## NOTES

# An Acid-catalyzed Reaction of Methyl Ethers with Acetyl Fluoride. Syntheses of 1-Fluorobicyclo[2.2.2]octanes[1]

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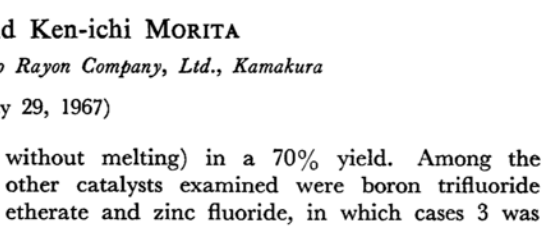
We have previously reported convenient methods for the syntheses of 1-chloro-, 1-bromo-, and 1-iodobicyclo[2.2.2]octane by the reaction of 1-methoxybicyclo[2.2.2]octane with acetylhalides in the presence of an acid catalyst. The reaction has now been extended to the preparation of 1-fluorobicyclo[2.2.2]octane derivatives.[2−4]

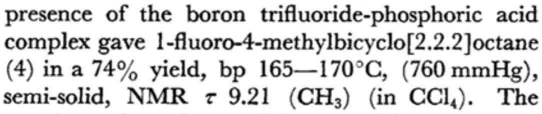
It has been theorized that the reaction of ethers with acyl halides proceeds *via* acyl oxonium ions.[1] The synthetic utility of acyl oxonium ions as a carbonium ion generator has been confirmed. Diazonium ions,[4] isocarboxonium ions,[5] and carboxylium ions[6] have been established as carbonium ion sources.

The treatment of 1-methoxybicyclo[2.2.2]octane (1) with an excess of acetyl fluoride in the presence of a catalytic amount of anhydrous stannic chloride gave a mixture (*ca.* 1 : 1) of 1-fluoro- and 1-chlorobicyclo[2.2.2]octane in about an 80% yield. When the boron trifluoride-phosphoric acid complex was used as a catalyst, the reaction between 1 and acetyl fluoride afforded 1-fluorobicyclo-[2.2.2]octane (3), mp *ca.* 152°C (most of it sublimes without melting) in a 70% yield. Among the other catalysts examined were boron trifluoride etherate and zinc fluoride, in which cases 3 was also obtained.

An analogous treatment of 1-methoxy-4-methylbicyclo[2.2.2]octane (2) with acetyl fluoride in the presence of the boron trifluoride-phosphoric acid complex gave 1-fluoro-4-methylbicyclo[2.2.2]octane (4) in a 74% yield, bp 165—170°C, (760 mmHg), semi-solid, NMR $\tau$ 9.21 ($CH_3$) (in $CCl_4$). The reaction of methoxycyclohexane (5) with acetyl fluoride in the presence of the boron trifluoride-phosphoric acid complex furnished a mixture of fluorocyclohexane (6) (25%), cyclohexene (7) (6%), and acetoxycyclohexane (8) (18%).



1 R=H
2 R=CH$_3$
3 R=H
4 R=CH$_3$



5
6
8

The formation of 1-acetoxybicyclo[2.2.2]octanes could not be detected when either 1 or 2 was reacted with acetyl fluoride in the presence of an acid catalyst. The formation of acetoxycyclohexane (8) in the case of 5 suggests that a 1-bicyclo[2.2.2]-octyl cation is more stable than a cyclohexyl cation. The mass spectra imply that a methyl carbonium ion is less stable than an ethyl carbonium ion[7]

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1) Bridged Ring Compounds. IX. Paper VIII: Z. Suzuki and K. Morita, *J. Org. Chem.*, **32**, 31 (1967).

2) The following reagents has been used for the introduction of fluorine atom by the cleavage of carbon-oxygen bonds: a) $Et_2NCF_2CHFCl$: D. E. Ager, *Tetrahedron Letters*, **1962**, 1065; L. H. Knox, E. Velarde, S. Berger, D. Cuadriells and A. C. Cross, *J. Org. Chem.*, **29**, 2187 (1964); *Russ. Chem. Rev.*, **12**, 926 (1966). b) $Bu_4N^+F^-$: H. B. Henbest and W. R. Jackson, *J. Chem. Soc.*, **1962**, 954, c) HF: G. P. Mueller, *J. Org. Chem.*, **26**, 2403 (1961); C. W. Shoppee, *J. Chem. Soc.*, **1957**, 4813; C. G. Bergstrom, *J. Am. Chem. Soc.*, **82**, 3479 (1960).

3) It has been reported that the reaction of acetyl fluoride with boron trifluoride etherate furniches ethyl fluoride; [F. See], *Z. Anorg. Allgem. Chem.*, **250**, 331 (1943).

4) H. E. Zollinger, "Azo and Diazo Chemistry, Aliphatic and Aromatic Compounds," Interscience Publishers, New York, N. Y. (1961).

5) P. S. Skell and I. Starer, *J. Am. Chem. Soc.*, **81**, 4117 (1959); J. Landgrebe, *Tetrahedron Letters*, **1965**, 105.

6) P. Beak, R. J. Trancik, J. B. Mooberry and P. Y. Hohnson, *J. Am. Chem. Soc.*, **88**, 4288 (1966).

