Electrophilic Substitution at Saturated Carbon. XLII. Trimethyleneketo Carbanions as Intermediates in Base-Catalyzed Epimerization, Racemization, and Cleavage Reactions of Optically Active Diastereomers of 1,2-Dimethyl-2-phenylcyclopentanols[1]

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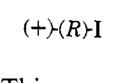
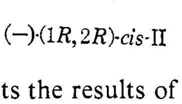
Abstract: The reactions have been studied of base-catalyzed epimerization, racemization, and cleavage of optically pure (+)-(*R*)-2-methyl-2-phenylcyclopentanone ((+)-I), of (−)-(1*R*,2*R*)-1,2-dimethyl-2-phenylcyclopentanol ((−)-*cis*-II), and of (−)-*trans*-(1*S*,2*R*)-1,2-dimethyl-2-phenylcyclopentanol ((−)-*trans*-II). Cleavage of ketone (+)-(*R*)-I in a variety of solvents gave (+)-(*S*)-5-phenylhexanoic acid ((+)-III) with varying amounts of retention of configuration: in *t*-butyl alcohol–potassium *t*-butoxide, ~61% net retention; in dimethyl sulfoxide–*t*-butyl alcohol–potassium *t*-butoxide, ~1% net retention; in diethylene glycol–potassium diethylene glycoxide, ~27% net retention. In the run conducted in dimethyl sulfoxide, recovered starting material was optically pure. Cleavage of (+)-(*R*)-5,5-dideuterio-2-methyl-2-phenylcyclopentanone in *t*-butyl alcohol-O-*d*–potassium *t*-butoxide gave acid (+)-III (62% net retention) that contained only 71% of one atom of deuterium at the methine carbon. Apparently, the carbanion intermediate was captured by protons donated by methyl groups of the medium. Optically pure (−)-*cis*-II was partially isomerized in dimethyl sulfoxide–dimsylsodium at 25° to give 93.5% starting material of 96.2% optical purity and 6.5% (−)-*trans*-II of 43% optical purity. Optically pure (−)-*trans*-II was partially isomerized in dimethyl sulfoxide–dimsylsodium at 25° to give 92% starting material of 75% optical purity and 8% of (−)-*cis*-II of 35% optical purity. Clearly, epimerization occurred at both asymmetric centers, but considerably faster at the oxygen-carrying than the phenyl-carrying center. In dilute solution in *t*-butyl alcohol–potassium *t*-butoxide at 135°, optically pure (−)-*cis*-II gave 35% (−)-*cis*-II of 99.4% optical purity, 2.4% of (−)-*trans*-II of 90% optical purity, and 20% (+)-(*S*)-6-phenyl-2-heptanone ((+)-IV) of 61% optical purity. The cleavage reaction occurred with 61% *net retention of configuration* at the benzyl carbon. In dilute solution in *t*-butyl alcohol–potassium *t*-butoxide at 135°, optically pure (−)-*trans*-II gave 36.4% (−)-*trans*-II of 99.9% optical purity, 2.5% (−)-*cis*-II of 96% optical purity, and 18% (−)-(*R*)-6-phenyl-2-heptanone ((−)-IV) of 56% optical purity. The cleavage reaction occurred with 56% *net inversion of configuration* at the benzyl carbon. Even in *t*-butyl alcohol, epimerization occurred but mainly at the asymmetric center carrying oxygen. The stereochemical course of the cleavage reaction depends on the relative configuration of the two asymmetric centers. These reactions are interpreted in terms of trimethyleneketo carbanion intermediates whose fates depend on the relative rates and direction of rotation of the phenyl-carrying and oxygen-carrying carbons, the rate of proton capture at the benzyl carbon atom, and the rate of recombination of the carbanion with the carbonyl group.

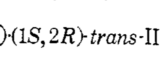
The previous paper of this series[2] describes the preparation, determination of configuration, and maximum rotations of cyclic ketone (+)-(*R*)-I, the diastereomeric alcohols, (−)-(1*R*,2*R*)-*cis*-II and (−)-(1*S*,2*R*)-*trans*-II, the acid (−)-(*R*)-III, and the open-chain ketone (−)-(*R*)-IV. The complete equilibration and racemization of (−)-*cis*-II and (−)-*trans*-II at 25° in dimethyl sulfoxide–dimsylsodium also was reported, and was interpreted as occurring through a trimethyleneketo carbanion (V) in which both asymmetric centers lost their configurational history.



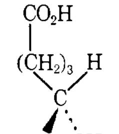
(+)-(*R*)-I



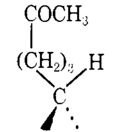
(−)-(1*R*, 2*R*)-*cis*-II



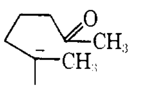
(−)-(1*S*, 2*R*)-*trans*-II



(+)-(*S*)-III



(+)-(*S*)-IV



V

This paper reports the results of studies of the stereochemical course of the base-catalyzed cleavage of cyclic ketone I to acid III, and of diastereomeric alcohols II to open-chain ketone IV. The accompanying reactions of epimerization and racemization of the optically active diastereomeric alcohols II has also been studied. The presence of the two asymmetric centers in II provides a means of monitoring the relative rates at which the carbons carrying the phenyl and the oxygen in the intermediate keto carbanion V rotate with respect to one another, recombine to give back cyclic alcohol, and protonate to give open-chain ketone IV. Comparison of the behavior of these cyclic alcohols in electrophilic substitution reactions at saturated carbon with that of similar open-chain alcohols is particularly interesting since in the cyclic systems the leaving group cannot become completely separated from the carbanion as in open-chain systems.

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(1) This research was sponsored by the U. S. Army Research Office, Durham, N. C. The authors extend their thanks.

(2) T. D. Hoffman and D. J. Cram, *J. Am. Chem. Soc.*, 90, 1000 (1968).

Table I. Cleavage of Optically Pure (+)-(*R*)-2-Methyl-2-phenylcyclopentanone ((+)-(*R*)-I)[a] to (+)-(*S*)-5-Phenylhexanoic Acid ((+)-(*S*)-III)

Run no.	Solvent	(−)-(*R*)-I concn, *M*	Base		Temp, °C	Time, hr	(+)-(*S*)-III		
			Nature	Concn, *M*			Yield, %	$[\alpha]^{25}_{546}$,[b] deg	Retention net, %
1	*t*-BuOH	0.19	*t*-BuOK	0.444	165	22.6	43	+17.7	62
2	*t*-BuOH	0.19	*t*-BuOK	0.418	165	22.8	37	+17.2	60
3[c]	*t*-BuOD[d]	0.19	*t*-BuOK	0.408	165	22.8	32	+17.7	62
4	$(CH_3)_2SO$-*t*-BuOH[e]	0.069	*t*-BuOK	0.150	75	48	25	+0.2	0.7
5	$(CH_3)_2SO$-*t*-BuOH[e]	0.069	*t*-BuOK	0.150	75	87	12	+0.3	1
6	$O(CH_2CH_2OH)_2$	0.21	$H(OCH_2CH_2)_2OK$	0.362	190	24	6.5	+7.77	27

[a] $[\alpha]^{25}_{546}$ +114.0° (*c* 3.9, ethanol). [b] *c* 2.7–2.85, benzene. [c] (+)-(*R*)-I contained 1.84 atoms of deuterium per molecule in position α to ketone, $[\alpha]^{25}_{546}$ +116.1° (*c* 4, benzene). [d] 0.99 atom of deuterium per molecule. [e] 2.1 *M* in *t*-BuOH.

Table II. Equilibration of Sodium Alkoxides of *cis*- and *trans*-1,2-Dimethyl-2-phenylcyclopentanols (*cis*- and *trans*-II) in Dimethyl Sulfoxide

Run no.	Starting material		Base		Time, hr	Temp, °C	%[a] *trans*-II	%[a] *cis*-II	*K* *trans*-II/*cis*-II
	Nature	Concn, *M*	Nature	Concn, *M*					
7	(±)-*cis*-II	0.073	$NaCH_2SOCH_3$	0.413	33.75	25.2	9.16	90.84	9.92
8	(±)-*trans*-II	0.074	$NaCH_2SOCH_3$	0.413	33.75	25.2	9.10	90.90	9.99

[a] Glpc analysis based on *cis*-II and *trans*-II = 100%; <0.1% 6-phenyl-2-heptanone by tlc and infrared.

Results

Optically pure cyclic ketone (+)-I was submitted to cleavage reaction in *t*-butyl alcohol–potassium *t*-butoxide, in dimethyl sulfoxide–*t*-butyl alcohol–potassium *t*-butoxide, and in diethylene glycol–potassium ethylene glycoxide. These three media gave three different stereochemical results in cleavages of open-chain β-arylethanols[3a] and α-phenyl ketones.[3b] Table I records the results obtained with the cyclic ketones. In run 4, unreacted cyclic ketone was recovered from the reaction mixture and found to be optically pure. Acid III was produced with net retention of configuration which varied from 61% in *t*-butyl alcohol to 27% in diethylene glycol to 1% in dimethyl sulfoxide–*t*-butyl alcohol. In run 1 made in *t*-butyl alcohol, besides acid III, 11% starting material and 14% *t*-butyl 5-phenylhexanoate were obtained from the reaction mixture. In runs 4 and 5, considerable sulfur-containing unidentified materials were separated from acid III (low yield) before analysis. In run 6 in ethylene glycol, both starting material and glycol ester of acid III produced were found to go to high molecular weight materials, and as a result the yield of III produced was low.

The starting ketone in run 3 contained 1.84 atoms of deuterium per molecule (mass spectral analysis) introduced by exchanging the α protons of I with deuterium oxide (40%) in dioxane (60% by volume) to which had been added dry potassium carbonate. The cleavage was carried out in *t*-butyl alcohol-O-*d* (0.99 atom of deuterium per molecule) to give a 32% yield of (+)-5-phenylhexanoic acid of 62.2% optical purity (retention). By nmr analysis the acid contained 29% of one hydrogen atom at the methine carbon.

The previous paper[2] reports the fact that the sodium alkoxides of (−)-*cis*-II and (−)-*trans*-II in dimethyl sulfoxide at 25° completely equilibrated to give only racemic material with *trans*-II/*cis*-II = 2.51. Similarly in dimethyl sulfoxide, 1.8 *M* in *t*-butyl alcohol and 0.16 *M* in potassium *t*-butoxide, the racemic *cis*- and *trans*-II equilibrated at 37° to give *trans*-II/*cis*-II = 2.22.

