expose fresh surfaces of the oil. After 1 hr the sample tube was frozen and degassed. After warming, the sample tube was removed and a gain of 0.00945 g was noted (theoretically 1 equiv = 0.01029 g): nmr spectrum ($CDCl_3$) singlets at δ 1.34 and 1.40; very small signals at 1.16, 1.17, 1.24, 1.51, 1.57 (sum <10% of major signals); ir (neat) major ν_{max} at 2950, 1600, 1550, 1480, 1310, 1065, 995, and 895 cm^{-1}. A sample crystallized from aqueous ethanol was analyzed.

Anal. Calcd for $C_9H_{18}N_2O_2$: C, 58.03; H, 9.74; N, 15.04; mol wt, 186.25. Found: C, 58.12; H, 9.86; N, 14.96; mol wt, 195 (vapor pressure osmometry, benzene, 37°); λ_{max} (cyclohexane) 270 nm (ϵ 460).

Reaction with 1,4-Cyclohexadiene. A mixture of 0.05940 g of **1**, 0.437 g of $CDCl_3$, and 0.06255 g of 1,4-cyclohexadiene (Columbia, distilled from triphenylphosphine and $MgSO_4$) decolorized rapidly with evolution of heat. Glc comparison (2 m × 0.25 in. SE-30 column at 60°, FGM Model 700 instrument) of the peak areas of benzene and cyclohexadiene indicated the yield of benzene was 90.3 ± 0.5%. The nmr spectrum of the solution showed resonances at δ 1.22, 1.40 (di-*tert*-butyl ketoxime), 2.62, 5.64 (1,4-cyclohexadiene), and 7.3 (benzene, yield calculated to be 90.3 ± 1.6%). Two small peaks also appeared at δ 1.29 and 1.32, each about 10% of the height of the oxime signals. Evaporation of the reaction solution gave a colorless, crystalline residue of di-*tert*-butyl ketoxime, 0.05360 g (90.4%), identified by comparison of ir and mass spectrum with those of an authentic sample.

Reaction with Cumene, Ethylbenzene, and Toluene. The epr kinetic studies were done on a Varian E-3 epr spectrometer equipped with a signal integrator. The general experimental procedure has been described in previous papers in this series.[1]

Mixtures of **1** in the alkyl aromatic hydrocarbon, triphenylphosphine (to destroy any hydroperoxides present in the solvent), and magnesium sulfate were degassed three times and distilled *in vacuo* into the epr tube. After admitting argon, the tubes were sealed and placed in the preheated cavity of the instrument. The decay of **1** in cumene, ethylbenzene, and toluene was pseudo first order for 5–11 half-lives. Small initial deviations (Figure 6) were ascribed to line-broadening effects at high concentrations. At very small concentrations (~10^{-5} *M*) of **1** the rate frequently decreased. This was probably due to regeneration of **1** from the oxime and radicals formed by slow decomposition of products or some adventitious material. Second-order rate constants were obtained by dividing by the concentration of hydrocarbon in pure solvent. This requires a knowledge of the density at the temperature involved. For toluene the density at 100° was calculated as 0.792 from a published formula.[47] The density of cumene at 100° was measured as 0.791 and the densities of ethylbenzene and cumene-α-*d* were assumed to be 0.79. The errors arising from use of these densities at 80 and 120° are small.

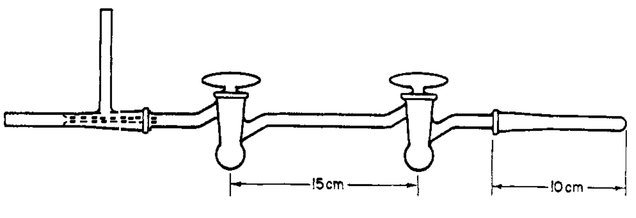

Figure 11.

The samples of **1** in styrene and in vinyl acetate were prepared in the same way as the alkylbenzene samples, except that magnesium sulfate was omitted.

Acknowledgment. One of us (G. D. M.) is grateful to the National Research Council of Canada for a postdoctorate fellowship (1971–1973). We wish to thank Dr. H. D. Hartzler (Du Pont) for a sample of di-*tert*-butyl ketimine.

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[47] "International Critical Tables," Vol. 3, 1st ed, McGraw-Hill, New York, N. Y., 1928, p 29.

Some Unusual Stereochemistry in a Transamination Reaction

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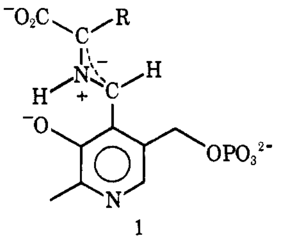
Abstract: In contrast to all potassium *tert*-butoxide catalyzed methylene–azomethine rearrangements previously studied in *tert*-butyl alcohol, the interconversion of *N*-(α-methyl-4-methoxybenzylidene)-α-phenylethylamine (I) and *N*-(α-methylbenzylidene)-α-(4-methoxyphenyl)ethylamine (II) has been found to occur with a very low degree of stereospecificity. Several explanations are offered and the intermediacy of a twisted carbanion is suggested.

The study of base-catalyzed isomerization of methylene–azomethine systems has provided some interesting stereochemical analogies to the enzymatic reactions by which amino acids are reversibly produced from the corresponding keto acids. The mechanism of the enzymatic reaction involves a proton shift in an imine formed by condensation of the requisite keto acid with enzyme bound pyridoxamine phosphate which in turn arises from pyridoxal phosphate cofactor. The incisive studies of Dunathan, Snell, and their coworkers[1] have shown that the stereochemistry of such transaminase catalyzed reactions is explicable in terms of suprafacial transfer in a system of the geometry displayed in 1. This geometry is presumably specified by



1

some combination of steric effects, electrostatic interactions of charged sites, and geometry of the surrounding protein. The suprafacial stereochemistry must be dictated by an immobilization of the substrate-cofactor compound relative to the proton vehicle on the enzyme surface.

