derivative as well as the amidoxime. The last one apparently was the result of hydrolysis of *O*-acetyl derivative by water which was produced during oxadiazole formation. Compound **1b** cyclized a little faster (~5 h) compared to **1a,c,d** (~6-7 h). After reaction, the pure compound in each case was obtained by column chromatography over silica gel (Merck) using benzene-hexane (1:1) as eluent. The yields were as follows: **2a**, 82.8%; **2b**, 64.3%; **2c**, 56.6%; and **2d** 83.0%.

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Registry No. **1a**, 942-87-0; **1b**, 88303-26-8; **1c**, 88303-27-9; **1d**, 88303-28-0; **2a**, 1198-98-7; **2b**, 87944-74-9; **2c**, 87944-75-0; **2d**, 81386-30-3; benzamidoxime, 613-92-3.

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Synthesis of 3-Aryl-1-adamantanemethylamines

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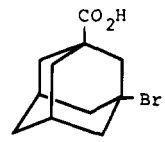
Friedel-Crafts alkylations of fluorobenzene, thioanisole, and thiophene with 3-bromo-1-adamantanecarboxylic acid are reported. Various Lewis acids ($AlCl_3$, $FeCl_3$, $ZnCl_2$, $SnCl_4$) served as effective catalysts for these substitution reactions. The products were 3-aryl-1-adamantanecarboxylic acids. Substitution took place in fluorobenzene and thioanisole at the para position and in thiophene at positions 2 and 3. These acids were reacted with phosphorus pentachloride and then ammonia to form amides which were reduced by lithium aluminum hydride to provide the corresponding 3-aryl-1-adamantanemethylamines.

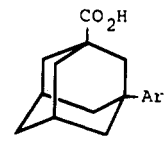
In connection with the synthesis of potential radiation-protective drugs (*1*), a number of 3-aryl-1-adamantanemethylamines were required. Ideally, these could be prepared by the lithium aluminum hydride reduction of the corresponding 3-aryl-1-adamantanecarboxamides or the Hofmann degradation of 3-aryl-1-adamantaneacetamides. Attempts to introduce a carboxylic or acetic acid group directly at position 3 of a 1-aryladamantane failed. For example, the standard Koch-Haaf carboxylation (*2*) of 1-phenyladamantane produced no 3-phenyl-1-adamantanecarboxylic acid, **2** (Ar = C_6H_5), and only starting material was recovered. The well-established synthesis of 1-adamantaneacetic acid (*3*) from adamantane, 1,1-dichloroethene, sulfuric acid, boron trifluoride, and *tert*-butyl alcohol was applied to 1-phenyl-and 1-(4-bromophenyl)-adamantanes at various temperatures gave back starting materials. No immediate explanation can be advanced to account for the failure of 1-aryladamantanes to undergo these substitution reactions at another bridgehead carbon.

The successful approach to **2** was by means of the Friedel-Crafts reaction of 3-bromo-1-adamantanecarboxylic acid with arenes. 1-Adamantyl halides are known to substitute arenes to provide 1-aryladamantanes (*4-7*). Alkylation of toluene (*8*), xylene (*8*), and anisole (*9*) readily furnished 3-(para-substituted aryl)-1-adamantanecarboxylic acids, **2**. Such alkylations with **1** were extended to the synthesis of a number of additional acids, **2**. With fluorobenzene, a good yield of the *p*-fluorophenyl derivative was obtained. However, with thioanisole only a moderate amount of **2** (Ar = 4-$CH_3SC_6H_4$) was obtained. Relatively few Friedel-Crafts reaction have been reported with thioanisole. Complexation of the sulfide group with the Lewis acid to create an electron-attracting sulfonium ion moiety is attributed to decreased reactivity of the ring toward electrophilic substitution (*10*).

