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(10) Note Added in Proof. Methyl 4,6-*O*-benzylidene-3-*O*-methyl-*α*- and -*β*-D-*arabino*-hexopyranosid-2-uloses **1** and **2** were prepared by Antonakis, *et al.*[11]

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Reactions of Naphthalene and Anthracene Derivatives with Trifluoromethyl Hypofluorite

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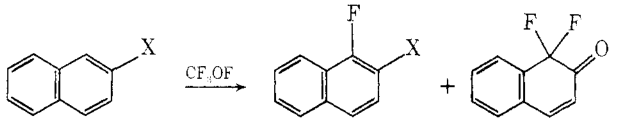
The recent discoveries that trifluoromethyl hypofluorite (CF_3OF) is useful in the fluorination of aromatic compounds[2,3] coupled with our interests in preparing fluoroaromatic compounds[4] led us to investigate the reaction of CF_3OF with some naphthalene and anthracene derivatives. Barton and coworkers'[2] report on the preparation of 1-fluoro-2-acetylaminonaphthalene (**2a**) from reaction of CF_3OF with 2-acetylaminonaphthalene (**1a**) led us to reinvestigate this reaction as a starting point for our own work.

Reaction of **1a** with CF_3OF was carried out in chloroform solution at room temperature. The reaction was performed until all **1a** was consumed as discerned from glpc and tlc analyses of the reaction progress. When all **1a** had been consumed two major products were present, 1-fluoro-2-acetylaminonaphthalene (**2a**) and 1,1-difluoro-2-naphthone (**3**), in 25 and 43% yields, respectively. The structure of **2a** was confirmed by conversion to 1-fluoro-2-aminonaphthalene (**2b**). Compound **3** was identified by its spectral and elemental analyses and by spectral analysis of its hydrogenation product.



1a, X = $NHCOCH_3$
b, X = NH_2
c, X = OH

2a–c

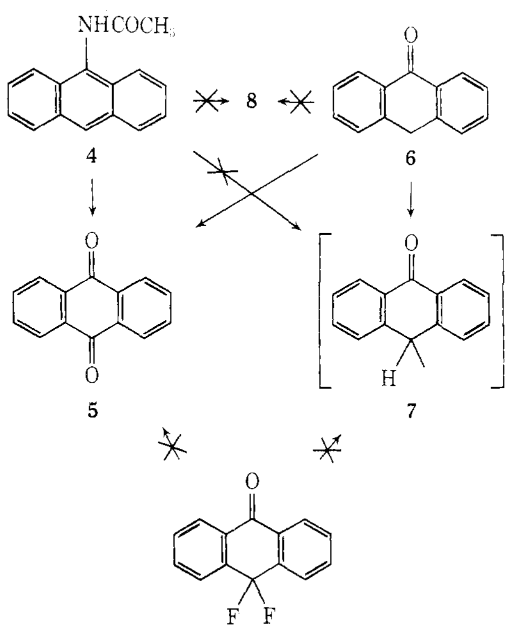
3

Reaction of 2-naphthylamine (**1b**) with CF_3OF produced a mixture from which 1-fluoro-2-naphthylamine (**2b**) was obtained in 9% yield and **3** was obtained in 19% yield. Facile decomposition of **2b** on exposure to air may account partially for its low yield. 2-Naphthol (**1c**) reacted with CF_3OF to yield 1-fluoro-2-naphthol (**2c**) in 14% yield and **3** in 20% yield. Analytical data established the composition of **2c**, but analogy with reaction products from **1a** and **1b** was used to determine the orientation of the fluorine atom. The hydroxyl proton showed long-range coupling to the fluorine atom, giving further evidence that the fluoro and hydroxyl groups are adjacent.[5] Attempts to prepare **2c** unambiguously from 1-amino-2-naphthol failed.

A gray solid (mp 295–298°) was formed in the reactions of **1a**, **1b**, and **1c** with CF_3OF. This material was insoluble in most organic solvents except dimethyl sulfoxide. The composition of the solid was not determined owing to slow continuous decomposition and our inability to obtain a pure sample. The infrared spectrum showed absorbances characteristic of an amine salt[6] at 2200 and 1800 cm^{-1} if the spectrum was obtained on freshly prepared material. On standing, these absorbances disappeared.

Treatment of pure samples of **2a**, **2b**, **2c**, and **3** with CF_3OF produced a complex mixture of at least seven components (tlc and glpc). We could therefore not show that **3** was formed by further fluorination of **2a**, **2b**, and **2c**. Yields of products are based on a parallel reaction scheme: $1 \rightarrow 2$; $1 \rightarrow 3$.

Reaction between 9-acetylaminoanthracene (**4**) and CF_3OF yielded anthraquinone (**5**) in 95% yield. No other compound was detected by tlc or glpc. Attempts to determine a mechanism for this reaction were made by treating feasible intermediates with CF_3OF. Anthrone (**6**) produced both **5** (55%) and 10,10-bianthronyl (**7**, 30%) on reaction with CF_3OF. 10,10-Difluoroanthrone (**8**) and **7** are reported products from the reaction of **6** with sulfur tetrafluoride in the presence of radical scavengers.[7] We were unable to detect either **5** or **7** on reaction of **8** with CF_3OF. Our detection methods (tlc and glpc) could have detected at least 0.1% of the components as determined from standard solutions of **5** and **7**. Careful reexamination of the products from **4** failed to show any **7**. These results are presently taken as evidence against the intermediacy of either **6** or **8**. Investigations which should provide useful information regarding the mechanism and synthetic potential of these and similar reactions are in progress.



