The infrared spectrum showed bands (μ): 3.05 (w), 3.4 (w), 5.7 (s), 6.0 (m), 6.5 (m), 6.9 (w), 7.3 (m), 7.8 (m), 8.3 (m), 8.8 (w), 9.1 (w), and 9.7 (m).

DL-**Diethyl N-acetylglutamate** was prepared similarly, 10 g. (0.068 mole) of DL-glutamic acid (Calbiochem, New York, N. Y.) leading to 6.3 g. (0.026 mole), 38% yield of the product, b.p. 163–165° (<1mm.), n^{25}D 1.4540. The infrared spectrum was identical with that of the L-compound.

Anal. Found: C, 53.8; H, 7.6.

D-(+)-**Diethyl N-acetylglutamate** was prepared similarly, 5.0 g. (0.034 mole) of D-glutamic acid (Calbiochem, New York, N. Y.) leading to 3.9 g. (0.016 mole), 48% yield, of **diethyl D-glutamate hydrochloride**, m.p. 113–115°, $[\alpha]^{21}$D −22.9° (*c* 2.56, ethanol) and thence to the product, 1.5 g. (0.0061 mole), 38% yield, m.p. 160–161° (<1 mm.), n^{27}D 1.4566, $[\alpha]^{21}$D +20.2° (*c* 2.94, ethanol). The infrared spectrum was identical with that of the L-compound.

Anal. Found: C, 53.8; H, 7.6; N, 6.0.

L-(+)-γ-**Ethyl-α-hydrogen N-Acetylglutamate**.—L-γ-Ethyl-α-hydrogen glutamate (3.0 g., 0.017 mole, Nutritional Biochemical Corp.) was dissolved in 5 ml. of water, neutralized with 1 *N* sodium hydroxide, boiled under reflux for 1 hr. with 15 ml. of acetic anhydride, and concentrated. The residue was extracted with 30 ml. of acetone and the extract was filtered and concentrated. This residue was dissolved in chloroform, chromatographed on silica gel, and eluted with 10% ethanol–chloroform, leading to an oil, b.p. 178–180° (0.4 mm.), n^{25}D 1.4660, $[\alpha]^{21}$D +4.67° (*c* 2.57, ethanol).

Anal. Calcd. for $C_9H_{15}NO_5$: C, 49.7; H, 6.91; N, 6.45. Found: C, 48.8; H, 6.91; N, 6.56.

The infrared spectrum, liquid film, showed bands (μ): 3.0 (m), 3.4 (m), 3.95 (w), 5.15 (w), 5.8 (s), 6.05 (s), 6.45 (s), 6.9 (m), 7.25 (s), 7.75 (s), 8.25 (s), 8.8 (m), 9.7 (m), 11.6 (w), and 12.7 (w).

L-(−)-**Diethyl N-acetylglutamate**, 0.66 g. (2.7 mmoles), was hydrolyzed at pH 7.2 by 0.020 g. of α-chymotrypsin, as described for diethyl malonate, 1.88 ml. of 1 *N* sodium hydroxide being consumed in 26 min., 70% hydrolysis of one ester group. (In another experiment, carried out for a longer time, hydrolysis stopped after 90% hydrolysis of one ester group.) The resulting solution was extracted, acidified, concentrated, extracted in the usual way, and chromatographed as described above, leading to L-(+)-γ-**ethyl-α-hydrogen N-acetylglutamate**, 0.40 g. (1.8 mmoles), $[\alpha]^{21}$D +4.90° (*c* 2.07, ethanol). Its infrared spectrum was identical with that of the synthesized sample. Attempts to prepare derivatives of this by treatment with 1,3-bis(*p*-dimethylaminophenyl)carbodiimide, with α-bromo-*p*-phenylacetophenone, and with *p*-toluidine failed.

