Table XIV. Relative Intensities in the Parent Ion Region in the Mass Spectra of IV-D and IV-H at 12 eV

	P − 2	P − 1	P	P + 1	P + 2
IV-D	15.7	5.3	100	17.7	1.9
IV-H	10.3	4.8	100	16.5	1.8

The ratio F ((P − 1)/P) for protio material was zero. Therefore, the (P − 1) contribution of deuterio material (mol wt 242) to m/e 241 probably was zero also.

The solid samples analyzed above had been purified by recrystallization, and it was assumed that no isotopic fractionation occurred. The mixture melting point data above support this assumption. Also, Cram and Whitney[36] demonstrated that isotopic fractionation did not occur in the recrystallization of partially deuterated material in another system.

For deuterium analysis of *N*-(neopentyl-*1-d*)-α-phenylethylamine (IV-D) from the reduction of II-D of run 23, 12- and 70-eV ionization potentials were employed with a heated inlet of *ca.* 125°. None of the above calculated methods could be used because the (P − 1)/P ratio for IV-H was high even at low ionization potential. Therefore, the region about the parent ion in the mass spectrum of IV-D (mol wt 192) at 12 eV was compared with that of IV-H (mol wt 191) at 12 eV. These data are summarized below in Table XIV and led to the conclusion that IV-D contained >0.99 atom of excess deuterium per molecule. Also, comparisons of the relative intensities of other fragments in the mass spectra of IV-D and IV-H at 70 eV showed that excess deuterium was located only at the methylene position.

Yield Controls. To 0.40 ml of a mixture of I and bicyclohexyl, 56.2% I by glc (column F, 160°), was added 3.0 ml of *tert*-butyl alcohol, 0.431 *M* in potassium *tert*-butoxide. The resulting solution was *ca.* 0.3 *M* in I. After 9.67×10^4 sec at 80°, the reaction mixture was worked up in the usual manner. By glc analysis as above, the isolated imine–bicyclohexyl mixture contained 55.6% I + II, and this corresponds to an imine yield of 98 ± 1%. Isomerization of I to II was 39.2%. To an aliquot of the above glc-analyzed I–bicyclohexyl mixture was added a dimethyl sulfoxide solution 2.9 *M* in methanol and 0.30 *M* in potassium methoxide; the resulting solution was *ca.* 0.2 *M* in I. After 33.0 min at 80°, the reaction mixture was worked up in the usual manner. By glc analysis as above, the isolated imine–bicyclohexyl mixture contained 54.5% I + II, and this corresponds to an imine yield of 93 ± 1%. Isomerization of I to II was 66.7%.

Thermal Conductivity of I *vs.* II. Mixtures of I and II were prepared by weight and analyzed by glc (column G, 140°). The results below indicated that glc analyses of I–II mixtures represented the actual compositions of those mixtures.

% II by weight	% II by glc
1.95	1.95 ± 0.04
3.57	3.61 ± 0.05
13.5	13.7 ± 0.2

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(36) D. J. Cram and T. A. Whitney, *J. Amer. Chem. Soc.*, **89**, 4651 (1967).

Electrophilic Substitution at Saturated Carbon. XLIX. A Stereospecific Transamination[1,2]

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Abstract: Imines (−)-(*S*)-*N*-(α-methylneopentylidene)-α-phenylethylamine (I) and (+)-(*S*)-*N*-(α-methylbenzylidene)pinacolylamine (II) were prepared in optically pure forms. Potassium *tert*-butoxide catalyzed equilibration of I and II in *tert*-butyl alcohol at 175° gave K = II/I = 4.1 ± 0.3. Under the same reaction conditions, racemization of (−)-I and isomerization of (−)-I to II proceeded at comparable rates. For example, after 11.0% isomerization, (−)-I had undergone 26 ± 1% racemization, and the (−)-II produced was 86 ± 1% optically pure. Since some racemic II was produced from (−)-I that had become racemic prior to rearrangement the optical purity of (−)-II represented a minimal and time-dependent value for the per cent stereospecificity of the isomerization. Use of a kinetic model gave the corrected value, 100 ± 6%. The model treated (+)-II (inverted product) as the stereospecific isomerization product of (+)-I (inverted starting material). The high stereospecificity was interpreted in terms of the intermediacy of a single inherently symmetrical azaallylic carbanion A asymmetrically ion paired with potassium. Azaallylic carbanion A has the two bulky substituents, *tert*-butyl and phenyl, in the two least-hindered positions. The isomerization occurred in a cis or suprafacial manner across the face of delocalized carbanion A. Collapse of A favored I over II by a factor of *ca.* 200 in *tert*-butyl alcohol–potassium *tert*-butoxide at 175°. In *tert*-butyl alcohol-*O-d*-potassium *tert*-butoxide, (−)-I underwent isotopic exchange 41 times as fast as it racemized. In dimethyl sulfoxide–*tert*-butyl alcohol the isomerization of (−)-I to II proceeded with a complete lack of stereospecificity.

Biological transamination[3] involves the base-catalyzed isomerization of intermediate imines derived from pyridoxal and α-amino acids and from pyridoxamine and α-keto acids.[4] The intermediacy of aza-

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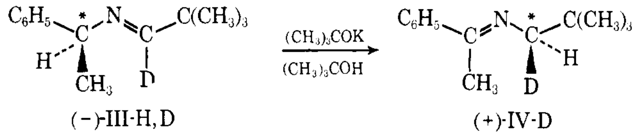
(1) This investigation was supported by the U. S. Public Health Service, Research Grant No. GM 12640-05 from the Department of Health, Education, and Welfare.

(2) Some of these results have been published in preliminary form: W. Meister, R. D. Guthrie, J. L. Maxwell, D. A. Jaeger, and D. J. Cram, *J. Amer. Chem. Soc.*, **91**, 4452 (1969).

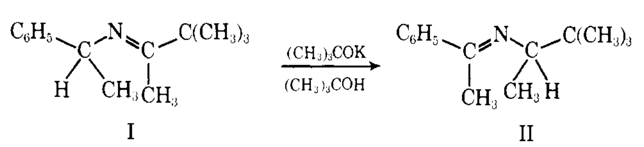
(3) (a) E. E. Snell in "Chemical and Biological Aspects of Pyridoxal Catalysis," P. M. Fasella, A. E. Braunstein, and A. Rossi-Fanelli, Ed., Macmillan, New York, N. Y., 1963, pp 1–12; (b) E. E. Snell, A. E. Braunstein, E. S. Severin, and Yu. M. Torchinsky, Ed., "Pyridoxal Catalysis: Enzymes and Model Systems," Interscience, New York, N. Y., 1968; (c) B. M. Guirard and E. E. Snell in "Comprehensive Biochemistry," Vol. 15, M. Florkin and E. H. Stotz, Ed., Elsevier, New York, N. Y., 1964, Chapter 5; (d) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. 2, W. A. Benjamin, New York, N. Y., 1966, Chapter 8.

(4) (a) D. E. Metzler, M. Ikawa, and E. E. Snell, *J. Amer. Chem. Soc.*, **76**, 648 (1954); (b) A. E. Braunstein and M. M. Shemyakin, *Biokhimiya*, **18**, 393 (1953).

allylic carbanions in base-catalyzed imine isomerizations has been demonstrated,[5] and essentially 100% stereospecificity was observed[6] in the potassium *tert*-butoxide catalyzed isomerization of imine (−)-III-H,D to (+)-IV-D in *tert*-butyl alcohol. The high stereospecificity of this isomerization was interpreted in terms of the sole intermediacy of one of four possible geometrically isomeric azaallylic carbanions ion paired with potassium ion on only one side.

