increment 2, etc., X_1 the percentage of X formed during time increment 1, X_2 during time increment 2, etc., X_t the total percentage of X formed during reaction time t, then the activity α_A of X theoretically to be expected for the internal mechanism, which is independent of the concentration and activity of M present in the reaction mixture, is approximately

$$\alpha_A = \beta_1 X_1/X_t + \beta_2 X_2/X_t + \ldots\ldots + \beta_i X_i/X_t$$

The activity α_B of X expected for external mechanism is dependent on the concentration of N and M. The decrease of the starting material N is due to formation of X with time and can be extrapolated from the plot $\% X_t$ *vs.* time.

It was noted that some M sublimes out of the reaction mixture. The amount of M actually present during the reaction time was determined by titration.

Considering these two factors, the activity α_B of X theoretically to be expected for the external mechanism is approximately

$$\alpha_B = [(\beta_0 - \beta_1)X_1/X_t]N_1/M_1 + [(\beta_0 - \beta_2)X_2/X_t]N_2/M_2 + \ldots\ldots + [(\beta_0 - \beta_i)X_i/X_t]N_i/M_i,$$

where $\beta_0 - \beta_1$ is the average activity of M during time increment 1, $\beta_0 - \beta_2$ during time increment 2, etc., N_1 the average amount of N present in the reaction mixture during time increment 1, N_2 during time increment 2, etc., M_1 the average amount of M present in the reaction mixture during time increment 1, M_2 during time increment 2, etc.

The theoretical and experimental activities expressed in percentage of the original activity of N obtained are shown for a reaction time of 10 min. (Table II).

Table II. Radioactivity of X[a]

		% of original activity of N
Calculated	internal pathway only	70
	external pathway only	31[b]
Experimental (two runs)[c]		32.4 ± 1.5
		32.3 ± 1.5

[a] For a reaction time of 10 min. [b] A small correction for the rate of exchange of X with outside M (see Table I) is included here. [c] The starting concentrations were 0.267 *M* radioactive N (441.56 μc./mole) and 0.267 *M* inactive M. The activities α_t (143.18 μc./mole, respectively, 142.73 μc./mole) of X formed after time t were calculated from the activities α_r (27.66 μc./mole, respectively, 26.95 μc./mole) of recovered X (determined by isotope-dilution technique), using the formula $\alpha_r = (\alpha_s X_s + \alpha_t X_t)/(X_s + X_t)$, where α_s and X_s are the activity and weight of inactive X added and X_t (13.4%, respectively, 13.15%) the weight of X formed after time t (determined by n.m.r. integration in the same run as α_r).

The results exclude the internal pathway for the thermal interconversion of N to X in *t*-pentylbenzene and for the reasons given above render it highly unlikely in decalin as well.[15] The mechanism appears to be a retrogression of the formation of the *endo* adduct followed by recombination, contrary to the Alder rule,[16] to give the *exo* isomer.

(15) However, Professor J. A. Berson has suggested that it is conceivable that an internal mechanism depending on complex formation between M and diene might not occur in an aromatic solvent such as *t*-pentylbenzene because of competitive solvent–M complexing.

(16) K. Alder and G. Stein, *Angew Chem.*, 50, 510 (1937).

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Received April 28, 1965

Acid-Catalyzed 1,5-Hydride Transfer in Acyclic Molecules. Mechanism and Stereochemistry

Sir:

In contrast to the common occurrence of intramolecular 1,2-hydride transfer to carbonium ions (*e.g.*, in many pinacol rearrangements and solvolytic reactions) and of intermolecular analogs,[1] there are relatively few reports of intramolecular transfer of hydride to more remote carbonium ions.[2] Most examples of such reactions are restricted to medium rings[3] or rigid polycyclic compounds in which the reacting sites are in close proximity[4] and have been regarded as due largely to the special geometrical features of these molecules. A single example of an acid-catalyzed 1,5-hydride transfer in a flexible system is the isomerization[5] of steroidal sapogenins at C-25.

Recently the polyphosphoric acid (PPA) catalyzed isomerization of a series of γ-hydroxy olefins to saturated ketones was reported[6] (eq. 1). Several conceivable

$$R_1R_2C{=}CH(CH_2)_2CHOHCH_3 \xrightarrow{PPA} R_1R_2CH(CH_2)_3COCH_3 \quad (1)$$

I, $R_1 = R_2 = CH_3$ III, $R_1 = R_2 = CH_3$
II, $R_1 = CH_3$, $R_2 = C_6H_5$ IV, $R_1 = CH_3$, $R_2 = C_6H_5$

mechanisms for this transformation were listed, including (a) migration of the double bond to an enolic position, (b) internal hydride transfer of the O–H hydrogen, and (c) internal transfer of the carbinol C–H. We wish to report evidence that this latter mechanism is the correct one and that consequently this reaction represents a simple, clear-cut example of intramolecular 1,5-hydride transfer to an acyclic carbonium ion.