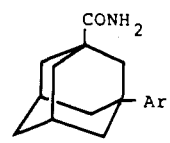
The reaction of 1- and 2-adamantyl bromides with thiophene has been reported. There was isolated a mixture of 2- and



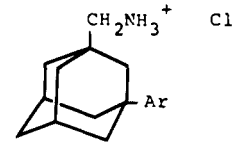
1



2a, Ar = 4-FC_6H_4
b, Ar = 4-$CH_3SC_6H_4$
c, Ar = 2-C_4H_3S
d, Ar = 3-C_4H_3S



3a, Ar = 4-$CH_3OC_6H_4$
b, Ar = 4-FC_6H_4
c, Ar = 4-$CH_3SC_6H_4$
d, Ar = 2-C_4H_3S
e, Ar = 3-C_4H_3S



4a, Ar = 4-$CH_3C_6H_4$
b, Ar = 4-$CH_3OC_6H_4$
c, Ar = 4-FC_6H_4
d, Ar = 4-$CH_3SC_6H_4$
e, Ar = 2-C_4H_3S

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3-(1-adamantyl)thiophenes (*11*). A mixture of these isomers was converted first to chloromercuri derivatives which were separated by fractional crystallization (*11*). The pure isomers were regenerated by protolysis of the pure chloromercuri derivative.

The reaction of thiophene with **1** yielded a mixture of 3-(2- and 3-thienyl)-1-adamantanecarboxylic acids, **2c,d**, in the ratio of 2:1 (estimated by GC of their methyl esters). Attempts to separate these isomeric acids by conversion to chloromercuri derivatives proved unsuccessful. Preparative liquid chromatography enabled the separation of **3d**, which was identified by its 180-MHz ^{1}H NMR spectrum. Although the coupling constants between the various protons in similar 2- and 3-substituted thiophenes are relatively close, the chemical shifts of the ring protons in **3d** compared well with those published for 2-methylthiophene (*12*). Attempts to isolate pure **3e** by further chromatographic separations proved futile. This amide was always admixed with **3d** as was evident from 180-MHz spectra of various fractions. The ^{1}H NMR parameters for the thiophene ring in **3d,e** agreed with those reported for 2- and 3-methylthiophene (*13*) and 2- and 3-(1-adamantyl)thiophene (*11*).

The acids, **2**, were transformed to the amides, **3**, which were reduced by lithium aluminum hydride to the required methylamines. The amines were isolated as the hydrochlorides, **4**.

Experimental Section

All melting points were taken on a Hoover-Thomas capillary melting point apparatus and are uncorrected. Proton NMR spectra were recorded on a Varian T60A spectrometer fitted with a Nicolet TT-7 Fourier transform accessory or by means of a 180-MHz Bruker CXP-180 instrument. Chemical shifts are reported in ppm (δ) downfield from internal $(CH_3)_4Si$. Adamantane proton resonances were not resolved and appeared as broad multiplets between 1.5 and 2.3 ppm and their chemical shifts are not reported for each compound.

Mass spectra were obtained by Mr. Richard Dvorak at 70 eV on a Perkin-Elmer Hitachi RMU-6D or Varian MAT 112 spectrometer. The ions which are listed usually are those above *m/e* 100 and with intensities greater than 20% of base peak. Relative intensities are shown in parentheses. Microanalyses were performed by MicroTech Labs, Skokie, IL. Satisfactory elemental analyses were obtained for new compounds and were submitted for review.

Solvents in various workup procedures were removed in vacuo by means of a rotary flash evaporator at the lowest possible temperature.

***3-Bromo-1-adamantanecarboxylic Acid* (1).** The literature bromination of 1-adamantanecarboxylic acid in the presence of anhydrous aluminum bromide worked well but aluminum chloride can be substituted for the bromide and **1** was obtained (81%): mp 145–146 °C (lit. (*14*) mp 146.5 °C); ^{1}H NMR ($CDCl_3$), δ 1.70–2.49 (complex m for adamantane protons), 10.20 (s, CO_2H).