In order to examine the isomerization of optically pure *cis*- and *trans*-II, the concentrations of dimsylsodium and substrate were increased *ca.* 20-fold over that of the previous equilibrium study.[2] Preliminary experiments indicated the isomerization proceeded more slowly at the higher base concentrations. The isomerizations of both *cis*- and *trans*-II were allowed to approach equilibrium. After 33.75 hr at 25° the reaction was stopped. The mixtures were found to contain only trace amounts (<0.1%) of 6-phenyl-2-heptanone and its condensation products. Approximately the same balance of diastereomers was obtained from both *cis*- and *trans*-II. At 25° an average equilibrium constant of $K = trans/cis = 9.96$ was obtained (*cf.* Table II). This dramatic increase in the value of *K* (factor of 4) confirms the fact that the *trans*-alkoxide's steric requirements are much greater in effect than O^- itself. Apparently, the state of aggregation of the *trans*-alkoxide has been significantly raised. The strongly basic dimsyl solution probably intercepted any 6-phenyl-2-heptanone generated during the isomerization. The progress of the reaction was followed as equilibrium was approached. The effective rate constants of a simple first-order rate process are equal to the sum of the constants for the forward and reverse reactions ($k_f + k_r$).[4] The two sums were calculated. Both diastereomers as expected approached equilibrium at approximately the same rate: run 7 (*cis*), $k_f + k_r = 6.8 \pm 1.1 \times 10^{-5}$ sec^{-1} (five points); run 8 (*trans*), $k_f + k_r = 7.0 \pm 1.1 \times 10^{-5}$ sec^{-1} (three points).

In the present work optically pure (−)-*cis*-II was dissolved in dimethyl sulfoxide containing dimsylsodium at 25°. After 255 sec, the reaction mixture was quenched and analyzed by glpc and found to have

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(3) (a) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen, and J. Allinger, *J. Am. Chem. Soc.*, 81, 5774 (1959); (b) D. J. Cram, K. R. Kopecky, F. Hauck, and A. Langemann, *ibid.*, 81, 5754 (1959).

(4) A. Frost and R. Pearson, "Kinetics and Mechanisms," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1961, p 186.

Table III. Isomerization of Optically Pure (−)-*cis*- and (−)-*trans*-1,2-Dimethyl-2-phenylcyclopentanols ((−)-*cis*-II and (−)-*trans*-II) in Dimethyl Sulfoxide–Dimsylsodium at 25°

Run no.	Starting material		Dimsylsodium concn, M	Time, sec	(−)-*cis*-II			(−)-*trans*-II		
	Nature	Concn, M			Yield, %	$[\alpha]^{25}_{546}$,[a] deg	Optical purity, %[b]	Yield, %	$[\alpha]^{25}_{546}$,[a] deg	Optical purity, %[b]
9	(−)-*cis*-II[c]	0.084	0.424	375	95.7	−129.4	99.6[d]	4.3	−24.6	48.0
10	(−)-*cis*-II[c]	0.083	0.340	255	93.5	−122.6	96.2[d]	6.5	−22.3	43.0
11	(−)-*trans*-II[e]	0.072	0.409	20,760	7.9	−44.9	35.0[d]	92.1	−39.0	75.2[d]

[a] c 2.45, benzene, weighings on a Cahn Gram Electrobalance. [b] Compared to optically pure material measured at the same concentration. [c] $[\alpha]^{25}_{546}$ −127.5° (c 2.45, benzene). [d] ±0.2. [e] $[\alpha]^{25}_{546}$ −51.9° (c 2.80, benzene).

Table IV. Epimerization, Racemization, and Cleavage of *cis*- and *trans*-1,2-Dimethyl-2-phenylcyclopentanols (*cis*- and *trans*-II) to 6-Phenyl-2-heptanone (IV) in *t*-Butyl Alcohol–Potassium *t*-Butoxide

Run no.	Starting material		Base concn, M	Time, hr	Temp, °C	Total yield, %[a]	*cis*-II			*trans*-II			IV		
	Nature	Concn, M					Yield, %	$[\alpha]^{25}_{546}$,[b] deg	Optical purity, %[c]	Yield, %	$[\alpha]^{25}_{546}$,[b] deg	Optical purity, %[c]	Yield, %	$[\alpha]^{25}_{546}$,[b] deg	Optical purity, %[c]
12	(±)-*cis*-II	0.0030	0.242	10	150		17			5			78		
13	(±)-*trans*-II	0.0030	0.246	10	150		8			35			57		
14	(±)-*cis*-II	0.030	0.209	48	135	27	9			2.4			15		
15	(±)-*trans*-II	0.030	0.209	48	135	36	2			18			15		
16	(−)-*cis*-II[d]	0.0053	0.244	43	135[e]		42	−126.7	99.3	2			56	+17.3[f]	66.7
17	(−)-*trans*-II[g]	0.0053	0.247	47	135[e]		4	−114	89.2	57	−49.25	94.8	39	−13.0[h]	50.4
18	(−)-*cis*-II[d]	0.031	0.239	51	135[i]	57	35	−127.3	99.4	2.4	−45.6	89.8	20	+16.0[f]	61.1
19	(−)-*trans*-II[g]	0.031	0.229	51	135[i]	57	2.5	−122.4	95.7	36	−51.91	99.9	18	−14.6	55.7

[a] Based on glpc internal standard. [b] c 2.45–2.80, benzene, weighings taken on a Cahn Gram Electrobalance. [c] Compared to optically pure material at the same concentration. [d] $[\alpha]^{25}_{546}$ −127.5° (c 2.45, benzene). [e] ±5°. [f] Optically pure (−)-(*R*)-IV has $[\alpha]^{25}_{546}$ −26.1° (c 1.85, benzene). Reaction went with net retention of configuration. [g] $[\alpha]^{25}_{546}$ −51.9° (c 2.80, benzene). [h] Optically pure (−)-(*R*)-IV has $[\alpha]^{25}_{546}$ −26.1° (c 1.85, benzene). Reaction went with net inversion of configuration. [i] ±0.1°.

only partially racemized and epimerized. The diastereomers were separated by preparative glpc and each diastereomer was examined for optical purity. The same experiment was performed starting with optically pure (−)-*trans*-II. Table III contains the results. In both reactions, (−)-*cis*-II → (−)-*trans*-II, or (−)-*trans*-II → (−)-*cis*-II, epimerization about the carbon atom carrying the oxygen occurred faster than about the carbon atom carrying the phenyl group.

Initial attempts to cleave *cis*- and *trans*-II in hydroxylic solvents led to condensation products of the initially produced 6-phenyl-2-heptanone (IV). Reasonable yields of open-chain ketone IV were obtained by carrying out the reaction of II in dilute solution in *t*-butyl alcohol about 0.25 M in potassium *t*-butoxide at minimum temperatures and reaction times. None of the runs were carried to completion. The mixture of starting and epimerized starting material and ketonic product was reduced with lithium aluminum hydride since no direct means of separating the two alcohols and ketone was found. The three alcohols were analyzed by glpc with an internal standard to provide a basis for yield calculation. In the four runs (16–19) that involved optically pure starting material the three alcohols were separated by column chromatography and shown to be pure by tlc. The rotations of *cis*-II and *trans*-II were determined. The secondary alcohol, 6-phenyl-2-heptanol, produced by reduction of 6-phenyl-2-heptanone was oxidized with chromic acid back to 6-phenyl-2-heptanone (IV) whose rotation was taken. Table IV records the results.

Of the conditions employed for cleavage of either optically active I or II, those that involved dimethyl sulfoxide, 2.1 M in *t*-butyl alcohol and 0.15 M in potassium *t*-butoxide at 75°, were the most drastic (run 4, Table I). To determine if the low optical activity of the acid (+)-III produced in this run was due to racemization of the compound once formed, optically active (+)-III was submitted to the conditions of run 4 except that the reaction time was more than doubled. The substance was only 10% racemized. In other work[5] 2-phenylbutane was found not to racemize appreciably under conditions more drastic than those of runs 1–3 and 6. Cleavages of alcohols II were all conducted under conditions more mild than the cleavages of ketone I. The acidity of the benzyl proton in 2-phenylbutane, acid III, and ketone IV should all be comparable. It is safe to conclude that the open-chain products, III and IV, were optically stable under conditions of their formation in the runs of Tables I and IV.

Discussion

The isomerization of the optically active diastereomeric alcohols, (−)-*cis*-II and (−)-*trans*-II, into one another and the accompanying racemization will be discussed first, followed by a mechanistic interpretation of the stereochemical course of the cleavage of these cyclic alcohols into open-chain ketone IV. The cleavage of optically active cyclic ketone (+)-I to give open-chain acid III will then be examined. At each stage the behavior of these cyclic systems will be compared with that of their open-chain counterparts. Finally, the mechanistic notions developed here will be placed in context with respect to other investigations.

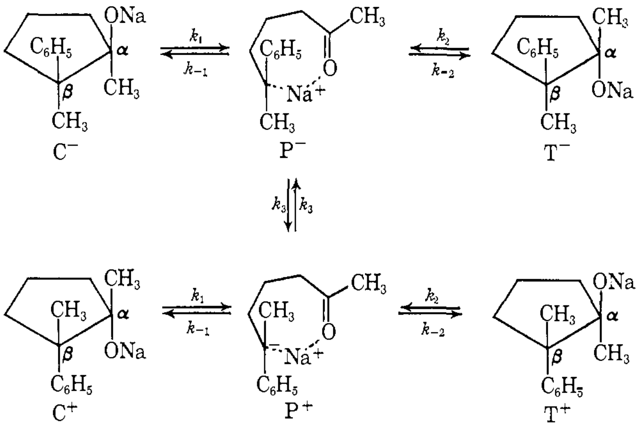
(5) D. J. Cram, A. Langemann, and F. Hauck, *J. Am. Chem. Soc.*, **81**, 5750 (1959).

Interconversion of (−)-*cis*- and (−)-*trans*-1,2-Dimethyl-2-phenylcyclopentanol (*cis*- and *trans*-II) and the Accompanying Racemization. Simple dissolution of (−)-*cis*-II and (−)-*trans*-II in a solution of dimsylsodium in dimethyl sulfoxide at 25° produces an equilibrium mixture of racemic diastereomers.[2] Interruption of the equilibrating process after a short time by quenching the mixture provided the results of Table III.

In the following discussion, C^- will refer to (−)-*cis*-II, C^+ to (+)-*cis*-II, T^- to (−)-*trans*-II, and T^+ to (+)-*trans*-II. The reaction, $C^- \rightarrow T^-$, represents an epimerization at the carbon-carrying oxygen (C_α), whereas $C^- \rightarrow T^+$ represents an epimerization at the carbon-carrying phenyl (C_β). The yields of product from the various reactions that occurred in runs 10 and 11 are summarized (run 9 is not included since the reaction, $C^- \rightarrow C^+$, was not carried far enough to provide accurate data): run 10, $C^- \rightarrow 92\%\ C^- + 1.8\%\ C^+ + 4.7\%\ T^- + 1.8\%\ T^+$; run 11, $T^- \rightarrow 5.3\%\ C^- + 2.6\%\ C^+ + 81\%\ T^- + 11\%\ T^+$. The ratio T^-/T^+ from C^-, or $(T^-/T^+)_{C^-}$, provides a measure of the relative tendencies for epimerization to occur at the two asymmetric centers during reaction of C^-. Similarly, $(C^-/C^-)_{T^-}$ provides a measure of the same thing during reaction of T^-. From either starting material, epimerization occurs over twice as frequently at C_α as at C_β. In a formal sense, epimerization at C_α is an electrophilic substitution at saturated carbon that occurs with predominant retention, $(T^-/T^+)_{C^-} \sim 2.6$ (run 10) and $(C^-/C^+)_{T^-} \sim 2.0$ (run 11), and where carbonyl acts as both leaving group and electrophile.