7) R. W. Taft, R. H. Mortin and F. W. Lampe, *J. Am. Chem. Soc.*, **87**, 2490 (1965).

and that the latter is in turn less stable than a 1-bicyclo[2.2.2]octyl ion.[8] No data concerning the stability of a cyclohexyl ion is available, however.

## Experimental

**1-Fluorobicyclo[2.2.2]octane (3).** *A. The Boron Trifluoride-phosphoric Acid Complex as a Catalyst.* To a stirred mixture of 2.84 g (0.02 mol) of 1 and 3.10 g (0.05 mol) of acetyl fluoride,[9] twelve drops of the boron trifluoride-phosphoric acid complex were added with ice-bath cooling. After the mixture had been stirred for thirty minutes at 0°C, the reaction temperature was allowed to rise to 10—20°C, after which stirring was continued for 3 more hours. The reaction mixture was then poured onto cracked ice, and the mixture was stirred for 10 min and extracted three times with 25-m*l* portions of ether. The ether layers were then combined, washed with aqueous sodium bicarbonate and water, and dried over anhydrous calcium chloride. The ether was distilled off through a 10-in packed column, and the residue was sublimed to give 1.8 g (70%) of 3 mp *ca.* 152°C (most of it sublimes without melting).

Found: F, 14.7%. Calcd for $C_8H_{13}F$: F, 14.82%.

*B. Boron Trifluoride Etherate as a Catalyst.* An experiment similar to that described above was carried out using 0.5 m*l* of boron trifluoride etherate instead of twelve drops of the boron trifluoride-phosphoric acid complex; we thus obtained 1.6 g of 3.

*C. Zinc Fluoride as a Catalyst.* To a stirred suspension of 0.5 g (4.8 mmole) of zinc fluoride in 1.2 g (8.6 mmol) of 1, 2 m*l* of acetyl fluoride were added at 0°C over a 15-min period. The reaction temperature was then allowed to rise at room temperature (15—20°C), and stirring was continued for 24 hr. After the usual treatment (described for Procedure A), 1.0 g of an oil was obtained. Gas chromatographic analysis (PEG 6000 column at 180°C) showed that the product was about a 1-to-1.5 mixture of 3 and the starting material(1).

*D. Stannic Chloride as a Catalyst.* To a stirred mixture of 1.2 g (8.6 mmoles) of 3 and 2.1 g of acetyl fluoride 0.1 m*l* of stannic chloride was added with ice-bath cooling. An exothermic reaction was observed. The reaction mixture was then stirred for 4 hr at 4°C. After the usual treatment, the residue was crystallized from aqueous methanol to give 0.75 g of crystals with a mp of 112—123°C (in a sealed capillary tube). Gas chromatographic analysis (PEG 6000 column at 180°C) showed that the product was *ca.* a 1-to-1 mixture of 3 and 1-chlorobicyclo[2.2.2]octane.[1] The two materials were separated by preparative v.p.c. and identified.

**1-Fluoro-4-methoxybicyclo[2.2.2]octane (4).** To a stirred mixture of 3.12 g (0.02 mol) of 2 and 3.1 g (0.05 mol) of acetyl fluoride, fifteen drops of the boron trifluoride-phosphoric acid complex were added with ice-bath cooling. The mixture was then stirred for 3 hr at about 10°C. After the usual treatment, the product was collected by distillation (bp 165—170°C at 760 mmHg) to furnish 2.1 g (74%) of 4, $n_D^{20}$ 1.4501, semi-solid, NMR τ 9.21[10] (in carbon tetrachloride).

Found: F, 13.3%. Calcd for $C_9H_{15}F$: F, 13.36%,

**Fluorocyclohexane (6).** To a stirred mixture of 4.56 g (0.04 mol) of methoxycyclohexane (5)[11] and 6.2 g (0.1 mol) of acetyl fluoride, twenty drops of the boron trifluoride-phosphoric acid complex were added with ice-bath cooling. After the mixture had been stirred for thirty minutes at 0°C, the reaction temperature was allowed to rise to 3—5°C and stirring was continued for two more hours. After the usual treatment, we obtained 2.83 g of an oil. The oil was separated by preparative vapor-phase chromatography (DC 550 column at 145°C) to give 1 g (25%) of fluorocyclohexane (6), $n_D^{20}$ 1.4145 (lit.[12], $n_D^{25}$ 1.4130), (Found: F, 18.25%. Calcd for $C_6H_{11}F$: F, 18.61%), 1 g (18%) of acetoxycyclohexane (8) and 0.2 (6%) of cyclohexene (7). The identity of 7 and 8 was established by a comparison of their infrared spectra and v.p.c. retention times with those of authentic samples.

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8) J. L. Franklin, *J. Chem. Educ,* **40**, 28 (1963).

9) C. G. Swarin and C. B. Scott, *J. Am. Chem. Soc.,* **75**, 246 (1953).

10) The analysis of the NMR spectra of 1-fluorobicyclo[2.2.2]octanes (3 and 4) was presented at the 6th Meeting of the NMR symposium, Kyoto, October, 1967.

11) A. I. Vogel, *J. Chem. Soc.,* **1948**, 108.

12) S. M. McElvain J. W. Langston, *J. Am. Chem. Soc.,* **66**, 1759 (1944).