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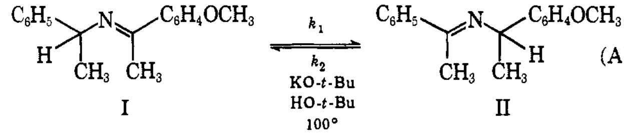
[1] (a) H. C. Dunathan, *Vitam. Horm.* (*New York*), **28**, 399 (1970); (b) H. C. Dunathan, L. Davis, P. G. Kury, and M. Kaplan, *Biochemistry*, 7, 4532 (1968); (c) J. E. Ayling, H. C. Dunathan, and E. E. Snell, *ibid.*, 7, 4537 (1968); (d) H. Wada and E. E. Snell, *J. Biol. Chem.*, 237, 133 (1962).

The parallelism of the chemical model systems is remarkable when the relative simplicity of the reaction environment is considered, yet stereospecificity and intramolecularity are common features of both reactions when the chemical models are reactions carried out in *tert*-butyl alcohol catalyzed by potassium *tert*-butoxide.[2,3] Interestingly, an entire class of enzymes, the racemases,[4] use pyridoxal phosphate as cofactor and presumably operate by mechanisms analogous to those of the transaminases with the exception of those features responsible for stereospecificity. Stereospecificity can also be removed in the chemical model systems by a variety of medium and counterion changes but to date has been an inviolate rule in *tert*-butyl alcohol with potassium *tert*-butoxide as catalyst. This paper reports an example of racemization in this medium and discusses possible origins of the phenomenon.

Results

Equilibration and Isomerization. Imines I and II



I II (A)

were prepared by the usual methods and subjected to potassium *tert*-butoxide catalyzed isomerization at 100°. Table I shows results obtained after 10 half-lives for the equilibrium of eq A which allow calculation of K_{eq} = II/I = 0.521. The data given in Table II show that the isomerization follows first-order kinetics for approach to equilibrium with a rate constant $k = k_1 + k_2 = 1.85 \pm 0.13 \times 10^{-5}\ M^{-1}\ \text{sec}^{-1}$ and thus $k_1 = 0.633 \times 10^{-5}\ M^{-1}\ \text{sec}^{-1}$ and $k_2 = 1.21 \times 10^{5}\ M^{-1}\ \text{sec}^{-1}$.

Table I. Potassium *tert*-Butoxide Catalyzed Equilibrations of Imines I and II in *tert*-Butyl Alcohol

	Substrate					
Run	Nature	Concn, *M*	Base	Time,[a] min	% I[b]	% II[b]
1	I	0.022	0.547	11,555	65.4 ± 0.3	34.6
2	II	0.016	0.547	11,400	66.0 ± 1.4	34.0

[a] One half-life = 1140 min. [b] Average of three uv analyses.

Table II. Potassium *tert*-Butoxide (0.547 *M*) Catalyzed Isomerization of Imines I and II in *tert*-Butyl Alcohol at 100°

Run no.	Substrate	% isom	10^5k,[a] M^{-1} sec^{-1}
3–10	I-H	6–26	1.86 ± 0.23[b]
11–20	II-H	10–44	1.84 ± 0.20

[a] Rate constant for approach to equilibrium. [b] Error limit is one standard deviation.

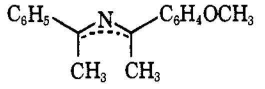
Exchange and the Collapse Ratio. Table III shows the results of experiments which attempt to determine the collapse ratio ($k_{\text{exchange}}/k_{\text{isomerization}}$) by studying the isomerization of I to II in *tert*-butyl alcohol-*O-d* and the concomitant deuterium incorporation in I. Because deuterium incorporation in I would be expected to slow the isomerization, an effort was made to obtain data at low conversions and the isomerization rate constants, therefore, show appreciable scatter. A value of $0.8 \times 10^{-5}\ M^{-1}\ \text{sec}^{-1}$ would seem a reasonable lower limit for the initial isomerization rate constant and this would lead to a calculated maximum collapse ratio, k_e/k_i, of 4. The true value is clearly between 2 and 4. Similar experiments were carried out using I prepared from α-phenylethylamine-α-*d* (Id) and these results are presented in Table IV. Unfortunately our method of preparing α-phenylamine-α-*d* gave only 92.4% of one atom of deuterium incorporation, but the data could be corrected for the predictable fate of the 7.6% protio impurity and this led to a calculated collapse ratio ranging from 1.9 to 3.4. An alternate method of arriving at the collapse ratio from optical activity loss will be discussed later.

Table III also shows that the amount of intramolecular proton transfer, *ca.* 50%, in *tert*-butyl alcohol-*O-d* is typical of that previously observed in other systems,[2,5] as is the lower value, *ca.* 10%, for intramolecular transfer of deuterium in *tert*-butyl alcohol-*O-h*.

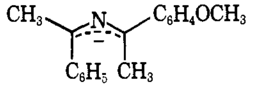
Isomerizations with Chiral Substrate. Table V summarizes data obtained by partial isomerization of chiral substrate and measurement of the optical rotation of the amines isolated from hydrolysis of the isomeric mixture. It is apparent that, in contrast to previous studies in this medium, there is appreciable racemization of both starting material and product. Starting from I, initially formed II is about 60% racemized and the same is true of I formed starting with II. It will be noticed that the racemization observed in II when it is starting material is relatively small as predicted for a system with a collapse ratio favoring product.