Another informative comparison involves the values of $(C^+/T^+)_{C^-}$ and $(C^+/T^+)_{T^-}$. Had C^+ and T^+ arisen only from a reaction intermediate [$(C^+/T^+)_{C^-} \sim 1$ (run 10) and $(C^+/T^+)_{T^-} \sim 0.24$ (run 11)] produced from both C^- and T^-, and had the products once formed not undergone subsequent reactions, the value of the ratio C^+/T^+ should be independent of starting material. The observed values differ by a factor of 4, which indicates that either one or both of these conditions are not fulfilled. Clearly, these products once formed do undergo further reaction, and at different rates. The *cis* isomer reacts about ten times faster than the *trans*. Possibly the value of $(C^+/T^+)_{C^-} = 1$ for run 10 represents a collapse ratio of an intermediate in an essentially kinetically controlled process, whereas $(C^+/T^+)_{T^-} = 0.24$ represents a value intermediate between kinetically and thermodynamically controlled processes. This interpretation is compatible with $T/C = K = 10$, which was observed.

Chart I



Although more complex interpretations can be envisioned and probably apply (see next section), the simplest mechanism is found in Chart I. In this mechanism the enantiomeric ion pairs P^+ and P^- are the key intermediates, and k_{-1} and $k_{-2} > k_3$. This scheme accounts for the fact that epimerization at C_α exceeds that at C_β. Epimerization at C_α can occur without ligand detachment from the metal cation, but epimerization at C_β requires ligand detachment at one face of the benzyl anion and attachment at the opposite face. Thus, rotation (epimerization) at C_α should be faster than at C_β, as is observed.

Since the recovery of II from runs 9–11 was high, it is clear that recapture of the carbonyl group by the carbanion in the trimethyleneketo carbanion is a process more kinetically favored that proton abstraction from dimethyl sulfoxide. In the equilibration[2] of *cis*- and *trans*-II, the recovery was about 50–60%, and in the equilibration the keto carbanion was formed many times. The pK_a's of toluene and dimethyl sulfoxide are close to one another,[6] but apparently the intramolecularity of the ring-closing reaction made it favored over proton transfer.

Cleavage of (−)-*cis*- and (−)-*trans*-1,2-Dimethyl-2-phenylcyclopentanol ((−)-*cis*-II and (−)-*trans*-II) to 6-Phenyl-2-heptanone (IV) and the Accompanying Epimerization and Racemization Reactions. Table IV contains the results of the cleavage, epimerization, and racemization reactions of both (−)-*cis*- and (−)-*trans*-II in *t*-butyl alcohol–potassium *t*-butoxide at 135°. The data of runs 16–19 make it clear that the same processes occur in *t*-butyl alcohol that were observed in dimethyl sulfoxide, in addition to the reaction of proton donation by solvent to the intermediate trimethyleneketo carbanion. The yield pattern for runs 17 and 18 provide a second set of interesting ratios.

$$C^- \xrightarrow[18]{\text{run}} 2.3\%\ T^- + 0.12\%\ T^+ + 35\%\ C^- + 0.10\%\ C^+ + 3.9\%\ (-)\text{-IV} + 16\%\ (+)\text{-IV}$$

$$T^- \xrightarrow[17]{\text{run}} 56\%\ T^- + 1.5\%\ T^+ + 3.8\%\ C^- + 0.22\%\ C^+ + 29\%\ (-)\text{-IV} + 9.5\%\ (+)\text{-IV}$$

$$(T^-/T^+)_{C^-} \sim 19 \text{ (run 18)}$$
$$(C^-/C^+)_{T^-} \sim 17 \text{ (run 17)}$$
$$(C^+/T^+)_{C^-} \sim 0.87 \text{ (run 18)}$$
$$(C^+/T^+)_{T^-} \sim 0.15 \text{ (run 17)}$$

In this hydroxylic solvent the values of $(T^-/T^+)_{C^-}$ and $(C^-/C^+)_{T^-}$ are 19 and 17, respectively, much higher than in dimethyl sulfoxide. Thus, epimerization at C_α exceeds epimerization at C_β by over a power of 10 in this medium. In other words, electrophilic substitution at saturated carbon with a carbonyl leaving group and the same carbonyl group as electrophile occurs with high retention of configuration, much higher than in dimethyl sulfoxide. Equally striking is the fact that this process is fast enough to be com-

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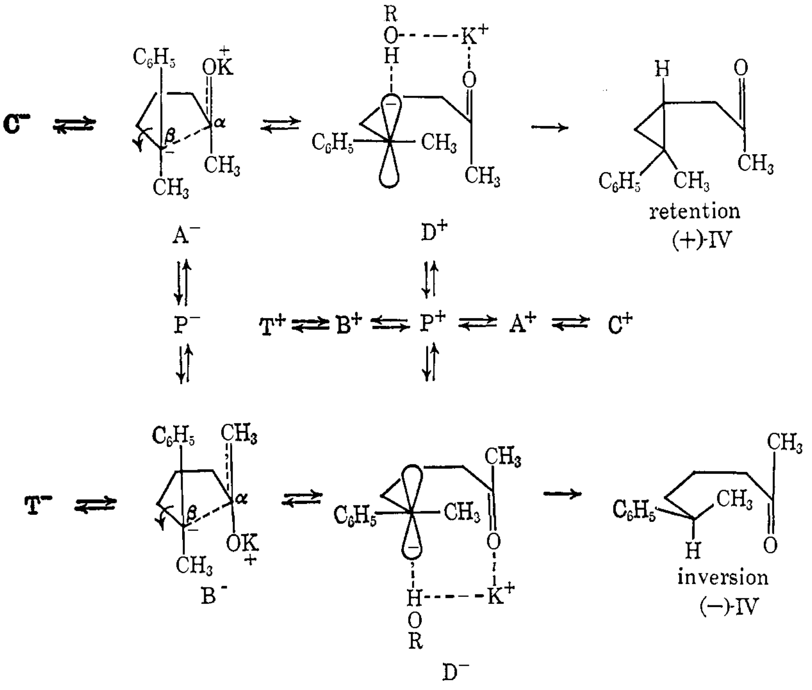
[6] D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 19, 43.

Chart II



petitive with proton transfer from the hydroxylic medium.

The ratios of C$^+$/T$^+$ from both C$^-$ and T$^-$ are both considerably less than unity. The values are grossly inaccurate since they depend on very small percentage yields which were not accurately determined. No significance can be attached to the fact that these two ratios are not the same. However, it is clear from these values that the trimethyleneketo carbanion collapses preferentially to the *trans* isomer. The yield data and reaction times suggest that C$^+$ and T$^+$ once formed do not undergo further reaction at widely different rates.

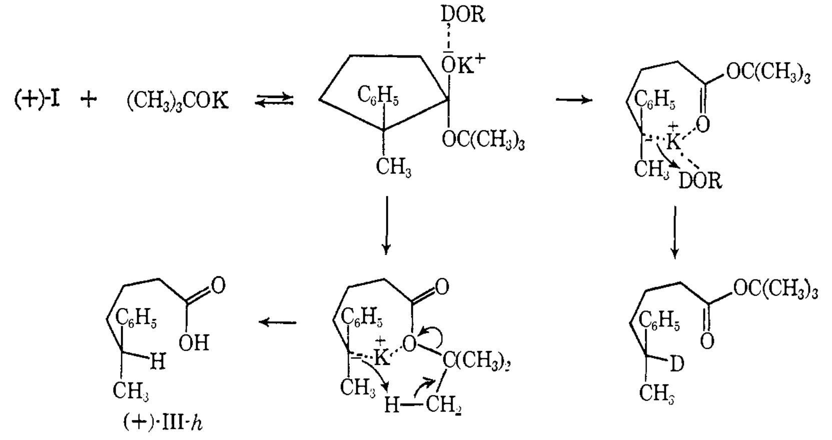
A remarkable feature of these reactions is the dependence of the stereochemical course of cleavage and protonation on the configuration of the starting material. In run 18, (−)-*cis*-II gave predominantly open-chain ketone (+)-IV in a reaction in which *retention dominated over inversion* by a factor of about 4. In run 19, (−)-*trans*-II gave open-chain ketone (−)-IV in a reaction in which *inversion dominated over retention* by a factor of about 3. Clearly, a mechanism for these reactions is required in which the diastereomeric character of the starting material is felt in the intermediate trimethyleneketo carbanion. The simple scheme of Chart I cannot apply since intermediate ion pair P$^-$ is produced directly from C$^-$ and T$^-$, and the diastereomeric memory is lost.

Chart II symbolizes a mechanism enough more elaborate than that of Chart I to accommodate the stereochemical course of the protonation reaction. Intermediates such as P$^-$, P$^+$, A$^-$, and B$^-$ and products C$^+$ and T$^+$ are not formulated but are included. In this scheme, C$^-$ produces an intermediate ion pair A$^-$ in which the C$_\alpha$–C$_\beta$ bond has been broken to generate a species in which the p orbitals at C$_\alpha$ and at C$_\beta$ are electrostatically involved enough to preserve configuration at both centers. By rotation counterclockwise at C$_\alpha$, A$^-$ → P$^-$ which, in turn, produces B$^-$. *Rotation in A$^-$ should occur predominantly clockwise for steric reasons*, since compressing methyl against methyl is energetically more feasible than phenyl against the potassium oxide group and its ligands. This brings a lobe of the p orbital at C$_\beta$ into the vicinity of the proton donors that act as ligands to the potassium ion. These alcohol molecules first hydrogen bond to the carbanion as in D$^+$ which *mainly collapses to product (+)-IV with retention of configuration.* Alternatively, D$^+$ continues to rotate and gives P$^+$. This species partitions to give B$^+$ or A$^+$ which, in turn, generate T$^+$ and C$^+$.

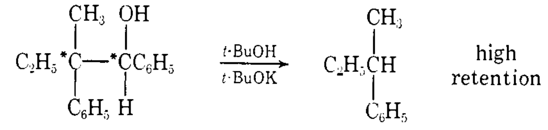
With T$^-$ as starting material, B$^-$ is produced directly. In this species rotation of C$_\beta$ is also clockwise for steric reasons since compression of methyl against the potassium oxide group is a lower energy process than phenyl against methyl. Thus, B$^-$ gives D$^-$ at which point a lobe of the p orbital of C$_\beta$ is in position to hydrogen bond with alcohol molecules serving as potassium's ligands. Collapse to the covalent state by proton transfer gives (−)-IV, *an over-all substitution with inversion.* Alternatively, D$^-$ can go to P$^+$, which partitions to give ultimately T$^+$ and C$^+$. This mechanism, although complex, is required to account for all the stereochemical transformations observed. It is difficult to envision any reasonable alternative explanation to account for (−)-*cis*-II giving (+)-IV (predominating retention) and (−)-*trans*-II, (−)-IV (predominating inversion). In both the retention and inversion pathways, potassium *t*-butoxide contact ion pairs are produced. Any mechanism not involving rotation of C$_\beta$ would lead to dissociated potassium and *t*-butoxide ions, an unfavorable process in this low dielectric medium.

