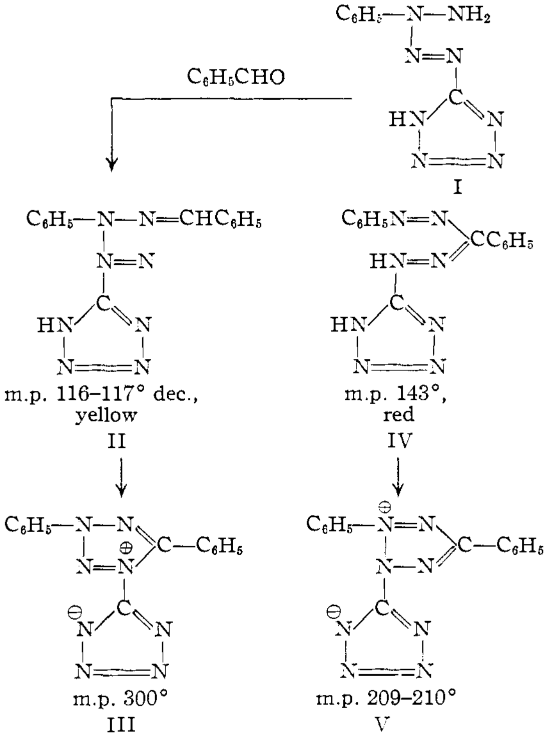
recent study confirms Busch's initial hypothesis and, furthermore, suggests that the rearrangement is probably intramolecular.[5] However, we have found that the interaction of 1-(5′-tetrazolyl)-3-phenyltetrazene (I) and benzaldehyde yields a relatively stable benzaltetrazene (II), m.p. 116–117 dec. (*Anal.* Calcd. for $C_{14}H_{12}N_8$: C, 57.52; H, 4.14; N, 38.34. Found: C, 57.30; H, 4.33; N, 38.04) instead of the corresponding formazan (IV). Oxidation of this yellow solid (II) with cold concentrated nitric acid gave 3,5-diphenyl-1-(5′-tetrazolyl)(1H)-tetrazolium betaine (III), m.p. 300° (*Anal.* Calcd. for $C_{14}H_{10}N_8$: C, 57.92; H, 3.47; N, 38.61. Found: C, 58.12; H, 3.76; N, 38.50). That the oxidation product (III) was, indeed, a tetrazolium betaine was established from the degradation of this solid with hot concentrated hydrochloric acid which gave a mixture of 5-hydroxytetrazole (60% yield) and 2,5-diphenyltetrazole (98% yield). However, the degradative evidence did not permit the unequivocal assignment of the relative positions of the tetrazolyl and N-phenyl substituents. Thus, it is conceivable that structure V might afford the same degradation products.



Quite fortunately, Kuhn and Kainer had earlier described the synthesis of 2,5-diphenyl-3-(5′-tetrazolyl)(2H)tetrazolium betaine (V), m.p. 209–210°, which was obtained by the oxidation of the corresponding formazan (IV) with N-bromosuccinimide.[6] Compound IV, m.p. 143°, possesses the red color that characterizes the formazans[2] and was obtained by the action of benzenediazonium chloride on benzal 5-tetrazolylhydrazone.

The differences noted between II and IV, and III and V preclude the possibility of a tetrazene–formazan rearrangement in the present study and hence lend credence to the (1H)-tetrazolium structure assigned to III.

We have employed the procedure described above for the preparation of a variety of 3,5-diaryl-1-(5′-tetrazolyl)(1H)tetrazolium betaines by introducing electronegative substituents in the benzene residue of I together with the use of substituted benzaldehydes. These compounds will be described in detail in a future communication.