Discussion

In the highly stereospecific imine isomerizations studied previously,[2,3] it was a necessary conclusion that only one geometric isomer of the intermediate carbanion could be involved in the isomerization. If it is assumed that carbanions III and IV are both involved



III



IV

in the interconversion of I and II the racemization of product is readily explained. (Anisyl and phenyl can be interchanged in IV.) The intermediacy of IV seems unlikely for several reasons. In the first place, Ela and Cram[6] were able to estimate that *trans*-1,3-diphenyl-1-butene gave carbanion V 70 times more rapidly than it gave carbanion VI. We would expect the difference in stability of III, with a methyl–methyl interaction, to produce an even greater selectivity for III over IV. A more direct argument is provided by the stereochemical outcome of the isomerization of *N*-(α-methylneopentylidene)-α-phenylethylamine (VII).[3] In this case, the observed facial retention ruled out the intermedi-

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(2) (a) R. D. Guthrie, W. Meister, and D. J. Cram, *J. Amer. Chem. Soc.*, **89**, 5288 (1967); (b) R. D. Guthrie, D. A. Jaeger, W. Meister, and D. J. Cram, *ibid.*, **93**, 5137 (1971).

(3) D. A. Jaeger and D. J. Cram, *ibid.*, **93**, 5153 (1971).

(4) (a) G. Rosso, K. Takashima, and E. Adams, *Biochem. Biophys. Res. Commun.*, **34**, 134 (1969); (b) E. Adams and I. L. Norton, *J. Biol. Chem.*, **239**, 1525 (1964).

(5) D. J. Cram in "Fundamentals of Carbanion Chemistry," A. T. Blomquist, Ed., Academic Press, New York, N. Y., 1965, p 176.

(6) S. W. Ela and D. J. Cram, *J. Amer. Chem. Soc.*, **88**, 5777 (1966).

Table III. Deuterium Analysis of I and II from Isomerization of I to II Catalyzed by 0.514 *N* Potassium *tert*-Butoxide in *tert*-Butyl Alcohol-*O-d* at 100°

	Run								
	21	22	23	24	25	26	27	28	29
Time, min	120	66	135	215	315	375	420	515	630
% isom	2.78	2.49	6.50	6.15	7.04	8.36	9.50	10.6	12.7
% of one atom D in I[a]	11.8	6.67	12.4						
% of one atom D (benzyl)[b]		5.2	11.7						
% of one atom D in II[a]	51.3								
$10^5 k_i$,[c] M^{-1} sec^{-1}	0.69	1.26	1.72	1.01	0.80	0.82	0.85	0.78	0.81
$10^5 k_e$,[d] M^{-1} sec^{-1}	3.33	3.33	3.18						

[a] Mass spectroscopic analysis of benzamide of α-phenylethylamine. [b] Nmr determination for α-phenylethylamine. [c] Rate constant for isomerization of I to II calculated from *k* for approach to equilibrium and K_{eq}. [d] Rate constant for exchange of I.

Table IV. Deuterium Analysis of I and II from Isomerization of Id[a] to II in *tert*-Butyl Alcohol Catalyzed by 0.49 *N* Potassium *tert*-Butoxide at 100°

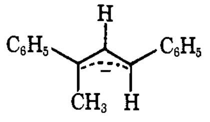
	Run				
	30	31	32	33	34
Time, min	1000	1560	3300	4260	6420
% isom	Small	6.0	10.9	11.7	15.5
% of one atom D[b]	87.2	84.1	69.9	65.3	57.1
% of one atom D (benzyl)[c]		81	67		
% of one atom D in II[b]		2.7	10.4		
$10^6 k_i$,[d] M^{-1} sec^{-1}		1.05	1.03	0.86	0.86
$10^6 k_e$,[e] M^{-1} sec^{-1}	1.97	2.05	2.87	2.90	2.55
k_e/k_i		1.9	2.8	3.4	3.0

[a] Contained 92.4% of one atom of D based on mass spectral analysis of benzamide of amine from hydrolysis. [b] Mass spectral analysis of benzamides of amines from hydrolysis. [c] Nmr analysis of recovered amine. [d] Rate constant for isomerization based on rate of approach to equilibrium and k_{eq}. [e] Rate constant for exchange of Id.

Table V. Stereochemical Consequences of the Treatment of I and II with Potassium *tert*-Butoxide in *tert*-Butyl Alcohol at 100°

					α-Phenylethylamine		*p*-Methoxy-α-phenylethylamine	
Run	Subst	Time, min	[KO-*t*-Bu]	% isom	$[\alpha]^{25}$D,[a] deg	% rac	$[\alpha]^{25}$D,[a] deg	% rac
35	(*S*)-I	500	0.457	7.3	−35.5	12.0		
36	(*S*)-I	840	0.452	13.1	−30.0[b]	26.3	+15.5	59.6
37	(*S*)-I	1200	0.457	15.1	−26.3[b]	35.4	+12.7	66.9
38	(*S*)-I	1230	0.457	16.1	−25.2[b]	38.1	+12.7	66.9
39	(*S*)-I	1560	0.452	18.1	−23.7[b]	40.2	+12.6	67.2
40	(*S*)-I	1860	0.457	20.5	−21.2[b]	48.0	+11.0	71.3
41	(*S*)-I	1950	0.457	20.9	−18.6[b]	54.3		
42	(*S*)-I	2940	0.457	25.6	−13.6	66.6	+9.7	74.8
43	(*R*)-II	280	0.509	9.4	−17.2[c]	57.7	+36.9[c]	3.9
44	(*R*)-II	540	0.509	16.7	−17.0	58.2	+37.3	2.9
45	(*R*)-II	900	0.509	26.7	−14.5[c]	64.4	+35.2[c]	8.3
46	(*R*)-II	1350	0.509	36.4	−13.2	67.6	+32.1[c]	16.4
47	(*R*)-II	1980	0.509	45.9	−10.7	73.7	+27.5	28.4

