underwent *cis* opening to give XIII and XV, and that XIV and some of XIII were formed from non-bridged ions. A similar interpretation might be applied to the rearrangement of optically active 1-phenyl-1-*o*-tolylglycol to optically active phenyl-*o*-tolylacetaldehyde, observed by Mislow and Siegel.[38]

Experimental

Preparation of the 3-Cyclohexyl-2-butanols (I).—The physical properties of the 3-phenyl-2-butanols used for preparation of the saturated alcohol I are listed as follows: L-(+)-*threo*-3-phenyl-2-butanol, $n^{25}D$ 1.5167, $\alpha^{24}D$ +31.61°, l = 1 dm., neat; D-(−)-*erythro*-3-phenyl-2-butanol, $n^{25}D$ 1.5162, $\alpha^{24}D$ −0.77°, l = 1 dm., neat; racemic *threo*-3-phenyl-2-butanol-3-*d*, $n^{25}D$ 1.5158; and racemic *erythro*-3-phenyl-2-butanol-3-*d*, $n^{25}D$ 1.5166. The reduction of these alcohols was accomplished by a procedure illustrated by that employed for the L-(+)-*threo* isomer. A mixture of 23.2 g. of the alcohol, 200 ml. of glacial acetic acid (Baker analyzed reagent) and 1.0 g. of platinum dioxide was shaken in a hydrogen atmosphere until no more hydrogen was absorbed, and then for an additional half-hour. The catalyst was collected, and the solution was shaken with 500 ml. of purified pentane and one liter of ice-water. The aqueous phase was washed with 500 ml. of pentane and 500 ml. of ether. The combined organic layers were washed with dilute base, water, were dried, and evaporated through two 24″ Vigreux columns. The residual oil was distilled at a pot temperature of 85° at 1.4 mm. pressure to give 23.6 g. of L-(+)-*threo*-I, $n^{25}D$ 1.4695, $\alpha^{27}D$ +17.76° (l = 1 dm., neat). The same procedure also provided D-(−)-*erythro*-I, $\alpha^{27}D$ −2.49°, m.p. 28–29°. Neither alcohol absorbed in the ultraviolet in the region, 215–300 mμ. The infrared spectra contained no bands associated with any unsaturated linkages. Reduction of the *erythro* isomer took 1.7 hours, and the *threo* isomer took 3.7 hours.

Preparation of the 3-Cyclohexyl-2-butyl *p*-Toluenesulfonates.—The procedure is illustrated: A solution of 6.0 g. of L-(+)-*threo*-I was dissolved in 30 ml. of Karl Fischer reagent pyridine and was cooled to 0°. To this mixture was added in one portion 7.6 g. of *p*-toluenesulfonyl chloride. The mixture was swirled until homogeneous, and allowed to stand at 0° for 8 hours and then to come to room temperature. The reaction mixture was shaken with cold 2 *N* sulfuric acid and purified pentane. The aqueous layer was washed twice with pentane and once with ether. The combined organic layers were washed with water, dilute base, with water, and dried and evaporated to an oil without being heated above 40°. The residual oil (10.4 g.) was crystallized and recrystallized to constant melting point from fractionated pentane, m.p. 71.2–72.2°.

Anal. Calcd. for $C_{17}H_{26}O_3S$: C, 65.77; H, 8.44. Found: C, 65.88; H, 8.36.

The other diastereomeric *p*-toluenesulfonates of I had the following properties and analyses: racemic *threo*, m.p. 49–50° (Found: C, 65.56; H, 8.49); racemic *erythro*, m.p. 39–40° (Found: C, 65.71; H, 8.48); D-(−)-*erythro*, m.p. 62.5–63.5° (Found: C, 65.82; H, 8.24).