***3-Aryl-1-adamantanecarboxylic Acids* (2). *General Procedure*.** A mixture of **1** (0.01 mol), the anhydrous metal halide (0.01 mol), and the arene (15 mL) was stirred in an oil bath at specified temperatures over a period of time. The reaction mixture was cooled and poured into ice water (100 mL) containing concentrated HCl (5 mL). The organic layer was separated and the aqueous solution extracted with benzene (3 × 50 mL). The combined organic extract was washed first with water and then with 10% NaOH solution (75 mL) which had previously been saturated with NaCl. The sodium salt of **2** which appeared at the interphase was filtered and washed several times with saturated NaCl solution. The salt was suspended in water and neutralized by the addition of concentrated HCl. The acid was filtered, washed with water, and recrystallized from methanol.

***3-(4-Fluorophenyl)-1-adamantanecarboxylic Acid* (2a).** **2a** was prepared (62%) from fluorobenzene, by using $FeCl_3$, 90 °C (3 h): mp 168–170 °C; ^{1}H NMR (CCl_4) δ 6.76–7.29 (complex m, ArH), 11.82 (br s, CO_2H); mass spectrum, *m/e* (relative intensity) 276 (2), 275 (19), 274 (M^+, 100), 229 (73), 173 (46), 153 (29), 136 (29), 109 (50).

***3-(4-Methylthiophenyl)-1-adamantanecarboxylic Acid* (2b).** **2b** was made (35%) from thioanisole, $ZnCl_2$ at 100 °C, (3 h): mp 143–144 °C; ^{1}H NMR (CCl_4) δ 2.40 (s, SCH_3), 7.15 (br s, ArH), 10.85 (s, CO_2H); mass spectrum, *m/e* (relative intensity) 304 (10), 303 (28), 302 (M^+, 100), 288 (13), 201 (17), 179 (38).

An increase in reaction time did not improve the yield. Reactions conducted in boiling CS_2 or CH_2Cl_2 with $AlCl_3$ (3 h) led to the recovery of **1**. A reaction in nitrobenzene at 100 °C ($AlCl_3$, 4 h) yielded neither **1** or **3**.

A mixture of 3-(2- and 3-thienyl)-1-adamantanecarboxylic acids was obtained (47%) when thiophene was used ($SnCl_4$, 85 °C, 1 h). The acids were esterified with diazomethane and were analyzed by GC (Hewlitt-Packard gas chromatograph 14492) using a 3% OV-225 Gaschrome Q column at 215 °C. The 2- and 3-isomeric esters were detected (2:1) at 10.0 and 11.3 min, respectively. This mixture of acids was, converted to the amides, as described below.

***3-Aryl-1-adamantanecarboxamides* (3).** A mixture of **2** (0.01 mol) and phosphorus pentachloride (0.01 mol) in carbon tetrachloride (50 mL) was refluxed for 1 h. After the solvents were evaporated in vacuo, the residue was evaporated in vacuo twice with 20 mL of carbon tetrachloride each time to remove volatile phosphorus halides. The remaining acid chloride was dissolved in anhydrous tetrahydrofuran and added dropwise to stirred ice-cold ammonium hydroxide (28%, 60 mL) (15 h). The product was filtered, washed with water, and recrystallized from ethanol.

***3-(4-Methoxyphenyl)-1-adamantanecarboxamide* (3a).** **3a** was made (82%) from the corresponding acid (*9*): mp 145–146 °C; ^{1}H NMR ($CDCl_3$) δ 3.78 (s, CH_3), 5.60 (br s, NH_2), 6.77–7.35 (AA′BB′ pattern for ArH); mass spectrum, *m/e* (relative intensity) 286 (21.17), 285 (M^+, 100), 241 (59), 185 (29), 121 (19).

***3-(4-Fluorophenyl)-1-adamantanecarboxamide* (3b).** **3b** was prepared (64%): mp 160–162 °C; ^{1}H NMR ($CDCl_3$) δ 5.50 (br s, NH_2), 6.83–7.44 (AA′BB′, ArH); mass spectrum, *m/e* (relative intensity) 275 (2), 274 (9), 273 (M^+, 40), 229 (100), 173 (26).