[a] Run in cyclohexane at concentrations of 30 to 100 mg/ml unless otherwise specified. [b] Run neat. [c] Average of two determinations.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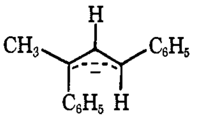
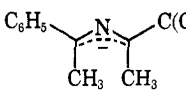
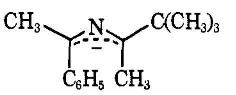

VI

VII →


VIII

or


IX

acy of IX which is related to VIII in the same way that IV is related to III.

The most remarkable part of this study is the observed racemization of starting material in the reactions of I and II. A possible explanation involves Scheme I

Scheme I

$$(S)\text{-I} \xrightarrow{k_1} \text{II} \underset{k_1}{\overset{k_2}{\rightleftharpoons}} \text{I}$$

wherein racemized starting material is viewed as having arisen from racemized product, where (*S*)-I is optically pure starting material and I is racemic. This scheme has been discussed by Ingold[7] who derived eq 1. Table

$$[\text{I}] = [(S)\text{-I}]_0\left[\frac{k_2}{k_1 + k_2} - e^{-k_1 t} + \left(1 - \frac{k_2}{k_1 + k_2}\right)e^{-(k_1 + k_2)t}\right] \quad (1)$$

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(7) (a) C. K. Ingold and C. L. Wilson, *J. Chem. Soc.*, 93 (1934); (b) S. K. Hsu, C. K. Ingold, and C. L. Wilson, *ibid.*, 1778 (1935).

Table VI. Calculated and Experimental Percentages of Racemization of Imines I and II

Run	% A[b,d]	% A′ [c,d]	% rac of starting material Calcd[d]	 Exptl	f[a]
35	91.7	0.7	1.0	12.0	0.42
36	86.6	1.7	1.9	26.3	0.34
37	81.2	3.2	3.8	35.4	0.34
38	80.7	3.3	3.9	38.1	0.33
39	76.5	4.9	6.0	40.2	0.37
40	72.4	6.7	8.5	48.0	0.36
41	71.2	7.2	9.2	54.3	0.31
42	60.0	13.5	18.4	66.6	0.36
43	90.1	9.3	0.3	3.9	0.74[e]
44	81.9	0.9	1.1	2.9	0.92[e]
45	71.6	2.2	3.0	8.3	0.86[e]
46	60.6	4.4	6.8	16.4	0.82[e]
47	48.0	7.8	14.0	28.4	0.80[e]

[a] f represents the fraction of starting material which passes on to product from the intermediate carbanion, $k_c/(k_b + k_c)$ of Scheme II. [b] % A represents the amount of unreacted starting imine isomer, (*S*)-I in Scheme I. [c] % A′ represents the amount of starting material which, having passed through the product isomer, returns to starting isomer A racemic, I in Scheme I. [d] Using eq 1. [e] For these cases, $f = k_b/(k_b + k_c)$.

VI shows the values of % racemization calculated using eq 1 in comparison with the experimentally determined values for runs 35 through 47. Since in all runs the isomeric products were never completely racemic, values calculated and listed in Table VI represent the maximum values that could be obtained. It is quite apparent that a discrepancy exists between the experimental and calculated values. It has been pointed out[7] that if the reaction proceeds through a carbanion, Scheme II, the kinetically determined rate constants k_1 and k_2 can be written in terms of the kinetically unobtainable rate constants: $k_1 = k_ak_c/(k_b + k_c)$ and $k_2 = k_dk_b/(k_b + k_c)$. If racemization occurs at the carbanion stage, the fraction of optical activity retained in starting material is given by eq 2. The fraction $f = k_c/(k_b + k_c)$ is the fraction of material proceeding to product after having reached the intermediate stage, C. If this fraction is unity, all material passes directly from C to product and return from product will account for all racemization observed in the starting material. Since the calculated fraction of racemization does not agree with that determined experimentally, as indicated in Table VI, it is evident that f is less than unity and that racemization occurs at the intermediate stage, C. Because it is now well established that carbanions are intermediate in the methylene–azomethine rearrangement, racemization of the carbanion which is intermediate in the interconversion of I and II provides a reasonable explanation of our data.

Scheme II

$$\begin{tikzcd}
\mathrm{I} \arrow[r, shift left, "k_a"] & \mathrm{C} \arrow[l, shift left, "k_b"] \arrow[r, shift left, "k_c"] & \mathrm{II} \arrow[l, shift left, "k_d"] \\
& (S)\text{-I} \arrow[u] &
\end{tikzcd}$$

$$F = \frac{k_1 + k_2}{[\exp(k_1t/f)][k_2 + k_1\exp(-k_1t - k_2t)]} \qquad (2)$$

Because the per cent retention of configuration of starting material is known and k_1 and k_2 have been determined, f can be calculated from eq 2, and values are listed in Table VI. For runs starting with I, this allows determination of the collapse ratio, $R = k_b/k_c = 1.9 \pm 0.1$, in a manner independent of hydrogen–deuterium exchange data. The collapse ratio determined in this way is a minimum value because it does not take into account return to starting material from the carbanion with excess retention of configuration, a process which almost certainly occurs.