Preparation of Diastereomeric Mixture of 3-Phenyl-2-butanol-3-*d*.—A mixture of 256 g. of pure *p*-toluenesulfonyl chloride and 200 g. of 99.8% deuterium oxide was refluxed (stirred) until a clear solution was produced. Sodium phenylmethylglycidate was prepared,[39] and recrystallized from ethanol and dried at 100° at 2 mm. pressure for 48 hours. This material (420 g.) was added to the hot solution of acid with vigorous stirring and over a period of 1.5 hours. The reaction was exothermic, and was accompanied by gentle reflux. The reaction mixture was then stirred for 20 minutes, refluxed for one hour, cooled, and the organic phase was decanted. The aqueous phase was washed with pentane, and the combined organic phases were dried and evaporated to an oil. This material was added to methyl Grignard reagent prepared from 300 g. of methyl iodide and 51 g. of magnesium in the usual manner. The product was isolated to give 75 g. of 3-phenyl-2-butanol-3-*d*, $n^{25}D$ 1.5171, b.p. 88° at 5.5 mm.

The two racemic diastereomers were separated through the usual derivatives,[10] the *erythro* as the 3-nitrophthalic acid ester (82 g., m.p. 156–157°), and the *threo* as the acid phthalate (30 g., m.p. 129–131°). Hydrolysis of these derivatives[10] gave the corresponding alcohols, *threo*, $n^{25}D$ 1.5168, and *erythro*, 1.5166. Catalytic reduction of these materials (see above procedure) gave *threo*-I-3-*d*, $n^{25}D$ 1.4689, and *erythro*-I-3-*d*, $n^{25}D$ 1.4695.

Portions of these labeled alcohols were converted directly to their respective *p*-toluenesulfonates, which were recrystallized to constant melting point. For the *threo* isomer, m.p. 49–50°; for the *erythro*-isomer, m.p. 39–40°. Other portions were converted to their respective acid phthalates, which were recrystallized to constant melting point: *threo*-acid phthalate, m.p. 93–94.5°; *erythro*-acid phthalate, m.p. 76.5–78.5°. These esters were hydrolyzed back to *threo*-I-3-*d*, $n^{25}D$ 1.4688, and *erythro*-I-3-*d*, $n^{25}D$ 1.4695, which were converted to their *p*-toluenesulfonates, *threo* isomer, m.p. 48–49°; *erythro* isomer, m.p. 39–40°.

Optically Active and Racemic 2-Cyclohexyl-2-butanol (II).—A mixture of 2.0 g. of racemic 2-phenyl-2-butanol,[12] 30 ml. of glacial acetic acid and 0.5 g. of platinum oxide was shaken in an atmosphere of 30 lb. of hydrogen until absorption of hydrogen was complete. The alcohol was isolated in the usual way and distilled at low pressure to

(37) D. J. Cram, THIS JOURNAL, **75**, 332 (1953).

(38) K. Mislow and M. Siegel, *ibid.*, **74**, 1060 (1952).

(39) "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 733.

give 1.56 g. of a colorless oil. This material was chromatographed on neutral activity I alumina, and the hydrocarbon formed in the hydrogenation was washed through with pentane. The alcohol was eluted with ether, and was distilled through a short still, pot temperature 92° (3 mm.), wt. 0.95 g., $n^{25}D$ 1.4698.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 76.92; H, 13.12.

This material was also prepared by addition of methylmagnesium iodide to ethyl cyclohexyl ketone in the usual kind of Grignard reaction. From 8.3 g. of ketone, 2.43 g. of magnesium and 14.2 g. of methyl iodide was obtained on distillation of the product 8.8 g. of II, $n^{25}D$ 1.4695. The infrared spectra of the two samples of alcohol II were identical.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 76.87; H, 12.91.

The catalytic reduction procedure was applied to 2.65 g. of optically pure 2-phenyl-2-butanol,[10] $n^{25}D$ 1.5161, $\alpha^{25}D$ +18.35, l = 1 dm., neat. A mixture of hydrocarbon and alcohol was produced (2.35 g.) which was separated by chromatography to give 1.42 g. of optically pure 2-cyclohexyl-2-butanol, $n^{25}D$ 1.4698, $\alpha^{24}D$ −3.52° (neat, l = 1 dm.), and 0.68 g. of 2-cyclohexylbutane, $n^{25}D$ 1.4442, $\alpha^{23}D$ +0.22° (neat, l = 1 dm.).

