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Base-Catalyzed Intramolecular 1,3- and 1,5-Proton Transfers

Sir:

Since the report of the first base-catalyzed intramolecular 1,3-proton transfer,¹ enough other examples² have appeared in the literature to suggest that the phenomena might be rather general. Support for this view is found in a number of examples of enzyme-catalyzed intramolecular proton transfers that have been observed.³

molecular proton transfers which lend substantial support to these "conducted tour" mechanisms.

Compound III,⁵ when treated with various bases in a variety of deuterated solvents, gave IV⁶ with intramolecularity that varied from 17 to 98% (Table

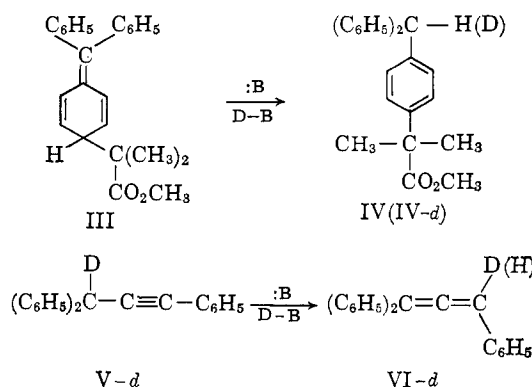


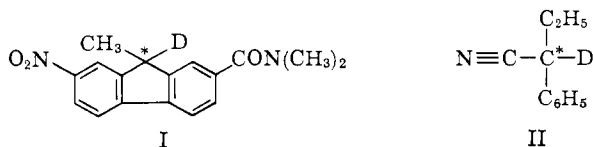
TABLE I

INTRAMOLECULARITY IN BASE-CATALYZED PROTON (DEUTERON) TRANSFERS IN TRIENE III TO GIVE TRIARYLMETHANE IV AND IN DEUTERATED ACETYLENE (V) TO GIVE ALLENE VI^a

Run no.	Compd.	Solvent ^b	Base	T, °C.	% intramolecular
1	III	$(\text{CH}_2\text{OD})_2$	$\text{DOCH}_2\text{CH}_2\text{OK}$	55	17
2	III	$(\text{CH}_2)_4\text{O}-10\% \text{D}_2\text{O}$	DONa	25	34
3	III	$(\text{CD}_3)_2\text{SO}-10\% \text{CH}_3\text{OD}$	CH_3OK	25	40
4	III	CH_3OD	CH_3ONa	25	47
5	III	<i>t</i> -BuOD	<i>t</i> -BuOK	25	50
6	III	$(\text{C}_2\text{H}_5)_3\text{COD}$	$(\text{C}_2\text{H}_5)_3\text{N}$	75	98
7	III	$(\text{C}_2\text{H}_5)_3\text{COD}^c$	$(\text{C}_2\text{H}_7)_3\text{N}$	75	97
8	III	$(\text{C}_2\text{H}_5)_3\text{COD}^d$	$(\text{C}_2\text{H}_7)_3\text{N}$	75	98
9	V	<i>t</i> -BuOD	<i>t</i> -BuOK	30	22 ± 3
10	V-d ^e	CH_3OH	CH_3OK	30	19
11	V-d ^e	$(\text{CH}_3)_2\text{SO}-1.6 \text{ M } t\text{-BuOH}$	$\text{N}(\text{CH}_2\text{CH}_2)_3\text{N}$	30	88
12	V-d ^e	$(\text{CH}_3)_2\text{SO}-3.9 \text{ M } \text{CH}_3\text{OH}$	$\text{N}(\text{CH}_2\text{CH}_2)_3\text{N}$	30	88
13	V-d ^e	$(\text{CH}_3)_2\text{SO}-3.9 \text{ M } \text{CH}_3\text{OH}^f$	$\text{N}(\text{CH}_2\text{CH}_2)_3\text{N}$	30	85
14	V-d ^e	$(\text{CH}_3)_2\text{SO}-3.9 \text{ M } \text{CH}_3\text{OH}^f$	$(\text{CH}_2)_5\text{NH}$	30	58

^a All deuterium analyses were made by combustion and falling drop method (J. Nemeth). Products once formed underwent little if any exchange under conditions of their formation. ^b Solvents 97–100% deuterated where deuterium is indicated. ^c Solution was 0.1 M in $(\text{C}_4\text{H}_9)_4\text{NI}$. ^d Solution was 0.1 M in $(\text{C}_2\text{H}_7)_3\text{NDI}$. ^e 95% of 1 atom of deuterium. Results were corrected accordingly. ^f Solution was 0.14 M in $\text{N}(\text{CH}_2\text{CH}_2)_3\text{NHI}$.

In studies of the stereochemistry of base-catalyzed hydrogen–deuterium exchange of I and II, examples of intramolecular racemization (isoracemization) were interpreted as occurring by a series of intramolecular proton transfers (conducted tour mechanism).⁴ Some of the steps involved 1,6-proton transfers across an aromatic system (I), others 1,3-proton transfers from carbon α to a cyano group to nitrogen and back to



carbon. We have now observed examples of intra-

(1) D. J. Cram and R. T. Uyeda, *J. Am. Chem. Soc.*, **84**, 4358 (1962).

(2) (a) S. Bank, C. A. Rowe, Jr., and A. Schriesheim, *ibid.*, **85**, 2115 (1963); (b) R. B. Bates, R. H. Carnahan, and C. E. Staples, *ibid.*, **85**, 3032 (1963); (c) W. von E. Doering and P. P. Gaspar, *ibid.*, **85**, 3043 (1963); (d) G. Bergsen and A. M. Weidler, *Acta Chem. Scand.*, **17**, 862, 1798 (1963); (e) G. Bergsen, *ibid.*, **17**, 2691 (1963); (f) D. J. Cram and R. T. Uyeda, *J. Am. Chem. Soc.*, in press.

(3) (a) F. S. Kawahara and P. Talalay, *J. Biol. Chem.*, **235**, PC 1 (1960); (b) B. W. Agronoff, H. Eggerer, U. Henning, and F. Lynen, *ibid.*, **235**, 326 (1960); (c) H. C. Rilling and M. J. Coon, *ibid.*, **235**, 3087 (1960).

(4) D. J. Cram and L. Gosser, *J. Am. Chem. Soc.*, **86**, 2950 (1964).

I). This rearrangement involves proton transfer across the face of a benzene ring. Compound V (deuterated) under similar conditions with base in protonated solvents gave VI with intramolecularity that varied between about 20 and 88% (Table I).

The isomerization of triene III to aryl compound IV can be visualized as occurring by one 1,5-rearrangement, or by two successive 1,3-rearrangements. Evidence that the latter type of mechanism makes little, if any, contribution is shown by the fact that no deuterium could be detected in the aromatic rings of IV (combination of n.m.r. and combustion techniques) produced in those runs which gave low intramolecularity (1–5). Had intermediates such as VII-d intervened, some deuterium should have been incorporated into the *ortho* position of the *para*-substituted ring of IV.

These rearrangements are interpreted as occurring largely through ion-pair intermediates whose carbanion is hydrogen bonded to the molecule of oxygen or nitrogen acid generated by proton (deuterium) abstract-

(5) R. Heck, P. S. Magee, and S. Winstein, *Tetrahedron Letters*, **30**, 2033 (1964).

(6) All new compounds used in this investigation gave carbon and hydrogen analysis within 0.3% of theory. All old compounds gave physical properties which corresponded to literature values.