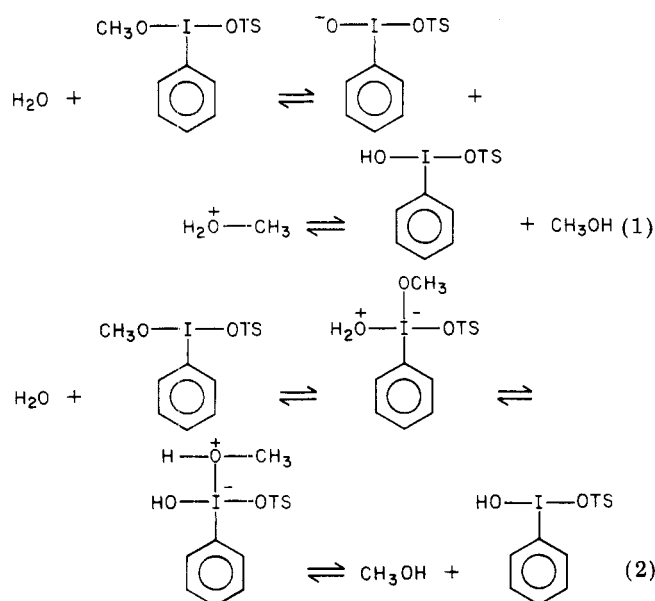


Scheme I

Table I^a

	δ	δ (H ₂) ^{obsd}	δ (H ₂) ^{calcd}
CH ₃ OD in CD ₂ Cl ₂	3.37	202	
PhI(OCH ₃)OTS	3.87	232	
1 equiv of CD ₃ OD	3.67	220	217
2 equiv of CD ₃ OD	3.52	211	212
6 equiv of CD ₃ OD	3.40	204	206

^a 110 mg of 7 in CD₂Cl₂.

The second mechanism might involve the intermediate formation of a four-coordinate iodine species in which iodine bears a negative charge. A similar intermediate was first proposed by Beringer and Chang in ligand exchange reactions of iodonium salts with aryllithiums¹¹ and subsequently by Martin and Amey in ligand exchange reactions of 5 with R₂OH/R₂OK.⁵ However, such a species need not necessarily form if 7 exists as an ion pair PhI⁺(OCH₃)-OTS in solution.

With water as nucleophile, the products of either mechanism would be identical. However, with methanol as nucleophile instead of H₂O, mechanism 1 would yield 8 and dimethyl ether while mechanism 2 would result in degenerate exchange. For that reason, we studied the reaction between 7 and methanol-*d*₄ in CD₂Cl₂ by NMR spectroscopy at probe temperature. The result was degenerate exchange.

There was no observable formation of 8 (which is very insoluble in CH₂Cl₂ and would precipitate as formed) nor was CH₃OCD₃ detected by ¹H NMR analysis. The results of the exchange study are summarized in Table I. The addition of methanol-*d*₄ to 7 in CH₂Cl₂ led to broadening of the singlet at δ 3.87 and, within 10 min, to a shift of that singlet to a new position and some renarrowing of the line width. The observed chemical shifts after exchange with various added quantities of CD₃OD are compared in Table I to calculated values for rapid exchange between 7 and CH₃OD (on the NMR time scale).

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Experimental Section

General. NMR spectra were recorded on a Varian EM-360 spectrometer. Melting points are uncorrected. Compound 7 was sent out for elemental analysis.

Synthesis of [Methoxy(tosyloxy)iodo]benzene (7). Trimethyl orthoformate (ca. 2.0 mL) was added to 2.00 g (5.10 mmol) of [hydroxy(tosyloxy)iodo]benzene (8); the reaction vessel was purged with nitrogen and capped. After ca. 10 min, the solid 8 had disappeared, and a yellow solution resulted. The reaction mixture was then allowed to stand at room temperature whereupon large glassy plates slowly crystallized from the liquid. After 8 h the liquid was decanted and [methoxy(tosyloxy)iodo]benzene (7) was obtained as a crystalline aggregate (yield 1.79 g (86%), mp 88–92 °C). No further crystallization occurred from the mother liquor over a period of 48 h. The product was blown dry under a stream of nitrogen and subsequently stored under nitrogen; ¹H NMR (CD₃CN/Me₄Si) δ 2.28 (s, 3 H, (tosyloxy)methyl), 3.92 (s, 3 H, OCH₃), 7.0–8.2 (complex m, 9 H, aromatic).

Anal. Calcd for C₁₄H₁₅ISO₄: C, 41.39; H, 3.72; I, 31.24. Found: C, 41.22; H, 3.61; I, 31.16.

Hydrolysis of 7. 7 (0.90 g) was dissolved in CH₃CN (2 mL). To this solution was added 0.1 g of H₂O, and it was immediately filled with fine glassy crystals of 8 which were subsequently isolated and dried: yield 0.72 g (83%); mp 135–137 °C.

