ANTINEOPLASTIC AGENTS

X. N-BIS(2-FLUOROETHYL)AMINES[1,2]

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Received September 30, 1963

ABSTRACT

Successive conversion of N-bis(2-hydroxyethyl)-*p*-toluenesulphonamide (I*b*) to respective dimethanesulphonate and difluoro derivatives (II*a*, III*a*, and III*c*) was found to provide a convenient route to N-bis(2-fluoroethyl)amine. Reaction of N-bis(2-methanesulphonyloxyethyl)-*p*-toluenesulphonamide (III*a*) with limited quantities of potassium fluoride, in several protic solvents, was shown to yield N-(*p*-toluenesulphonyl)morpholine (IV). Utility of N-bis(2-fluoroethyl)amine as a precursor of fluoro-nitrogen mustards was illustrated by synthesis of two N-bis(2-fluoroethyl)benzylamines (IX*b* and X*a*). Application of an aluminum chloride – lithium aluminum hydride reagent for hydrogenolysis of carbon–fluorine bonds was also suggested.

Greater versatility in design of potential antineoplastic agents should be possible by utilizing predictable differences in the chemical reactivity expected for N-bis(2-fluoroethyl)amines, as compared to other N-bis(2-haloethyl)amines. For example, neighboring group displacement of halogen from a 2-fluoroethylamine should proceed substantially more slowly than with related 2-haloethylamines.[3] Intensive study of fluoro-nitrogen mustards might, therefore, lead to substances with more specific and prolonged antitumor activity.

Advantage might also be taken of the known ability of certain fluorine derivatives to inhibit the citric acid cycle (2, 3). The pronounced toxicity of fluoroacetic acid and several even-numbered linear homologs has been attributed to their eventual in vivo conversion to fluorocitric acid. Apparently, the odd-numbered homologs do not yield one of the necessary precursors, fluoroacetic acid, and are considerably less toxic. Fluorocitric acid, in turn, is believed to block the citric acid cycle during the tricarboxylic acid sequence. Although utilization of glycolytic products at this stage, by neoplastic tissue, appears less important than conversion to lactic acid, interruption of glycolysis during the citric acid cycle might be useful in control of certain neoplasms.

The above considerations and general paucity of information relating to synthesis and biological properties[4] of N-bis(2-fluoroethyl)amines has led to the present investigation. Syntheses of N-bis(2-fluoroethyl)-3,4-methylenedioxybenzylamine and N-bis(2-fluoroethyl)-3,4,5-trimethoxybenzylamine were first considered, as the corresponding chloro derivatives (5) gave encouraging results in the Dunning leukemia test system.

Synthesis of N-bis(2-fluoroethyl)amine (6) from 1-bromo-2-fluoroethane and ammonia illustrates the method employed for obtaining the two previously reported (6, 7) fluoro-nitrogen mustards. However, appropriate N-substitution of N-bis(2-fluoroethyl)amine was

[1]*Part IX. G. R. Pettit, D. S. Blonda, and E. C. Harrington. Can. J. Chem. 41, 2962 (1963).*

[2]*Abstracted in part from the Master of Science thesis submitted by R. L. Smith to the Graduate School, University of Maine, August, 1963.*

[3]*A proton magnetic resonance study of several N-bis(2-haloethyl)amines, in deuterium oxide, has indicated that the fluoro compounds undergo hydrolysis (see also ref. 1) and intermolecular condensation reactions at a markedly slower rate than, for example, the chloro derivatives. Details of this investigation will be reported by G. R. Pettit, J. A. Settepani, and R. A. Hill.*

[4]*Only one N-bis(2-fluoroethyl)amine appears in the comprehensive survey of alkylating agents prepared by R. B. Ross and colleagues (ref. 4). By contrast, over 2200 other nitrogen mustards are included in this valuable review.*

considered a more convenient approach to the required benzylamines and, in general, to fluoro-nitrogen mustards. Initially, N-bis(2-fluoroethyl)amine was prepared using the Childs procedure (6). When requirements for the amine increased, a more practical laboratory synthesis based on 2,2′-iminodiethanol (I) was undertaken.