8

Experimental Section

All temperature reading are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Nmr spectra were determined on a Varian T-60 spectrometer using tetramethylsilane (δ 0.0) as an internal standard. Molecular weights were determined from mass spectra obtained on a Varian MAT-111 spectrometer. Infrared spectra were determined on a Perkin-Elmer Model 337 grating spectrophotometer using polystyrene for calibration. Trifluoromethyl hypofluorite was obtained from PCR, Inc., Gainesville, Fla. Aldrich spectroquality chloroform was used as the solvent in all reactions with CF_3OF. Glpc analyses were performed on a Varian 1440 flame ionization gas chromatograph using a 5 ft × 0.13 in. stainless steel column of 3% SE-30 on Chromosorb W and helium flow rate of 60 ml/min.

Reactions with Trifluoromethyl Hypofluorite (CF_3OF). 2-Acetylaminonaphthalene (1a). A solution of 1.5 g (7.2 mmol) of **1a** in 25–30 ml of chloroform was treated with CF_3OF at room temperature. The reaction mixture became dark. The course of the reaction was followed by glpc and tlc (silica gel). Two major products were formed and all **1a** was consumed within 40–60min. Nitrogen was bubbled through the reaction mixture to assist in the removal of residual CF_3OF. The mixture was filtered to give 0.7 g of gray material, mp 295–298° dec. *Anal.* Found: C, 75.2; H, 4.7; N, 7.9; F, 3.6. This material was not identified because its properties (ir, nmr, melting point) continuously changed.

The filtrate was concentrated on a rotary evaporator, giving 1.8 g of brown oil. Trituration with petroleum ether (bp 40–60°) gave a yellow solution and a dark residue. Recrystallization of the residue from benzene-cyclohexane furnished 0.4 g (25%) of 1-fluoro-2-acetylaminonaphthalene (**2a**), mp 117-120° (lit.[2] mp 120-121°). Hydrolysis of 0.25 g (1.1 mmol) of **2a** with 30 ml of 6 *N* hydrochloric acid followed by neutralization with sodium hydroxide solution furnished 0.17 g (96%) of 1-fluoro-2-naphthylamine (**2b**), mp 34-35°.[8] *Anal.* Calcd for $C_{10}H_8FN$: C, 74.5; H, 4.97; F, 11.8; N, 8.70; mol wt, 161. Found: C, 74.2; H, 5.04; F, 11.6; N, 8.66; mol wt, 161.

Reaction of **2b** (50 mg, 0.3 mmol) with isoamyl nitrite (0.5 mmol) in tetrahydrofuran[9] (1 ml) furnished 1-fluoronaphthalene (23%) which was identical with authentic material.

The cooled petroleum ether solution furnished 0.55 g (43%) of 1,1-difluoro-2-naphthone (**3**) as pale yellow needles, mp 49-50.5°. Sublimation at 40° (0.5 mm) furnished pure **3** with little loss of material: mp 50.5-52°; ir (melt between salt plates) 1700 cm^{-1} (C=O); nmr (CCl_4) δ 6.12 (two sets of triplets, 1 H, C=CHC=O, J_{H-H} = 10, J_{H-F} = 2.8 Hz), 7.31-7.99 (m, 5 H, aromatic and CH=CC=O). Irradiation at δ 6.12 resulted in the collapse of a doublet centered at δ 7.36 among the aromatic protons. *Anal.* Calcd for $C_{10}H_6F_2O$: C, 66.7; H, 3.3; F, 21.1; N, 0.00; mol wt, 180. Found: C, 66.4; H, 3.4; F, 21.9; N, 0.05; mol wt, 180.

Reduction of 0.15 g of **3** in 30 ml of absolute alcohol using 0.1 g of 5% palladium on carbon at 15 psi for 2 hr furnished, after work-up, material which showed hydroxyl but no carbonyl absorption in its ir spectrum and no olefinic protons in its nmr spectrum. An analytically pure sample was not obtained.

2-Naphthylamine (1b). CF_3OF was bubbled into a solution of 3.0 g (0.02 mol) of **1b** in 60 ml of chloroform. 2-Naphthylamine was consumed completely within 15-60 min. Glpc showed the presence of **3**, **2b**, and a third unidentified component in a 3:1:5 ratio, respectively. Filtration of the mixture furnished 1.2 g of gray residue. The filtrate was concentrated on a rotary evaporator at room temperature. The ir spectrum of the mixture showed strong absorptions at 2200 and 1800 cm^{-1} characteristic of an amine salt.[6] Chromatography of the crude mixture on a 15 × 1 in. Florisil column (1:1 benzene-hexane) furnished 0.7 g (19%) of **3**. Benzene eluent furnished 1-fluoro-2-naphthylamine (**2b**, 9%). A pink solid (0.4 g) identical with the material filtered from the reaction mixture from **1a** was obtained on further elution with ether. The solid did not contain the 2200 and 1800 cm^{-1} ir absorbances.