Registry No. 7, 75067-08-2; 8, 27126-76-7; trimethyl orthoformate, 149-73-5.

Heterocycles. 8. Synthesis of Oxaflozane^{1,2}

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Received April 24, 1980

Oxaflozane (1) is a potent antidepressant agent.⁴ Previous synthesis^{4a} of this compound employed a Grignard reaction of 2 and 3 to give dihalo ether 4 and, finally, reaction of 4 with isopropylamine. We report an alternative synthesis of 1, taking advantage of hemiketal formation of β -oxoethanolamine^{5,6} which obviates the use of the potentially explosive reagents 2.⁷

Thus, *N*-isopropylethanolamine was condensed with α -bromo-3-(trifluoromethyl)acetophenone to give hemiketal 7. Acid-catalyzed dehydration of 7 with 1.1 equiv of *p*-toluenesulfonic acid gave 8. When less than 1 equiv of catalyst was used, the reaction did not go to completion as measured by the water collected. Hydrogenation of 8 gave oxaflozane (1)^{4a} in an overall yield of 34% (compared to 27% for the previous process).^{4a}

(1) For part 7, see P. M. Weintraub, *J. Heterocycl. Chem.*, **16**, 1081 (1979).

(2) Presented in part at the 10th Central Regional ACS Meeting, March 1979, Abstracts p 93.

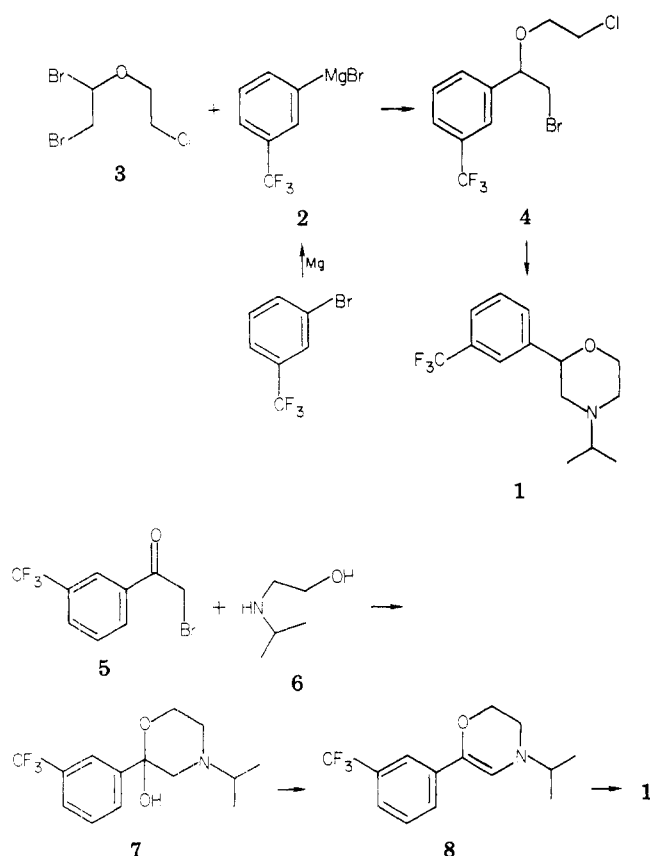
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Experimental Section

IR spectra (neat film) were recorded on a Perkin-Elmer 521 grating spectrophotometer. UV spectra (ethanol) were recorded on a Perkin-Elmer 350 spectrophotometer; extinction values are given as log ϵ . NMR (CDCl_3 with internal Me_4Si) spectra were run on a Varian A-60A. The solvents were removed in vacuo on a rotary evaporator. Kieselgel (SiO_2) was used for chromatography. Elemental analyses are within $\pm 0.4\%$ of theory.

Tetrahydro-4-isopropyl-2-[3-(trifluoromethyl)phenyl]-2H-1,4-oxazin-2-ol (7). A stirred solution of 3-(trifluoromethyl)acetophenone (93.5 g, 0.5 mol) in CHCl_3 (500 mL) at room temperature was treated dropwise over 1.5 h with a solution of Br_2 (80.0 g, 0.5 mol) in CHCl_3 (200 mL). The reaction was stirred for 1.5 h after the addition was completed and then the mixture was extracted with H_2O (3×250 mL) and aqueous NaCl (100 mL), dried (Na_2SO_4), filtered, and concentrated. The residue was distilled to give 5 (124 g, 92.9%), bp $85-90^\circ\text{C}$ (1.2 mm) [lit.⁸ bp $71-72$ (0.25 mm)].