The collapse ratio, R, represents the fraction: carbanion returning to I/carbanion proceeding to II; it is possible to estimate the fraction racemization occurring at the carbanion stage, P, using eq 3, where Y is the

$$Y = RP[\mathrm{II}]/([\mathrm{I}] + [\mathrm{II}]) + Z \qquad (3)$$

total observed fraction racemization in I and Z is the contribution to the total racemization from returned product. Because the initially formed product imine is about 60% racemized, regardless of the choice of starting isomer, it is interesting to use eq 3 to calculate R assuming that $P = 0.60$. Collapse ratios obtained in this way are listed in Table VII and indicate $R = 3.3 \pm 0.2$.

Table VII. Collapse Ratios from Racemization Data

Run	Collapse ratio[a]	Run	Collapse ratio[a]
35	2.5	39	3.2
36	3.1	40	3.2
37	3.5	41	3.6
38	3.5		

[a] Assuming 60% racemization in the ion.

These considerations establish with reasonable certainty that the carbanion intermediate formed from either I or II undergoes racemization at a rate comparable with its reprotonation. When I is starting material, it can be seen in Table V that the fraction of racemic material in recovered I is roughly double the amount of II formed at low conversions. With a collapse ratio of 2–4 it is evident that $k_e/k_\alpha(k_{\text{exchange}}/k_{\text{racemization}}) = 1\text{–}2$. This is a striking result when it is considered that VII shows $k_e/k_\alpha = 41$ and that *N*-neopentylidene-α-phenylethylamine (X) also gives exchange with high retention, $k_e/k_\alpha = 21\text{–}36$, both results being obtained under conditions which were identical, except for temperature, with those of this study.[2,3]

The normally observed high stereospecificity for prototropy in the medium of this study has been explained by invoking an asymmetric carbanion-potassium ion pair which is stereospecifically formed and destroyed. The cases for which this stereospecificity is not observed can usually be rationalized by some variation of the conducted tour mechanism.[8] It is conceivable that the *p*-methoxy group functions to permit such a mechanism in III, although this seems very unlikely on the grounds that two systems bearing methoxy substituents attached directly to the reaction site have not exhibited the phenomenon.[9]

Another possible explanation is that the ion-pair intermediate between I and II, having phenyl substituents at both ends of the allylic system, is more de-

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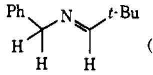
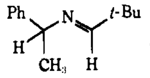
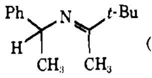
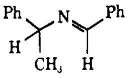
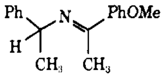
(8) Reference 5, p 85.

(9) (a) W. D. Kollmeyer and D. J. Cram, *J. Amer. Chem. Soc.*, **90**, 1779 (1968); (b) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *ibid.*, **83**, 3688 (1961).

Table VIII. Rate Constants for Ionization of Variously Substituted Imines in *tert*-Butyl Alcohol with Potassium *tert*-Butoxide

Compd (ref)	$10^5 k_{obsd}$,[a] sec^{-1}	[KO-*t*-Bu]	Temp, °C	$10^5 k_{75}$[b], M^{-1} sec^{-1}	k_{rel}
 (*c*)	12.2	0.59	50	200	13,300
 (*d*)	4.98	0.47	75	4.98	330
 (*e*)	48.3	0.40	175	0.0151	1.00
 (*c*)	38	0.61	30	8100	538,000
 (*f*)	4.2	0.51	100	0.38	25

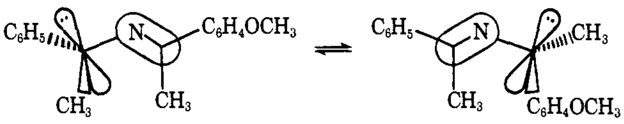
[a] Observed first-order rate constant at indicated temperature. [b] Calculated second-order rate constant at 75° assuming E_a = 25 kcal/mol. [c] R. D. Guthrie, F. Lovell, and L. Burdon, unpublished results. [d] Reference 2. [e] Reference 3. [f] Present work.

localized, lives longer, and consequently has a chance to become partially racemized before protonation occurs. The most difficult part of this argument is that I is less reactive than X and the latter shows high retention behavior. Normally a less reactive substrate is associated with a more reactive intermediate, although III could be an exception to the rule. In this connection, it is interesting to compare approximate rates of ionization for the several substituted imines listed in Table VIII.

It can be seen from these data that the effect of introduction of one methyl group at the carbon from which the proton is to be removed has the effect of slowing ionization by a factor of about 40 (first and second entries). Introduction of a second methyl group lowers the rate by an additional factor of 300. This increased effect must be due to steric inhibition of resonance reducing the rate of ionization by a factor of at least 7–8 even assuming that electronic effects of the second methyl would be as great as those of the first.

A more interesting comparison involves the second and fourth entries for which the rate difference of over 1600 reflects the replacement of a *tert*-butyl group by a phenyl group at the 3 position. When the same comparison is drawn between the third and fifth entries, the effect of changing a *p*-methoxyphenyl for a *tert*-butyl group results in a rate change of only 25. The difference between a *p*-methoxyphenyl and a phenyl should not have a large effect on the rate of ionization as can be roughly guessed from the results of Shoppee who studied the isomerization of a series of substituted benzylidenebenzylamines and found that methoxy had an effect comparable to methyl.[10] The effect of hydrogen substitution should certainly be more comparable to these groups than to that of the halogens which increased the rate by only a factor of 20. We therefore conclude that the diminished effect of replacing aryl by *tert*-butyl in the system containing methyl groups at both the 1 and 3 positions results from the fact that the —N=C part of the system is not providing the resonance stabilization to the incipient carbanion that it is capable of providing when one of the methyl groups is removed. The residual rate increase of 25 between the third and fifth entries in Table VIII might be expected from inductive considerations alone.