Deuterium labeling showed that it is the hydrogen attached to the carbinol carbon which migrates in the isomerization. 2-Deuterio-6-methylhept-5-en-2-ol (I-D), heated with PPA, gave 6-deuterio-6-methylheptanone-2 (III-D) in 47% yield. The position of the label was shown unequivocally by the n.m.r. spectrum of the semicarbazone of III-D, m.p. 154–155°, in which the *gem*-dimethyl group appeared as a sharp

(1) N. C. Deno, H. J. Peterson, and G. S. Saines, *Chem. Rev.*, 60, 7 (1960).

(2) For examples of 1,3-hydride shifts see (a) J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *J. Am. Chem. Soc.*, 76, 4501 (1954); (b) N. L. Wendler, R. P. Graber, C. S. Snoddy, Jr., and F. W. Bollinger, *ibid.*, 79, 4476 (1957); (c) J. A. Berson in "Molecular Rearrangements," Part I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp. 139–155.

(3) For reviews see (a) A. C. Cope in "Proceedings of the Robert A. Welch Foundation Conferences on Chemical Research. IV. Molecular Structure and Organic Reactions," W. O. Milligan, Ed., Houston, Texas, 1961, p. 11; (b) V. Prelog and J. G. Traynham in ref. 2c, p. 593

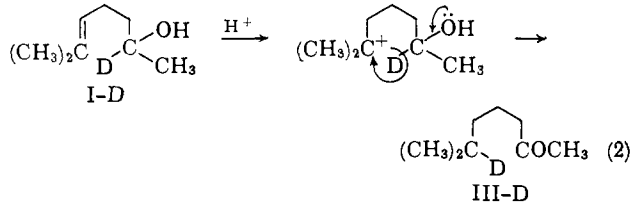
(4) (a) R. L. Letsinger and P. T. Lansbury, *J. Am. Chem. Soc.*, 81, 935 (1959); (b) R. C. Cookson and E. Crundwell, *Chem. Ind.* (London), 703 (1959); (c) S. Winstein and R. L. Hansen, *J. Am. Chem. Soc.*, 82, 6206 (1960); (d) C. F. Murphy and W. C. Wildman, *Tetrahedron Letters*, 3863 (1964); *cf.* W. C. Wildman, *Chem. Ind.* (London), 123 (1956).

(5) R. B. Woodward, F. Sondheimer, and Y. Mazur, *J. Am. Chem. Soc.*, 80, 6693 (1958).

(6) J. Colonge and J. C. Brunie, *Bull. soc. chim. France*, 1799 (1963).

singlet (6 H) at τ 0.87. The mass spectrum was consistent with this structure, with the parent peak shifted completely to *m/e* 129, and peaks of considerably higher intensity, relative to the spectrum of the undeuterated ketone, at *m/e* 114, 97, 86, 72, 30, and 28.

Since both intra- and intermolecular hydride transfer are feasible, a crossover experiment was designed to determine which mechanism is operative in this case. A 1:2 mixture of alcohols I-D and II was heated in PPA and the ketonic products were isolated. Mass spectrometric examination of the methylheptanone showed it to be completely identical with the deuterated ketone III-D obtained above, with no detectable amount (<5%) of III. The reaction is consequently entirely intramolecular and may be described by the cyclic mechanism shown in eq. 2.



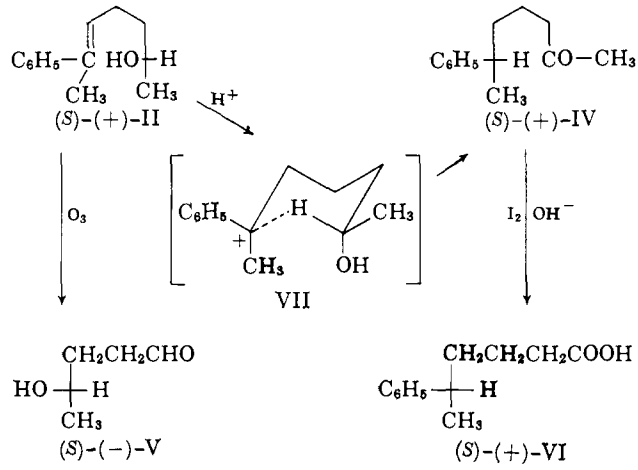
I-D

III-D (2)

It was anticipated that this isomerization, in common with other reactions involving six-membered cyclic transition states, would exhibit distinct stereospecificity. This expectation was realized by isomerizing the dextrorotatory isomer of 6-phenylhept-5-en-2-ol (II), $[\alpha]_D$ +16.9°, to 6-phenylheptanone-2 (IV, 63% yield), which proved to be optically active, $[\alpha]_D$ +2.3°. The oriented creation of a new asymmetric center simultaneous with the destruction of the original one is in accord with the demands of the cyclic transfer mechanism.