A solution of 5 (26.7 g, 0.10 mol) in toluene (250 mL) was treated with *N*-isopropylethanolamine (20.6 g, 0.20 mol) and stirred at room temperature for 24 h. The resulting mixture was extracted with 10% aqueous HCl (2×250 mL). The combined aqueous extract was cooled with ice, made basic by slow addition of concentrated NH_4OH , and extracted with Et_2O (2×300 mL). The combined Et_2O extract was dried (MgSO_4), treated with charcoal, filtered, and concentrated to a yellow liquid (25.4 g). This was purified by chromatography on SiO_2 (500 g), eluting with toluene-1% Et_3N (3.5 L) and with toluene-50% CHCl_3 -2% Et_3N (4 L), taking 500-mL fractions. The product was obtained by combining and concentrating fractions 8-13 to give 7 (18.8 g, 65.1%) as a yellow liquid: IR ν 3420, 1330, 1115 cm^{-1} ; UV λ 256 (2.812), 263 (2.826); ^1H NMR δ 1.04 (6 H, d, $J = 6.5$ Hz, $2 \times \text{CH}_3$), 2.25-3.03 (5 H, m, $2 \times \text{CH}_2\text{N} + \text{CH}$), 3.63-4.28 (2 H, CH_2O), 5.30 (s, 1 H, exchangeable, OH), 7.30-8.07 (4 H, m, aromatic). Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{F}_3\text{NO}_2$: C, 58.12; H, 6.27; N, 4.84. Found: C, 57.62; H, 6.35; N, 4.66.

3,4-Dihydro-4-isopropyl-6-[3-(trifluoromethyl)phenyl]-2H-1,4-oxazine (8). A stirred mixture of 7 (15.5 g, 53.6 mmol),

p-toluenesulfonic acid monohydrate (11.2 g, 58.9 mmol), and benzene (400 mL) was heated at reflux under a Dean-Stark water separator for 2 h. The reaction mixture was cooled to room temperature and extracted with saturated aqueous NaHCO_3 (2×200 mL). The organic layer was dried ($\text{K}_2\text{CO}_3/\text{MgSO}_4$), treated with charcoal, filtered, and concentrated to a red-brown liquid which was distilled to give 8 (11.47 g, 79.1%): bp (Kugelrohr) $150-155^\circ\text{C}$ (0.025 mm); IR ν 1640, 1600, 1585, 1115 cm^{-1} ; UV λ 243 (3.617), 329 (4.108); ^1H NMR δ 1.15 (6 H, d, $J = 6.5$ Hz, $2 \times \text{CH}_3$), 2.92-3.52 (3 H, m, $\text{CH}_2\text{N} + \text{CH}$), 4.18 (2 H, t, $J = 5$ Hz, CH_2O), 6.25 (1 H, s, $\text{C}=\text{CH}$), 7.13-7.73 (4 H, m, aromatic). Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{F}_3\text{NO}$: C, 61.98; H, 5.95; N, 5.16. Found: C, 61.22; H, 5.87; N, 4.94.

Tetrahydro-4-isopropyl-[3-(trifluoromethyl)phenyl]-2H-1,4-oxazine (1). A mixture of 8 (1.0 g, 3.69 mmol), PtO_2 (0.12 g), and AcOH (75 mL) was shaken under a H_2 atmosphere for 18 h. The mixture was diluted with 95% EtOH (50 mL), filtered through Celite, and concentrated. The residue was chromatographed on SiO_2 (35 g), taking 25-mL fractions and eluting with CHCl_3 -5.5% MeOH -0.5% Et_3N . Fractions 3 and 4 were combined and concentrated to give 1 (0.66 g, 66%): bp 52°C (0.005 mm); ^1H NMR δ 1.07 (6 H, d, $J = 6$ Hz, $2 \times \text{CH}_3$), 1.98-3.10 (5 H, m, $2 \times \text{CH}_2\text{N} + \text{NCH}$), 3.58-4.25 (2 H, m, CH_2O), 4.62 (1 H, d, $J = 2.5$ and 10 Hz, CHO), 7.45-7.78 (4 H, m, aromatic). Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{F}_3\text{NO}$: C, 61.53; H, 6.64; N, 5.13. Found: C, 61.64; H, 6.76; N, 5.34.

Registry No. 1, 26629-87-8; 5, 2003-10-3; 6, 109-56-8; 7, 75247-59-5; 8, 75232-80-3; 3-(trifluoromethyl)acetophenone, 349-76-8.

Evidence for 1,2-Dehydroadamantane as a Gas-Phase Product in Time-Resolved Field-Ionization Mass Spectrometry of 2-Adamantyl Trifluoroacetate

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Received August 7, 1980

Introduction

Demonstration of 1,2-dehydroadamantane (adamantene) as an intermediate in photolysis of the adamantyl phenylacetates¹ led us to investigate the possibility that the radical ion of this highly strained olefin might be detected in the mass spectrometer. Of particular use in this attempt was the ability of the field-ionization (FI) mass spectrometer to present a time-resolved view of low-energy processes occurring at times as short as 10^{-12} s and thus to isolate unimolecular gas-phase processes with lifetimes approaching this value.² A recent report provides evidence for formation of neutral adamantene in a McLafferty rearrangement of 2-(1-adamantyl)cyclohexanone following EIMS^{3a} and reviews briefly the complex history of this

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