We consider this evidence to indicate that anions III and VIII are not normal allylic carbanions in the sense that they are not planar. We suggest instead that the intermediate in the interconversion of I and II is a mixture of the two equilibrating carbanions IIIa and IIIb.


IIIa IIIb

These are not resonance forms but, because the nonbonded interaction of the methyl groups in III forces a twisting of the allylic anion, they change geometry as the negative charge is transferred from one end of the system to the other. The main geometric change is a movement of the nitrogen atom. In the particular case of perpendicular p orbitals represented above, the C–N–C plane is displaced by 90° (the drawing of IIIb has been rotated to facilitate representation). As the charge is moved from one p orbital to another the potassium ion also changes position. If it can be transferred to both sides of the developing p orbital, the observed racemization is rationalized.

This explanation must be reconciled with the fact that anion VIII can be protonated at the α-methylneopentyl end with stereospecificity.[3] We suggest that the analogous second anion is not available in this system due to lack of appreciable negative charge density at its non-phenyl-bearing end. For this case the anion must be forced to a nearly planar state to allow development of sufficient charge density for protonation.

Experimental Section

Solvents and Solutions. *tert*-Butyl alcohol was purified by distillation from calcium oxide through a 1-m helices packed column. *tert*-Butyl alcohol-*O-d* (98+ % of one atom of D) was prepared by the method of Young and Guthrie.[11] Cyclohexane was purified by the method of Linnell and Umar.[12] Pentane was distilled before use.

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(10) C. W. Shoppee, *J. Chem. Soc.*, 1225 (1931).

(11) A. T. Young and R. D. Guthrie, *J. Org. Chem.*, 35, 853 (1970).

(12) R. H. Linnell and S. Umar, *Chemist-Analyst*, 43, 90 (1954).

Other solvents were reagent grade and used without purification. Solutions of potassium *tert*-butoxide were prepared by reacting potassium metal with *tert*-butyl alcohol under oxygen-free nitrogen.

***N*-(α-Methyl-4-methoxybenzylidene)-α-phenylethylamine** (I). α-Phenylethylamine (0.5 g) was added to 5.3 g of saturated aqueous zinc chloride. After addition of 40 ml of water, the mixture was digested on a steam bath for 30 min, filtered, and dried in a vacuum desiccator overnight. This material (300 mg) was added to a solution of freshly distilled 4-methoxyacetophenone (15.0 g, 0.10 mol) and α-phenylethylamine (12.0 g, 0.10 mol) in 175 ml of toluene. The mixture was refluxed for 12 hr over a Dean–Stark trap. The reaction mixture was filtered through Celite and the solvent evaporated at 20 mm to leave an oil liquid. Addition of 100–200 ml of pentane precipitated the product which was recrystallized six times from pentane to give 12.1 g of product (48%), mp 53–54°. The ir spectrum of this material showed a strong band at 6.3 μ (C═N stretch); $\lambda_{\max}^{\text{cyclohexene}}$ 262 mμ (log ε 4.28); nmr (CCl_4) δ 6.79–7.87 (m, 9, aromatic), 4.80 (q, 1, benzyl), 3.79 (s, 3, methoxy), 2.21 (s, 3, benzylidene methyl), 1.52 (d, 3, benzyl methyl).

Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.55; N, 5.52. Found: C, 80.49; H, 7.71; N, 5.62.

All imine samples were stored in well-stoppered flasks at 0° to avoid slow changes that occurred at room temperature.

4-Methoxyacetophenone Oxime. 4-Methoxyacetophenone (150.0 g, 1.00 mol) was treated with 500 ml of ethanol, 600 ml of water, hydroxylamine hydrochloride (75.0 g, 1.05 mol), and potassium hydroxide (115 g, 2.05 mol) and stirred for about 12 hr. The solution was poured into 1.5 l. of water and treated with excess solid carbon dioxide. Filtration and recrystallization from ether–pentane gave 96.0 g, 58%, mp 85–86°, lit.[13] 86–87°.

α-(4-Methoxyphenyl)ethylamine. This was prepared by the following modification of a literature procedure.[14] 4-Methoxyacetophenone oxime (40.0 g, 0.24 mol) was dissolved in 200 ml of absolute ethanol and treated with 2 g of 10% palladium on carbon. Hydrogenation was carried out at 40 psi on a standard Parr apparatus until the calculated amount of hydrogen was consumed. Following filtration through Celite, the solvent was removed by evaporation at reduced pressure. The crude amine (36.5 g) was taken into 200 ml of ether and treated with 50 ml of 15% hydrochloric acid. The acidic layer was made basic to litmus with 50% sodium hydroxide solution and the amine which separated was taken into 150 ml of ether. After drying over sodium sulfate the ether was boiled off through a short Vigreux column and the crude amine was distilled through a 2-ft helices packed column to give 28.7 g of product, bp 137–138° (20 mm).