A useful synthesis of N-bis(2-fluoroethyl)amine was eventually developed[5] employing the ready nucleophilic displacement of sulphonate esters by fluoride ion (12, 13). The bismethanesulphonate derivative (II*a*) of *p*-toluenesulphonamide I*b* was prepared, in cold pyridine solution (12), and allowed to react with excess anhydrous potassium fluoride. Treating the resulting N-bis(2-fluoroethyl)sulphonamide (III*a*) with hydrogen bromide (14), in glacial acetic acid, led to N-bis(2-fluoroethyl)amine (III*c*) hydrobromide. In this manner, substantial quantities (>50 g) of amine III*c* hydrobromide were routinely prepared. Similar transformation of methanesulphonamide II*b* to amine III*c* was less satisfactory.

Interestingly, an attempt to prepare the monofluoro derivative of sulphonate II*a* using almost equimolar quantities of ester (II*a*) and potassium fluoride, in diethylene glycol, gave N-(*p*-toluenesulphonyl)morpholine (IV) as major product. Repeating the reaction with formamide (13) as solvent led to a 72% yield of morpholine IV, while only unreacted sulphonamide II*a* was recovered when diglyme or dimethylformamide was used as solvent. These experiments suggest that potassium fluoride may first promote an exchange reaction (II*a* → V) between the sulphonate ester and protic solvent and then catalyze (15) intramolecular nucleophilic displacement (V → VI, see also ref. 16) of the second sulphonate group.[6]

Synthesis of the required benzylamines was initiated as described (5) for preparing the corresponding chloro analogs. Amine III*c* was easily converted to both 3,4-methylenedioxy- and 3,4,5-trimethoxy-benzamide derivatives (VII*a* and VIII*a*). Subjecting amide VII*a* to the aluminum chloride – lithium aluminum hydride reduction reaction, successfully used[1] (5) for obtaining N-bis(2-chloroethyl)benzylamines, unexpectedly caused nearly complete hydrogenolysis of the carbon–fluorine bond to yield N,N-diethyl-3,4-methylenedioxybenzylamine (IX*a*)[7] as major product. Subsequently, a reduction technique employing only lithium aluminum hydride was developed, using N,N-diethyl-3,4,5-trimethoxybenzamide (VIII*b*) as model substrate, and found suitable for reducing amides VII*a* and VIII*a* to N-bis(2-fluoroethyl)benzylamines IX*b* and X*a*.

