Except in cases possessing special symmetry axes, two alternative conrotatory or disrotatory processes are possible and physically differentiable (cf. XVIII and XIX). Ordinarily, simple steric factors will be expected to direct the changes preferentially along one of the two paths, but in some cases, very interesting special stereoelectronic factors may be definitive. Thus, when a cyclopropyl cation is produced by ionization of a group X, and suffers concerted electrocyclic transformation to an allyl cation, our calculations indicate that the favored processes are XX and XXI.

XX   XXI
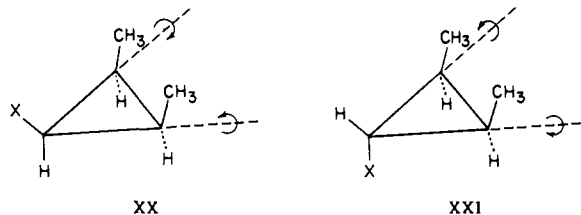
(10) Junior Fellow, Society of Fellows, Harvard University.
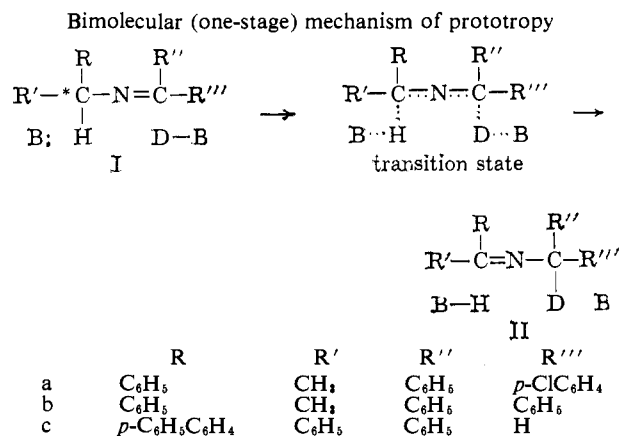
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On the Claim of a Bimolecular Mechanism of Prototropy

Sir:

The claim of a "bimolecular mechanism of prototropy" was based on an identity of values for the initial rate constants for k_i (isomerization), k_e (isotopic exchange), and k_α (loss of optical activity) for ethoxide ion catalyzed conversion of I to II in solvents such as 2:1 dioxane–ethanol-O-d or ethanol-O-d.[1]

Bimolecular (one-stage) mechanism of prototropy

|	R	R'	R''	R'''
a	C_6H_5	CH_3	C_6H_5	p-ClC_6H_4
b	C_6H_5	CH_3	C_6H_5	C_6H_5
c	p-$C_6H_5C_6H_4$	C_6H_5	C_6H_5	H

The discovery of an intramolecular component in the base-catalyzed rearrangement of 3-phenyl-1-butene to cis- and trans-3-phenyl-2-butene,[2] coupled with the fact that the rearrangement competes with simple isotopic exchange,[2b] led us to re-examine the evidence for a one-stage mechanism in the similar methylene-azomethine rearrangement.[3] Interconversions of III

(1) (a) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 572; (b) C. K. Ingold and C. L. Wilson, *J. Chem. Soc.*, 1493 (1933); (c) C. K. Ingold and C. L. Wilson, *ibid.*, 93 (1934); (d) S. K. Hsu, C. K. Ingold, and C. L. Wilson, *ibid.*, 1774 (1935); (e) R. P. Ossorio and E. D. Hughes, *ibid.*, 426 (1952).
(2) (a) D. J. Cram and R. T. Uyeda, *J. Am. Chem. Soc.*, **84**, 4358 (1962); (b) D. J. Cram and R. T. Uyeda, *ibid.*, **86**, 5466 (1964).

and IV and of V and VI were investigated.[4] Values of 1.2 for k_{eq}(IV/III) and of 14.9 for K_{eq}(VI/V) were obtained at 100°.