***N*-(α-Methylbenzylidene)-α-(4-methoxyphenyl)ethylamine (II).** The reaction was carried out in a manner identical with that described above for I, using α-(4-methoxyphenyl)ethylamine (12.1 g, 0.080 mol) and acetophenone (11.0 g, 0.092 mol). After removal of the solvent, the residue was distilled in a modified Hickman still[15] to give 5.88 g (29%) of slightly yellow liquid imine. After some difficulty the product was induced to crystallize. Four recrystallizations from pentane gave material with mp 55–56°. The ir spectrum of this material showed a strong band at 6.3 μ (C═N stretch); $\lambda_{\max}^{\text{cyclohexane}}$ 230 mμ (log ε 4.218); nmr (CCl_4) δ 6.63–7.86 (m, 9, aromatic), 4.69 (q, 1, benzyl), 3.68 (s, 3, methoxy), 2.17 (s, 3, benzylidene methyl), 1.24 (d, 3, benzyl methyl).

Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.55; N, 5.52. Found: C, 80.37; H, 7.60; N, 5.28.

(−)-α-Phenylethylamine was prepared by a published procedure,[16] $\alpha^{25}\text{D}$ − 19.11° (0.5 dm, neat), lit.[16] $\alpha^{22}\text{D}$ − 38.3 (1 dm, neat).

(+)- and -(−)-α-(4-Methoxyphenyl)ethylamine. *dl*-α-(4-Methoxyphenyl)ethylamine (68 g, 0.45 mol) was added slowly to a boiling solution of *d*-tartaric acid (75.0 g, 0.5 mol) in 300 ml of 95% ethanol. After standing at room temperature for 2 hr, the tartrate salt crystallized. Warming the crystalline mass gently caused the mass of fine needle-like crystals to redissolve leaving behind the coarse transparent crystals of the (+)-amine tartrate. The (+)-amine tartrate (58.8 g) was recovered by filtration and the (−)-amine tartrate precipitated from the warm filtrate on cooling. After recrystallization once from 95% ethanol, 19.8 g of the (−)-amine tartrate was recovered. The (−)-amine was brought to constant rotation $\alpha^{25}\text{D}$ −17.33° (0.5 dm, neat) after four recrystallizations of the tartrate from a 2:1 mixture of ethyl acetate–methanol. It was recovered in 11.5% yield after treatment of the tartrate with excess 10% aqueous sodium hydroxide and ether extraction. The (+)-amine was recovered in 21.8% yield after eight recrystallizations of the tartrate from 95% ethanol, $\alpha^{25}\text{D}$ −17.16° (0.5 dm, neat), lit.[17] $[\alpha]^{23}\text{D}$ 22.68° (*c* 3.70, benzene).

(*R*)-*N*-(α-Methylbenzylidene)-α-(4-methoxyphenyl)ethylamine ((*R*)-II). The chiral imine was prepared using (−)-α-(4-methoxyphenyl)ethylamine by the procedure described for the racemic material. The product had mp 58–59.

(*S*)-*N*-(α-Methyl-4-methoxybenzylidene)-α-phenylethylamine ((*S*)-I). The chiral imine was prepared using (−)-α-phenylethylamine by the procedure described for the racemic material. The product had mp 63–64°.

Optical Rotatory Dispersion Data on Chiral Imines. These data are given in Table IX.

Table IX. Optical Rotatory Dispersion Data on Optically Active Imines in Cyclohexane at *ca.* 25°

Substrate	λ_0, mμ	First extremum, mμ	Second extremum,[a] mμ	Specific rotation first extremum, deg
(*S*)-I	257	274	243	+1263
(*S*)-II	243	261	228	+2175

[a] Absorption superimposed on the Cotton curve in this region.

α-Phenylethylamine-α-*d*. Acetophenone oxime (10.0 g, 0.074 mol) was dissolved in ether and exchanged by shaking with ten 0.6-ml portions of deuterium oxide. The OH proton was more than 98% exchanged by nmr. The ether was evaporated and the residue dissolved in 25 ml of methanol-*O*-*d*,[18] 0.50 g of 10% palladium on carbon added, and the mixture shaken for 2 hr under 30 psi of deuterium gas. The reaction was judged to be complete by comparison of the nmr spectra of starting material and product (the oxime aromatic region is characteristic). The methanol was removed from the reaction mixture using a rotary evaporator. The crude amine was taken into ether and treated with excess 6 *N* HCl. The acidic extract was made basic with sodium hydroxide and the amine extracted with ether. The ether was boiled off through a short Vigreux column. Distillation through a 2-ft glass helices packed column gave 5.0 g, 56%, bp 82–83 (22 mm). Nmr analysis showed 95% of one atom of D in the benzyl position. Conversion of this material to I, followed by hydrolysis, separation of the amine, and conversion of the amine to the benzamide allowed mass spectral analysis which showed 0.924 of one atom of D with small amounts of multideuterated material.

Kinetic Runs. Thick-walled tubes constricted at the top were treated with chromic acid solution, washed with water and ammonia, and dried at 110°. A weighed amount of sample was introduced into the tube and the tube evacuated and filled with oxygen-free nitrogen. The solvent–base solution was introduced through a septum and frozen in liquid nitrogen. The tube was evacuated and allowed to warm to room temperature. After refreezing and reevacuation, the tube was sealed.

In a typical isomerization run, I (294 mg, 1.16 mmol) was placed in a tube with 5.15 ml of 0.547 *N* potassium *tert*-butoxide in *tert*-butyl alchol. The tube was placed in a constant-temperature bath at 100° for 1324 min. The tube was then removed, cooled, and opened. Two aliquots of 0.50 ml were pipeted into two small separatory funnels containing 15 ml of Spectroquality cyclohexane and 25 ml of water. The cyclohexane layer was washed twice more with a total of 50 ml of water. The cyclohexane layer was separated and dried over anhydrous sodium sulfate. A 5.0-ml aliquot was taken from each of the samples and diluted to 50 ml with cyclohexane for uv analysis. Simultaneous solution of eq 4 and 5 gave

$$(1.925 \times 10^4)c_1 + (0.589 \times 10^4)c_2 = A_{262} \qquad (4)$$

$$(0.295 \times 10^4)c_1 + (1.656 \times 10^4)c_2 = A_{230} \qquad (5)$$

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[15] K. B. Wiberg, "Laboratory Technique in Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, p 66.