(−)-Cyclohexylisopropylcarbinol.—A mixture of 2.0 g. of (+)-phenylisopropylcarbinol[33] ($\alpha^{23}D$ −20.85°, l = 1 dm., neat), 30 ml. of glacial acetic acid and 0.25 g. of platinum oxide was shaken under 30 lb. of hydrogen until no more hydrogen was absorbed (120 min.). The product was isolated in the usual way to give 1.93 g. of distilled product, which showed no absorption in the ultraviolet from 215–300 mμ. This material was chromatographed on 100 g. of neutral activity I alumina, and the hydrocarbon contaminant was eluted with pentane. The alcohol was eluted with ether and distilled to give 1.08 g. of cyclohexylisopropylcarbinol, $n^{25}D$ 1.4657, $\alpha^{24}D$ −8.35° (l = 1 dm., neat).

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 76.74; H, 12.77.

Lithium Aluminum Hydride Reduction of *p*-Toluenesulfonates of the Isomeric 3-Cyclohexyl-2-butanols to Give 2-Cyclohexylbutane.—A solution of 4.45 g. of the *p*-toluenesulfonate of L-(+)-*threo*-3-cyclohexyl-2-butanol in 60 ml. of ether was added to a slurry of 4.5 g. of lithium aluminum hydride in 300 ml. of ether. After the addition was complete, the reaction mixture was allowed to stand at room temperature for 20 hours. Ice-water was cautiously added to the mixture followed by 2 *N* hydrochloric acid, and the hydrocarbon was isolated in the usual way to give 1.48 g. of a mixture of olefin and 2-cyclohexylbutane. To remove olefin, this material was dissolved in 4.0 ml. of glacial acetic acid, and 5.0 g. of 2,4-dinitrobenzenesulfenyl chloride was added. The resulting solution was heated to 100° for 40 minutes, cooled, and shaken with 250 ml. of pure pentane and 250 ml. of water. The organic layer was washed with water, dried and the solution was passed through 50 g. of neutral activity I alumina. The pentane was evaporated and the saturated hydrocarbon was distilled at 25 mm., pot temperature, 85°, wt. 0.396 g., $n^{25}D$ 1.4452, $\alpha^{25}D$ −1.62° (l = 1 dm., neat).

In a similar experiment, D-(−)-*erythro*-3-cyclohexyl-2-butyl *p*-toluenesulfonate was reduced to give 2-cyclohexylbutane, $n^{25}D$ 1.4452, $\alpha^{25}D$ +1.51° (l = 1 dm., neat).

The hydrocarbon 2-cyclohexylbutane was also prepared by catalytic reduction of optically active 2-phenylbutane.[13] From 0.7 g. of 2-phenylbutane, $\alpha^{24}D$ +24.2° (l = 1 dm., neat), hydrogenated in glacial acetic acid with a platinum catalyst, was obtained 0.58 g. of 2-cyclohexylbutane, $n^{25}D$ 1.4441, $\alpha^{25}D$ −1.56.[15] Levene and co-workers[15] reported $n^{20}D$ 1.4460 for this compound.

Kinetic Measurements.—For the kinetic determinations, anhydrous formic and acetic acid were prepared as previously described.[19] Dioxane was purified by the method of Fieser.[40] The acetolysis solutions containing potassium acetate were prepared with anhydrous potassium carbonate. Enough acetic anhydride was added to react with the water produced (solutions were refluxed for 8 hours before use). The formolysis solutions were prepared with anhydrous sodium formate. The acetolysis rates were carried out with the ampoule technique. The samples were quenched by immersion of the vials in a Dry Ice–acetone-bath. After the samples returned to room temperature, 5.00-ml. aliquots were titrated with standard solutions of perchloric acid in glacial acetic acid, with an indicator of several drops of a standard solution of brom phenol blue in acetic acid.