III   IV

V   VI
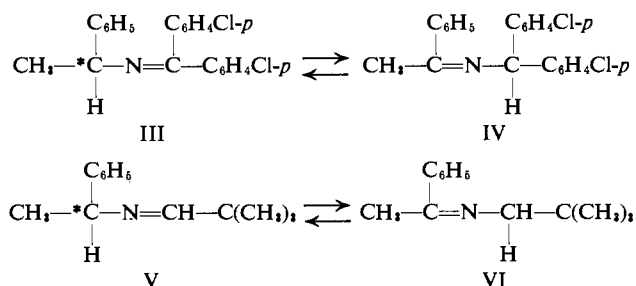
Optically active III was allowed to undergo about 8% isomerization to IV as a 0.18 M solution in 1:1 dioxane–ethylene glycol-O-d, 0.22 N in potassium glycoxide at 100°. The amount of product present was determined by an n.m.r. technique with an added internal standard. The mixture was hydrolyzed, and the α-phenylethylamine (isolated by v.p.c.) had undergone 2.8 ± 2% racemization and no isotopic exchange (n.m.r. with an internal standard). These observations are compatible with $k_i = k_\alpha = k_e$ for III → IV.

After a 0.17 M solution of IV in a 1:1 dioxane–ethylene glycol-O-d mixture (0.22 M in potassium glycoxide) at 100° was about 10% isomerized, the methyl and benzhydryl hydrogens of the starting material (n.m.r.) were >95% exchanged ($k_e \gg k_i$). After a 0.26 M solution of IV in t-butyl alcohol-O-d (0.0782 N in potassium t-butoxide) at 75° was 2.5 ± 0.1% isomerized (hydrolysis and v.p.c. with internal standard), the starting material was 38.2% exchanged at the benzhydryl (combustion and falling drop method), and 68 ± 4% (of 3 protons) exchanged at the methyl position (n.m.r.). If k_e' is the rate constant for isotopic exchange of IV at the benzhydryl position, then $k_e'/k_i \sim 19$. This value approximates the ratio of rate constants for collapse of a carbanion intermediate in t-butyl alcohol to give IV and III, respectively (k_a/k_b). The results of the run made in dioxane–ethylene glycol indicate that $k_e'/k_i > 10$ in this solvent as well.
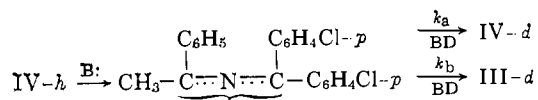
The high values of this collapse ratio indicate why the rate constants k_i, k_α, and k_e were equal for III → IV in spite of the fact that a carbanion intervened as an intermediate. Compound III structurally resembles Ia, and dioxane–ethylene glycol–glycoxide *is* similar to dioxane–ethanol–ethoxide. We conclude that carbanions intervened as intermediates in the conversions of I to II, and that the observed equalities of k_i and k_α, and of k_i, k_α, and k_e of the previous work, reflect a carbanion collapse ratio that strongly favored product, as in the conversion of III → IV.

A 0.305 M solution of optically active V in t-butyl alcohol-O-d, 0.441 M in potassium t-butoxide at 75°,
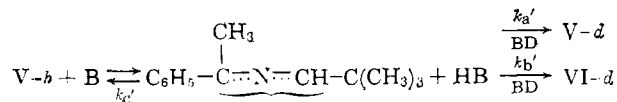
(4) Carbon and hydrogen analyses for all new compounds gave values within 0.3% of theory, and the physical properties of known compounds checked literature values.

was 16.6% isomerized (ultraviolet and v.p.c. analysis). The recovered starting material (v.p.c.) was 57% isotopically exchanged (combustion and falling drop method) but only 3.02 ± 0.06% racemized. The isolated (v.p.c.) product, VI, had undergone 62% exchange of one atom of hydrogen for deuterium in the neopentyl position. The imine was hydrolyzed in acid, and the benzamide of the amine produced was analyzed (combustion and falling drop method). In a control experiment, V did not isomerize, racemize, or exchange in t-butyl alcohol at 75° in the absence of base.