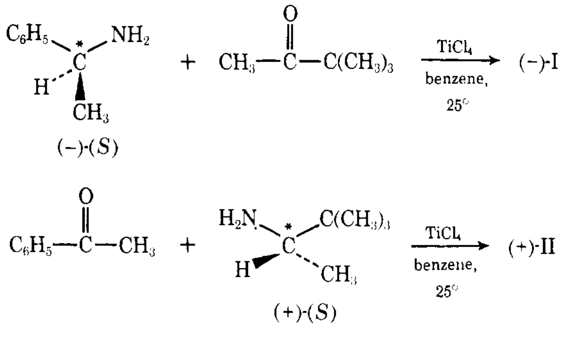


The present study was undertaken for several reasons. (1) The reaction, I → II, is a model for biological transamination, which of course occurs stereospecifically. Study of III → IV demonstrated that stereospecificity can be realized in a transamination without mediation of an enzyme. However I, unlike III, is a ketimine, and more closely approximates the steric properties of the groups involved in most of the transaminations observed in nature. (2) Optically pure (+)-IV-D displayed an unusually high optical rotation, and a comparison of (+)-IV-D with (+)-II revealed the source of this property.[2] (3) Both I and II possess chiral centers not dependent on the absence or presence of deuterium in the molecule (unlike IV). (4) The absolute configurations and maximum rotations of α-phenylethylamine[7,8] and pinacolylamine[9] are known, and therefore those of I and II could be determined simply by synthesis. (5) Both I and II proved stable to and preparatively separable by glc. (6) Imine I was found to be favored in equilibrium mixtures of I and II. Thus the isomerizations of I to II could be carried out under conditions of low conversion such that II, once formed, did not react further. (7) The bulk of the *tert*-butyl and phenyl groups was expected to enforce geometrical homogeneity at the azaallylic anion stage. Such homogeneity is a condition for stereospecificity in I → II.



Results

Syntheses. The syntheses of *N*-(α-methylneopentylidene)-α-phenylethylamine[10] (I) and *N*-(α-methylbenzylidene)pinacolylamine (II) employed the method of Weingarten, *et al.*,[11] with several modifications. Titanium tetrachloride catalyzed condensation of (−)-α-phenylethylamine, $\alpha^{25}D$ −38.16 ± 0.03° (neat, 1 dm),[8] with pinacolone in benzene at 25° yielded (−)-I, $[\alpha]^{25}D$ −21.2 ± 0.2° (*c* 5.18, chloroform). Likewise, titanium tetrachloride catalyzed condensation of (+)-pinacolylamine, $\alpha^{25}D$ 4.39 ± 0.03° (neat, 1 dm), with acetophenone in benzene at 25° yielded (+)-II, $[\alpha]^{25}D$ 86.9 ± 0.7° (*c* 1.21, chloroform).



Since (−)-α-phenylethylamine and (+)-pinacolylamine have the *S* configuration,[8,9] the absolute configurations of (−)-I and (+)-II were known as indicated because the asymmetric centers were not affected in the syntheses from the respective amines. In another preparation of I, condensation of (−)-α-phenylethylamine, $\alpha^{25}D$ 37.88 ± 0.03° (neat, 1 dm),[8] with pinacolone in refluxing decalin using α-phenylethylamine–zinc chloride complex[12] as catalyst, gave (+)-I, $[\alpha]^{25}D$ 21.0 ± 0.2° (*c* 5.02, chloroform). It was apparent that no racemization occurred in either this or the titanium tetrachloride catalyzed condensation since, within experimental error, I of the same absolute rotation was obtained by both methods.

Nuclear magnetic resonance spectra of I and II taken at ambient probe temperature (*ca.* 40°) indicated the presence of only one geometric isomer for each imine. Presumably I and II were both in the more sterically stable anti forms as indicated, and Staab, *et al.*,[10] reached the same conclusion for imine I.

Equilibria. Table I summarizes the results of potassium *tert*-butoxide catalyzed equilibrations of I and II in *tert*-butyl alcohol. Runs 1 and 2 were made at 175°, and runs 3 and 4 at about 190°. From the data of runs 1 and 2, an average equilibrium constant K = II/I = 4.1 ± 0.3 was calculated. The equilibrium constant at 175° was not determined more accurately for two reasons. First it was doubtful whether exactly the same I–II mixture could have been attained starting from both I and II since control experiments demon-

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

	Substrate		Base			
Run	Nature	Concn, *M*	concn, *M*	*T*, °C	Time, hr	% II[a]
1	I	0.32	0.48	175[b]	310	79.1 ± 0.1
2	II	0.31	0.48	175[b]	310	81.5 ± 0.2
3	I	0.22	0.5	205[b,c]	114	80
4	II	0.37	0.41	205[b,c]	288	78

[a] An average of at least three glc analyses. [b] ±3. [c] The sealed tube was about two-thirds immersed in a bath at this temperature, and the mixture refluxed, so the actual temperature in the tube was about 10–20° lower.

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(5) D. J. Cram and R. D. Guthrie, *J. Amer. Chem. Soc.*, **88**, 5760 (1966).

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

(7) W. Leithe, *Chem. Ber.*, **64**, 2827 (1931).

(8) W. Theilacker and H. G. Winkler, *ibid.*, **87**, 690 (1954).

(9) H. Pracejus and S. Winter, *ibid.*, **97**, 3173 (1964).

(10) D. Wurmb-Gerlich, F. Vögtle, A. Mannschreck, and H. A. Staab, *Justus Liebigs Ann. Chem.*, **708**, 36 (1967).

(11) H. Weingarten, J. P. Chupp, and W. A. White, *J. Org. Chem.*, **32**, 3246 (1967).

(12) R. P. Ossorio, F. G. Herrara, and A. Hidalgo, *An. Real Soc. Espan. Fis. Quim., Ser. B*, **50**, 875 (1954).

Table II. Base-Catalyzed Isomerizations of I to II

Run	Substrate Nature	Substrate Concn, *M*	Solvent	Base Nature	Base Concn, *M*	*T*, °C	Time, sec × 10^{-4}	% II[a]
5	(−)-I	0.34	$(CH_3)_3COH$	$(CH_3)_3COK$	0.41	175[b]	4.56	11.0 ± 0.1
6	(−)-I	0.34	$(CH_3)_3COH$	$(CH_3)_3COK$	0.48	175[c]	4.32	11.9 ± 0.2
7	(−)-I	0.34	$(CH_3)_3COH$	$(CH_3)_3COK$	0.48	175[c]	4.34	11.6 ± 0.3
8	(+)-I	0.22	$(CH_3)_3COH$	$(CH_3)_3COK$	0.5	205[b,d]	40.89	79.6
9	(−)-I	0.10	$(CH_3)_3COD$[e]	$(CH_3)_3COK$	0.40	175[b]	0.720	1.00 ± 0.04
10	(±)-I	0.31	$(CH_3)_3COH$	No base		175[b]	4.61	⩽0.1[f]
11	(−)-I	0.33	$(CH_3)_3COD$[g]	No base		175[b]	4.68	⩽0.1[f]
12	(−)-I	0.32	$(CH_3)_2SO$[h]	$(CH_3)_3COK$	0.06	75[i]	46.13	25.1 ± 0.2

[a] An average of at least three glc analyses. [b] ±3. [c] ±0.3. [d] The sealed tube was about two-thirds immersed in a bath at this temperature, and the mixture refluxed, so the actual temperature in the tube was about 10–20° lower. [e] 0.99 atom of excess deuterium per molecule. [f] Lower limit for detection by glc. [g] 0.92 atom of excess deuterium per molecule. [h] Solution was 1.5 *M* in *tert*-butyl alcohol. [i] ±1.

strated that I, and possibly II, decomposed slowly under these conditions. Secondly, the calculations and conclusions for the asymmetric induction runs below did not depend on a precise value of *K*. At 75°, a value of *K* greater than 4.1 (175°) would be expected since in the very similar III–IV system the equilibrium constant, *K* = IV/III, increased dramatically with a decrease in temperature: 15 at 100°; 23 at 75°; *ca.* 50 at 25°.[6b,13] Knowledge that *K* was greater than 4.1 at 75° was sufficient for the present study.

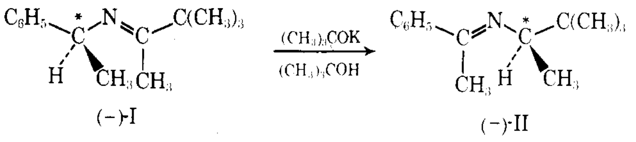
Base-Catalyzed Isomerizations of Imine I to II. Tables II and III summarize the results of potassium *tert*-butoxide catalyzed isomerizations of I to II in two solvent systems, *tert*-butyl alcohol (runs 5–9, 175°) and dimethyl sulfoxide–*tert*-butyl alcohol (run 12, 75°). Runs 10 and 11 served as controls and were made without base in *tert*-butyl alcohol and *tert*-butyl alcohol-*O-d*, respectively.

Uniformly the reaction mixtures were prepared in nitrogen-flushed glass tubes, which were degassed with nitrogen and sealed under vacuum (*ca.* 0.1 mm). After isolation the product mixtures were analyzed and preparatively separated by glc. Isolated I and II were analyzed polarimetrically and for deuterium content as required.