DL-**Diethyl N-acetylglutamate**, 1.69 g. (6.9 mmoles), was hydrolyzed at pH 7.2 by 0.035 g. of α-chymotrypsin in the usual way, 3.47 ml. of 1 *N* sodium hydroxide being consumed in 2 hr., indicating 100% hydrolysis of one ester group of one enantiomorph. The solution was extracted with three 50-ml. portions of ether and the extract was dried and concentrated, leading to D-(+)-**diethyl N-acetylglutamate**, 0.70 g. (2.8 mmoles), 83% yield, $[\alpha]^{21}$D +19.5° (*c* 6.0, ethanol). Its infrared spectrum was identical with that of the synthesized sample. The aqueous reaction solution, after extraction, was brought to pH 3 with 5 *N* hydrochloric acid, concentrated, and extracted with three 30-ml. portions of acetone. The extract was dried and concentrated, leading to L-(+)-γ-**ethyl-α-hydrogen N-acetylglutamate**, 0.73 g. (3.3 mmoles), 97% yield, $[\alpha]^{21}$D +4.80° (*c* 7.3, ethanol). Its infrared spectrum was identical with that of the synthesized sample.

D-(+)-**Diethyl N-acetylglutamate**, 0.078 g. (0.32 mmole), was treated with 0.010 g. of α-chymotrypsin as described in the kinetic procedure; 0.1 ml. of 0.1 *N* NaOH was consumed in 25 min. and 0.017 ml. in the next 55 min., the reaction essentially stopping, 3.7% hydrolysis of one ester group.

α-**Chymotrypsin** was from Worthington Biochemical Corp., three times recrystallized, salt free. The molecular weight was assumed to be 25,000 in the calculations.

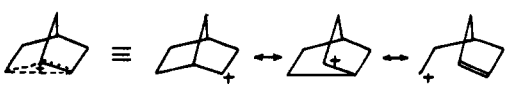
Kinetics of Hydrolysis by α-Chymotrypsin.—Reactions were carried out in the pH stat as previously described,[2] at pH 7.2, 25.0 ± 0.1°, in 20 ml. of 0.1 *M* sodium chloride, with magnetic stirring, under nitrogen. The nonenzymatic hydrolyses were followed for 20 min. and the needed corrections ascertained. In some cases the enzyme was added then as a solid, 0.010 g. dry weight, and the pH brought quickly back to 7.2. In other cases 5 ml. of a solution containing 0.010 g. of the enzyme in 0.1 *N* sodium chloride at pH 7.2 was added to 15 ml. of solution containing the substrate. Both methods led to the same results. The enzymatic hydrolysis was followed by the consumption of 0.1 *N* sodium hydroxide for 10–25 min., depending upon the reactivity of the substrate. Plots of alkali consumed due to enzymatic hydrolysis were linear with time. The results are summarized in Table I. The average corrections for nonenzymatic hydrolysis, referred to above, were for diethyl malonate 8%, succinate 1.4%, glutarate 4.3%, α-acetamidomalonate 1.8%, L-N-acetylglutamate 0.3%, and DL-N-acetylglutamate 0.6% of the enzymatic rates.

COMMUNICATIONS TO THE EDITOR

Rate of Solvolysis of 1-(*p*-Anisyl)camphene Hydrochloride. Evidence for the Absence of Significant Carbon Participation in the Solvolysis of a Tertiary Norbornyl Derivative

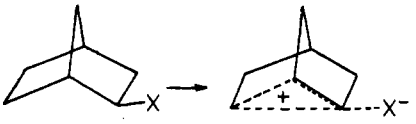
Sir:

The proposed nonclassical structure for the norbornyl cation distributes positive charge from the 2-position to the 1- and 6-carbon atoms[1] (I). Such delocalization



I

of the charge is presumed to stabilize the nonclassical structure over the classical and to stabilize the transition state with a partially formed nonclassical cation (II). It follows that it should be possible to explore the importance of such carbon participation in the transition state for the solvolysis of specific norbornyl