In order to determine the degree and direction of this specificity, II and IV were converted to compounds of known absolute configuration and optical purity. Ozonolysis of II, $[\alpha]_D$ +15.3°, gave (*S*)-(−)-4-hydroxyvaleraldehyde[7] (V), $[\alpha]_D$ −3.45°, while oxidation of (+)-IV with hypoiodite led to (*S*)-(+)-5-phenylcaproic acid (VI),[8] $[\alpha]_D$ +2.3°. These correlations establish first that, based on maximum rotations recorded in the literature, the reaction proceeds with an optical purity of 15%, and second that it proceeds in the steric direction shown. This result is in satisfying agreement with the prediction that the six-membered cycle would adopt a conformation resembling the cyclohexane chair (VII), with the phenyl at C-6 and the methyl at C-2 occupying equatorial positions, consonant with their larger steric requirements than methyl and hydroxyl, respectively.[11]

This discovery of an intramolecular 1,5-hydride transfer to a simple acyclic carbonium ion implies that this reaction should be much more common than heretofore realized. We are continuing studies on the stereochemistry of acid-catalyzed hydride transfer reactions.



(*S*)-(+)-II

(*S*)-(+)-IV

VII

(*S*)-(−)-V

(*S*)-(+)-VI

(7) P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **83**, 177 (1929), report $[\alpha]_D$ −7.8° for V.

(8) The absolute configuration of (+)-VI is assigned from its synthesis[9] from (+)-β-phenylbutyric acid; the correlation of (+)-β-phenylbutyric acid with (*R*)-(−)-hydratropic acid is summarized by J. H. Brewster and M. W. Kline, *J. Am. Chem. Soc.*, **74**, 5180 (1952). Since 3-phenyl-1-bromobutane with $[\alpha]_D$ +6.03° gave VI with $[\alpha]_D$ +2.01°, and the highest recorded rotation of 3-phenyl-1-bromobutane[10] is 104.3°, the maximum rotation of VI is at least 34.8°.

(9) P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **93**, 749 (1931).

(10) D. J. Cram, *J. Am. Chem. Soc.*, **74**, 2138 (1952).

(11) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 236.

(12) Alfred P. Sloan Foundation Research Fellow, 1963–1965.

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Received April 4, 1965

The Stereoselective Total Synthesis of Alantolactone

Sir:

Alantolactone (**15**) and its derivatives play a premier role in the structural elucidation of numerous eudesmane sesquiterpenes.[1] We delineate in this communication a stereoselective total synthesis of racemic alantolactone which confirms the structure[2] of the natural compound and illustrates an approach to related sesquiterpene lactones. The essential stages of the present synthesis involve: (1) construction of the carbocyclic framework *via* cationic olefin cyclization (**2** → **3**); (2) modification of the carbon framework by stereoselective photooxygenation of olefin **9** and dehydration of the related dihydro alcohol (**11** → **12**); (3) application of the recently discovered α-methylene-γ-butyrolactone synthesis (**12** → **15**).[3]

Alkylation of Hagemann's ester[4] with 4-bromobutene[5] using sodium hydride in refluxing toluene followed by saponification and thermal decarboxylation of the resulting keto acid afforded unsaturated ketone **1** [λ_{max}^{EtOH} 243 mμ (ε 12,000)]. Alcohol **2**, obtained by addition of ethereal methyllithium to ketone **1**, cyclized smoothly in formic acid under conditions employed by Johnson and co-workers for analogous compounds.[6] The resulting formate **3** was directly saponified and the alcohol **4** thus produced was oxidized with chromic acid reagent[7] giving octalone **5** whose structure was con-

(1) *Cf.* W. Cocker and T. B. H. McMurry, *Tetrahedron*, **8**, 181 (1960); W. Herz, G. Högenauer, and A. Romo de Vivar, *J. Org. Chem.*, **29**, 1700 (1964), and references therein; V. Benešová, V. Herout, and W. Klyne, *Collection Czech. Chem. Commun.*, 27, 498 (1962).

(2) J. A. Marshall and N. Cohen, *J. Org. Chem.*, **29**, 3727 (1964), and references therein.

(3) J. A. Marshall and N. Cohen, *Tetrahedron Letters*, No. 30, 1997 (1964).

(4) A. J. B. Edgar, S. H. Harper, and M. A. Kazi, *J. Chem. Soc.*, 1083 (1957).

(5) R. P. Linstead and H. N. Rydon, *ibid.*, 1995 (1934).

(6) W. S. Johnson, W. H. Lunn, and K. Fitzi, *J. Am. Chem. Soc.*, **86**, 1972 (1964).

(7) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).