The formolysis rates were conducted in a reaction flask immersed in a thermostated oil-bath at 25°. Aliquots (5.00 ml.) were withdrawn and quenched in 50 ml. of purified dioxane. The samples were titrated with standard solutions of perchloric acid in dioxane with an indicator of several drops of a saturated solution of brom cresol green in acetic acid.

The reactions were followed from 30 to 70–90% of completion, and were found to be first order. The precisions of the measurements were calculated from the mean deviations of the individual rate constants in each run.

3,5-Dinitrobenzoates of Racemic and (−)-2-Cyclohexyl-2-butanol (II).—The procedure is illustrated with the preparation of racemic ester. A mixture of 0.396 g. of racemic II and a 10% excess of freshly prepared 3,5-dinitrobenzoyl chloride was dissolved in 4.0 ml. of Karl Fischer reagent pyridine, and the mixture was heated to 82° for one hour. The resulting solution was cooled and shaken with a mixture of 1 *N* sulfuric acid and ether. The ether layer was washed with water, dilute base, and again with water. The solution was then dried, the solvent was evaporated, and the residual orange solid was chromatographed on 50 g. of neutral activity I alumina. The ester was eluted with ether to give 0.718 g. of material. This ester was recrystallized from hexane to give 0.485 g. of product, m.p. 97–98°.

Anal. Calcd. for $C_{17}H_{22}O_6N_2$: C, 58.28; H, 6.34. Found: C, 58.15; H, 6.53.

When optically pure (−)-II was converted to the ester, material was obtained, m.p. 115.5–116.5°, $[\alpha]^{23}D$ −0.91° (10% in $CHCl_3$).

Anal. Calcd. for $C_{17}H_{22}O_6N_2$: C, 58.28; H, 6.34. Found: C, 58.02; H, 6.14.

Acetolysis Reactions for Product Analysis.—A mixture of 6.0 g. of the *p*-toluenesulfonate of L-(+)-I in 125 ml. of acetolysis solution (see kinetic section) was swirled until the solid dissolved, and the resulting solution was kept at 35° for eight half-lives (extrapolated from rate data at 50° and 75°) (run 21). The reaction solution was shaken with a mixture of 800 ml. of water, 200 g. of ice, 50 g. of sodium chloride and 600 ml. of purified pentane. The aqueous layer was washed with ether, and the combined organic layers were washed with water and dilute base. The resulting solution was dried, evaporated through two 24" Vigreux columns. The residue was distilled at 25 mm. pressure to give 2.49 g. of colorless oil (the pot residue was neutral). This material was added dropwise to a slurry of 2.17 g. of lithium aluminum hydride and 100 ml. of anhydrous ether. The product was isolated in the usual way to give 2.24 g. of distilled colorless oil. This material was chromatographed on 130 g. of neutral, activity I alumina. The olefin was eluted with two 250-ml. portions of purified pentane, and alcohol was eluted with ether. The alcohol was distilled under vacuum to give 0.375 g., $\alpha^{23}D$ −1.19° (l = 1 dm., neat). The infrared spectrum of this material was superimposable on that of authentic 2-cyclohexyl-2-butanol.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 76.84; H, 12.89.

The olefin fraction was distilled at 25 mm. pressure to give 1.44 g. of material, $n^{25}D$ 1.4620, $\alpha^{23}D$ −0.190° (l = 1 dm., neat).

The same procedure was applied to the acetolysis of D-(−)-*erythro*-3-cyclohexyl-2-butyl *p*-toluenesulfonate (run 22). From 6.0 g. of starting material was obtained 2.67 g. of acetate–olefin mixture, which was converted to 2.32 g. of alcohol–olefin mixture. When separated, 0.392 g. of alcohol was obtained, $\alpha^{25}D$ +0.454° (l = 1 dm., neat). The infrared spectrum was superimposable on that of pure II. The olefin fraction came to 1.62 g., $n^{25}D$ 1.4631, $\alpha^{21}D$ −0.06° (l = 1 dm., neat).