One-point pseudo-first-order (base concentration remained constant) and second-order rate constants for the isomerizations of I to II, k_i and k_i', respectively, are listed in Table III. These values were calculated from the glc analyses with the assumption that, once formed, II did not return to I. This assumption ignores the fact that isomerizations of I to II do not proceed to completion: at 175°, $K = 4.1$, and at 75°, $K > 4.1$. However, it was valid under conditions of the low conversions of I to II employed in all runs.[14] Run 8 qualitatively demonstrated that imine II was less reactive than I because after 79.6% conversion of I to II (at about equilibrium) isolated II was 19.8% optically pure whereas I was essentially racemic. Use of an internal standard in the glc measurements established that under run 5 conditions, *ca.* 96%, and under 12 conditions, *ca.* 94% of the starting material could be accounted for in the form of either I or II. Additional controls established that under run 5 conditions loss of imine was due to decomposition of I *before* isolation. Correction for this loss of I gave rate constants within experimental error of those calculated assuming no loss of I.[14]

Discussion

Stereochemical Course of the Potassium *tert*-Butoxide Catalyzed Isomerization of I to II in *tert*-Butyl Alcohol. In runs 5–8, recovered II was optically active, so asymmetric induction did indeed occur in the potassium *tert*-butoxide catalyzed isomerization of I to II in *tert*-butyl alcohol at 175°. As indicated for runs 5–7, (−)-I yielded (−)-II, and in run 8, (+)-I yielded (+)-II.



(−)-I (−)-II

Also, in run 9 after 1% isomerization to II in *tert*-butyl alcohol-*O-d*, the (−)-I isolated was 3.3% racemized and contained 74.7% deuterium at the benzyl position by nmr. One-point pseudo-first-order rate constants for racemization and exchange were calculated, k_α and k_e, respectively. A ratio of $k_e/k_\alpha = 41$ resulted. This value indicated that the exchange of deuterium for protium in (−)-I occurred with high retention of configuration.[15]

Calculation of the Stereospecificity of the Isomerization of I to II in Runs 5 and 6. The stereospecificity of the isomerization of I to II could not be determined simply by comparison of the rotation of isolated II with that of optically pure II because I racemized faster than it isomerized to II, *i.e.*, $k_\alpha = 6.55 \times 10^{-6}$ sec^{-1} and $k_i = 2.56 \times 10^{-6}$ sec^{-1} for (−)-I in run 5. Such a calculation gives a minimal and time-dependent value for the stereospecificity. Therefore, the kinetic scheme (Chart I) and corresponding equations of the previous paper[6b] were employed which take into account the competing racemization of (−)-I. Under the conditions of runs 5 and 6, the return of II to I and the racemization of II were negligible and could be neglected.

Chart I

$$\begin{tikzcd}
(-)\text{-I} \arrow[r, "k_1"] \arrow[d, shift right, "k_2"'] \arrow[dr] & (-)\text{-II} \\
(+)\text{-I} \arrow[r, "k_1"] \arrow[u, shift right] \arrow[ur, "k_3"] & (+)\text{-II}
\end{tikzcd}$$

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(13) R. D. Guthrie and D. J. Cram, unpublished results.

(14) D. A. Jaeger, Ph.D. Thesis, University of California at Los Angeles, 1970, Appendix I. For example it was calculated that if the 11% of II had been present during the *entire* reaction period of run 5, only 0.2% of recovered I would have resulted from isomerization of II.

(15) For a discussion and interpretation of various k_e/k_α values, see D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 52–54.

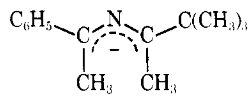
Table III. Rate Constants and Stereochemical Data[a] for Isomerizations of I to II

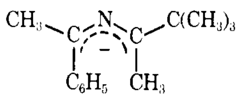
Isomerization rate consts	Run 5	6	7	8	9	11	12
$k_i \times 10^6$, sec^{-1}	2.56 ± 0.13	2.93 ± 0.15	2.84 ± 0.14		1.4		0.63
$k_i' \times 10^6$, l. mol^{-1} sec^{-1}	6.24 ± 0.50	6.10 ± 0.50	5.92 ± 0.50		3.5		10.4
Initial rotation of I	−24.4 ± 0.2° [b]	−24.4 ± 0.2° [b]	−24.4 ± 0.2° [b]	21.0 ± 0.2° [c]	−24.4 ± 0.2° [b]	−24.4 ± 0.2° [b]	−24.4 ±0.2° [b]
Rotation of recovd I	−18.1 ± 0.2° [d]	−16.9 ± 0.2° [e]		0.8 ± 0.3° [f]	−23.6 ± 0.2° [g,h]	−24.5 ± 0.2° [i,j]	0[k]
% racemization of recovd I	26 ± 1	31 ± 1		96 ± 1	3.3 ± 0.2	0	100
Racemization rate consts for I							
$k_\alpha \times 10^6$, sec^{-1}	6.55 ± 0.33	8.51 ± 0.43			4.50 ± 0.22		
$k_\alpha' \times 10^6$, l. mol^{-1} sec^{-1}	16.0 ± 1.0	17.7 ± 1.1			9.37 ± 0.56		
Rotation of recovd II	−91.8 ± 0.6° [l]	−89.5 ± 0.6° [m]	−88.9 ± 0.6° [n]	17.2 ± 0.2° [o]			−0.2 ± 0.3° [p]
Optical purity of recovd II[q]	86 ± 1	84 ± 1	84 ± 1	19.8 ± 0.2			0

[a] All rotations were taken in chloroform solution. [b] $[\alpha]^{25}_{546}$ (c 0.821). [c] $[\alpha]^{25}\text{D}$ (c 5.02). [d] $[\alpha]^{25}_{546}$, an average of three values: −18.1° (c 0.821); −18.0° (c 0.986); −18.2° (c 1.15). [e] $[\alpha]^{25}_{546}$, an average of two values: −16.8° (c 0.620); −17.0° (c 0.676). [f] $[\alpha]^{25}\text{D}$ (c 1.06). [g] $[\alpha]^{25}_{546}$ (c 0.593). [h] Material contained 74.7% deuterium at the benzyl position by nmr. [i] $[\alpha]^{25}_{546}$ (c 0.754). [j] Material contained no excess deuterium at the benzyl position by nmr. [k] $[\alpha]^{25}_{546}$ (c 1.17). [l] $[\alpha]^{25}_{546}$ (c 1.10). [m] $[\alpha]^{25}_{546}$ (c 0.668). [n] $[\alpha]^{25}_{546}$ (c 0.711). [o] $[\alpha]^{25}\text{D}$ (c 2.58). [p] $[\alpha]^{25}_{546}$ (c 1.31). [q] Based on optically pure (+)-II, $[\alpha]^{25}_{546}$ 106.2 ± 0.8°, $[\alpha]^{25}\text{D}$ 86.9 ± 0.7° (c 1.21).

The values of k_1, k_2, and k_3 were all calculated for runs 5 and 6 and are listed in Table IV. The ratio $k_1/(k_1 + k_3)100$ represents the per cent stereospecificity of the isomerization, and values of 99.6 ± 6 and 100.3 ± 6% were obtained for runs 5 and 6, respectively. *Therefore, the potassium tert-butoxide catalyzed isomerization of I to II in tert-butyl alcohol at 175° was essentially stereospecific when allowance was made for the competitive racemization of I.* Thus (−)-I isomerized only to (−)-II, and (+)-I to only (+)-II.

Mechanistic Description of the Stereospecific Isomerization of I to II. Since the isomerization of I to II occurred with 100 ± 6% stereospecificity, the reaction necessarily proceeded along an asymmetric structural coordinate, which can be described with models analogous to those employed previously.[6b] Four geometrically isomeric azaallylic carbanions are conceivable as intermediates in the proton transfer, A, B, C, and D.


A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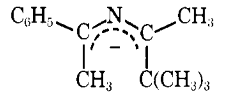
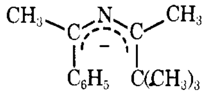

C


D

Solvation and ion pairing with potassium on only one side would provide an intermediate carbanion with an element of asymmetry which is obviously necessary since asymmetric induction was observed. On the basis of steric interactions, carbanion A is the most favorable intermediate because the 1,3 methyl–methyl interaction is of lower energy than any of the other 1,3 interactions in carbanions B, C, or D.

