+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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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.

$$\underset{\text{I}}{\mathrm{H{-}CR_2{-}\overset{\delta+}{C}R_2\cdots\cdots\overset{\delta-}{X}}} \longleftrightarrow \underset{\text{II}}{\mathrm{H^+\ CR_2{=}CR_2\ X^-}}$$

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.

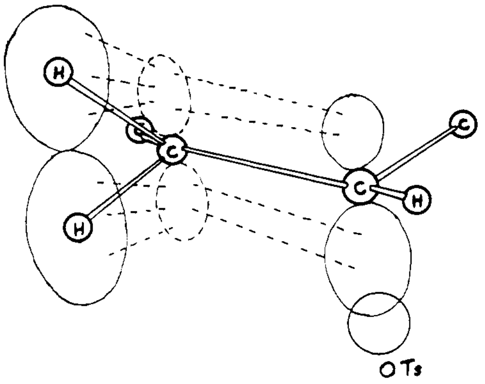

Fig. 1.—Transition state of a solvolytic reaction of cyclopentyl tosylate illustrating a molecular orbital viewpoint of hyperconjugation.

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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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-