***3-(4-Methylthiophenyl)-1-adamantanecarboxamide* (3c).** **3c** was obtained in 68% yield: mp 89–91 °C; NMR (CCl_4) δ 2.45 (s, CH_3), 5.85 (br s, NH_2), 7.24 (s, ArH); mass spectrum *m/e* (relative intensity) 303 (9), 302 (23.45), 301 (M^+, 100), 283 (89), 257 (32), 226 (17).

Complete separation of 3-(2- and 3-thienyl)-1-adamantanecarboxamides (**3d,e**) by medium-pressure column chromatography or thin-layer chromatography (silica gel or alumina) proved difficult. For example, TLC on 0.25-mm silica gel with a fluorescent indicator, Polygram SIL G/UV_{254} (Brinkmann Instruments Inc.), gave only one spot, detected by UV light, R_f = 0.45 (chloroform–95% ethanol 9:1). Preparative liquid chromatography on a Waters Auto-500A chromatograph, and a Prep Pak Silica (5.7 × 30.0 cm) column, flow rate 250 mL/min (refractive index detector), separated 0.120 g of **3d** from a 1.5-g mixture of **3d** and **3e** using ethyl actate–chloroform (3:1) as solvent: mp 120–122 °C; 180-MHz ^{1}H NMR ($CDCl_3$) δ 5.85 (d, $CONH_2$), 6.75 (dd, H-3 of thiophene), 6.84 (dd, H-4 of thiophene), 7.05 (dd, H-5 of thiophene) ($J_{4,5}$ = 5.1, $J_{3,4}$ = 3.6, $J_{3,5}$ = 1.2 Hz); mass spectrum, *m/e* (relative intensity) 263 (5), 262 (14), 261 (M^+, 66), 217 (97), 161 (30), 149 (100).

***3-Aryl-1-adamantanemethylamine Hydrochlorides* (4).** A suspension of **3** (0.02 mol) in anhydrous ether or tetrahydrofuran

(100 mL) was added dropwise to a well-stirred suspension of lithium aluminum hydride (0.10 mol) in either solvent (400 mL). After the addition, the reaction mixture was refluxed for 12 h, cooled to 0 °C, and decomposed by adding water (3.8 mL), 20% sodium hydroxide (11.4 mL), and again water (3.8 mL). The precipitate was filtered and washed 3 times with ether. The combined ether extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was dissolved in anhydrous ether, filtered to remove insoluble material, and treated with dry hydrogen chloride gas. The amine hydrochlorides were filtered and recrystallized from aqueous ethanol.

***3-(4-Methylphenyl)-1-adamantanemethylamine Hydrochloride* (4a).** **4a** was synthesized from the corresponding amide (*8*) (75%): mp 214–216 °C; ^{1}H NMR (Me_2SO-d_6) δ 2.59 (br s, CH_2N), 7.11–7.29 (m, ArH), 7.97 (br s, NH_3^+); mass spectrum, *m/e* (relative intensity) 256 (20), 255 (M^+ – HCl, 60), 238 (41), 225 (100), 183 (128), 168 (92).

***3-(4-Methoxyphenyl)-1-adamantanemethylamine Hydrochloride* (4b).** **4b** was prepared (77%): mp 237–238 °C; ^{1}H NMR (Me_2SO-d_6) δ 2.55 (br s, CH_2N), 6.77–7.36 (AA′BB′, ArH), 8.06 (br s, NH_3); mass spectrum, *m/e* (relative intensity) 273 (8), 272 (41), 271 (M^+, 70), 242 (57), 241 (100), 185 (62), 149 (25), 121 (30).

***3-(4-Fluorophenyl)-1-adamantanemethylamine Hydrochloride* (4c).** **4c** was obtained in 76% yield: mp 208–210 °C; ^{1}H NMR (Me_2SO-d_6) δ 2.56 (br s, CH_2N), 6.95–7.5 (m, ArH), 8.06 (br s, NH_3); mass spectrum, *m/e* (relative intensity) 259 (M^+ – HCl, 32), 238 (100), 229 (67), 173 (59), 153 (21), 109 (50).