II

derivatives by determining the effect of alkyl or aryl substituents at the 1- and 6-positions on the rate of solvolysis. The well-known ability of such substituents to stabilize positively charged structures leads one to expect a marked rate-enhancing effect for such substituents *provided carbon participation is a significant factor in stabilizing the transition state for the norbornyl system under examination.*[2]

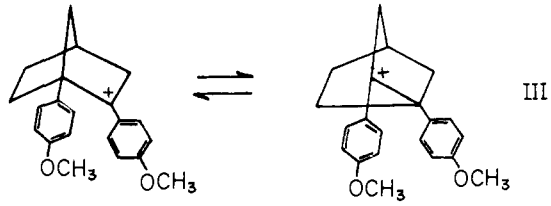
Both the n.m.r. spectra and the chemical data indicate that only one of the two anisyl groups stabilizes the 1,2-dianisylnorbornyl cation.[3] Consequently, it has been concluded that this ion must exist as a pair

(1) S. Winstein and D. Trifan, *J. Am. Chem. Soc.*, **74**, 1154 (1952).

(2) For a recent application of this approach to the bicyclo[3.1.0]hexane system, see E. J. Corey and H. Uda, *ibid.*, **85**, 1788 (1963).

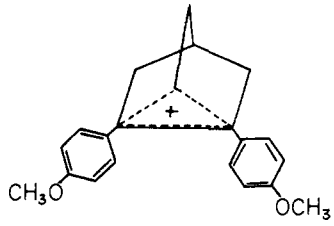
(3) P. von R. Schleyer, D. C. Kleinfelter, and H. G. Richey, Jr., *ibid.*, **85**, 479 (1963).

of equilibrating ions with essentially classical structures (III).



III

This interesting conclusion cannot be generalized to other norbornyl derivatives because of two possible difficulties. First, it has been argued that the classical structure of the 1,2-dianisylnorbornyl cation is the result of the great stabilization of the electron-deficient center by the anisyl group, thereby making unnecessary participation of the 1,6-bonding pair to stabilize the structure.[4] Second, it is possible that the failure of the second anisyl group to contribute to the stabilization of the cation may be due to steric difficulties in achieving ideal orientations for both anisyl groups (IV).

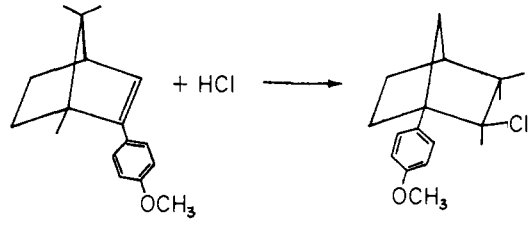


IV

It appeared that the 1-anisyl-2-methylnorbornyl system would provide a more energetic carbonium ion with much smaller steric difficulties.[5] Accordingly, we undertook to synthesize such a derivative and to determine its rate of solvolysis in order to establish whether carbon participation would be a factor in the rate. Fortunately, the synthesis of 2-(*p*-anisyl)-borneol, 2-(*p*-anisyl)bornylene, and 1-(*p*-anisyl)camphene have recently been described and the structures of the products established both by independent unambiguous syntheses and critical n.m.r. examination.[6] Consequently, we decided to work in this series.

Hydrogen chloride was added at -5 to $-10°$ to 10 g. of 2-(*p*-anisyl)bornylene in 50 ml. of methylene chloride until absorption was complete. The solution was concentrated by rotary evaporation and the white solid was recrystallized from dichloromethane. There was obtained 10.0 g. (87% yield) of a white solid, m.p. 113.5–114.5°. *Anal.* Calcd. for $C_{17}H_{23}ClO$: C, 73.21; H, 8.31; Cl, 12.72. Found: C, 72.95; H, 8.50; Cl, 12.98.