2-Naphthol (1c). CF_3OF was slowly bubbled into a solution of 2.9 g (13.0 mmol) of **1c** in 30 ml of chloroform until glpc analysis no longer showed the presence of **1c**. Two major products were indicated by both glpc and tlc. Nitrogen was bubbled into the reaction mixture to facilitate the removal of residual CF_3OF. The reaction mixture was filtered (0.2 g residue) and concentrated on a rotary evaporator to give a dark, viscous oil. The crude material was chromatographed on a 8 × 0.5 in. column of neutral alumina [1:1 benzene-petroleum ether (60°)], furnishing 0.5 g (20%) of pure **3**. Chloroform-benzene (7:3) eluted 0.32 g of **2c**. Recrystallization from petroleum ether produced 0.3 g (14%) of **2c**: mp 74-75°; ir (KBr) 3250 cm^{-1} (OH); nmr ($CDCl_3$) δ 5.2 (broad, 1 H, OH) and 7.1-8.2 (m, 6 H, aromatic). On careful drying, the δ 5.2 absorption appeared as a doublet, J = 4 Hz. Since no change was observed in the aromatic portion of the spectrum, the coupling occurred between the hydroxyl proton and the fluorine atom. Intramolecular hydrogen bonding was negligable as deduced from the large hydroxyl proton chemical shift dependence on the concentration of the solution.

Anal. Calcd for $C_{10}H_7FO$: C, 74.1; H, 4.4; F, 11.7; mol wt, 162. Found: C, 74.3; H, 4.4; F, 12.0; mol wt, 162.

Attempted preparation of **2c** from 1-amino-2-naphthol hydrochloride by a Balz-Schiemann reaction failed in two attempts.

9-Acetylaminoanthracene (4). CF_3OF was bubbled into a solution of 0.78 g (3.3 mmol) of **4** in 30 ml of chloroform. The reaction was monitored by tlc on silica gel (chloroform). Three products were detected but one major component accounted for more than 90% of the products. All **4** was consumed in 2 hr. Nitrogen was passed through the reaction mixture to remove residual CF_3OF. The solvent was removed on a rotary evaporator and the tan residue was chromatographed on a 10 × 0.5 in. column of alumina (benzene), furnishing a light yellow solid which after recrystallization from benzene yielded 0.65 g (95%) of **5**, mp 282-284°. The identity was proven by comparison with authentic anthraquinone.

Anthrone (6). A solution of 1.5 g (7.0 mmol) of **6** in 50 ml of chloroform was treated with CF_3OF for 3 hr. Tlc on silica gel (chloroform) showed the presence of two components. Removal of the chloroform on a rotary evaporator gave 1.6 g of yellow solid. Chromatography on a 10 × 1 in. column of silica gel (benzene) furnished 0.9 g (55%) of yellow **6**. Benzene-chloroform (1:1) elution furnished an orange solid after removal of the solvents. Recrystallization from benzene-petroleum ether gave 0.55 g (35%) of 10,10-bianthronyl (**7**): mp 262-268° dec (lit.[10] mp *ca.* 270-275° dec); ir identical with a published spectrum; nmr ($CDCl_3$) δ 4.75 (s, 1 H, benzylic proton) and 6.7-8.0 (complex, 8 H, aromatic); mol wt, 386 (calcd mol wt, 386).

Acknowledgment. This research was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and by the office of Research and Projects, Southern Illinois University.

Registry No.—**1a**, 581-97-5; **1b**, 91-59-8; **1c**, 135-19-3; **2a**, 19580-15-5; **2b**, 14554-00-8; **2c**, 51417-63-1; **3**, 51417-64-2; **4**, 37170-96-0; **6**, 90-44-8; **7**, 4393-30-0; CF_3OF, 373-91-1.

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Nitroxides. LVIII. Structure of Steroidal Spin Labels

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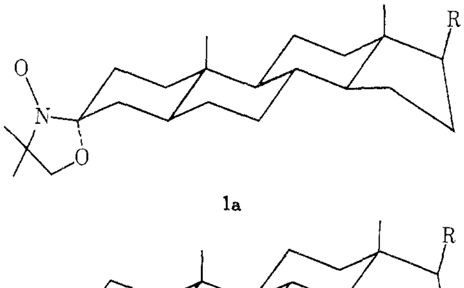
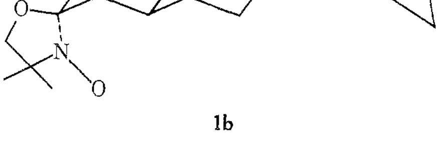
Spiro oxazolidine steroidal nitroxides[1] are widely used as spin labels in biological membranes.[2-4] In spite of its interest for orientation studies, the configuration of the spiro ring system has never been established. There are two possible isomers:[5] radical **1a**, in which the nitrogen is



1a



1b