The predominant formation of (−)-II from (−)-I is explained by invoking the intermediacy of carbanion A as follows. Abstraction of the benzyl proton of (−)-I in the conformation formulated (actually N should be above the plane of the page) by solvated potassium *tert*-butoxide contact ion pair yields carbanion (−)-A, solvated by *tert*-butyl alcohol and ion paired with potassium only on that face of the azaallylic anion from which the proton was abstracted. Protonation then occurs *within* this asymmetrically ion-paired carbanion to give

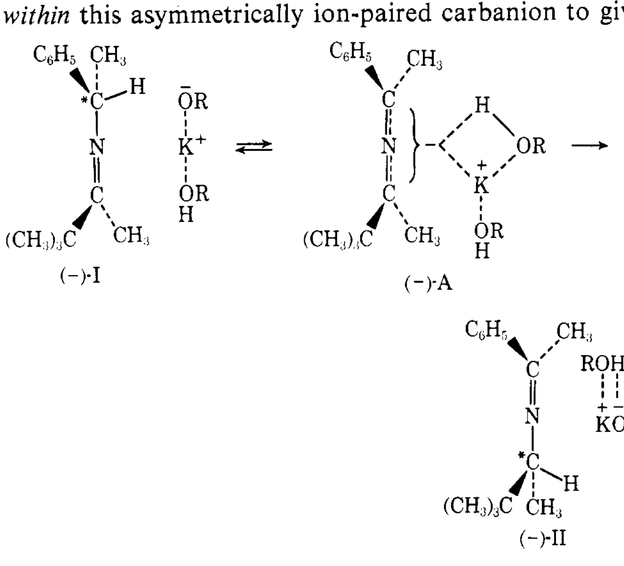


Table IV. Stereochemical Course of Potassium *tert*-Butoxide Catalyzed Isomerization of I to II in *tert*-Butyl Alcohol at 175°

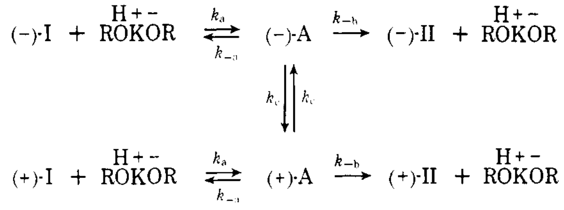
Process	Schematic designation	$k \times 10^6$, sec^{-1} [a] Run 5	$k \times 10^6$, sec^{-1} [a] Run 6	Rel rates Run 5	Rel rates Run 6
(−)-I → (−)-II (+)-I → (+)-II	k_1	2.55 ± 0.14	2.52 ± 0.14	1.00	1.00
(−)-I → (+)-I	k_2	3.27 ± 0.17	3.64 ± 0.17	1.28	1.45
(−)-I → (+)-II (+)-I → (−)-II	k_3	0.01 ± 0.14	−0.01 ± 0.14	0.004	−0.003
Stereospecificity of I → II	$(k_1 \times 100)/(k_1 + k_3)$			99.6	100.3

[a] Runs 5 and 6 were made with 0.41 and 0.48 M potassium *tert*-butoxide, respectively. Rates for run 6 were corrected to run 5 conditions by multiplication by the factor 0.41/0.48.

(−)-II, the product of stereospecific isomerization, and (−)-I, starting material, the product of an invisible reaction. With respect to carbanion A, the isomerization of I to II is described as having occurred in a cis or suprafacial manner, analogous to the stereochemical course of biological transamination.[16]

The fact that (−)-I racemized faster than it isomerized to II complicated the mechanistic description, and the overall stereochemical results can be explained by the intermediacy of carbanion A *alone* or by that of *both* carbanions A and B. The more probable mechanistic scheme utilizing the intermediacy of only carbanion A is outlined in Chart II. This scheme rationalizes the stereochemical results if the collapse ratio for carbanion A (k_{-a}/k_{-b}) is sufficiently large. The collapse ratio is simply the partitioning ratio of A between I and II.

Chart II

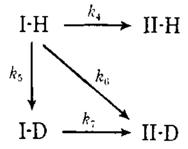


At zero time, only (−)-I is present, and abstraction of a proton by potassium *tert*-butoxide yields intermediate carbanion (−)-A. Carbanion (−)-A undergoes one of three competing reactions: (1) it collapses to (−)-I, the product of an invisible reaction (k_{-a}); (2) it collapses to (−)-II, the product of stereospecific isomerization (k_{-b}); (3) it rearranges to the enantiomeric ion pair (+)-A by ligand migration and/or carbanion rotation (k_c). Three analogous reaction paths are available to enantiomeric ion pair (+)-A formed, and they are also governed by rate constants k_{-a}, k_{-b}, and k_c. The simultaneous racemization of (−)-I and stereospecific isomerization of (−)-I to (−)-II are consistent with the mechanism of Chart II if the collapse of ion pair (+)-A yields (+)-I much more often than (+)-II, that is, if k_{-a}/k_{-b} is very large. The concentration of (+)-I increases as the reaction proceeds, and the kinetic scheme recognizes that (+)-II is its stereospecific isomerization product.

If the isomerization of (−)-I did proceed *only* through carbanion A as outlined above, then k_2/k_3 (where k_2 and k_3 are the rate constants for processes yielding (+)-I and (+)-II, respectively) is the collapse ratio of (+)-A and is equal, therefore, to k_{-a}/k_{-b}, the collapse ratio for the system as a whole. Within experimental error, the smallest values of k_2/k_3 obtainable from the calculations for runs 5 and 6 were 20 and 27, respectively (Table IV). Thus, the collapse ratio must be at least 20 if carbanion A is the only intermediate.

The collapse ratio also can be estimated in a different way that involves the rates of incorporation of deuterium into I and II from *tert*-butyl alcohol-*O*-*d* in run 9. The appropriate kinetic scheme (Chart III) and corresponding equations of the previous paper[6b] were employed.

Chart III



The rate constant ratio k_5/k_6 is the partitioning ratio of intermediate carbanion between exchanged starting material, I-D, and exchanged product, II-D, and is therefore the collapse ratio for carbanion with deuterium capture. If it is assumed that the collapse ratio has no *substrate* or *solvent* isotope effect, then k_5/k_6 is also the collapse ratio for intermediate carbanion in asymmetric induction runs 5 and 6 in which substrate and solvent both contained protium. The fact that this assumption is probably not strictly correct[6b] does not affect any conclusions drawn here.

With the equations[6b] for Chart III and the data of run 9, coupled with reasonable assumptions of the primary deuterium isotope effect for I → II and the per cent exchange of II in run 9, k_4, k_5, k_6, and k_7 were calculated and are compiled in Table V. As expected, the collapse ratio, k_5/k_5, and intramolecularity, $k_4/(k_4 + k_6)$, were very sensitive to variation in the assumed per cent exchange of II; over the range of 30–90% exchange, k_5/k_6 and $k_4/(k_4 + k_6)$ varied from 910 to 110 and from 0.89 to 0.13, respectively. Intramolecularity in the reaction of III → IV in *tert*-butyl alcohol-*O*-*d*-potassium *tert*-butoxide was 0.46.[6b] For another imine system with the same solvent–base it was about 0.5.[5] Furthermore, in the same solvent–base system similar values were obtained for the isomerizations of several allylic systems.[17] An analogous value for I → II would

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[16] (a) H. C. Dunathan, L. Davis, P. G. Kury, and M. Kaplan, *Biochemistry*, 7, 4532 (1968); (b) J. E. Ayling, H. C. Dunathan, and E. E. Snell, *ibid.*, 7, 4537 (1968).

[17] (a) D. H. Hunter and D. J. Cram, *J. Amer. Chem. Soc.*, **86**, 5478 (1964); (b) S. W. Ela and D. J. Cram, *ibid.*, **88**, 5791 (1966); (c) D. J. Cram and R. T. Uyeda, *ibid.*, **86**, 5466 (1964).