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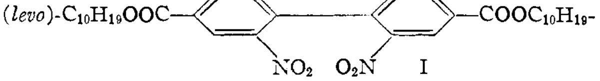
RECEIVED NOVEMBER 8, 1955

MOLECULAR DISSYMMETRY AND OPTICAL INACTIVITY

Sir:

We wish to report the synthesis of (*dextro*)-menthyl (*levo*)-menthyl 2,6,2′,6′-tetranitro-4,4′-diphenate (I)



I

an optically inactive and configurationally pure compound[1] *whose individual molecules are asymmetric.*

Despite the total lack of molecular reflection symmetry, *i.e.*, the absence of plane, point of 4*n*-fold alternating axis of symmetry, rotameric interconversions ensure statistically equal populations of enantiomeric conformations and thus account for the observed optical inactivity.[2]

Compound I may be variously regarded either as (1) a *meso* diastereomer for which no symmetric conformation is possible, or as (2) a non-resolvable racemic mixture of conformational type. In either case I appears unique in that its enantiomeric conformations are interconverted by rotameric changes which cannot involve passage through any symmetric conformation.[2] An adequate discussion of this and related matters requires the reexamination of certain fundamental generalizations pertaining to molecular dissymetry and optical activity, a task which we hope to approach in full publication.

The stereoisomers of I were prepared as follows. Action of copper on methyl 4-chloro-3,5-dinitrobenzoate gave methyl 2,6,2′,6′-tetranitro-4,4′-diphenate, m.p. 192–192.5°[3] (Found: C, 42.9; H, 2.0; N, 12.5), acid hydrolysis of which yielded 2,6,2′,6′-tetranitro-4,4′-diphenic acid (II), m.p. 338–342° (Found: C, 40.2; H, 1.8; N, 13.0). Conversion of II to the acid chloride with thionyl chloride, followed by treatment with (−)-menthol in pyridine, gave (−)-menthyl 2,6,2′,6′-tetranitro-4,4′-diphenate (III), m.p. 225–226°, $[\alpha]^{28}_{D}$ −59.4° (benzene); Found: C, 58.5; H, 5.6; N, 8.3. Similar treatment of the acid chloride of II with (+)-menthol yielded (+)-menthyl 2,6,2′,6′-tetranitro-4,4′-diphenate (IV), m.p. 225–226°, $[\alpha]^{28}_{D}$

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(5) H. Hauptmann and A. C. de M. Perisse, *Experientia*, **10**, 60 (1954).

(6) R. Kuhn and H. Kainer, *Angew. Chem.*, **65**, 442 (1953).

(1) As distinguished from a racemate or racemic mixture.

(2) K. Mislow, *Science*, **120**, 232 (1954).

(3) F. Ullmann and J. Bielecki, *Ber.*, **34**, 2174 (1901), report m.p. 173°.

+60.0° (benzene); Found: C, 58.7; H, 5.7; N, 8.0. The racemate, formed by recrystallization of a mixture of equal quantities of III and IV from benzene–methanol, melted at 264–265°. Partial hydrolysis of III with sodium hydroxide in aqueous dioxane yielded (−)-menthyl hydrogen 2,6,2′,6′-tetranitro-4,4′-diphenate (V), m.p. 216–218°, $[\alpha]^{31}\mathrm{D}$ −38.6° (acetic acid); Found: N, 9.7, 9.5; neut. eq. 562. Treatment of V with thionyl chloride, followed by addition of (−)-menthol in pyridine, gave III (m.p., mixed m.p., $[\alpha]_{\mathrm{D}}$). Similar treatment of the acid chloride of V with (+)-menthol afforded I, m.p. 247–248.5° (Found: C, 58.4; H, 6.3; N, 8.1). The optical activity of I was zero, as measured in pyridine and benzene solutions at 589, 578, 546 and 435 mμ.

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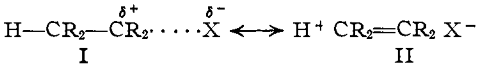
RECEIVED OCTOBER 14, 1955

THE STEREOCHEMISTRY OF HYPERCONJUGATION

Sir:

The most important recent evidence for the concept of hyperconjugation has been the finding of decreased reactivity in solvolytic reactions of tertiary halides and secondary sulfonates in which β-hydrogen atoms are substituted by deuterium.[1,2] The accepted explanation has involved the decreased effectiveness of hyperconjugation (I ⟷ II) because of the greater strength of the carbon–deuterium bond. Changes in inductive effect are not involved for HD has no dipole moment. The implied analogy between hyperconjugation and elimination reactions[1] and the suggested importance of the *trans*-hydrogen in II[3] have been scrutinized by a study of the stereospecificity of the deuterium isotope effect.