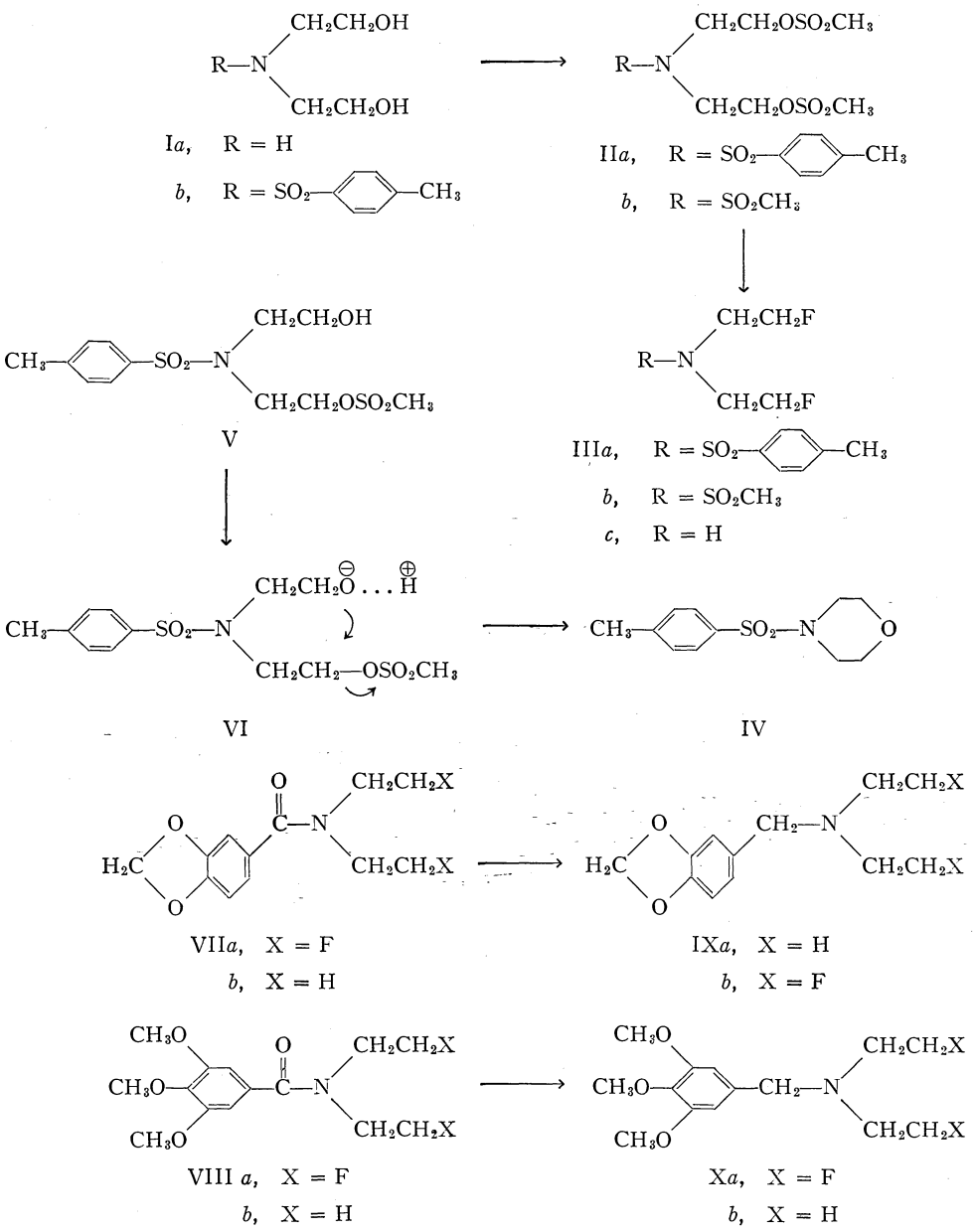
Biological evaluation of the fluoro-nitrogen mustards has been undertaken by the Cancer Chemotherapy National Service Center (National Institutes of Health, U. S. Public Health Service). Initial biological studies have shown that amine III*c* is a very toxic compound. No animals survived when random-bred albino rats were treated with N-bis(2-fluoroethyl)amine hydrobromide at a dose of 3 mg/kg in saline (by the intraperitoneal route). While a dose of 0.6 mg/kg was tolerated, only two of three survived at 1 mg/kg. By analogous experimental methods, the maleic acid salt of N-bis(2-chloroethyl)-amine was tolerated at 100 mg/kg, N-bis(2-bromoethyl)amine hydrobromide at 4 mg/kg, and N-bis(2-iodoethyl)amine hydroiodide at 10 mg/kg. Interestingly, when similar animals bearing Walker 256 (subcutaneous) were treated (saline solution, intraperitoneally, beginning on the first day of tumor transplant) with the above nitrogen mustards,

[5]*The approach employed was selected from among a number of potentially valuable methods (ref. 8, 9, 10, and 11).*

[6]*The major side reaction during displacement of p-toluenesulphonate esters by potassium fluoride, in diethylene glycol, has been attributed to ether formation (12).*

[7]*The aluminum chloride – lithium aluminum hydride reagent, used in this experiment, may provide a mild and general method for hydrogenolysis of carbon–fluorine bonds. Complex metal hydrides do not readily affect the carbon–fluorine bond (cf. Hudlický, ref. 3 (p. 161) and ref. 17).*

tumor growth was inhibited; 40% by the fluoro mustard (0.6 mg/kg), completely by the chloro (22 mg/kg), completely by the bromo (4 mg/kg), and 88% by the iodo (6.5 mg/kg). Tumor growth was measured on the 10th day.



EXPERIMENTAL

Glass apparatus employed for preparation and subsequent reduction of the benzamides was previously dried at 120° C. Tetrahydrofuran used in the reduction procedure was heated at reflux over sodium for 4 hours and then distilled (from lithium aluminum hydride) into the reaction container. The formamide and dimethylformamide were both distilled *in vacuo* and stored over molecular sieve type 4-A. Potassium fluoride was dried in a vacuum oven at 165° for 24 hours. All solvent extracts were dried over magnesium sulphate.

Melting points were observed using a Kofler apparatus. Infrared spectral data was recorded by Dr. R. A. Hill of this laboratory. Microanalyses were provided by Dr. A. Bernhardt, Max-Planck Institute, Mülheim (Ruhr), Germany, and Drs. Weiler and Strauss, Oxford, England.