***3-(4-Methylthiophenyl)-1-adamantanemethylamine Hydrochloride* (4).** **4d** was produced (65%): mp 210–212 °C; ^{1}H NMR (Me_2SO-d_6) δ 2.44 (s, SCH_3), 2.56 (br s, CH_2N), 7.26 (br s, ArH); mass spectrum, *m/e* (relative intensity) 290 (6), 289 (21), 288 (100), 287 (M^+ – HCl, 19), 257 (48), 201 (47), 169 (21), 165 (25), 137 (26).

***3-(2-Thienyl)-1-adamantanemethylamine*.** This compound was isolated as a pale yellow oil from the reduction of pure **3d** (81%): 180-MHz ^{1}H NMR ($CDCl_3$) δ 2.41 (d, CH_2N), 6.74 (dd, H-3 of thiophene), 6.83 (dd, H-4 of thiophene), 7.06 (dd, H-5 of thiophene), $J_{4,5}$ = 5.1, $J_{3,4}$ = 3.6, $J_{3,5}$ = 1.2 Hz. It was converted to the hydrochloride (**4e**): mp 255–260 °C (dec); mass spectrum, *m/e* (relative intensity) 249 (3), 248 (9), 247 (M^+ – HCl, 48) 218 (100), 217 (62), 135 (22), 134 (52), 133 (23); ^{1}H NMR (Me_2SO-d_6) δ 2.59 (br s, CH_2N), 6.90–7.46 (m, ArH), 8.01 (br s, NH_3^+).

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Registry No. **1**, 21816-08-0; **2** (Ar = H), 828-51-3; **2** (Ar = 4-$CH_3OC_6H_4$), 56531-56-7; **2a**, 88358-11-6; **2b**, 88358-12-7; **2c**, 88358-13-8; **2d**, 88358-14-9; **3** (Ar = 4-$CH_3C_6H_4$), 61051-22-7; **3a**, 61051-24-9; **3b**, 88376-63-0; **3c**, 88358-15-0; **3d**, 88358-16-1; **3e**, 88358-17-2; **4a**, 88358-18-3; **4b**, 88358-19-4; **4c**, 88358-20-7; **4d**, 88358-21-8; **4e**, 88358-22-9; 3-(2-thienyl)-1-adamantanemethylamine, 88358-23-0; fluorobenzene, 462-06-6; thioanisole, 100-68-5; thiophene, 110-02-1.

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Heterocycles. 3. Synthesis and Spectral Data of Some 2-Pyrazolines

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The reaction of 1,3-diaryl-2-propen-1-ones (Ia–o) with hydrazine and methyl- and phenylhydrazine produced different substituted 2-pyrazolines (III). The structures of these products were evident from their chemical and spectroscopic analysis.

The aim of the present work is to prepare different substituted 2-pyrazolines and to substantiate their structure by chemical and spectral tools. The importance of these pyrazoline derivatives arises from their wide applications for different purposes. Thus, the 1,3-diaryl-2-propen-1-ones (Ia–o) were condensed with hydrazines hydrate, phenylhydrazine, and methylhydrazine to produce 1*H*-3,5-diaryl-2-pyrazolines ($IIIa_1$–I_1), 1,3,5-triaryl-2-pyrazolines ($IIIf_2$–I_2), and 3,5-diaryl-1-methyl-2-pyrazolines ($IIId_3$–n_3), respectively (cf. Scheme I). The structures of all products were evident from their chemical and spectral data (cf. Tables I–IV).

The electronic spectra of all the 2-pyrazolines exhibit similar absorption patterns. Thus, the pyrazolines $IIIa_1$–I_1 absorb in the regions 302–273 and 238–221 nm, the pyrazolines $IIIf_2$–I_2 show two major maxima in the regions 364–350 and 253–222

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