Marked differences exist between the behavior of these cyclic alcohols and their open-chain counterparts. In *t*-butyl alcohol–potassium *t*-butoxide, optically pure diastereomeric open-chain alcohols α- and β-VI gave 2-phenylbutane with 81–82% retention of configuration,

Chart III

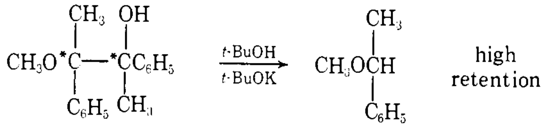


and optically pure α- and β-VII gave 1-phenylmethoxyethane with 94% retention.[7] Recovery of starting materials in some of these experiments and a number of others demonstrated the substances to be unchanged either with respect to epimerization or racemization.[7] Clearly, the leaving carbonyl group in the cyclic systems is more constrained to shield the front face of the carbanion than in an open-chain system. The same thing was observed in the thermal racemization of VIII in methanol and t-butyl alcohol. Protonation of the carbanion and alkoxylation of the carbonium ion of the intermediate carbonium ion–carbanion ion pair occurred as reactions competing with racemization.[8]



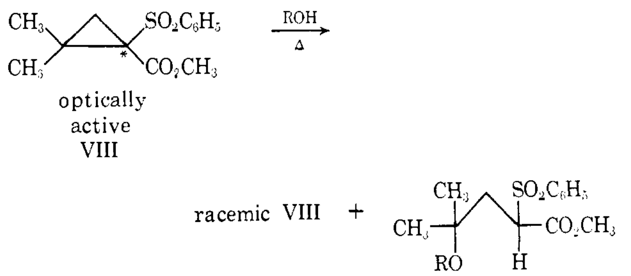
$$C_2H_5{}^*\overset{CH_3}{\underset{C_6H_5}{C}}-{}^*\overset{OH}{\underset{H}{C}}C_6H_5 \xrightarrow[t\text{-BuOK}]{t\text{-BuOH}} C_2H_5\overset{CH_3}{\underset{C_6H_5}{C}}H \quad \text{high retention}$$

α- or β-VI



$$CH_3O{}^*\overset{CH_3}{\underset{C_6H_5}{C}}-{}^*\overset{OH}{\underset{CH_3}{C}}C_6H_5 \xrightarrow[t\text{-BuOK}]{t\text{-BuOH}} CH_3O\overset{CH_3}{\underset{C_6H_5}{C}}H \quad \text{high retention}$$

α- or β-VII

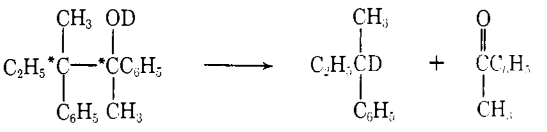


optically active VIII

racemic VIII +

Another example of isomerization through thermal ion-pair formation involves the thermal equilibration of substituted *cis*- and *trans*-aziridines, a reaction competitive with dipolar cycloaddition in the presence of appropriate olefins.[9]

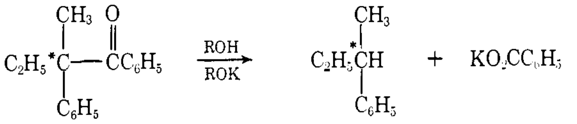
In a previous study, open-chain alcohol IX was cleaved in t-butyl alcohol-O-*d*-potassium t-butoxide, and the 2-phenylbutane produced (87% net retention) contained over 80% deuterium in the benzyl position.[10] Apparently, the acetophenone leaving group did not compete effectively with the t-butyl alcohol-O-*d* as a proton donor.



$$C_2H_5{}^*\overset{CH_3}{\underset{C_6H_5}{C}}-{}^*\overset{OD}{\underset{CH_3}{C}}C_6H_5 \longrightarrow C_2H_5\overset{CH_3}{\underset{C_6H_5}{C}}D + \overset{O}{\underset{CH_3}{\overset{\|}{C}}}C_6H_5$$

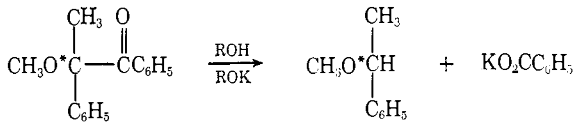
IX

Stereochemical Cleavage of (+)-2-Methyl-2-phenylcyclopentanone ((+)-I) to (+)-5-Phenylhexanoic Acid ((+)-III). The results of Table I demonstrate that ketone (+)-I cleaves to open-chain acid, and that in all media the reaction occurs with net retention. In t-butyl alcohol–potassium t-butoxide, 60–62% net retention was observed. In diethylene glycol–potassium diethylene glycoxide, net retention dropped to 27%. In dimethyl sulfoxide–t-butyl alcohol–potassium t-butoxide, only about 1% net retention was obtained. In this solvent starting material was recovered in one run (4), and was found not to have racemized detectably.



$$C_2H_5{}^*\overset{CH_3}{\underset{C_6H_5}{C}}-\overset{O}{\overset{\|}{C}}C_6H_5 \xrightarrow[ROK]{ROH} C_2H_5\overset{CH_3}{\underset{C_6H_5}{\overset{*}{C}}}H + KO_2CC_6H_5$$

X



$$CH_3O{}^*\overset{CH_3}{\underset{C_6H_5}{C}}-\overset{O}{\overset{\|}{C}}C_6H_5 \xrightarrow[ROK]{ROH} CH_3O{}^*\overset{CH_3}{\underset{C_6H_5}{C}}H + KO_2CC_6H_5$$

XI

The results in t-butyl alcohol resemble those obtained in the same medium from open-chain ketones X and XI,[3b] which underwent cleavage with 74 and 61% net retention, respectively. In this nondissociating medium, the potassium ion and its ligands of proton-donating alcohol molecules organize proton donors at the front of the carbanion, and products can be formed

[7] D. J. Cram, F. Hauck, K. R. Kopecky, and W. D. Nielsen, *J. Am. Chem. Soc.*, **81**, 5767 (1959).

[8] D. J. Cram and A. Ratajczak, *ibid.*, **90**, 2198 (1968).

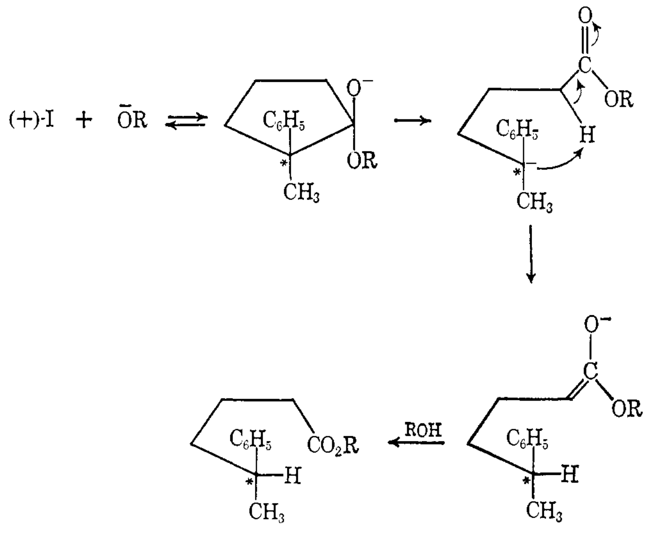
[9] (a) R. Huisgen, *Angew. Chem. Intern. Ed. Engl.*, **2**, 565, 633 (1963); (b) R. Huisgen, W. Scheer, and H. Huber, *J. Am. Chem. Soc.*, **89**, 1753 (1967).

[10] D. J. Cram and B. Rickborn, *ibid.*, **83**, 2178 (1961).

without generation of dissociated ions by simple proton transfer. Three possible proton sources can be envisioned: the hydroxyl groups of the solvent; the methylene hydrogens α to the carbonyl group; the methyl groups of the *t*-butyl alcohol. Run 3 carried out in *t*-butyl alcohol-O-*d* with α,α-dideuterated ketone gave acid with 29% of one atom of protium attached to the benzyl carbon. Apparently, 71% of the carbanions captured deuterium from either the hydroxyl group of the alcohol or the methylene group α to the carbonyl, and the remaining 29% from the methyl groups of the *t*-butyl alcohol. Chart III details two of the three probable mechanisms. Although not formulated, some of the reaction probably involves proton transfer from the methylene group α to the ester leaving group. The fact that a mixture of ester and acid was obtained supports the notion that the reaction is initiated by alkoxide attack on the carbonyl group. In this solvent the open-chain and cyclic systems give about the same results.

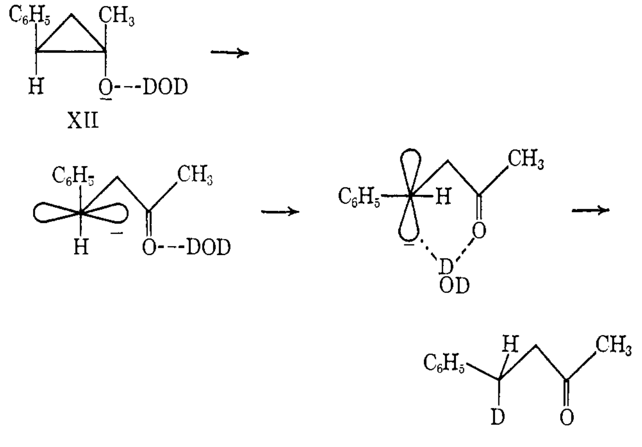
The results of cleavage of ketone I in diethylene glycol (27% net retention) contrasts with the 38 and 17% net inversion observed for open-chain ketones X and XI.[3b] Cyclic ketone I contains two acidic α-hydrogens that cannot leave the molecule, whereas the open-chain ketones have no α-hydrogens. This structural feature may explain the tendency of the cyclic ketone to give retention. In this connection it was observed that when 2-phenyl-2-butylpotassium was treated with 2-butanone, only 2-phenylbutane was produced. Thus, the ketone served as a proton source for the benzyl anion.[11] Chart IV details the mechanism considered mainly responsible for the net retention observed in diethylene glycol.

Chart IV



The results of cleavage of (+)-I in dimethyl sulfoxide–*t*-butyl alcohol–potassium *t*-butoxide (~1% retention) contrast with the 40% net retention found in cleavage of open-chain ketone VIII.[12] Cleavage of alcohols VII and IX in the same medium gave almost complete racemization.[3a] As pointed out by Gassman and Zalar[13] in connection with cleavage of bicyclic ketones, addition of dimsylpotassium to a ketone provides a very acidic leaving group at the front face of the carbanion. Possibly, dimsylpotassium serves as the adding base for the open-chain ketone and *t*-butoxide anion the adding base for the cyclic ketone—the former leading to net retention and the latter to racemization, as in the cleavage of the open-chain alcohols. Apparently, the stereochemistry depends on a subtle balance between structural features of the substrate and medium.