N-bis(2-methanesulphonyloxyethyl)-p-toluenesulphonamide (IIa)

Methanesulphonyl chloride (115 g) was added dropwise with stirring over a 5.5 hour period to a cold (ice bath) solution of N-bis(2-hydroxyethyl)-*p*-toluenesulphonamide (I*b*, 130 g, ref. 18) in dry pyridine (107 ml). The resulting pale yellow mixture was stirred with cooling for 1.5 hours and then allowed to stand 2.5 hours. After the mixture was washed with ice water and 6 *N* hydrochloric acid the residue was extracted with chloroform. The combined extract was washed successively with water, 6 *N* hydrochloric acid, and water. Following removal of solvent *in vacuo* and trituration with ether, the pale yellow residue solidified. Recrystallization from chloroform–benzene gave colorless crystals; yield, 136 g (66%), m.p. 58–62°. Four recrystallizations from benzene (Norit-A) afforded an analytical sample melting at 63–63.5°; ν_{max}^{KBr} 1355–1318 (broad), 1180–1154 (broad), 1015, 998, 980, 910, 820, and 720 cm^{-1}. Calc. for $C_{13}H_{21}NO_8S_3$: C, 37.58; H, 5.09; N, 3.37; S, 23.16%. Found: C, 37.30 to 41.68; H, 4.92 to 5.39; N, 3.08 to 3.19; S, 22.04 to 22.18%.

Three apparently pure analytical samples of sulphonamide II*a*, m.p. 63–64°, were prepared using different methods and submitted for elemental analysis. However, the product (II*a*) was generally accompanied by a tenacious impurity as evidenced by the above analytical data.

N-Bis(2-fluoroethyl)-p-toluenesulphonamide (IIIa)

A mixture of sulphonamide II*a* (18.0 g, 0.01 mole), anhydrous potassium fluoride (10.0 g, 0.17 mole) and diethylene glycol (180 ml) was stirred at 130–140° for 4.5 hours. The solution was cooled to room temperature and diluted with ice water (150 ml). The resulting mixture was extracted with chloroform and the extract was concentrated to a colorless oil, which crystallized upon trituration with ether. Recrystallization from benzene – ethyl ether yielded (4.0 g, 32%) colorless needles melting at 76–78°. Childs (6) reported a melting point of 79°. Four recrystallizations from ethyl ether (Norit-A) gave an analytical specimen melting at 79–79.4°; ν_{max}^{KBr} 1598, 1468, 1447, 1400, 1365, 1342–1330 (broad), 1293, 1172–1148 (broad), 1038, 937–922, 858, 720, and 700 cm^{-1}. Calc. for $C_{11}H_{15}F_2NO_2S$: C, 50.18; H, 5.74; F, 14.43; N, 5.32; S, 12.18%. Found: C, 50.40; H, 5.67; F, 14.29; N, 5.13; S, 12.36%.

N-Bis(2-methanesulphonyloxyethyl)methanesulphonamide (IIb)

Methanesulphonyl chloride (115 ml) was added (dropwise) over 1 hour to a cold (ice bath) solution composed of 2′,2′-iminodiethanol (52.6 g) and dry pyridine (160 ml). The resulting yellow suspension was stirred for 0.25 hours and then the solution was filtered. The solid phase was washed well with water, with 6 *N* hydrochloric acid (250 ml), and again with water. Following crystallization from acetone, the product (137 g, 81%), m.p. 110–112°, was recrystallized from chloroform to yield pale yellow needles melting at 114.5–115.5°; yield, 50.0 g (33%). Several recrystallizations from acetone raised the melting point to 117–118°; ν_{max}^{KBr} 1368–1320 (broad), 1176, 1148, 1135, 1020, 978, 900, 808, 778, 740, and 727 cm^{-1}. Calc. for $C_7H_{17}NO_8S_3$: C, 24.76; H, 5.05; N, 4.13; S, 28.34%. Found: C, 24.95; H, 4.97; N, 3.94; S, 27.98%.