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 76.81; H, 12.72.

(40) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., 1955, p. 284.

Control experiments demonstrated that II must contain 5% or more of I before the latter component can be detected in the infrared of a mixture.

Formolysis of Racemic *threo*-3-Cyclohexyl-2-butyl *p*-Toluenesulfonate.—A solution of 4.5 g. of the above ester was allowed to stand in a 0.159 *M* solution of sodium formate in dry formic acid (100 ml.) at 25° for a period of 12 hours. The reaction mixture was subjected to the same procedure employed in the acetolysis (through the lithium aluminum hydride treatment). The oil recovered (1.69 g.) gave an infrared spectrum essentially free of an O–H stretching band.

Hydrolysis of *p*-Toluenesulfonates of L-(+)-*threo*- and D-(−)-*erythro*-3-Cyclohexyl-2-butanol (I).—The L-(+)-*threo* ester (6.0 g.) was dissolved in 250 ml. of 80% (by weight) purified dioxane[40] which was 0.0772 *M* in sodium acetate (run 23). The resulting solution was held at 50° for 9 days (5 days for the *erythro* isomer). The products were isolated as in the acetolysis runs to give 0.869 g. of alcohol fraction, $\alpha^{24}D$ −1.45° (*l* = 1 dm., neat), $n^{25}D$ 1.4698, and 1.18 g. of olefin. The alcohol fraction contained a small carbonyl band in the infrared due to a trace of acetate, so the alcohol fraction was submitted to a lithium aluminum hydride treatment, and 0.692 g. of product was isolated, $\alpha^{25}D$ −1.33° (*l* = 1 dm., neat).

The D-(−)-*erythro* ester (6.0 g.) when submitted to the same treatment (run 24) gave 0.690 g. of product before the lithium aluminum hydride treatment and 0.612 g. after, αD +0.47° (*l* = 1 dm., neat). The olefin fraction amounted to 1.42 g.

Separation of Secondary Alcohols from 2-Cyclohexyl-2-butanol (II).—Control procedures were developed for separating secondary alcohols from II. The following procedure is illustrative. A solution was prepared from 0.187 g. of L-(+)-*threo*-I (optically pure) and 0.8014 g. of racemic II, which was distilled to ensure homogeneity, $\alpha^{25}D$ −3.38° (*l* = 1 dm., neat). Phthalic anhydride (0.69 g.) and 0.659 g. of the alcohol mixture was dissolved in 2.0 ml. of pure pyridine, and the solution was heated to 100° for 4 hours. The solution was cooled and shaken with 250 ml. of cold 1 *N* sulfuric acid and 100 ml. of ether. The aqueous portion was extracted with 100-ml. portions of ether, and the combined ether portions were washed with water and cold 0.5 *N* sodium hydroxide solution, and finally with water. The solution was dried, evaporated through a 24″ column packed with glass helices, and the residual oil was distilled at 6 mm., pot temperature 94°, to give 0.377 g. of alcohol II, $n^{25}D$ 1.4696, $\alpha^{24}D$ +0.01° (*l* = 1 dm., neat).

The same control was carried out with 20.3% by weight of optically pure D-(−)-*erythro*-I in racemic II, $\alpha^{24}D$ −0.26° (*l* = 1 dm., neat). An 84% recovery of II was made, $\alpha^{25}D$ +0.02° (*l* = 1 dm., neat). The same control was applied to a 20.5% by weight of optically active (−)-isopropylcyclohexylcarbinol in racemic II, $\alpha^{26}D$ −1.96° (*l* = 1 dm., neat). An 89% recovery of II was made, $\alpha^{24}D$ 0.00° (*l* = 1 dm., neat). The same control was run with a sample of 20.8% optically pure II alone, $\alpha^{25}D$ −0.73° (*l* = 1 dm., neat). Recovery of material amounted to 87%, $\alpha^{24}D$ −0.75° (*l* = 1 dm., neat). This material when analyzed for carbon and hydrogen gave a good hydrogen analysis, but carbon was about 0.8% low due to contamination with a small amount of phthalic anhydride. This contaminant was removed as follows. A mixture of 0.500 g. of the above material and 5 ml. of 10% sodium hydroxide solution was refluxed for one hour, cooled, and the alcohol was extracted with ether and distilled to give 0.411 g. of II, $\alpha^{26}D$ −0.71° (*l* = 1 dm., neat).