Dependence of Stereochemical Course of Cleavage Reactions of Alcohols on Structural Features. The cleavage results of DePuy, *et al.*,[14] on optically active cyclopropanol XII in 50:50 dioxane–water–sodium hydroxide provide an interesting basis for comparison with our results. These authors observed high inversion in a solvent comparable to those (ethylene glycol or methanol) used for cleavage of such open-chain systems as VI, VII, or IX to give moderately high inversion. Since we observed that in *t*-butyl alcohol our cyclic alcohols both epimerized and racemized, and that the stereochemical course of the cleavage reaction depended on the diastereomeric configuration of the starting material, the same might be true in the cyclopropanol system XII. Compound XII possesses a steric disposition such that upon cleavage, the benzyl carbon should rotate in a direction to undo the compression of the phenyl and methyl groups, rotate the benzyl hydrogen past the carbonyl group, and bring the remote lobe of the p orbital into the vicinity of the alcohol molecules hydrogen bonding the carbonyl group. Proton transfer then might occur to provide the net inversion observed. This process might be more favored sterically than in our system because the two ends of the broken ring have less opportunity to separate, and because a benzyl hydrogen is smaller than a benzyl methyl group. This mechanism also possesses the distinct advantage of not having to disrupt the solvent structure any more than it is disrupted already by the initial hydrogen bonding in the alkoxide itself.


XII

This "rotation mechanism" to provide inversion cannot accommodate the high inversion observed by

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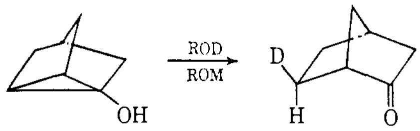
[11] D. J. Cram, A. Langemann, J. Allinger, and K. R. Kopecky, *J. Am. Chem. Soc.*, **81**, 5740 (1959).

[12] D. J. Cram and H. P. Fischer, in ref 6, p 148.

[13] (a) P. G. Gassman and F. V. Zalar, *Tetrahedron Letters*, 3031 (1964); (b) *J. Am. Chem. Soc.*, **88**, 3070 (1966); (c) P. G. Gassman, J. T. Lumb, and F. V. Zalar, *ibid.*, **89**, 946 (1967).

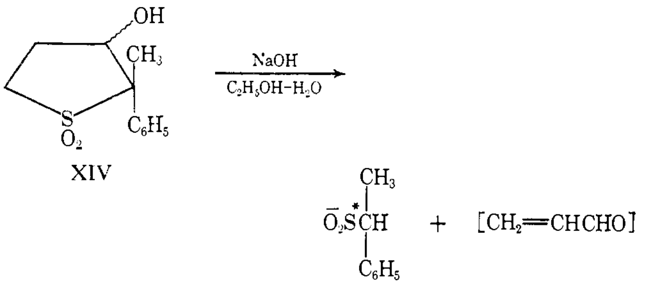
[14] (a) C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, *ibid.*, **88**, 3347 (1966); (b) C. H. DePuy, *Accounts Chem. Res.*, **1**, 33 (1968).

Nickon, *et al.*,[15] in his cleavage of polycyclic alcohol XIII in a variety of media. Rotation is prohibited by the ring system of XIII.



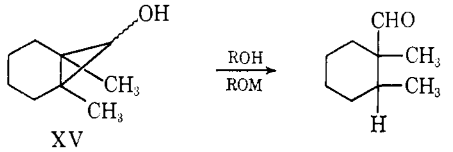
XIII

The results of the present work bring up interesting questions about the mechanism of the cleavage of cyclic sulfone XIV studies by Corey and Lowry.[16] These authors observed cleavage of alcohol of unidentified configuration at the carbon bearing the hydroxyl group in ethanol–water. High inversion was the stereochemical result, one that contrasted with high retention found for open-chain sulfones. The same complications of epimerization and dependence of cleavage results on diastereomeric structure might apply to XIV as were observed in our cyclopentanols. The ring sizes of XIV and II are the same. A thorough study of possible epimerization and cleavage of both diastereomers of XIV would be informative.



XIV

In the cleavage of the *exo* and *endo* isomers of XV, only high retention was observed in *t*-butyl alcohol–potassium *t*-butoxide. However, in ethylene glycol–sodium glycoxide, *endo*-XV gave 20% net retention and *exo*-XV, 40% net inversion.[17] Again conformation appears to play some role in the stereochemistry of this electrophilic substitution reaction at saturated carbon.



XV

Experimental Section

General. The same general techniques, instruments, and solvents were employed that were detailed in the previous paper.[2] The starting materials and products described there[2] were used in this investigation. Polarimetric analyses of (−)-*cis*- and (−)-*trans*-II were performed in all cases as follows.

Weighings were performed on a Cahn Gram Electrobalance (Cahn Instruments Co., Paramount, Calif.) and are accurate to ±0.001 mg. Small aluminum weighing pans were employed. Liquids were delivered to the pans *via* micropipets under a positive pressure of dry nitrogen. The pan containing the weighed sample was transferred to the neck of a calibrated 1-ml volumetric flask and the contents washed into the flask with dry benzene. The weighing pan was freed of solvent with a stream of nitrogen and then removed from the flask. Solvent was added to the mark with a dry syringe and the pan replaced in the neck. The solution was then made homogeneous and its rotation measured in a 1-dm tube. Solvent blanks were taken before and after the solution was analyzed. An average zero reading was recorded for each wavelength; these corrections were made on crude data. All rotations were taken in the same volumetric flask and the same polarimeter cell. The optical purity of each sample was determined by running a sample of optically pure material at the same concentration immediately after the sample whose optical purity was being determined. The Perkin-Elmer Model 141 polarimeter was most sensitive at the three lower mercury lines (546–365 mμ); the less intense sodium line often gave sluggish response. The variations in rotations observed at the 365-mμ line are due to an inherent peculiarity of the machine to overshoot. Readings could only be approached from one side. All other lines allowed approach from below as well as above.

Cleavages of (+)-2-Methyl-2-phenylcyclopentanone (+)-I. In all cases optically pure material was used. The procedure for cleavage in *t*-butyl alcohol (runs 1, 2, and 3) was reported previously.[2] The deuterated (+)-I used in run 3 was prepared by a modification of a procedure used for other substances.[18]

To a rigorously dried 100-ml flask were added 20 ml of deuterium oxide (Volk Chemical Co., >99.6% D), 30 ml of pure dioxane, 0.55 g of potassium carbonate (dried at 500° for 48 hr), and 1.75 g (10 mmol) of optically pure (+)-2-methyl-2-phenylcyclopentanone. The nonhomogeneous reaction mixture was stirred at 30° for 20 hr in a dry atmosphere, and then heated at 55° for 30 min. The solution was still nonhomogeneous but colorless. The solvents were removed at 25° (0.57 mm), after which the flask was recharged with 50 ml of a 60:40 dioxane–deuterium oxide solution. The reaction sequence was repeated, and the solvents were removed at reduced pressure. Deuterium oxide (25 ml) was added and the ketone extracted with pure ether. The solvent was washed with deuterium oxide and brine and dried. Removal of the solvent gave 1.55 g of an oil which was homogeneous by tlc. The residual oil was flash distilled and then chromatographed on silica gel. Fractions 3–7 were eluted with 1:99 ether–pentane to give, after distillation, 1.42 g of a colorless oil: $[\alpha]^{25}\mathrm{D}$ +95.7°; $[\alpha]^{25}{}_{546}$ +115.0° (*c* 1.19, C_2H_5OH).

The ketone was homogeneous to glpc (30% SE 30 on Firebrick at 175°, helium carrier gas). By nmr the ketone contained *ca.* one-half of one methylene hydrogen α to the keto group. The exchange process was repeated. The cyclopentanone (0.820 g) was added to a mixture of 20 ml of deuterium oxide, 45 ml of pure dioxane, and 0.50 g of dry potassium carbonate. The reaction mixture was stirred at *ca.* 30° for 12 hr, then the solvents were removed, and the product extracted in the usual way. The crude product was chromatographed on silica gel, then flash distilled (95° (1 mm)) to give 0.673 g of 2-methyl-2-phenyl-5,5-dideuteriocyclopentanone: $[\alpha]^{25}\mathrm{D}$ +97.30°, $[\alpha]^{25}{}_{546}$ +116.1°, $[\alpha]^{25}{}_{365}$ +364.0° (*c* 3.97, C_2H_5OH); $n^{25}\mathrm{D}$ 1.5337; ir (carbon tetrachloride) 5.75 μ (C=O); nmr (carbon tetrachloride) τ 2.70 (aromatic CH, m, 5), 7.10–8.50, center of gravity, 8.22 ($(-CH_2-)_2$, m, 4), 8.70 (CH_3, s, 3); mass spectrum (70 eV) *m/e* (relative intensity) 177 (6), 176 (42), 175 (7), 133 (13), 118 (100), 117 (22), 78 (10), 77 (8), and 28 (5).

The mass spectrum (12 eV) indicated the isotopic distributions: 0.75% h_2, 13.1% *d*, 85.3% d_2, 0.60% d_3, 0.22% d_4.

Anal. Calcd for $C_{12}H_{12}D_2O$: C, 81.77; H, 9.14. Found: C, 81.90, 81.88; H, 9.31, 9.06.

For run 3 this deuterated ketone (0.4338 g, 2.46 mmol) was syringed into a clean Carius tube which had been evacuated while hot and then filled with dry nitrogen. A solution of 13 ml of *t*-butyl alcohol-O-*d*, 0.408 *M* in potassium *t*-butoxide, was pipetted in under a blanket of nitrogen. The tube was frozen, evacuated, and sealed. The tube was warmed to 25°, shaken to ensure homogeneity, and totally immersed in a stirred oil bath at 165 ± 1° for 22.75 hr. The ampoule was quickly cooled to 25°, then frozen, and the contents worked up in a manner completely analogous to that with the protio compound.[2] By tlc and ir the nonacidic fraction contained both *t*-butyl ester and starting ketone. The acid was obtained in 31.7% yield as a yellow oil which was flash distilled in a microstill: ir (carbon tetrachloride) 2.80–4.40 (OH) and 5.85 μ (C=O); $n^{25}\mathrm{D}$ 1.5077; nmr (carbon tetrachloride) τ −1.19 (OH, s, 1), 2.88 (aromatic CH, singlet with fine structure, 5), 7.43–8.17 (–CH, $CH_2C{=}O$,

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[15] A. Nickon, J. L. Lambert, R. O. Williams, N. H. Westiuk, *J. Am. Chem. Soc.*, **88**, 3354 (1966).

[16] (a) E. J. Corey and T. H. Lowry, *Tetrahedron Letters*, 793 (1965); (b) *ibid.*, 803 (1965).

[17] P. S. Warton and T. I. Bair, *J. Org. Chem.*, **31**, 2480 (1966).

[18] P. Natalis, *Bull. Soc. Chim. Belges*, **67**, 599 (1958).

m, 0.75 H), 8.47 ($(CH_2)_2$, s, 4), 8.78 (CH_3, s, 3); $[\alpha]^{25}D$ +15.1°, $[\alpha]^{25}_{546}$ +17.9°, $[\alpha]^{25}_{436}$ +32.3° (*c* 2.85, benzene).