N-Bis(2-fluoroethyl)methanesulphonamide (IIIb)

A mixture composed of anhydrous potassium fluoride (70.0 g, 1.2 mole), methanesulphonamide II*b* (10.0 g, 0.3 mole), and diethylene glycol (500 ml) was stirred and heated at 150–155° for 6 hours. As the reaction proceeded, the mixture began to gel and darken. After cooling, and dilution with cold water (750 ml), the mixture was extracted with chloroform. The extract was concentrated *in vacuo* to a brown oil and triturated with ethyl ether. Next, the waxy residue was extracted with benzene (50 ml) and the extract was treated with Norit-A. Following dilution with ethyl ether and cooling, two crystal crops were obtained: the first 5.9 g (10%), m.p. 42.5–45.5°, and the second 10.1 g (18%), m.p. 38–42°. Three recrystallizations of the higher melting specimen from carbon tetrachloride led to an analytical sample of colorless needles, m.p. 46.2–46.7°; ν_{max}^{KBr} 1346–1320 (broad), 1155–1144 (broad), 1012, 966, 922, 843, and 776 cm^{-1}. Calc. for $C_5H_{11}F_2NO_2S$: C, 32.08; H, 5.92; F, 20.03; N, 7.48; S, 17.13%. Found: C, 32.35; H, 5.72; F, 20.01; N, 7.73; S, 16.90%.

N-Bis(2-fluoroethyl)amine (IIIc) Hydrobromide

Procedure A

Toluenesulphonamide III*a* (1.32 g) was added to a solution of phenol (0.47 g) in anhydrous 3:7 hydrogen bromide – glacial acetic acid and the pale yellow solution was allowed to remain at room temperature for 13 hours. After dilution with ethyl ether (30 ml) the colorless crystalline hydrobromide weighed 0.25 g (26%) and melted at 186–188°. Increasing the reaction time to 2.5 or to 4 days afforded respectively 48 to 60% yields of amine III*c* hydrobromide.[8] Three recrystallizations from methanol – ethyl ether gave a pure sample, m.p. 187–189°; ν_{max}^{KBr} 3000–2900 (broad), 2760, 1563, 1455, 1422, 1273, 1058, 925, and 785 cm^{-1}. Calc. for $C_4H_{10}BrF_2N$: C, 25.28; H, 5.30; F, 19.99%. Found: C, 25.46; H, 5.23; F, 20.26%.

By mixture melting point determination and infrared spectral comparison in potassium bromide, the

[8]*Experiments conducted by T. P. Habif and M. Sciaraffa.*

hydrobromide salt was found to be identical with a specimen prepared from N-bis(2-fluoroethyl)amine hydrochloride (see below). Fluoro-nitrogen mustard III*c* was further characterized by conversion to *N-bis(2-fluoroethyl)-3,4,5-triiodobenzamide.* The amide was prepared (cf. VII*a*) using the amine corresponding to 4.2 g of N-bis(2-fluoroethyl)amine hydrobromide and 5.2 g of 3,4,5-triiodobenzoyl chloride (19). The crude pale yellow solid was recrystallized from benzene (Norit-A) to yield 2.9 g (49%) of colorless needles melting at 152–154.5°. Concentrating the mother liquor gave a second crop (0.2 g) melting at 151–153.5°. Several recrystallizations from benzene–hexane afforded an analytical specimen melting at 154–155° with sublimation from 150°, ν_{max}^{KBr} 1630 cm^{-1}. Calc. for $C_{11}H_{10}F_2I_3NO$: C, 22.35; H, 1.71; I, 64.42; N, 2.37%. Found: C, 22.56; H, 1.64; I, 64.22; N, 2.23%.

Procedure B

When the general cleavage reaction over a 13 hour period described in procedure A was applied to methanesulphonamide III*b* (3.7 g), the yield of N-bis(2-fluoroethyl)amine hydrobromide (0.3 g), m.p. 183–187°, was 8%. Two recrystallizations from methanol – ethyl ether led to a pure sample, m.p. 187–189°, which was identical with the hydrobromide obtained using procedure A. The identical composition of both products was established by infrared spectral comparison (in potassium bromide) and mixture melting point determination.