Table V. One-Point Pseudo-First-Order Rate Constants for Reactions of I-H in *tert*-Butyl Alcohol-O-*d* 0.40 *M* in Potassium *tert*-Butoxide at 175° (Run 9)

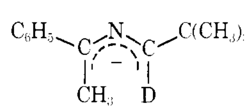
Process	Schematic designation	$k \times 10^5$, sec^{-1}, for assumed % exchange of II with $(k^H/k^D)^a$ = 1.6, 2.7, or 5.0 90	70	50	30
Isom without exchange	k_4	0.0256	0.077	0.128	0.179
Exchange of starting material	k_5	19.1	19.1	19.1	19.1
Isom with exchange	k_6	0.174	0.123	0.072	0.021
Isom of exchanged starting material	k_7	*b*	*b*	*b*	*b*
Intramolecularity	$k_4/(k_4 + k_6)$	0.13	0.38	0.64	0.89
Collapse ratio	k_5/k_6	110	155	265	910

[a] Primary deuterium isotope effect = $(k_4 + k_6)/k_7$. [b] k_7 varied with the value of (k^H/k^D); k_7 = 0.125, 0.075, and 0.040 × 10^{-5} sec^{-1} for (k^H/k^D) = 1.6, 2.7, and 5.0, respectively.

give a collapse ratio between 155 and 265.[18] Thus, a collapse ratio greater than 20 appears likely, and the reaction mechanism with carbanion A as the major intermediate in the isomerization of I to II is considered highly probable.

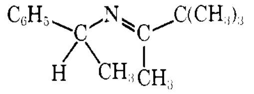
Other mechanisms would involve either the very high energy carbanion D or the isomerization of carbanion (−)-A to B without movement of potassium ion with respect to the neopentyl center. However, several open-chain allylic carbanions have been shown to be configurationally stable in *tert*-butyl alcohol–potassium *tert*-butoxide.[17a,b,19] Freedman, *et al.*,[20] have investigated the behavior of several allyl alkali metal salts in tetrahydrofuran by nmr, and one allylic carbanion has been shown[20a] to be configurationally unstable. However, geometric isomerization through the intermediacy of covalent allyllithium species was not ruled out.

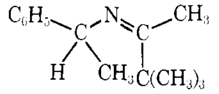
Comparison of the I → II and III → IV Reactions. In the previous section, we concluded that A is the only azaallylic carbanion that contributes materially to the course of the reaction, and that the collapse ratio is high valued. These conclusions are consistent with the results of the III–IV system.[6] The potassium *tert*-butoxide catalyzed isomerization of (−)-III-H,D to (+)-IV-D was also 100% stereospecific, and carbanion E was invoked as the sole intermediate. Carbanion E is analogous to carbanion A in the sense that it is the most sterically favored of the four geometrically isomeric carbanions available to the system. With respect to carbanion E, the stereospecific proton transfer occurred in a cis or suprafacial manner.

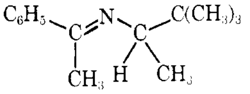

E

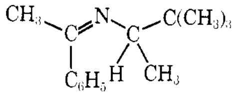
Similarity between the two systems was further demonstrated by comparison of k_e/k_α values for (−)-I-H and (−)-III-H in *tert*-butyl alcohol-*O*-*d*–potassium *tert*-butoxide: 41 for (−)-I-H at 175° (run 9) and 35 for (−)-III-H at 75°. Both of these values are actually too high because the calculated rates of racemization, k_α, were lower than the actual rates. Using a kinetic scheme a corrected value of $k_e/k_\alpha = 21$ has been calculated[6] for (−)-III-H, and the corrected k_e/k_α value for (−)-I-H would probably be about the same. The similar k_e/k_α values point directly to a similarity of intermediates in the two systems, namely carbanions A and E.

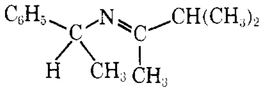
Syn–Anti Isomerization of Imines I and II. We have formulated I and II as present only as the anti isomers since only the anti isomers were detected at 40° by nmr. In the nmr spectrum of imine V at about 40°, the syn isomer was observed and the syn–anti ratio was 7:93.[10] It would seem reasonable that small equilibrium amounts of *syn*-I and *syn*-II were present at 175°. However, the isomerization of I → II almost certainly proceeded exclusively through *anti*-I for the following reasons. By Hammond's postulate,[21] the transition state for ionization of I closely resembles the high-energy carbanion intermediate, and without geometric isomerization concomitant with ionization, only carbanions C and D, both very unfavorable species, could result from the ionization of *syn*-I. Simultaneous geometric isomerization is unlikely if the transition states resemble carbanion because allylic carbanions have been shown to be geometrically stable.[19,20] The behavior of other similar systems[10] indicates that at 175° the equilibrium between *syn*- and *anti*-I was established much more rapidly than I isomerized to II.

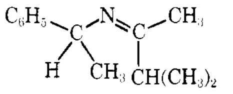

anti-I


syn-I


anti-II


syn-II


anti-V


syn-V

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(18) For isomerization of I to II with carbanion A as intermediate

$$\mathrm{I} \underset{k_{-a}}{\overset{k_a}{\rightleftarrows}} \mathrm{A} \underset{k_{-b}}{\overset{k_b}{\leftrightarrows}} \mathrm{II}$$

and $K = \mathrm{II}/\mathrm{I} = (k_a/k_b)(k_{-b}/k_{-a}) = k_i/k_{-i} = 4.1$. With k_{-a}/k_{-b} = *ca.* 200, essentially every ionization of II resulted in isomerization (stereospecific) to I, and therefore, II did not racemize once formed. The ratio of kinetic acidities, k_a/k_b, is *ca.* 800. The high collapse ratio k_{-a}/k_{-b} masked this tremendous difference in ionization rates and resulted in comparable isomerization rates, k_i and k_{-i}.

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

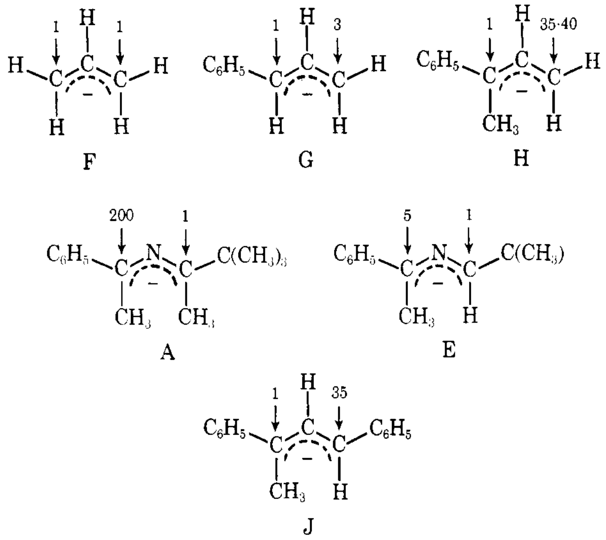
(20) (a) H. H. Freedman, V. R. Sandel, and B. P. Thill, *ibid.*, **89**, 1762 (1967); (b) V. R. Sandell, S. V. McKinley, and H. H. Freedman, *ibid.*, **90**, 495 (1968).

(21) G. S. Hammond, *ibid.*, **77**, 334 (1955).

Dependence of Stereospecificity on Potassium. Run 12 was made in dimethyl sulfoxide–*tert*-butyl alcohol–potassium *tert*-butoxide at 75°, and both recovered starting material and product were racemic. For dimethyl sulfoxide–*tert*-butyl alcohol–potassium *tert*-butoxide mixtures similar to that used in run 12, it was concluded[22] that free *tert*-butoxide ion was the active base in proton abstraction. In the present system, *tert*-butoxide also was probably the active base, and abstraction of a proton by *tert*-butoxide would yield a carbanion intermediate not ion paired to potassium. As noted, no asymmetric induction was observed in run 12, and this fact is consistent with the interpretation that potassium carbanide ion pair intermediates were requisite for stereospecific isomerization of I to II.

Collapse Ratio Comparisons. It is interesting to compare the collapse ratios of azaallylic carbanions A and E in *tert*-butyl alcohol–potassium *tert*-butoxide with those of several allylic carbanions in the same solvent–base system: F, G,[17b] H,[17c] and J[19] (Chart IV). By definition, the collapse ratio of symmetrical carbanion F is unity. Substitution of a phenyl group for a pseudoequatorial hydrogen gives carbanion G with a collapse ratio of only about 3 favoring the unsubstituted center. Further substitution of a methyl group for a pseudoaxial hydrogen of G gives carbanion H with a collapse ratio of about 35–40 favoring the unsubstituted center. Finally, substitution of an additional phenyl group for the remaining pseudoequatorial hydrogen of H gives carbanion J with essentially the same collapse ratio of about 35. The similarity of collapse ratios for H and J and the low value for G led to the conclusion that a phenyl group has little effect on a collapse ratio. The marked unbalancing of the collapse ratio on going from F and G to H and J must therefore be due to inductive and steric effects of the methyl group. Perhaps the corresponding effects for a phenyl group cancel each other. In carbanion E, the effect of the *tert*-butyl group overpowers that of the methyl group, and the collapse ratio favors the benzylic center. Substitution of a methyl group for the remaining hydrogen of E gives carbanion A with a collapse ratio of about 200 favoring the benzylic center. The effects of the two methyl groups probably are cancelled, and the great unbalancing of the collapse ratio is due to the inductive and steric effects of the *tert*-butyl group.