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 76.63; H, 12.84.

The alcohol products from acetolysis runs 21 and 22 were submitted to the above procedures, and the final rotations are recorded in Table IV. The alcoholic products from the hydrolysis runs 23 and 24 were also subjected to the above procedures, and the final rotations are recorded in Table IV. The analyses are recorded here.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found for alcohol in run 23: C, 76.90; H, 12.82. Found for alcohol in run 24: C, 77.11; H, 13.02.

A control separation was run for the actual isolation of I from a mixture of I and II. A solution was prepared from 0.411 g. of *threo*-I and 0.407 g. of *erythro*-I, and this mixture was flash distilled to ensure homogeneity, and an infrared spectrum of this solution was taken. This material (0.427 g.) was mixed with 1.012 g. of II, and the solution was distilled to ensure homogeneity. A mixture of 1.301 g. of this ternary solution was mixed with 1.38 g. of phthalic anhydride and 3.9 ml. of pure pyridine and heated to 100° for one hour. The resulting mixture was cooled, and shaken with excess 1 *N* sulfuric acid solution and ether. The aqueous phase was washed with ether, and the combined organic solutions were washed with water, and were then extracted with three 100-ml. portions of cold 0.5 *N* sodium hydroxide solution. The basic extracts were combined, acidified with 200 ml. of 1 *N* sulfuric acid, and extracted twice with 400-ml. portions of ether. The combined ether layers were washed with water, dried and evaporated. The resulting acid phthalate residue was refluxed for 24 hours with a solution of 0.8 g. of sodium hydroxide, 1.12 g. of potassium hydroxide and 18 ml. of water. The reaction mixture was cooled, extracted with ether, and the organic extract was washed with dilute basic solution and with water. The ether solutions were dried, evaporated through two 24″ Vigreux columns, and the residue was distilled at 3 mm. to give 0.346 g. (90% recovery) of secondary alcohols. The infrared spectrum of this mixture was superimposable on that of the initially prepared mixture (50% *threo*-I, 50% *erythro*-I).

Hydrolysis of *p*-Toluenesulfonates of Racemic *threo*- and *erythro*-3-Cyclohexyl-2-butanol (I).—For analysis of the secondary alcohols formed in hydrolysis of these esters, relatively large runs were carried out with racemic materials under the conditions used for the optically active esters (runs 23 and 24). In run 25, 27.8 g. of racemic *threo*-3-cyclohexyl-2-butyl *p*-toluenesulfonate was employed as starting material, and the alcohol mixture, 3.77 g. (I and II) was isolated as in runs 23 and 24. The secondary alcoholic component I was isolated through its acid phthalate as in the above control experiment, and 0.35 g. of I was obtained. This material was submitted to infrared analysis (see later section).

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 77.09; H, 12.63.

The tertiary alcohol component II was also isolated as in runs 23 and 24, wt. 3.27 g. This material was converted to its 3,5-dinitrobenzoate (see procedure recorded earlier) in 50% yield, m.p. 96.5–97°, undepressed by admixture of an authentic sample of the same derivative of racemic II.

In runs 27, racemic *erythro*-3-cyclohexyl-2-butyl *p*-toluenesulfonate was subjected to the same treatment to give yields of I and II recorded in Table IV. Alcohol I was analyzed.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 76.99; H, 12.65.

Alcohol II was converted to its 3,5-dinitrobenzoate, m.p. 97–98°, undepressed by admixture with an authentic sample.