The n.m.r. spectrum exhibited methyl proton absorption at 1.05, 1.25, and 1.50 p.p.m., and a doublet at 2.73 p.p.m. (J = 9 c.p.s.) amounting to one proton. The three methyl groups of bornyl or isobornyl derivatives exhibit absorptions below 1.0 p.p.m., closely bunched,[6] whereas the observed shifts are consistent with those anticipated for the methyl groups in a camphene hydrochloride structure. The doublet at 2.73 p.p.m. is assigned to the hydrogen of the 7-methylene group *syn* to the chlorine substituent. Both its position and the magnitude of the splitting are consistent with the assigned structure.[7] Therefore, addition of hydrogen chloride to 2-(*p*-anisyl)bornylene proceeds with Wagner–Meerwein rearrangement to yield 1-(*p*-anisyl)camphene hydrochloride[8] (V).



V

Solvolysis of 1-(*p*-anisyl)camphene hydrochloride in ethanol exhibits simple first-order kinetics for over 90% of the reaction. The observed rate constant at 25.0°, 686 × 10^{-6} sec.$^{-1}$, compares with the value 1160 × 10^{-6} sec.$^{-1}$ observed for camphene hydrochloride itself. Thus the 1-*p*-anisyl substituent results, not in an increase, but in an actual *decrease* in the rate constant. It follows that participation by the 6-carbon atom cannot be a significant factor in the transition state for the solvolysis.

The failure of the 1-anisyl substituent to facilitate the rate of solvolysis of camphene hydrochloride would appear to support the conclusion that such tertiary norbornyl derivatives undergo solvolysis *via* cations that are essentially classical in nature.[9]

(4) S. Winstein, Reaction Mechanisms Conference at Brookhaven National Laboratory, Upton, N. Y., Sept. 5, 1962.

(5) The remarkable stability of the 2-(*p*-anisyl)camphenilyl cation suggests that the ability of the *p*-anisyl group to conjugate with the carbonium center is not significantly affected by the presence of the two methyl substituents in the adjacent 3-position: P. D. Bartlett, E. R. Webster, C. E. Dills, and H. G. Richey, Jr., *Ann.*, **623**, 217 (1959). Consequently, significant steric difficulties in a 1-anisyl-2-methylnorbornyl cation would not be anticipated.

(6) W. F. Erman and T. J. Flautt, *J. Org. Chem.*, **27**, 1526 (1962).

(7) Private communications from Dr. T. J. Flautt and Professor P. von R. Schleyer.

(8) Treatment of 2-(*p*-anisyl)camphenilol with hydrogen chloride in ether likewise yields the Wagner–Meerwein rearranged product, 1-(*p*-anisyl)-apoisobornyl chloride (P. D. Bartlett, *et al.*, ref. 5).

(9) C. A. Bunton, "Nucleophilic Substitution at a Saturated Carbon Atom," Elsevier Publishing Co., New York, N. Y., 1963, p. 62.

(10) Ethyl Corporation Fellow, 1963–1964.

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Rates of Solvolysis of the *p*-Nitrobenzoates of 1,2-Dimethyl-*exo*- and 1,2-Dimethyl-*endo*-norborneols. Further Evidence for the Absence of Significant Carbon Participation in the Solvolysis of a Tertiary Norbornyl Derivative

Sir:

The 1-*p*-anisyl substituent fails to stabilize the 1,2-di-*p*-anisylnorbornyl cation.[1] Similarly, the 1-*p*-anisyl substituent fails to enhance the rate of solvolysis of 1-*p*-anisylcamphene hydrochloride over camphene hydrochloride itself.[2] These results strongly support the conclusion that tertiary norbornyl cations are essentially classical in nature.[3]

However, there is a possible ambiguity in the interpretation of the results. It can be argued that steric difficulties and not lack of participation are responsible

(1) P. von R. Schleyer, D. C. Kleinfelter, and H. C. Richey, Jr., *J. Am. Chem. Soc.*, **85**, 479 (1963).

(2) H. C. Brown and H. M. Bell, *ibid.*, **86**, 5003 (1964).

(3) C. A. Bunton, "Nucleophilic Substitution at a Saturated Carbon Atom," Elsevier Publishing Co., New York, N. Y., 1963, p. 62.