The methyl singlet was bracketed by a doublet, $J = 6$ Hz. The methyl region of the spectrum was scanned at a sweep width of 100 cps; the peak heights of the methyls were measured. The doublet which was assigned to the methyl of the 5-phenyl-5-protiohexanoic acid constituted 28.8% of the total resonance in the methyl region. The base line chosen found the peak heights of the methyl doublet in a ratio of 56:44 which agrees exactly with the ratio of the methyl doublet of the pure protio compound.

For runs 4 and 5 carried out in *t*-butyl alcohol–dimethyl sulfoxide, the following procedure is illustrative. Under a blanket of pure, dry nitrogen were mixed 0.722 g (0.00412 mol) of (+)-I, 50 ml of pure dimethyl sulfoxide, and 10 ml of *t*-butyl alcohol, 0.899 *M* in potassium *t*-butoxide. The mixture was swirled until homogeneous and held under nitrogen at 75 ± 0.01°. After 48 hr the flask was removed and the contents poured into a rapidly stirred mixture of 100 ml of ice and water. The yellow solution was extracted with three, 250-ml portions of 1:1 ether–pentane. The combined organic phases were washed with excess water and brine and dried. The solvent was removed to give 0.208 g of a mobile oil: ir (carbon tetrachloride) 5.75, 5.85 (C=O), 6.05, and 6.10 μ (C=C). By tlc the oil contained starting ketone and a trace of *t*-butyl 5-phenylhexanoate. The oil was dissolved in 1:99 ether–pentane and subjected to elution chromatography on 36 g of silica gel packed in a column 50 cm high and 18 mm wide. The ketone was eluted with 7.5:92.5 ether–pentane. Fraction 5 was 0.046 g of pure 2-methyl-2-phenylcyclopentanone which was flash distilled: $[\alpha]^{25}D$ +95.1°, $[\alpha]^{25}_{546}$ +114.0° (*c* 2.20, ethanol); $n^{25}D$ 1.5342.

Run 6 in diethylene glycol was made as follows. Under pure nitrogen were mixed 25.2 ml of diethylene glycol, 0.362 *M* in potassium diethylene glycoxide, and 0.8385 g of optically pure (+)-I. The mixture under nitrogen in a closed system was heated in a Wood's metal bath at 190 ± 1° for 24 hr. The solution was homogeneous before and after the run. By tlc the crude reaction mixture contained a trace of starting material. An equal volume of 15% aqueous potassium hydroxide was added; the reaction mixture was stirred at 110° for 30 min and then allowed to cool. The solution was shaken with 25 ml of water and 40 ml of ether. The organic layer was washed with several portions of water, then brine, and dried. Analysis of the ir spectrum of the residual oil indicated the presence of starting material and its aldol dimers. The aqueous layer was shaken with three, 40-ml portions of 1:1 ether–pentane, and then made strongly acidic with concentrated hydrochloric acid. A milky white suspension developed, and the product was extracted with ether which was washed with water and brine and dried. Solvent was removed on a steam bath to give 0.200 g of a yellow oil. By tlc the acid was contaminated by materials of greater and smaller R_f. The oil was dissolved in 50 ml of 1:1 ether–pentane and shaken with an equal volume of 5% aqueous sodium bicarbonate. The basic aqueous layer was extracted with three more equal volumes of 1:1 ether–pentane, then neutralized with concentrated hydrochloric acid and ice. The product was extracted from the strongly acidic aqueous phase with dichloromethane which was then shaken with brine and dried. By tlc a small impurity of low R_f was still present. The above process was repeated and the acid was extracted with ether to give 0.0548 g (6.54%) of a yellow oil. The ir and nmr spectra were superimposable with those of an authentic sample. The 5-phenylhexanoic acid was distilled in a micro Hickman flask (pot 139° 0.2 mm)): $[\alpha]^{25}D$ +6.48°, $[\alpha]^{25}_{546}$ +7.77° (*c* 2.69, benzene); $n^{25}D$ 1.5079.

Partial Epimerization and Racemization of (−)-*cis*-1,2-Dimethyl-2-phenylcyclopentanol ((−)-*cis*-II) in Dimethyl Sulfoxide at 25° (Run 8). To a dry, 250-ml, three-necked flask equipped with a pressure-equilibrating dropping funnel, nitrogen inlet, and Teflon stirring bar, was pipetted 100 ml of dry dimethyl sulfoxide. The flask was immersed in a water bath at 25° and a few crystals of triphenylmethane (Matheson Coleman and Bell, mp 93.1–93.9°, recrystallized from methanol) and 1.989 g (10.4 mmol) of optically pure (+)-*cis*-II were added. While the homogeneous solution of (−)-*cis*-II in dimethyl sulfoxide was stirred at 25°, a 1.70 *M* dimsylsodium solution was prepared in the dropping funnel from 1.99 g (51 mmol) of practical grade sodium amide (Matheson Coleman and Bell, >95% pure) and 30 ml of dry dimethyl sulfoxide. The ammonia was removed from the dimsyl solution by a stream of dry nitrogen. After 30 min the exit gas contained no ammonia (test with wet litmus).

The dimsylsodium solution was added rapidly to the dimethyl sulfoxide solution. After 10 sec a pink color appeared. After 25 sec the solution became deep red (time zero). The total addition time was 45 sec. The reaction mixture was stirred for an additional 250 sec from the time the solution became deep red. The contents of the flask were then poured into a rapidly stirred solution of 500 ml of ice and water (10 sec). The residual solution in the reaction flask was not combined with the quenched solution. Total reaction time was computed as 255 sec, from appearance of first deep red to halfway through the quenching procedure.

The product was isolated in a way completely analogous to that described for the equilibrium runs.[2] By tlc no 6-phenyl-2-heptanone was present (visualization by 10% phosphomolybdic acid in ethanol, then, 2,4-DPNH spray). The crude reaction mixture was dissolved in pentane and analyzed by glpc and found to contain 6.5% *trans*-II and 93.5% starting material ((−)-*cis*-II). A mixture of racemic diastereomeric cyclopentanols was made up to contain 6.50% *cis*-II and 93.50% *trans*-II (w/w). By glpc this standard mixture was analyzed and found to contain 6.47% *cis*-II and 93.53% *trans*-II. The crude reaction mixture, in pentane, was placed on a column of 350 g of silica gel prepared in 5:95 ether–pentane. The column measured 68 cm in height and 32 mm in diameter. Fifty fractions were taken as the solvent was varied from 5:95, 7.5:92.5, and 10:90 ether–pentane. Fractions 1–12 were yellow oils which contained neither cyclopentane nor open-chain ketone by tlc. Qualitative tests, performed in capillary tubes for olefin (bromine in carbon tetrachloride) and ketone (2,4-DNPH in ethanol), were also negative. Fractions 3–50 (100 ml each) were composed of 10:90 ether–pentane. Fractions 13–24 gave 1.484 g of the *cis*-epimer (II). These fractions were flash distilled through a short-path still. The resulting white crystalline solid had a nmr spectrum superimposable with that of an authentic sample of II. By tlc and glpc no epimeric *trans*-II was present. The entire sample was melted under nitrogen on a steam bath and its optical purity measured in dry benzene. To minimize errors, the solutions were made up in the same calibrated 1-ml volumetric flask, and the polarimetric analyses were performed within 30 min of one another. The readings were checked for zero drift before and after each analysis. Table V reports the results.

Table V. Rotations of *cis*-II Recovered from Run 8

α^{25}_{obsd}, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	α^{25}_{obsd}, deg
−2.495	−102.0	96.16	589	−106.0	−2.628
−2.606	−106.5	96.16	578	−110.8	−2.745
−2.997	−122.6	96.15	546	−127.5	−3.159
−5.363	−219.2	96.28	436	−227.6	−5.642
−8.961	−366.2	96.20	365	−380.7	−9.435
	Av	96.21			

[a] *c* 2.417, benzene, for partially racemized material. [b] *c* 2.448, benzene, for optically pure *cis*-II.

Fractions 25–30 contained 0.115 g of *cis*-II contaminated by a trace (~1% by glpc) of *trans*-II. Fractions 31–39 were essentially blank, but a trace amount of each isomer was indicated by tlc. Fractions 40–50 provided 125 mg of an oil that contained 1.3% *cis*-II by glpc. The nmr spectrum in carbon tetrachloride of fractions 40–50 had the characteristic methyl absorption at high field (τ 9.12) and a broad singlet at τ 8.42 corresponding to the hydroxyl proton *trans* to a neighboring phenyl. The spectrum was de-

Table VI. Rotations of *trans*-II Recovered from Run 8

α^{25}_{obsd}, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	α^{25}_{obsd}, deg
−0.063	−18.2	43.05	589	−42.3	−0.178
−0.067	−19.4	43.59	578	−44.4	−0.187
−0.077	−22.2	43.78	546	−50.8	−0.214
−0.137	−39.6	42.63	436	−92.9	−0.391
−0.234	−67.6	42.12	365	−160.6	−0.676
	Av	43.0			

[a] *c* 0.3419, benzene, for partially racemized material. [b] *c* 0.4160, benzene, for optically pure (−)-*trans*-II. Run 7 was carried out similarly to run 8.

finitive for *trans*-II. No *cis*-II was detectable by nmr. The sample was subjected to preparative glpc on a 6 ft × 0.25 in. column of 10% KOH–10% Carbowax 4000 on Chromosorb W NAW at 150°. The material was collected at 25° in a clean capillary tube. No epimeric *cis*-II was detected by glpc or tlc. The polarimetric analyses are given in Table VI. The optical purity was determined by measurement of the specific rotation of a sample of optically pure (−)-*trans*-II along with that of the partially racemized material.

Partial Isomerization and Racemization of (−)-*trans*-1,2-Dimethyl-2-phenylcyclopentanol ((−)-*trans*-II) in Dimethyl Sulfoxide at 25° (Run 9). Conditions for *ca.* 5% isomerization were first obtained with the racemic *trans*-II. Then run 9 was made. A solution of 1.518 g (7.97 mmol) of optically pure (−)-*trans*-II in 110 ml of dimethyl sulfoxide, 0.41 *M* in dimsylsodium, was placed in a water bath thermostated at 25° for 5.77 hr. The reaction mixture was then poured into excess ice–water and the product recovered in the usual way. By tlc no open-chain ketone was present. Analysis of the crude reaction mixture by glpc showed the presence of 7.9% *cis*-II and 92.1% *trans*-II. The reaction mixture (1.639 g) was dissolved in 5:95 ether–pentane and placed on a column of 290 g of silica gel packed in a column which measured 77 cm high and 31 mm wide. Fractions (56, *ca.* 75 ml each) were collected. The epimeric alcohols were eluted with 10:90 ether–pentane. Fractions 24–33 gave 112 mg of *cis*-II contaminated by some material of faster moving R_f. The material in these fractions was rechromatographed. The pure *cis* isomer was eluted with 5:95 ether–pentane and flash distilled to give a clear, colorless oil which could not be induced to crystallize. The results of the polarimeter analyses are given in Table VII.