Composition of Active 2-Cyclohexyl-2-butanol (II) Obtained from Solvolyses by Mixed Melting Point Experiments.—In Table IV are recorded the rotations and optical purities of the samples of II obtained from solvolysis runs 21, 22, 23 and 24. To confirm the degree of optical purity of these samples, each was converted to its 3,5-dinitrobenzoate derivative, and the melting point was compared to those of synthetic mixtures of varying composition of optically pure and racemic derivative of authentic II. In run 21, a 22% yield of 3,5-dinitrobenzoate was obtained, m.p. 98–104°. A synthetic mixture of 35% optically pure (from (−)-II) and 65% racemic ester was prepared, m.p. 97–103°, mixed melting point, 97–103°. In run 21, a 53% yield of ester was obtained, m.p. 98–99.2°. A synthetic mixture of 30% of optically pure (from (−)-II) and 70% of racemic ester was prepared, m.p. 98.5–100.5°. In run 22, a 54% yield of ester was obtained, m.p. 102–110°. A synthetic mixture of 59% of optically pure ester (from (−)-II) and 41% of racemic ester was prepared, m.p. 100.5–109°. A mixed melting point of these two samples gave 102–108.5°. In run 23, a 40% yield of ester was obtained, m.p. 98–106°. To this material was added 44% of optically pure ester (from (−)-II), and the melting point was 96.5–98°, undepressed by admixture with authentic ester. Ester from run 24 gave 50% yield of ester, m.p. 96.3–97.2°. Ester from run 25 gave a 62% yield of ester, m.p. 97–98°.

Infrared Analysis of Secondary Alcohols from Runs 25 and 26.—These alcohols were analyzed as a two-component

system (*threo*- and *erythro*-I) with a Perkin–Elmer recording spectrophotometer, model 21. The infrared spectra of pure *threo*- and *erythro*-I were examined from 4000–650 cm.$^{-1}$. The wave lengths most suitable for analysis and the optical densities of the pure alcohols were (resolution 940, suppression 0, speed 0, gain 5, response 1:1, cells NaCl, 0.10-mm. thickness, NaCl optics): at 1149.7 cm.$^{-1}$, *threo* 0.212, *erythro* 0.469; 1126.5 cm.$^{-1}$, *threo*, 0.631, *erythro*, 0.409; 1019.2 cm.$^{-1}$, *threo*, 0.287, *erythro*, 0.593; 987.1 cm.$^{-1}$, *threo*, 0.298, *erythro*, 0.726; 1129.2 cm.$^{-1}$, *threo*, 0.593, *erythro*, 0.392; 1197.0 cm.$^{-1}$, *threo*, 1.000, *erythro*, 0.629; 1081.6 cm.$^{-1}$, *threo*, 1022, *erythro*, 0.638; 1020.3 cm.$^{-1}$, *threo*, 0.286, *erythro*, 0.620. Known mixtures of about 25, 50 and 75% *threo*-I in *erythro*-I were prepared, and optical density *vs.* composition curves were prepared. The optical densities of the unknowns from runs 25 and 26 were then determined, and the composition thus became known. The results are listed in Table IV.

Preparation of 2,4-Dinitrobenzenesulfenyl Chloride Adducts from the Olefinic Mxitures Obtained from Runs 19 and 20.—The procedure is illustrated for the olefin obtained from run 19. A mixture of 0.217 g. of olefin, 4 ml. of glacial acetic acid and 0.378 g. of 2,4-dinitrobenzenesulfenyl chloride was heated to 80° for 20 minutes and then cooled. The yellow solid that separated was collected and extracted with boiling ethanol. The extract was filtered, and the filtrate was concentrated and cooled. The crude product that separated, 0.154 g. (26%), was recrystallized twice from ethanol, m.p. 147–148.5°.

Anal. Calcd. for $C_{16}H_{21}O_4N_2SCl$: C, 51.53; H, 5.63. Found: C, 51.70; H, 5.79.

The crude adduct obtained from olefin from run 20 was obtained in 25% yield. Two recrystallizations of the material from ethanol gave m.p. 147–149°. A mixed melting point of the two samples gave 146–149°.