N-Bis(2-fluoroethyl)amine Hydrochloride

A specimen of N-bis(2-fluoroethyl)amine prepared as described by Childs (6) was converted to the hydrochloride derivative by D. S. Blonda of this laboratory. Three recrystallizations from methanol – ethyl ether gave an analytical sample melting at 202°; ν_{max}^{KBr} 2990–2970, 2730, 2460, 1590–1578 (broad), 1460, 1058, 936–922 (broad), cm^{-1}. Calc. for $C_4H_{10}ClF_2N$: C, 33.00; H, 6.92; Cl, 24.35%. Found: C, 33.02; H, 6.84; Cl, 24.16%.

N-(p-Toluenesulphonyl)morpholine (IV)

Approximately 60 ml of a solution prepared from anhydrous potassium fluoride (1.4 g, 0.024 mole) and formamide (75 ml) was added dropwise over a 0.25 hour period to a warm (90°) solution of *p*-toluenesulphonamide II*a* (9.1 g, 0.22 mole) in formamide (50 ml). Before addition of the remaining potassium fluoride solution, over 0.25 hour, stirring and heating at 120–125° were continued 4 hours. Heating was then continued at 120–125° for 3 hours. The solution was cooled to room temperature and poured into cold water (125 ml). Following extraction with benzene the combined extract was concentrated *in vacuo* to a colorless solid; yield, 3.8 g (71.5%), m.p. 144.5°. Recrystallization from methanol gave colorless needles melting at 148–149°. By mixture melting point determination and infrared spectral comparison in potassium bromide, the product was found to be identical with an authentic sample (16).

When the above experiment was repeated essentially as described using diethylene glycol as solvent the crude yield of *p*-toluenesulphonamide IV was 5.6 g, m.p. 142–143.5°. Recrystallization from methanol gave 0.43 g of colorless needles melting at 147–148.5°. However, when the reaction was repeated using the dimethyl ether of diethylene glycol or dimethylformamide as solvent only starting material (II*a*) was isolated.

N-Bis-ethyl-3,4-methylenedioxybenzylamine (IXa) Hydrochloride[9]

(a) From N-bis(2-fluoroethyl)-3,4-methylenedioxybenzamide (VIIa)

In a typical experiment N-bis(2-fluoroethyl)amine hydrobromide (5.7 g) was treated with 1.3 g of sodium hydroxide in water (25 ml). The corresponding amine was extracted with benzene and the combined extract was dried. Next, a solution of 3,4-methylenedioxybenzoyl chloride (2.6 g, ref. 5) in benzene (25 ml) was added over a 1 hour period with cooling (ice bath). Stirring was continued while the mixture was heated at reflux for 5 hours. After it was cooled to room temperature, N-bis(2-fluoroethyl)amine hydrochloride was collected and the colorless filtrate was concentrated to a deep straw-colored oil; yield, 3.45 g, ν_{max}^{pure} 1640 cm^{-1}. Several attempts to crystallize the crude oily amide were unsuccessful.

The N-bis(2-fluoroethyl)amide (VII*a*, 9.2 g) was reduced using a mixture of aluminum chloride (4.8 g) and lithium aluminum hydride (1.2 g) as described for preparation of N-bis(2-chloroethyl)-3,4-methylenedioxybenzylamine hydrochloride in a prior investigation (5). In this case, addition of excess ethyl ether – hydrogen chloride solution did not precipitate the hydrochloride. However, removing the solvent *in vacuo* led to 3.5 g of colorless crystalline amine (IX*a*) hydrochloride, m.p. 190–195°. Four recrystallizations from methanol – ethyl ether raised the melting point to 203–204°, with darkening from 198°.

(b) From N-bis-ethyl-3,4-methylenedioxybenzamide (VIIb)

Preparation (cf. ref. 20) and conversion of amide VII*b* (9.7 g) to the corresponding amine (2.1 g, decomp. 210–211° with darkening from 209°) was accomplished essentially as described in the preceding experiment. Calc. for $C_{12}H_{18}ClNO_2$: C, 59.13; H, 7.44; N, 5.76%. Found: C, 59.39; H, 7.30; N, 5.86%.

Amine IX*a* hydrochloride prepared by procedure (*a*) was found to be identical (infrared spectral comparison) with the specimen prepared by this method. A mixture of both products melted at 206–207° (darkening from 203°). However, elemental analysis of the product from procedure (*a*) indicated that this specimen still contained a small amount (1.44%) of fluorine.