Chart IV



Experimental Section

General. The instruments used and data reported are as in paper XLVIII.[6b]

Solvents and Bases. The purification of *tert*-butyl alcohol has been described[17a] and *tert*-butyl alcohol-*O*-*d* was prepared using an established procedure.[23] The preparation of solutions of potassium *tert*-butoxide in *tert*-butyl alcohol and in *tert*-butyl alcohol-*O*-*d* has been described.[17a] Dimethyl sulfoxide (DMSO) was purified by distillation from potassium amide onto activated molecular sieves. Solutions of potassium *tert*-butoxide in DMSO–*tert*-butyl alcohol were prepared by the dilution of *tert*-butyl alcohol–potassium *tert*-butoxide solutions with DMSO. Other solvents were reagent grade and were used without further purification.

Gas–Liquid Chromatography (Glc). Analytical and Preparative. Analyses and preparative separations were carried out on four columns: column A, 6 ft × 1/4 in. aluminum column packed with 15–20% Carbowax 20M on 60–80 mesh firebrick; column B, 10 ft × 1/4 in. aluminum column packed with 30% Hyprose SP 80 on 60–80 mesh Chromosorb W NAW; column C, 6 ft × 1/4 in. aluminum column packed with 5% *m*-phenyl ether (five ring) on >20 mesh Fluoropak; column D, 3 ft × 1/4 in. aluminum column packed with 20% SE-30 on 60–80 mesh firebrick. Columns A, B, and C were installed in a Perkin-Elmer Model 154 gas chromatograph, and a helium carrier gas pressure of 15 psi was employed throughout. Column D was installed in a F and M Model 720 gas chromatograph, and a helium carrier gas flow rate of 60 ml/min was employed. For columns A and B, oven temperatures of 140–160° and 73°, respectively, were employed, and those for columns C and D were as noted. For most analytical determinations a cut-and-weigh method of integration was employed using Keuffel and Esser Co. Albanene tracing paper, with the remainder being done by disc integration. These two methods gave essentially identical results as determined by multiple analysis of the same glc trace. Also, Varian-Aerograph has reported[24] that the cut-and-weigh procedure is as accurate as disc integration. Retention times in minutes on column A at 143° were as follows: I, 24.8; II, 41.4; acetophenone, 23.4; α-phenylethylamine, *ca.* 17, severe tailing; pinacolone, 1.4; pinacolylamine, *ca.* 3, severe tailing; *n*-pentadecane, 12.8; DMSO, *ca.* 17, severe tailing.

Limits of Error. Generally, limits of error were determined using the total differential method. However, when calculations involved exponential or logarithmic expressions, they were determined by substitution of appropriate maximum and minimum values. The pseudo-first-order isomerization rate constants, k_i, of Table III were assigned errors of ±5% for *inter*-run comparisons; the limits of error for k_1 and k_3 of Table IV were determined for *intra*-run comparisons.

(±)-*N*-(α-Methylneopentylidene)-α-phenylethylamine [(±)-I][10] Using Titanium Tetrachloride. In a dry system under a pure nitrogen atmosphere, 43.1 g (0.228 mol) of titanium tetrachloride was added with stirring during 15 min to a solution of 216.0 g (1.78 mol) of α-phenylethylamine and 89.0 g (0.89 mol) of pinacolone in 100 ml of benzene at 0°. Brown solid immediately precipitated, and an additional 225 ml of benzene was added. Stirring was continued at 25° for 25 hr, after which time the reaction mixture was added to 2 l. of 0.5 *N* sodium hydroxide. The resulting mixture (pH 10) was extracted with ether, and all extracts were combined, washed with 300 ml of 0.8 *N* sodium hydroxide, and dried. Rotary evaporation left 284 g of a yellow oil, which was fractionally distilled to give 79.3 g (44%) of (±)-I, bp 136–141° (*ca.* 20 mm). This material was 100% pure by glc (column D, 175°) and was redistilled to give 71.3 g (39%) of (±)-I, bp 53–54° (0.08 mm). *Anal.* Calcd for $C_{14}H_{21}N$: C, 82.70; H, 10.41. Found: C, 82.74; H, 10.66.

The ir spectrum of I in chloroform showed an intense band at 6.07 μ assigned to the carbon–nitrogen double bond stretch. The uv spectrum of I in absolute ethanol displayed a complex series of absorptions with maxima at 248 nm, log ε 2.46; 252 nm, log ε 2.51; 258 nm, log ε 2.54; 261 nm, log ε 2.46. The nmr spectrum of I

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[22] D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Amer. Chem. Soc.*, **83**, 3688 (1961).

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

[24] "Research Notes," Varian-Aerograph, Walnut Creek, Calif., Fall, 1966.

in carbon tetrachloride exhibited a complex multiplet from τ 2.58 to 3.03 (phenyl protons, 4.92), a symmetrical quartet centered at 5.52, J = 6.5 Hz (benzyl proton, 0.90), a singlet at 8.29 (vinyl methyl protons, 2.89), a symmetrical doublet centered at 8.67, J = 6.5 Hz (benzyl methyl protons, 3.36), and a singlet at 8.90 (*tert*-butyl methyl protons, 8.99).

(−)-*N*-(α-Methylneopentylidene)-α-phenylethylamine [(−)-I] Using Titanium Tetrachloride. The procedure essentially followed that for the preparation of (±)-I. From (−)-α-phenylethylamine,[8] $\alpha^{25}\mathrm{D}$ −38.16 ± 0.03° (neat, 1 dm), was obtained (−)-I, $[\alpha]^{25}\mathrm{D}$ −21.2 ± 0.2°, $[\alpha]^{25}{}_{546}$ − 25.3 ± 0.2° (*c* 5.18, chloroform), and $[\alpha]^{25}{}_{546}$ −24.4 ± 0.2° (*c* 0.821, chloroform). Analysis of this material by glc (column A, 143°) indicated only one impurity, an unidentified component with retention time 38.9 min, present to the extent of less than 0.4%. Similarly, glc provided an analytical sample. *Anal.* Calcd for $C_{14}H_{21}N$: C, 82.70; H, 10.41. Found: C, 82.62; H, 10.55.

(+)-*N*-(α-Methylneopentylidene)-α-phenylethylamine [(+)-I] Using Zinc Chloride Complex. In a dry system under a pure nitrogen atmosphere, a mixture of 100 ml of *cis*- and *trans*-decalin, 11.7 g (0.097 mol) of (+)-α-phenylethylamine,[8] $\alpha^{25}\mathrm{D}$ 37.88 ± 0.03° (neat, 1 dm), 16.2 g (0.162 mol) of pinacolone, and 88 mg of zinc chloride-(±)-phenylethylamine complex[12] was refluxed for 19.5 hr. The reaction mixture was dried over sodium sulfate and saturated with dry hydrogen chloride to precipitate the hydrochlorides of (+)-I and (+)-α-phenylethylamine, which were collected by filtration. The hydrochloride mixture was added to 100 ml of 1.8 *N* sodium hydroxide, and the resulting alkaline mixture was extracted with three 30-ml portions of ether, which were combined and dried. The ether was rotary evaporated to leave 17.9 g of a yellow oil, which was fractionally distilled to remove excess α-phenylethylamine. Material up to bp 133° (*ca.* 20 mm) was collected, and the pot residue, 1.5 g, was distilled (0.1 mm) through a short, heated column to give 1.10 g (6%) of (+)-I, $[\alpha]^{25}\mathrm{D}$ 21.0 ± 0.2° (*c* 5.02, chloroform), which was pure by glc (column D, 175°).