Table VII. Rotations of *cis*-II Recovered from Run 9

$\alpha^{25}_{\text{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	$\alpha^{25}_{\text{obsd}}$, deg
−0.187	−37.3	35.01	589	−106	−0.524
−0.196	−39.1	35.15	578	−111	−0.547
−0.225	−44.9	35.14	546	−127	−0.628
−0.403	−80.4	34.95	436	−230.0	−1.131
−0.672	−134	34.8	365	−384.9	−1.893
	Av	35.0			

[a] *c* 0.494, benzene, taken on partially racemized material. [b] *c* 0.4859, benzene, taken on optically pure (−)-*cis*-II.

Fractions 39–56 gave 1.033 g of an oil that by tlc was only *trans*-II. Further fractions with solvent mixtures of 20:80 ether–pentane showed insignificant amounts of material. Only fractions 34–38, which gave 35 mg of material, contained both isomers. The total yield of recovered epimeric alcohols was 78% based on starting material. The fractions containing the pure *trans* isomer were flash distilled to yield a clear, colorless oil with a nmr spectrum identical with starting material. Table VIII reports the rotations.

Table VIII. Rotations of *trans*-II Recovered from Run 9

$\alpha^{25}_{\text{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	$\alpha^{25}_{\text{obsd}}$, deg
−0.911	−32.4	74.99	589	−43.18	−1.223
−0.952	−33.8	74.88	578	−45.19	−1.280
−1.098	−39.0	75.06	546	−51.97	−1.472
−1.989	−70.70	75.71	436	−93.38	−2.645
−3.385	−120.3	75.48	365	−159.4	−4.515
	Av	75.2			

[a] *c* 2.7796, benzene, taken on partially racemized material n^{25}_{D} 1.5410. [b] *c* 2.7984, benzene, taken on optically pure (−)-*trans*-II, n^{25}_{D} 1.5405.

Epimerization, Racemization, and Cleavage of (−)-*cis*-1,2-Dimethyl-2-phenylcyclopentanol in *t*-Butyl Alcohol. Conditions for cleavage and isomerizations of the *cis* isomer were obtained by running a series of sealed-tube reactions under various conditions. The progress of the reaction was followed by tlc and glpc. Reactions were run on a 20–200-mg scale in 35 ml of solvent. These results are summarized in Table IV. By tlc both epimeric alcohols, open-chain ketone, and its aldol products were present. The amount of isomerized epimeric alcohol was much less than starting material. By making the concentration of cyclopentanol *ca.* 0.1 to 0.01 of that of the base (*ca.* 0.24), the open-chain ketone, 6-phenyl-2-heptanone, could be preserved and isolated in reasonable yields. Attempts to run the cleavage reactions in a stainless steel bomb led to unreproducible results. The glass ampoule technique was employed. Details of run 18 are given below.

Into a previously dried Carius tube filled with dry nitrogen were placed 1.038 g of optically pure (−)-*cis*-II, 100 ml of *t*-butyl alcohol (0.419 *M* in potassium *t*-butoxide), and 75 ml of pure *t*-butyl alcohol. The tube was immersed in a bath at −78° and sealed at atmospheric pressure under a positive pressure of nitrogen. The cold bath was removed and the tube and its contents were warmed to 35°, shaken until homogeneous, and then immersed in a stirred oil bath at 135 ± 0.5°. The temperature dropped a few degrees. An asbestos cap was fitted and the tube immersed to the meniscus when the temperature equilibrated at 135 ± 0.5°. After 51 hr at this temperature the tube was removed, cooled, then frozen, and opened. The contents of the tube were transferred to a round-bottomed flask containing 2.45 g (0.046 mol) of granular ammonium chloride. The ampoule was washed with copious volumes of ether and water. The resulting solution was stirred until homogeneous, and then the solvents were removed at reduced pressure (25°). Sufficient water was added and the product extracted with ether. The pH of the aqueous layer was 6 to 8. The combined organic layers were washed with water and brine and dried. Solvent was removed at reduced pressure to give 1.234 g of a yellow oil. By tlc four major components were present: open-chain ketone, both epimeric alcohols, and aldol products of the ketone. The crude mixture of alcohols and ketones was dissolved in 30 ml of dry ether and 0.502 g (0.013 mol) of powdered lithium aluminum hydride added in small portions. The slurry was stirred at 25° for 12 hr. The flask was immersed in an ice–water bath at *ca.* 0° and the reaction mixture hydrolyzed with 0.5 ml of water, 0.5 ml of 10% sodium hydroxide, and 1.5 ml of water. When stirred, a white granular solid separated. The solvent was decanted and the solids were washed with dichloromethane and ether. The salts were placed in a Soxhlet extractor with refluxing dichloromethane for 8 hr. The combined organic layers were washed with water and brine, dried, then concentrated at reduced pressure to give 1.310 g of a yellow oil. By tlc the ketone was completely reduced. The R_f of 6-phenyl-2-heptanol was 0.13; that of the *cis*-II was 0.35, and *trans*-II, 0.23. Pure heptadecane, 83.5 mg, was syringed into the crude reaction mixture which was dissolved in 1 ml of pentane. The glpc analysis results are given in Table IV. The absolute yield was 57%. The crude reaction mixture (1.369 g) was dissolved in a minimum amount of 5:95 ether–pentane and placed on a column of 290 g of silica gel. The column was prepared in 5:95 ether–pentane and measured 61 cm in height and 25 mm in diameter. Fractions (106, *ca.* 75 ml each) were taken. The first three fractions were eluted with 5:95 ether–pentane. The alcohols were eluted with 10:90 ether–pentane. The 26th fraction contained the *cis*-II contaminated by material of higher R_f. Fractions 27–40 gave 423 mg of the pure *cis*-II as a clear oil. These fractions were flash distilled to give 0.326 g (31.4% gravimetric yield) of a white crystalline solid whose nmr spectrum was completely superimposable on that of an authentic sample. The entire sample was melted in a water bath under dry nitrogen and then subjected to polarimetric analysis (Table IX).

Table IX. Rotations of *cis*-II Recovered from Run 18

$\alpha^{25}_{\text{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	$\alpha^{25}_{\text{obsd}}$, deg
−1.377	−106.3	99.48	589	−106.8	−1.418
−1.436	−110.8	99.25	578	−111.7	−1.482
−1.649	−127.3	99.36	546	−128.1	−1.700
−2.941	−227.0	99.42	436	−228.3	−3.030
−4.924	−380.1	99.48	365	−382.0	−5.070
	Av	99.40 ± 0.2			

[a] *c* 1.2800, benzene, taken on partially racemized material. [b] *c* 1.3112, benzene, taken on optically pure (−)-*cis*-II.

Fractions 41–50 gave 37 mg of an oily two-component mixture. By tlc the mixture was composed of *cis*-II and a trace of the *trans*-II. Fractions 55–80 contained 361 mg of a four-component mixture rich in the *trans*-II. By glpc the mixture contained only the diastereomeric cyclopentanols. The other two components were held on the column by the potassium hydroxide–Carbowax liquid phase. The *cis*-II was removed by successive preparative tlc's (20 × 20 cm glass plate coated with 1 mm layer of silca gel G). The bands were identified by exposure to iodine vapor for 10–20 sec. The vapor was allowed to evaporate and the band scrapped off the plate. The alcohol was washed off the silica gel with acetone which was concentrated at reduced pressure. The resulting solution was subjected to preparative glpc (10% KOH–10% Carbowax 4000 at 15°). The pure *trans*-II was collected in a capillary and subjected to polarimetric analysis (Table X).

Table X. Rotations of *trans*-II Recovered from Run 18

$\alpha^{25}_{\mathrm{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	$\alpha^{25}_{\mathrm{obsd}}$, deg
−0.074	−38.5	91.0	589	−42.3	−0.084
−0.076	−39.3	88.5	578	−44.4	−0.088
−0.088	−45.6	89.6	546	−50.8	−0.101
−0.160	−83.6	90.0	436	−92.8	−0.185
−0.277	−144	89.8	365	−160	−0.329
	Av	89.8			

[a] *c* 0.1898, benzene, taken on partially racemized *trans*-II. [b] *c* 0.1969, benzene, taken on optically pure (−)-*trans*-II.

Fractions 81–100 contained 46 mg of an oil which by tlc contained *ca.* 10% of *trans*-II. The open-chain alcohol, 6-phenyl-2-heptanol (X), appeared in fractions 101–104, along with two materials of larger R_f values which were present in fractions 81–100. The solvent composition of fraction 102 was 20:80 ether–pentane. Fractions 105–108 gave 221 mg of X which was homogeneous by tlc. Further fractions with solvent mixtures ranging up to 1:1 ether–pentane showed an insignificant amount of material. The nmr and ir spectra of undistilled 6-phenyl-2-heptanol were in accord with expectations: ir (carbon tetrachloride) 2.73, 3.00 (OH), and 6.23 μ (aromatic C=C); nmr (carbon tetrachloride) τ 2.86 (aromatic CH, singlet with fine structure), 6.46 ($-C(CH_3)(OH)\mathit{H}$, m, J = 6–6.5 Hz), 6.95 (OH, broad singlet), 7.42 ($-C(CH_3)(C_6H_5)\mathit{H}$, m, J = 7 Hz), 8.10–9.30 ($-(CH_2)_3-$, m), 8.79 ($-C(C_6H_5)\mathit{CH}_3$, d, J = 7 Hz), and 8.97 ($-C(OH)\mathit{CH}_3$, d, J = 6.5 Hz). The observed rotation of an unknown weight of the chromatographed 6-phenyl-2-heptanol in 95% ethanol was strongly positive.

The open-chain alcohol was freed of solvent on a rotatory evaporator at reduced pressure and oxidized directly *via* the Jones[19] reagent. The Jones reagent consists of 26.72 g of chromium trioxide (J. T. Baker, reagent grade) and 23 ml of concentrated sulfuric acid (Baker and Adamson, reagent grade) diluted to 100 ml with distilled water. The reagent (0.5 ml, 1.37 mmol) was added dropwise to a well-stirred homogeneous solution of 154 mg (0.8 mmol) of (+)-6-phenyl-2-heptanol in 15 ml of reagent grade acetone held at *ca.* 2° by external cooling. During the addition period (*ca.* 7 min) the temperature of the solution never rose above 7°. A flocculent green solid precipitated from solution. After 0.4 ml was added, the solid coagulated and the solution became brown. An additional 0.1 ml of Jones reagent was added and the mixture was stirred at *ca.* 3° for 10 min. Ice and dichloromethane were added, and the solution was shaken. The layers were separated and the aqueous phase shaken with an equal volume of dichloromethane and discarded. The combined organic phases were shaken twice with water (pH of second wash was *ca.* 7) and brine and dried. The solvent was removed at reduced pressure to give 160 mg of a fragrant yellow brown oil. By tlc there was a trace of starting material and material of R_f 0.88 in addition to 6-phenyl-2-heptanone. The infrared spectrum showed weak absorption in the OH region at 2.95 μ and strong absorption at 5.80 μ. The crude reaction mixture was subjected to elution chromatography on 62 g of silica gel slurried with 5:95 ether–pentane. The column measured 59 cm in height and 15 mm in width. The product ketone was eluted with 10:90 ether–pentane. Fractions 27–31 gave 46 mg of 6-phenyl-2-heptanone (IV) which was homogeneous to tlc. The ir and nmr spectra were obtained: ir (carbon tetrachloride) 5.82 μ (C=O); nmr (carbon tetrachloride) τ 2.86 (aromatic CH, singlet with fine structure, 5), 7.41 (–CH, m, 1), 7.76 ($CH_2C{=}O$, m, 2), 8.08 ($O{=}CCH_3$, s, 3), 8.85 ($-(CH_2)_2-$, m, 4), and 8.87 (CH_3, d, 3, J = 7 Hz). The entire sample was flash distilled in a micro Hickman flask, and submitted to polarimetric analysis (Table XI).