$$\mathrm{H{-}CR_2{-}}\overset{\delta+}{\mathrm{CR_2}}\cdots\cdots\overset{\delta-}{\mathrm{X}} \longleftrightarrow \mathrm{H^+\ CR_2{=}CR_2\ X^-}$$

I II

Reaction of cyclopentene oxide with lithium aluminum deuteride gave *trans*-cyclopentanol-2-*d* (III) containing 0.98 ± 0.03 atom of D per molecule, which was converted to the tosylate, m.p. 28–29°, and displaced by tetramethylammonium acetate in pure acetone to afford, after hydrolysis, *cis*-cyclopentanol-2-*d* (IV). The infrared spectra of III and IV were different in many respects and demonstrated that each deuteroalcohol was free from its epimer.

Ten exchanges of cyclopentanone with excess weakly basic deuterium oxide gave cyclopentanone-2,2,5,5-d_4, which was reduced with lithium aluminum hydride at −80° to cyclopentanol-2,2,5,5-d_4 (V) containing 4.1 ± 0.1 atoms of D per molecule. The tosylate had m.p. 28–29°.

The acetolysis rates were determined at 50° for the tosylates of III, IV, V and cyclopentanol (Table I). There is no important stereochemical effect for deuterium substitution. The tosylates of III and IV solvolyzed at closely similar rates and showed one-fourth the logarithmic rate reduction of the tetradeutero derivative.

TABLE I

ACETOLYSIS RATES OF DEUTEROCYCLOPENTYL TOSYLATES

Tosylate of	10^5k (sec.$^{-1}$)[a] 50°	$\Delta\Delta F^{\ddagger}$ (per D), cal./mole
Cyclopentanol	4.21	. .
trans-Cyclopentanol-2-*d*	3.62	99
cis-Cyclopentanol-2-*d*	3.47	125
Cyclopentanol-2,2,5,5-d_4	2.05	116

[a] 0.1*M* solutions in acetic acid, 0.117*M* in sodium acetate. Rates were run in duplicate; reproducibility was 1%.

The results are clearly inconsistent with a common interpretation of resonance structures such as II. The results are completely consistent with a molecular orbital viewpoint formulated as in Fig. 1.

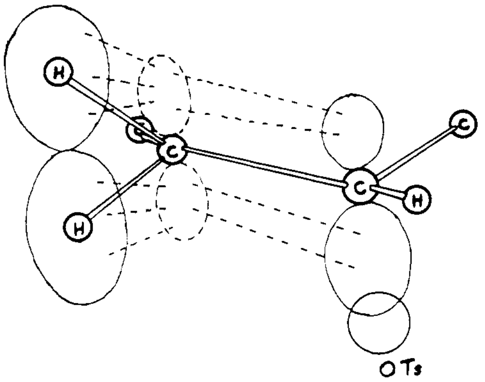


Fig. 1.—Transition state of a solvolytic reaction of cyclopentyl tosylate illustrating a molecular orbital viewpoint of hyperconjugation.

The sp^3 hybrid orbitals of the β-C–H bonds are not orthogonal to the developing p orbital at the reactive center; consequently, overlapping will occur. A molecular orbital of the proper symmetry may be constructed from the methylene hydrogen atoms which, by overlapping with the component p orbital of the β-carbon, forms a conjugated system with the developing p orbital formally analogous to that in an allyl carbonium ion. *Because the two methylene hydrogens are acting as a unit in a molecular orbital, substitution of either one by deuterium will have the same effect on the energy of the pseudo-π bond, to a close approximation.*

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RECEIVED OCTOBER 15, 1955

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(1) V. J. Shiner, Jr., THIS JOURNAL, **75**, 2925 (1953); **76**, 1603 (1954).

(2) E. S. Lewis and C. E. Boozer, *ibid.*, **76**, 791 (1954).

(3) G. Baddeley, *Ann. Repts. on Progress Chem.* (Chem. Soc. London), **51**, 169 (1954).

THE CARCINOSTATIC ACTIVITY OF SOME 2-AMINO-1,3,4-THIADIAZOLES

Sir:

During screening of compounds for their carcinostatic activity, several 2-amino-1,3,4-thiadiazole derivatives were found to be active against several transplanted animal tumors. A representative group of the derivatives and analogs synthesized and tested are listed, along with the results obtained, in Table I. The synthesis of these particu-