Anal. Calcd. for $C_{16}H_{21}O_4N_2SCl$: C, 51.53; H, 5.63. Found: C, 51.27; H, 5.91.

When the above reactions were carried out at 25° for 24 hours, the adducts were isolated as long yellow needles in 38% yield in each case.

LOS ANGELES, CALIF.

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

Studies in Stereochemistry. XXX. Models for Steric Control of Asymmetric Induction[1]

BY DONALD J. CRAM AND KARL R. KOPECKY

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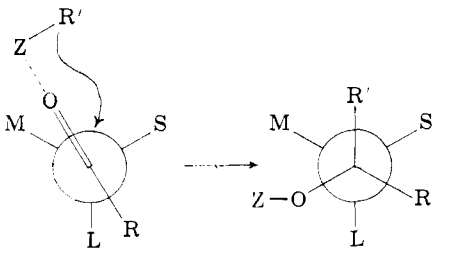
The application of two different models to explain the steric course of asymmetric induction has been investigated in systems where each model predicts a different result. In syntheses of 2,3-diphenyl-2,3-butanediol and its monomethyl ether from various ketones, an asymmetric center is created in the presence of one already in the molecule. With systems of this type, rigid model II rather then open-chain model I predicts the configuration of the predominant product. Models are proposed which rationalize the formation of isotactic and syndiotactic polymers.

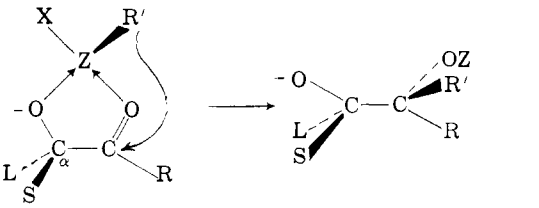
In previous papers of this series,[2] a model has been developed which correlates and rationalizes a large body of data pertaining to the steric direction of asymmetric induction. This model is represented by I, which depicts the reaction of an aldehyde or ketone with an organometallic reagent in which an asymmetric center is created on carbon adjacent to an asymmetric center already in the molecule. The symbols, L, M and S stand for large, medium and small groups attached to the old asymmetric center, and that conformation is selected which presents the least steric barrier to reaction.



transition state of lowest energy — predominant diastereomer

I (open-chain model)

A second model was also considered[2a] for systems in which the asymmetric center in the starting material carried a group such as OH or NH_2 which was capable of complexing with organometallic reagents. This model is represented by II, and it involves a relatively rigid, five-membered ring which fixes the conformation of the reacting species.



transition state of lowest energy — predominant diastereomer

II (rigid model)

In systems in which an amino or hydroxyl group on C_α is the medium sized group (*e.g.*, S is hydrogen and L is phenyl), the open-chain (I) and rigid models (II) predict the same result. All systems in which the configurations of the products have been clearly demonstrated belong to this class,[3] and none has been examined in which the two models unambiguously predict opposite results. To meet this condition, the complexing group on C_α(hydroxyl or amino) must be the small group.

(1) This work was sponsored by the Office of Ordnance Research, U. S. Army.

(2) (a) D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **74**, 5828 (1952); (b) D. J. Cram and J. D. Knight, *ibid.*, **74**, 5835, 5839 (1952); (c) D. J. Cram, F. A. Abd Elhafez and H. Weingarten, *ibid.*, **75**, 2293 (1953); (d) D. J. Cram and F. D. Greene, *ibid.*, **75**, 6005 (1953); D. J. Cram, F. A. Abd Elhafez, *ibid.*, **76**, 22 (1954); D. J. Cram and J. E. McCarty, *ibid.*, **76**, 5740 (1954).

(3) D. Y. Curtin, E. E. Harris and E. K. Meislich [*ibid.*, **74**, 2901 (1952)] developed a correlation between configuration of the predominant product and the order in which groups were introduced in the preparation of substituted, diastereomeric 1-hydroxyl-2-aminodibenzyl compounds.