Table XI. Rotations of Ketone IV Recovered from Run 18

$\alpha^{25}_{\mathrm{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	$\alpha^{25}_{\mathrm{obsd}}$, deg
+0.234	+13.3	61.4	589	−21.6	−0.403
+0.243	+13.8	61.0	578	−22.6	−0.423
+0.281	+16.0	61.1	546	−26.1	−0.488
+0.516	+29.3	61.0	436	−48.0	−0.900
+0.903	+51.3	61.1	365	−84.0	−1.574
	Av	61.1			

[a] *c* 1.74, benzene, taken on partially racemized material; n^{25}_{D} 1.5004. [b] *c* 1.85, benzene, taken on optically pure IV; n^{25}_{D} 1.4997. Run 16 was similarly performed (see Table III).

Isomerization and Cleavage of (−)-*trans*-1,2-Dimethyl-2-phenylcyclopentanol ((−)-*trans*-II) in *t*-Butyl Alcohol (Run 19). To a previously dried Carius tube filled with dry nitrogen was placed 0.842 g of optically pure (−)-*trans*-II, 35 ml of *t*-butyl alcohol, 0.980 *M* in potassium *t*-butoxide, and 115 ml of pure *t*-butyl alcohol. The tube was immersed in a bath at −78° and sealed under a stream of nitrogen. The tube and its contents were warmed, shaken until homogeneous, and immersed to the meniscus in a stirred bath at 135 ± 0.5° for 51 hr. Then the tube was removed, cooled, frozen (−78°), and opened. The content of the tube was transferred to a flask containing 1.83 g (34.3 mmol) of granular ammonium chloride. Isolation was completely analogous to that described for the *cis* isomer. The recovered tan oil (0.803 g) was analyzed by tlc and found to contain open-chain ketone (IV), *cis*-II, *trans*-II, and aldol condensation products of IV. Reduction of the entire crude reaction mixture with 0.407 g of powdered lithium aluminum hydride gave, after the usual work-up, 770 mg of a tan oil. By tlc no open-chain ketone IV was present (2,4-DNPH spray). Pure heptadecane, 0.302 g, was syringed into a 1-ml volumetric flask containing the crude reaction mixture. Pentane was added to the mark and the mixture analyzed by glpc (*cf.* Table IV). The total yield was 57%.

The crude reaction mixture was dissolved in a minimum volume of 5:95 ether–pentane and subjected to elution chromatography on 285 g of silica gel. The silica gel was slurried in 5:95 ether–pentane and packed in a column which measured 60 cm in height and 25 mm in diameter. Fractions (130, *ca.* 75 ml each) were taken. The first 32 fractions contained oils of R_f greater than *cis*-II. The epimeric alcohols were eluted with 10:90 ether–pentane. Fractions 33–45 contained *ca.* 42 mg of oil which by tlc contained *cis*-II contaminated by material of larger R_f. This material was purified by glpc, and pure *cis*-II was collected in a capillary and submitted to polarimetric analysis (Table XII).

Table XII. Rotations of *cis*-II Recovered from Run 19

$\alpha^{25}_{\mathrm{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	$\alpha^{25}_{\mathrm{obsd}}$, deg
−0.384	−102.2	95.9	589	106.5	−0.524
−0.400	−106.6	95.9	578	111.2	−0.547
−0.459	−122.4	95.8	546	127.7	−0.628
−0.822	−219.0	95.2	436	230.0	−1.131
−1.378	−367.3	95.4	365	384.9	−1.893
	Av	95.6 ± 0.3			

[a] *c* 3.7065, benzene, taken with partially racemized *cis*-II. [b] *c* 4.8590, benzene, taken with optically pure *cis*-II.

Fractions 46–55 gave *ca.* 42 mg of a yellow oil. By tlc neither isomeric cyclopentanol was present. Fractions 56–59 contained the *trans*-II contaminated by material with R_f identical with the oil contained in fractions 46–55. Fractions 60–85 gave 298 mg of

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(19) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, pp 81 ff.

pure *trans*-II. This material possessed an nmr spectrum identical with that of an authentic sample. The entire sample was flash distilled and submitted to polarimetric analysis (Table XIII).

Table XIII. Rotations of *trans*-II Recovered from Run 19

$\alpha^{25}_{\text{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	Optical purity, %	λ, mμ	$[\alpha]^{25}_{\lambda}$,[b] deg	$\alpha^{25}_{\text{obsd}}$, deg
−1.203	−43.18	100.0	589	−43.18	−1.223
−1.258	−45.20	100.0	578	−45.19	−1.280
−1.445	−51.91	99.88	546	−51.97	−1.472
−2.603	−93.51	100.1	436	−93.38	−2.645
−4.427	−159.0	99.75	365	−159.4	−4.515
	Av	99.9 ± 0.2			

[a] *c* 2.7500, benzene, taken with partially racemized *trans*-II.
[b] *c* 2.7984, benzene, taken with optically pure (−)-*trans*-II.

Fractions 86–100 contained a trace of the *trans* epimer contaminated by material of lower R_f. The solvent composition was changed to 20:80 ether–pentane. Fractions 101–128 gave 146 mg of a yellow oil which by tlc was pure 6-phenyl-2-heptanol (X). The ir and nmr spectra (carbon tetrachloride) of fractions 101–128 were superimposable with an authentic sample.

The entire sample of open-chain alcohol was dissolved in 5 ml of reagent grade acetone. An ice-water bath at *ca.* 4° was applied, and the Jones reagent (0.5 ml) was added to the stirred solution over a space of 5 min. The solution was stirred at 5° for an additional 5 min, and equal volumes of ice-water and dichloromethane were added. The product was isolated in the usual way to give *ca.* 140 mg of a yellow oil. By tlc ketone IV (R_f 0.36) was contaminated by materials of R_f 0.73 and 0.59. The crude reaction mixture was subjected to column chromatography on silica gel. Pure ketone IV was eluted with 5:95 ether–pentane. Fractions 26–37, containing the bulk of IV, possessed ir and nmr spectra (carbon tetrachloride) completely superimposable on spectra obtained with an authentic sample. The material was distilled in a micro Hickman still at 100° (pot temperature, 0.26 mm) and submitted to polarimetric analysis (Table XIV).

Table XIV. Rotations of Ketone IV Recovered from Run 20

$\alpha^{25}_{\text{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	λ, mμ	Optical purity,[b] %
−0.288	−12.1	589	55.9
−0.302	−12.6	578	55.8
−0.348	−14.6	546	55.9
−0.638	−26.7	436	55.9
−1.108	−46.39	365	55.7
		Av	55.8 ± 0.1

[a] *c* 2.36, benzene, n^{25}_{D} 1.4999. [b] Compared to optically pure IV (*c* 1.85, benzene), n^{25}_{D} 1.4997.

Control on the Reduction–Oxidation Reactions (IV → X → IV). Into a previously dried flask equipped with a Teflon stirring bar were placed 10 ml of dry diethyl ether and 99 mg, 0.52 mmol, of 68.5% optically pure (+)-IV, ($[\alpha]^{25}_{546}$ +17.3° (*c* 1.88, benzene)). Powdered lithium aluminum hydride, 60 mg (1.6 mmol), was added in small portions to the ethereal solution. A drying tube was fitted and the slurry stirred at 25° for 13 hr. A cooling bath was applied and the reaction mixture hydrolyzed with water; then 10% hydrochloric acid was delivered *via* a 50-μl syringe.

The solution was decanted and the lithium salts were triturated with warm dichloromethane. The combined organic phases were washed twice with water, then brine, and dried. Solvents were removed at reduced pressure to give 115 mg of a yellow oil. By tlc no ketone was present (2,4-DNPH spray). Two spots of unequal intensity and low R_f (0.16 and 0.22) were visible. The more intense spot (R_f 0.16) was identified as 6-phenyl-2-heptanol by comparison with an authentic sample.

The entire crude reaction mixture was dissolved in 15 ml of reagent grade acetone. A stirring bar and thermometer were added; the flask was cooled to 10° with an external ice bath. The Jones reagent, 1.5 ml (4 mmol), was added dropwise over a period of 5 min. The brown solution was stirred for an additional 5 min at *ca.* 10–15°. Ice and dichloromethane were then added and the solution was transferred to a separatory funnel. The layers were separated; the aqueous phase was shaken with an equal volume of dichloromethane and discarded. The combined organic phases were shaken with water until the aqueous phase was neutral, then washed with brine, and dried. Removal of solvent at reduced pressure afforded 121 mg of a fragrant yellow oil. By tlc there was a trace of 6-phenyl-2-heptanol (R_f ~0.16) in addition to product ketone (R_f 0.47).

The crude reaction mixture was subjected to elution chromatography on 55 g of silica gel slurried in 5:95 ether–pentane. The column measured 39 cm in height and 15 mm in width. The product ketone was eluted with 10:90 ether–pentane. Fractions 19–24 gave *ca.* 39 mg of ketone IV which was homogeneous to tlc. The ir and nmr spectra were superimposable with an authentic sample. The open-chain ketone was flash distilled in a micro Hickman flask and submitted to polarimetric analysis (Table XV).

Table XV. Rotations of Ketone IV Recovered from Control Run

$\alpha^{25}_{\text{obsd}}$, deg	$[\alpha]^{25}_{\lambda}$,[a] deg	λ, mμ	Optical purity,[b] %
+0.339	+14.8	589	68.4
+0.355	+15.5	578	68.7
+0.408	+17.8	546	68.4
+0.751	+32.8	436	68.4
+1.314	+57.4	365	68.4
		Av	68.5 ± 0.2

[a] *c* 2.26, benzene, n^{25}_{D} 1.4997. [b] Compared to optically pure ketone (+)-IV (*c* 1.85, benzene), n^{25}_{D} 1.4997.

Control Run. Optical Stability of 5-Phenylhexanoic Acid. Partially optically active (+)-5-phenylhexanoic acid ($[\alpha]^{25}_{546}$ +17.7° (*c* 2.79, benzene), n^{25}_{D} 1.5092) was dissolved in a solution of 9.5 ml of pure dimethyl sulfoxide and 1.9 ml of *t*-butyl alcohol, 0.899 *M* in potassium *t*-butoxide. The flask was immersed to the meniscus in a bath held at 75 ± 0.1° for 107 hr. After the usual work-up, the acid was subjected to elution chromatography on silica gel. The product was eluted with pure ether. The residual oil was flash distilled and subjected to polarimetric analyses: $[\alpha]^{25}_{\text{D}}$ +13.25°, $[\alpha]^{25}_{546}$ +15.9° (*c* 2.77, benzene), n^{25}_{D} 1.5080. This corresponds to 10.3% racemization.