(±)-*N*-(α-Methylbenzylidene)pinacolylamine [(±)-II] Using Titanium Tetrachloride. The procedure essentially followed that for the preparation of (±)-I. From 13.5 g (13.4 mmol) of (±)-pinacolylamine and 17.6 g (14.6 mmol) of acetophenone was obtained 5.40 g (20%) of (±)-II, bp 98–117° (*ca.* 20 mm). This material was redistilled to give (±)-II, bp 55–57° (0.2 mm), pure by glc (column A), and similarly, glc provided an analytical sample. *Anal.* Calcd for $C_{14}H_{21}N$: C, 82.70; H, 10.41. Found: C, 82.62; H, 10.26.

The ir spectrum of II taken neat and in chloroform showed an intense band at 6.10 μ, which was assigned to the carbon–nitrogen double bond stretch. The uv spectrum of II in cyclohexane displayed a broad absorption band with a maximum at 241 nm, log ε 4.16, and a shoulder at 280 nm, log ε 2.71; in absolute ethanol the uv spectrum was almost identical with a maximum at 239 nm, log ε 4.13, and a shoulder at 280 nm, log ε 2.66. The nmr spectrum of II in carbon tetrachloride displayed a complex multiplet from τ 2.08 to 2.35 (ortho protons, 1.93), a complex multiplet from 2.60 to 2.90 (meta and para protons, 3.20), a symmetrical quartet centered at 6.70, J = 6.5 Hz (methine proton, 0.98), a singlet at 7.90 (benzyl methyl protons, 2.88), one-half of a doublet at 8.96, and a singlet at 9.05, under which lay the other half of the doublet (neopentyl and *tert*-butyl methyl protons, respectively, 12.0 total).

(+)-*N*-(α-Methylbenzylidene)pinacolylamine [(+)-II] Using Titanium Tetrachloride. The procedure essentially followed that for the preparation of (±)-II. From (+)-pinacolylamine, $\alpha^{25}\mathrm{D}$ 4.39 ± 0.03° (neat, 1 dm), was obtained (+)-II in 53% crude yield. Preparative glc (column A) yielded (+)-II, $[\alpha]^{25}\mathrm{D}$ 86.9 ± 0.7°, $[\alpha]^{25}{}_{578}$ 91.3 ± 0.7°, $[\alpha]^{25}{}_{546}$ 106.2 ± 0.8°, $[\alpha]^{25}{}_{436}$ 211 ± 1°, $[\alpha]^{25}{}_{365}$ 454 ± 3° (*c* 1.21, chloroform). *Anal.* Calcd for $C_{14}H_{21}N$: C, 82.70; H, 10.41. Found: C, 82.78; H, 10.24.

The ORD spectrum of (+)-II in cyclohexane, 1.22 × 10^{-4} *M*, has been reported.[2]

Resolution of (±)-Pinacolylamine. The preparation of (±)-pinacolylamine employed a procedure similar to that of Stevens and Richmond,[25] and it was converted to and resolved through (±)-*N*-pinacolylphthalamide acid using known procedures.[9] Optically pure (+)-*N*-pinacolylphthalamide acid, $[\alpha]^{25}\mathrm{D}$ 26.3 ± 0.4° (*c* 2.00, ethyl acetate), on hydrolysis yielded (+)-pinacolylamine, bp 100–102°, $\alpha^{25}\mathrm{D}$ 4.084 ± 0.003° (neat, 1 dm). By glc (column B) ether was the only impurity. This material was redistilled from potassium hydroxide to give (+)-amine, bp 100–102°, $\alpha^{25}\mathrm{D}$ 4.39 ± 0.03°, $\alpha^{25}{}_{546}$ 5.37 ± 0.03° (neat, 1 dm). A further distillation from sodium hydroxide yielded material with the same rotations, and glc (column C, 40°) provided an analytical sample. *Anal.* Calcd for $C_6H_{15}N$: C, 71.22; H, 14.94. Found: C, 71.56; H, 14.90.

The rotation for optically pure (+)-pinacolylamine obtained above is higher than the value calculated from the data of Pracejus and Winter, $\alpha^{25}\mathrm{D}$ 4.11° (neat, 1 dm).[9, 26]

Isomerization Reactions. General Procedure. Thick-walled Pyrex glass tubes were treated with hot sodium dichromate-concentrated sulfuric acid and were rinsed with distilled water, with dilute ammonium hydroxide, and again with distilled water. They were dried at 115°.

The reaction mixture was prepared in a nitrogen-flushed glass tube. Liquid reagents were added by dry, nitrogen-flushed syringes, and the tube then was fitted with a septum cap and immersed in a Dry Ice–acetone bath. After evacuation the tube was filled with nitrogen, and its contents thawed. This degassing procedure was repeated twice more, and the tube was sealed under vacuum (*ca.* 0.1 mm). The tube was warmed until the reaction mixture thawed, and it was placed in the appropriate constant temperature bath for the desired period, after which time it was opened. After work-up, glc was used for analysis and preparative separation of the isolated imine mixture.

Run 5. In a glass tube were sealed 1.36 g (1.50 ml, 6.70 mmol) of (−)-I, $[\alpha]^{25}{}_{546}$ −24.4 ± 0.2° (*c* 0.821, chloroform), and 20.0 ml of *tert*-butyl alcohol 0.41 *M* in potassium *tert*-butoxide. After 760 min at 175 ± 3°, the tube was opened, and its contents were emptied into a separatory funnel containing 25 ml each of pentane and water. The layers were separated, and the aqueous layer (pH 10) was extracted twice with 10-ml pentane portions. The combined pentane extracts were back-extracted with 10 ml of water, dried over sodium sulfate, and concentrated on a steam bath under a gentle stream of nitrogen. By glc (column A) the concentrated mixture was composed solely of I, II, and a few very low retention time impurities. The I–II mixture contained 11.0 ± 0.1% II, and I and II were preparatively separated by glc. Optical rotations of recovered I and II were recorded in chloroform: for I, $[\alpha]^{25}{}_{546}$ −18.1 ± 0.2° (*c* 0.821); −18.0 ± 0.2° (*c* 0.986); −18.2 ± 0.2° (*c* 1.15); for II, $[\alpha]^{25}{}_{546}$ −91.8 ± 0.6° (*c* 1.10). By glc (column A) a sample of I from which the rotation solutions were made showed 0.9% pinacolone as the only impurity, most likely from the hydrolysis of I. No corresponding α-phenylethylamine was detected, but this is reasonable since it tailed severely on column A.

Runs 6 and 7. In a glass tube were sealed 0.68 g (0.75 ml, 3.35 mmol) of (−)-I, $[\alpha]^{25}{}_{546}$ −24.4 ± 0.2° (*c* 0.821, chloroform), and 10.0 ml of *tert*-butyl alcohol 0.48 *M* in potassium *tert*-butoxide. After the reaction period at 175.0 ± 0.3°, the tube was opened, and the reaction mixture was worked up employing essentially the same procedure used in run 5.

Run 6 was made for 760 min, and the I–II mixture contained 11.9 ± 0.2% II. Optical rotations of recovered I and II taken in chloroform were as follows: for I, $[\alpha]^{25}{}_{546}$ −16.8 ± 0.2° (*c* 0.620); −17.0 ± 0.2° (*c* 0.676); for II, $[\alpha]^{25}{}_{546}$ −89.5 ± 0.6° (*c* 0.668). By glc (column A) a sample of II from which the rotation sample was made showed 0.8% I as the only impurity.

Run 7 was made for 764 min, and the I–II mixture contained 11.6 ± 0.3% II. Recovered II gave rotation $[\alpha]^{25}{}_{546}$ −88.9 ± 0.6° (*c* 0.711, chloroform).

Run 8. In a glass tube were sealed 0.88 g (0.97 ml, 4.33 mmol) of (+)-I, $[\alpha]^{25}\mathrm{D}$ 21.0 ± 0.2° (*c* 5.02, chloroform), and 20.0 ml of *tert*-butyl alcohol 0.5 *M* in potassium *tert*-butoxide. After 6.785 × 10^3 min of being immersed approximately two-thirds in a bath at 205 ± 3°, the tube was opened, and its contents were emptied into a separatory funnel containing 50 ml of benzene and 25 ml of water. The layers were separated, and the aqueous layer was extracted twice with 10-ml portions of benzene. The combined extracts were dried and concentrated on a steam bath under a gentle stream of nitrogen. By glc (column D, 175°) the I–II mixture contained 80.2% II, and after residual benzene was removed on a rotary evaporator, the crude I–II mixture was distilled twice under vacuum (*ca.* 0.1 mm) through a short, heated column. The distilled I–II mixture contained 79.6% II by glc (column A). Optical rotations

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(25) P. G. Stevens and J. H. Richmond, *J. Amer. Chem. Soc.*, **63**, 3135 (1941).