If k_e' is the rate constant for exchange of V at the benzyl position, then $k_e'/k_i \sim 4.7$.[5] This value approximates the ratio of rate constants for collapse of a carbanion to give V and VI (k_a'/k_b') if all carbanion collapse to V involves exchange. The % intramolecularity for conversion of V to VI is calculated from the

(5) The amount of V regenerated from carbanion at 17% conversion of V to VI is too small to affect this value substantially. The primary isotope effect, however, does affect k_e'/k_i because the value of k_i decreases as deuterium accumulates in V. A run carried to 6.6% isomerization gave $k_e'/k_i \sim 3.6$.

exchange observed in VI to be a minimum of 38%. If exchange of V before isomerization is taken into account, the intramolecularity becomes roughly 50%. Correction of the collapse ratio accordingly gives $(k_a' + k_c')/k_b' \sim 7$. If k_α' is the rate constant for racemization of the starting material, then $k_e'/k_\alpha' \sim 28$. This value indicates that isotopic exchange of V occurs with high retention of configuration in t-butyl alcohol.

$$V\text{-}h + B \underset{k_c'}{\rightleftharpoons} C_6H_5 - \overset{\overset{\displaystyle CH_3}{|}}{C \cdots N \cdots CH} - C(CH_3)_3 + HB \quad \begin{array}{c} \xrightarrow[BD]{k_a'} V\text{-}d \\ \xrightarrow[BD]{k_b'} VI\text{-}d \end{array}$$

Clearly carbanions intervene as intermediates in these isomerization, racemization, and exchange reactions, and the claim for a bimolecular mechanism of prototropy is without secure foundation.

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Book Reviews

This book might have been given a title such as "Chromatography and Related Methods" since more than two-thirds of the book is devoted to chromatography. Much of the remainder discusses the related differential migration methods of counter-current distribution (one chapter) and electrophoresis (two chapters). There is also a chapter on membrane separation and one on miscellaneous methods (differential sedimentation and differential solubility). The part of the book on chromatography is organized into the classical divisions of adsorption, partition, and ion exchange. In each case there are separate chapters on theory, experimental methods, and applications. Paper chromatography is considered separately. There are also chapters on general theory and detection of solutes in effluents.

The emphasis on chromatography does not reflect a bias of the authors but rather the current state of biochemistry. As the authors note, it is only necessary to peruse recent biochemical journals to be impressed by the importance which chromatographic methods have achieved. This revolution has occurred in recent years and is only now approaching a plateau where further advances will be largely technical improvements. For this reason, this book appears at an opportune time. It includes the most recent techniques (such as gradient elution and molecular sieve chromatography) and should not soon be out of date.

Since the book has only two authors, it has the coherence which is so often lacking when there are many authors. At the same time it does not suffer greatly from the fact that two authors cannot be expert in every area discussed. The writing is clear, the organization is logical, and coverage of the subject is detailed and in general complete.

A good index, a comprehensive (though not complete) bibliography, and the inclusion of experimental details and numerous tables and figures make this book valuable as a reference. However, I would foresee its greatest use as a textbook for a graduate course in biochemical separation methods or chromatography. Its writing arose out of a series of lectures, and perhaps its availability will

stimulate the addition of this course to graduate school curriculums.

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The rapidly increasing application of radioactivation analysis makes this a most welcome book for anyone interested in problems in chemical analysis and for the student, especially in view of the paucity of books in the field.

Little knowledge of the phenomena of radioactivity is assumed. For those who feel the need of some review of such information, a summary of the fundamentals of radioactive decay characteristics and measurement is given in an appendix. As the title suggests, the discussion of activation analysis is limited to that following neutron irradiation, the most available type. In addition to the usual modern methods employed in activation analysis, with and without chemical separations, the use of the more recently developed technique of measuring the "prompt radiation" emitted after neutron capture is also emphasized.

Numerous illustrations of applications to analysis are given. These have been carefully selected with a view to bringing out the variety, sensitivity, errors, limitations, and difficulties of which one should be aware in making the necessary measurements. The application of automation, including possible use of computers, to instrumental radioactivation analysis is the subject of one chapter. The closing chapter takes a brief look at special applications, some current and some for future development.

The book is recommended as supplying an excellent review of the modern aspects of activation analysis. It is not intended as a text or operations manual; such information can be obtained from the numerous references to the original literature.

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