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THE ADDITION OF METHANOL TO SOME BICYCLOBUTANES (1)

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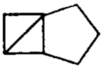
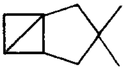
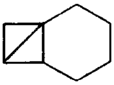
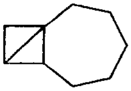
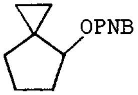
Several investigators (3a-i) have reported the addition of protic solvents to bicyclo[1.1.0]butanes. Very low concentrations of acid served to catalyze this reaction (3b,d,e), which in some cases proceeded only at elevated temperatures in neutral solvents (3b). Wiberg (3e) has noted that the acid catalyzed hydration of bicyclo[1.1.0]butane gave cyclopropylcarbinol and cyclobutanol in the same ratio as observed in the nitrous acid deamination of cyclopropylcarbinyl amine or cyclobutyl amine. Blanchard and Cairncross (3b) reported the hydration of 3-methylbicyclo[1.1.0]butanecarbonitrile at 100° (neutral conditions, 3.5 hr.) and at 25° (in 0.1N HCl) gave the same product. In some cases where additional strain has been introduced into a bicyclobutane nucleus (3f,g,h,i), rapid reactions with solvent under neutral conditions at room temperature have been observed, and in each case the product ratio was consistent with a carbonium ion intermediate. It has been proposed (3i,4,5) that solvent addition proceeds by protonation of the bicyclobutane, followed by solvent attack on a carbonium ion intermediate. It is possible, however, that in these cases of exceptional reactivity severe distortions or changes in the substitution pattern of the bicyclobutane altered the reaction path; i.e., initial solvent attack might be either concerted or nucleophilic rather than electrophilic. We would like to report preliminary results of the protic addition to some bicyclobutanes of intermediate strain.

Tricyclo[4.1.0.0^{1,5}]heptane, 3,3-dimethyltricyclo[4.1.0.0^{1,5}]heptane, tricyclo[5.1.0.0^{1,6}]octane, and tricyclo[6.1.0.0^{1,7}]nonane were prepared by ultraviolet irradiation of the corresponding 3-methylenecycloalkenes in aprotic solvents (3f,g,4,6,7). Isomeric monomers were separated from polymer by bulb-to-bulb distillation. Yields of tricycloalkane (8) varied between 25% and 35%, except for tricyclo[4.1.0.0^{1,5}]heptane, which was obtained in only 3% yield. Tricyclo[6.1.0.0^{1,7}]nonane was sufficiently stable to permit purification by preparative scale v.p.c. (9); $\nu_{max}^{CCl_4}$ 3021, 2915, 2841, 960 cm^{-1}; n.m.r. (δ, p.p.m.) 0.44 (1H, doublet, J = 1 c.p.s., endo (10) H at C_9), 0.71 (1H, multiplet, endo (10) H at C_7), 1.2 and 2.2 (12H, multiplets). This hydrocarbon could be stored up to three months at -5° under nitrogen without noticeable decomposition when it was separated from other impurities.

When placed in methanol (11), all of the tricycloalkanes added solvent to give cyclopropylcarbinyl and cyclobutyl methyl ethers. The structures of the ethers were proved by synthesis (12). In addition, 1-methoxybicyclo[3.2.0]heptane was shown to have a *cis*-fused ring system by hydroboration of bicyclo[3.2.0]hept-

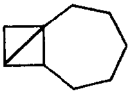
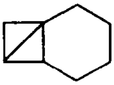
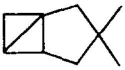
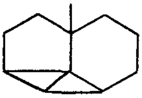
TABLE I. Comparison of Product Ratios

Protic Solvent Addition[a]	Relative Ratio	
	Cyclopropylcarbinyl	Cyclobutyl
	1.00	0.39
	1.00	0.32
	1.00	0.35
	1.00	0.28
Solvolysis[b]		
	1.00	0.41
	1.00	0.51

[a] Methanol. [b] Aqueous acetone.

1^5-ene (13) and conversion of the resulting bicyclo[3.2.0]heptanol to the desired methyl ether. The ratio of cyclopropylcarbinyl and cyclobutyl products was not only similar to that found in several solvolytic studies, but the products were stereochemically equivalent (12,14). The rate of methanol addition increased as the alkyl bridge was contracted. Fusion of an additional ring to the tricyclic nucleus produced a large increase in the rate of protic solvent addition (4). Solvent addition was very rapid in the presence of acid (0.01N perchloric acid), relative to neutral methanol, and was slightly retarded in the presence of base (0.01N sodium methoxide). However, there was no significant change in the relative proportion of the products as the hydrogen ion concentration was changed (15).

TABLE II. Rate of Methanol Addition

Substrate	Relative Rate[a]
	$1^{b,c}$
	$\sim 4^{d}$
	5^{d}
	$>500^{2a}$

[a] Methanol at 25°C.; [b] Followed by v.p.c. with an internal standard; [c] 1/2 = 48 hr.
[d] Followed by n.m.r.

These observations are consistant with a mechanism which involves carbonium ion formation followed by reaction with solvent and are supported by stereochemical studies of solvent addition to bicyclobutanes (3b,g; 16), which suggest proton addition to the underside of the bicyclobutane nucleus followed by solvent attack on the resulting carbonium ion (17). The rate profile, which levels off as methoxide is added to the solvent, as a function of hydrogen ion concentration suggests that methanol functions as a general acid catalyst (18) for solvent addition. The differences in reactivity observed for various bicyclobutanes can be explained by the strain energy differences in each of the substrates rather than a change in mechanism.

Studies on the physical and chemical properties of these systems are being continued.

References

1. This work was supported in part by PHS Grant No. 00709, National Institute of Arthritis and Metabolic Diseases, U.S. Public Health Service.
2. National Institutes of Health Predoctoral Fellow, 1965-1966.
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7. Dilute solutions (1g./1.) of 3-methylenecycloheptene or 3-methylenecyclooctene were irradiated with a 450 watt Hanovia lamp equipped with a vycor filter. The rate of bicyclobutane formation decreased as the size of the ring was reduced, and the reactivity of the tricycloalkanes increased. Optimum yields of bicyclobutanes from 3-methylenecyclohexene and 3,3-dimethyl-3-methylenecyclohexene were obtained by irradiation with a G.E. AH-6 lamp (1000 watt).
8. Based on the amount of ethers formed by reaction with methanol, except for tricyclo[6.1.0.0^{1,7}]nonane.
9. Base protected 10' x 3/8" 10% Carbowax 6000 on Chromsorb W, 80°.

10. K. B. Wiberg and J. M. Lavanish, *J. Am. Chem. Soc.*, **88**, 365 (1966). The exo alkyl substituent would shift the resonance about 0.3 p.p.m. downfield. The stereochemical assignment is in agreement with previous work (3g,h).

11. All glassware was washed with 2N ammonium hydroxide, rinsed with distilled water, and dried at 175° before use; methanol was freshly distilled from magnesium methoxide.

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15. A very slow isomerization of the cyclopropylcarbinyl ethers to cyclobutyl ethers was observed in the presence of 0.01N perchloric acid.

16. A. Cairncross, Private communication.

17. The acid catalyzed addition of alcohols to benzvalenes is not entirely compatible with this scheme, and the addition may follow another pathway. (K. E. Wilzback, J. S. Ritscher, and L. Kaplan, *J. Am. Chem. Soc.*, **89**, 1031 (1967).

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