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the concentrations c_1 and c_2 (of I and II, respectively) from A, the absorbance at the subscripted wavelength. The total concentration of the imine isomers calculated from the original sample weight was 7.67×10^{-5} M and the concentration calculated from uv absorbance after reaction was 7.45×10^{-5} M. Analysis of synthetic samples known to contain 25.0, 50.0, and 75.0% of I gave 25.3, 49.9, and 75.3% respectively. These values were not significantly altered by putting the synthetic mixtures through the work-up procedure.

Racemization Runs. In a typical racemization run, I (1.503 g, 5.94 mmol) was introduced into a tube with 49.4 ml of 0.457 N potassium *tert*-butoxide in *tert*-butyl alcohol. The tube was sealed and placed in a constant-temperature bath for 1230 min at 100°. The tube was cooled and opened and two 0.20-ml aliquots worked up as described above for uv analysis, showing 18.1 and 18.0% isomerization. The remainder of the reaction mixture was poured immediately into a mixture of 75 ml of pentane and 125 ml of water. After washing the pentane layer 3–4 times with water, it was dried and the pentane evaporated. The resultant imine mixture was treated with 20 ml of 20% aqueous sulfuric acid solution and refluxed for 1 hr to hydrolyze the imines. The mixture was cooled and continuously extracted with ether for 24 hr. The acidic layer was made basic with *ca.* 2 g of solid sodium hydroxide and the mixture of amines extracted with ether for 24 hr. The ether solution was dried, the ether was evaporated and the amines were separated by preparative glc on a 15 ft × $^3/_8$ in. column packed with 17% SE-30 on 45–60 mesh Chromosorb W at 195°. Care was taken to keep the amine samples in a carbon dioxide free atmosphere during collection. Samples were dissolved in cyclohexane which had been stored over potassium hydroxide for polarimetric analysis. Rotations determined on amines obtained by hydrolysis of the starting materials are listed in Table X.

Table X. Rotations at 25° of Optically Active Amines from the Hydrolysis of Chiral Imines I and II

Substrate	Amine	Concn,[a] mg/ml	Specific rotation, deg
(*S*)-I-H	(−)-α-Phenylethyl[b]	45.3	−40.0
		40.4	−41.6
		Neat	−40.5
(*S*)-II-H	(−)-α-(4-Methoxyphenyl)ethyl[c]	100.0	−36.2
(*R*)-II-H	(+)-α-(4-Methoxyphenyl)ethyl[c]	121.0	+38.1
		75.0	+38.1

[a] Solution of the amine in cyclohexane. [b] Lit.[17] $\alpha^{22}\mathrm{D}$ −38.3° (neat, 1 dm). [c] Predicted maximum specific rotation, $[\alpha]^{25}\mathrm{D}$ +36.0° based on nmr data on partially resolved material in chiral solvent: W. H. Pirkle, T. G. Burlingame, and S. D. Beare, *Tetrahedron Lett.*, **56**, 5849 (1968).

Amination of Toluene, Adamantane, and *tert*-Butyl Chloride with Monochloramine–Aluminum Chloride[1]

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Abstract: The reaction of monochloramine with toluene in the presence of aluminum chloride at −35° yielded 13–15% of *m*-toluidine, whereas trichloramine gave 39–43% yields. In order to rationalize the meta substitution, a mechanistic scheme entailing addition–elimination is proposed. Amination of adamantane with monochloramine under Friedel–Crafts conditions gave 1-aminoadamantane in 40% yield. An analogous reaction with trichloramine–aluminum chloride provided 1-aminoadamantane in 85% yield with no detectable 2-aminoadamantane. The reaction pathway presumably involves formation of the 1-adamantyl cation followed by attack by the nitrogen-containing nucleophile. Reaction of *tert*-butyl chloride, monochloramine, and aluminum chloride yielded *tert*-butylamine (7–20%). Similarly, trichloramine generated *tert*-butylamine in 50–56% yield and 2,2-dimethylaziridine in 7–12% yield. Mechanistically, the *tert*-butyl cation is thought to participate as an intermediate. Possible reasons are discussed for the lower yields in all cases with monochloramine, as compared to trichloramine.

This report is an outgrowth of our interest in the chemistry of *N*-haloamines, as well as our involvement with environmental chemistry.[3] Prior work[4] from this laboratory involved investigations of the trichloramine–aluminum chloride combination for amination of various organic substrates, *e.g.*, arenes, alkanes, and alkyl halides. The aromatic study included mono-[5,6] and *m*-dialkylbenzenes,[7] halobenzenes,[8] and biphenyl.[9] A striking feature was the essentially exclusive meta orientation observed in all cases. There was an accumulation of evidence[4–10] which pointed to an addition–elimination pathway. This comprised the first example of involvement of this type of mechanism to a fairly appreciable extent (yields as high as 36%) with simple benzenoid compounds. It is well known[11] that with uncomplicated benzene derivatives, the straightforward substitution route pertains almost exclusively for the classical methods.

With alkane substrates, replacement of hydrogen

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[1] Paper XIX. Chemistry of *N*-Haloamines. Contribution No. 81 from the Center for Great Lakes Studies, University of Wisconsin—Milwaukee.

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