[9]*These experiments were performed by D. S. Blonda.*

N-Bis-ethyl-3,4,5-trimethoxybenzylamine (Xb) Hydrochloride

A solution of N-bis-ethyl-3,4,5-trimethoxybenzamide (3.0 g, 0.011 mole (ref. 21)) in tetrahydrofuran (20 ml) was slowly (0.5 hour) added to a cold (ice bath) suspension of lithium aluminum hydride (0.24 g, 0.006 mole). The ice bath was removed and stirring was continued at room temperature for 24 hours. The reaction was conducted in a nitrogen atmosphere. After cautious addition of ethyl acetate, 95% ethanol, and water, the reaction mixture was concentrated *in vacuo* at 40–50°. The residual mixture was treated with 40% sodium hydroxide (20 ml) and extracted with benzene. Diluting the combined and dried extract with dry hydrogen chloride in ethyl ether gave 2.28 g (70.4%), m.p. 179.5–181°, of amine X*b* hydrochloride. Three recrystallizations from methanol – ethyl ether (Norit-A) led to a pure sample as colorless needles, m.p. 183–184°; ν_{max}^{KBr} 2920, 2600, 1590, 1512, 1470, 1428, 1335, 1260–1243 (broad), 1122, 1018, 860, and 780 cm^{-1}. Calc. for $C_{14}H_{24}ClNO_3$: C, 58.03; H, 8.35; N, 4.83%. Found: C, 58.30; H, 8.42; N, 4.93%.

N-Bis(2-fluoroethyl)-3,4-methylenedioxybenzylamine (IXb) Hydrochloride

Lithium aluminum hydride (0.5 g) was used to reduce N-bis(2-fluoroethyl)-3,4-methylenedioxybenzamide (VII*a*, 3.1 g) as described for preparation of diethyl amine X*b*. The crude hydrochloride was obtained as colorless crystals; yield, 1.73 g (52%), m.p. 176–178°. Four recrystallizations from methanol – ethyl ether led to an analytical specimen melting at 185° (sublimation at 150°), ν_{max}^{KBr} 2900, 2600–2500 (broad), 1510, 1494, 1445, 1255, 1140, 922, and 905 cm^{-1}. Calc. for $C_{12}H_{16}ClF_2NO_2$: C, 51.53; H, 5.77; N, 5.01%. Found: C, 51.42; H, 5.87; N, 4.88%.

N-Bis(2-fluoroethyl)-3,4,5-trimethoxybenzamide (VIIIa)

A 6.1 g sample of bis(2-fluoroethyl)amine hydrobromide was converted to the free base and allowed to react with 3,4,5-trimethoxybenzoyl chloride (3.5 g) in dry benzene (100 ml) as described for synthesis of amide VII*a*. The crude amide crystallized from benzene–hexane as colorless needles weighing 4.4 g (96%), m.p. 80.5–83.5°. Two recrystallizations from the same solvent afforded a pure sample melting at 83.7–84.5°, ν_{max}^{KBr} 1638 cm^{-1}. Calc. for $C_{14}H_{19}F_2NO_4$: C, 55.44; H, 6.31; F, 12.53; N, 4.61%. Found: C, 55.55; H, 6.36; F, 12.30; N, 4.56%.

N-Bis(2-fluoroethyl)-3,4,5-trimethoxybenzylamine (Xa) Hydrochloride

Lithium aluminum hydride (0.14 g) reduction of amide VIII*a* (2.0 g) was accomplished as described for preparation of amine X*b* hydrochloride. Recrystallizing the crude hydrochloride from methanol – ethyl ether (Norit-A) gave a first crop (0.75 g) melting at 132–134.5° and a second crop (0.14 g, total yield 41%) melting at 129.5–131.5°. Three recrystallizations of the higher melting specimen from the same solvent gave a pure sample of colorless platelets melting at 133.5–135°, ν_{max}^{KBr} 1589, 1510, 1468, 1422, 1335, 1258, 1172, and 965 cm^{-1}. Calc. for $C_{14}H_{22}ClF_2NO_3$: C, 51.62; H, 6.81; F, 11.66; N, 4.30%. Found: C, 51.75; H, 6.91; F, 11.44; N, 4.29%.

ACKNOWLEDGMENTS

This investigation was aided by Grants Number T-79C and T-79D from the American Cancer Society. We also wish to thank Dr. R. B. Ross for providing a summary of the N-bis(2-fluoroethyl)amine toxicity studies.

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