(26) The rotation of (+)-pinacolylamine was reported as a specific rotation for a neat sample rather than as an observed value for a neat sample. The rotation must have been the latter since the density of pinacolylamine has never been reported, and this would make the observed value even smaller since the density is certainly less than unity.

of recovered I and II taken in chloroform were as follows: for I, $[\alpha]^{25}\text{D}$ 0.8 ± 0.3° (*c* 1.06); for II, $[\alpha]^{25}\text{D}$ 17.2 ± 0.2° (*c* 2.58). A sample of II from which the rotation solution was made was analytically pure. *Anal.* Calcd for $C_{14}H_{21}H$: C, 82.70; H, 10.41. Found: C, 82.75; H, 10.43.

Run 9. In a glass tube were sealed 0.181 g (0.200 ml, 0.891 mmol) of (−)-I, $[\alpha]^{25}_{546}$ −24.4 ± 0.2° (*c* 0.821, chloroform), and 9.0 ml of *tert*-butyl alcohol-*O-d* (0.99 atom of excess deuterium per molecule by combustion and falling drop analysis) 0.40 *M* in potassium *tert*-butoxide. After 120 min at 175 ± 3°, the tube was opened, and the reaction mixture was worked up employing essentially the same procedure used in run 5. The I–II mixture contained 1.00 ± 0.04% II; recovered I gave rotation $[\alpha]^{25}_{546}$ −23.6 ± 0.2° (*c* 0.593, chloroform) and was analyzed by nmr for deuterium at the methine position using a reported procedure.[19] The integral ratio of the absorption of the residual methine proton *vs.* that of the phenyl protons was determined and compared to the analogous ratio for perprotio-I (0.93:5.00) determined under identical conditions. Two analyses on different days gave 74.5 and 74.9% exchange.

Run 10. In a glass tube were sealed 0.045 g (0.049 ml, 0.22 mmol) of (±)-I and 0.68 ml of *tert*-butyl alcohol. After 767 min at 175 ± 3°, the tube was opened, and the reaction mixture was worked up employing essentially the same procedure used in run 5 scaled down proportionately. Analysis by glc (column A) demonstrated the absence (⩽0.1%) of II in recovered imine I.

Run 11. In a glass tube were sealed 0.091 g (0.100 ml, 0.45 mmol) of (−)-I, $[\alpha]^{25}_{546}$ −24.4 ± 0.2° (*c* 0.821, chloroform), and 1.35 ml of *tert*-butyl alcohol-*O-d* (0.92 atom of excess deuterium per molecule by nmr). After 1080 min at 175 ± 3°, the tube was opened, and the reaction mixture was worked up employing essentially the same procedure used in run 5 scaled down proportionately. Analysis by glc (column A) demonstrated the absence (⩽0.1%) of II in recovered imine I, $[\alpha]^{25}_{546}$ −24.5 ± 0.2° (*c* 0.754, chloroform). Also, I was analyzed by nmr for deuterium at the benzyl position as in run 9. The integral ratio of the absorption of the methine proton *vs.* that of the phenyl protons was 0.92:5.00, and the absorption of the α-methyl group was a clean doublet even at high spectrum amplitude. Therefore, exchange of deuterium for protium occurred to an extent of less than 0.5%.

Run 12. In a glass tube were sealed 0.68 g (0.75 ml, 3.3 mmol) of (−)-I, $[\alpha]^{25}_{546}$ −24.4 ± 0.2° (*c* 0.821, chloroform), 9.0 ml of DMSO, and 1.5 ml of *tert*-butyl alcohol 0.41 *M* in potassium *tert*-butoxide. After 7.629×10^3 min at 75 ± 1°, the tube was opened, and its contents were emptied into a separatory funnel containing 15 ml each of pentane and water. The layers were separated, and the pentane layer was extracted three times with 5-ml portions of water. The aqueous extracts were combined with the original water layer and back-extracted with 15 ml of pentane. Finally, the combined pentane layers were dried over sodium sulfate and concentrated on a steam bath under a gentle stream of nitrogen. By glc (column A) the concentrated mixture was composed solely of I, II, and a few very low retention time components. The I–II mixture contained 25.1 ± 0.2% II, and rotations of recovered I and II were recorded in chloroform: for I, $[\alpha]^{25}_{546}$ 0° (*c* 1.17), observed α^{25}_{546} 0.000 ± 0.003°; for II, $[\alpha]^{25}_{546}$ −0.2 ± 0.3° (*c* 1.31), observed α^{25}_{546} −0.002 ± 0.003°. By glc (column A, 143°) a sample of I from which the rotation solution was made showed 0.2% of pinacolone and an even smaller impurity with retention time 0.9 min. Also, a small base-line drift was observed. A peak with retention time 0.9 min and a similar base-line drift was observed with the injection of DMSO, so it was estimated that an upper limit of 0.5% DMSO was present in I. On glc analysis of an analogous sample of II the same base-line drift and peak with retention time 0.9 min were observed.

Control Runs and Equilibration Runs of I and II. General Procedure. The reaction mixture was prepared in a glass tube using the general procedure for the isomerization runs. Work-up employed a procedure identical with that used for isomerization runs in the corresponding solvent–base system. The volumes of reagents were proportional to the amount of imine employed.

Yield Controls for Run 5. In a glass tube were sealed 0.10 ml of a mixture of I and *n*-pentadecane, 49.6 ± 0.2% I by glc (column A), and 0.70 ml of *tert*-butyl alcohol 0.41 *M* in potassium *tert*-butoxide; the resulting solution was 0.32 *M* in I. After 760 min at 175 ± 3°, the tube was opened and the reaction mixture was worked up. By glc (column A) the isolated imine–*n*-pentadecane mixture contained 48.6 ± 0.1% I + II, and this corresponds to an imine yield of 96.1 ± 0.6%.

In a glass tube were sealed 0.085 ml of a mixture of II and *n*-pentadecane, 50.5 ± 0.5% II by glc (column A), and 0.70 ml of *tert*-butyl alcohol 0.41 *M* in potassium *tert*-butyl alcohol. After 760 min at 175 ± 3°, the tube was opened, and the reaction mixture was worked up. By glc (column A) the isolated imine–*n*-pentadecane mixture contained 50.4 ± 0.1% I + II, and this corresponds to an imine yield of 100%. Of the I–II mixture, there was only 2.4% I, so a small amount of I decomposition during the reaction would not have been detected.

Yield Control for Run 12. In a glass tube were sealed 0.085 ml of a mixture of I and *n*-pentadecane, 48.6 ± 0.6% I by glc (column A), 0.6 ml of DMSO, and 0.10 ml of *tert*-butyl alcohol 0.41 *M* in potassium *tert*-butoxide. The resulting solution was 0.27 *M* in I. After 9.46×10^3 min at 75 ± 1°, the tube was opened, and the reaction mixture was worked up. By glc (column A) the isolated imine–*n*-pentadecane mixture contained 46.6 ± 0.4% I + II, and this corresponds to an imine yield of 94 ± 2%.

Stability of I to Isolation. To 0.10 ml of a mixture of I and *n*-pentadecane, 49.7 ± 0.5% I by glc (column A), was added 0.70 ml of *tert*-butyl alcohol 0.41 *M* in potassium *tert*-butoxide; the resulting solution was 0.32 *M* in I. The mixture was then worked up immediately, and by glc (column A) the I–*n*-pentadecane mixture contained 51.1 ± 0.5% I; this corresponds to a 100% yield for I.

Thermal Conductivity of I *vs.* II. A mixture of I and II was prepared containing 12.7 ± 0.1% II by weight. It was dissolved in a small amount of cyclohexane and by glc (column A) it contained 12.5 ± 0.1% II.

Stereochemical Stability of I and II to Glc (Column A). Imine (−)-I gave rotation $[\alpha]^{25}_{546}$ −24.4 ± 0.2° (*c* 0.821, chloroform) before and $[\alpha]^{25}_{546}$ −24.6 ± 0.2° (*c* 1.15, chloroform) after glc collection. Imine (+)-II gave rotation $[\alpha]^{25}_{546}$ 106.2 ± 0.8° (*c* 1.21, chloroform) before and $[\alpha]^{25}_{546}$ 105.7 ± 0.8° (*c* 1.25, chloroform) after an additional glc collection.