Synthesis of 1,2',3,3',5',6'-Hexahydro-3-phenylspiro[isobenzofuran-1,4'-thiopyrans] (2) and 1,2',3,3',5',6'-Hexahydro-3-phenylspiro-[isobenzofuran-1,4'-pyrans] (3) (1)

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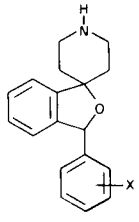
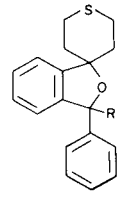
The 1,2',3,3',5',6'-hexahydro-3-phenylspiro[isobenzofuran-1,4'-thiopyran] ring system (**2a**) has been prepared from *o*-bromobenzoic acid. The 1,2',3,3',5',6'-hexahydro-3-phenylspiro[isobenzofuran-1,4'-pyran] ring system (**3a**) has been prepared from 2-bromobenzhydrol methyl ether. Several 3-(dimethylaminoalkyl) derivatives of both **2a** and **3a** were prepared by lithiation followed by alkylation.

J. Heterocyclic Chem., **19**, 1069 (1982).

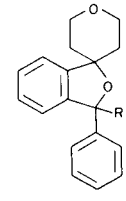
Our laboratory has been involved in an investigation of 3-aryl-1,3-dihydrospiro[isobenzofuran-1(3*H*),4'-piperidines] (**1**), as CNS agents (2-4). Particularly noteworthy are HP 505 (**1a**) and HRP 197 (**1b**) which are of clinical interest as antidepressant drugs.



1
a, X = H
b, X = *p*CH$_3$



2

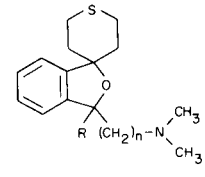


3

This paper describes the preparation of 1,2',3,3',5',6'-hexahydro-3-phenylspiro[isobenzofuran-1,4'-thiopyrans] **2** and 1,2',3,3',5',6'-hexahydro-3-phenylspiro[isobenzofuran-1,4'-pyrans] **3**. The thiopyrans **2** contain a sulfur rather than a nitrogen atom at the 1' position of the six-membered ring while the pyrans contain an oxygen atom at this position.

o-Bromobenzoic acid served as the starting material for the synthesis of **2**. The carboxyl group was protected as the oxazoline, employing the methodology of Meyers and Temple (5). Heating a suspension of 2-(2-bromophenyl)-4,4-dimethyl-2-oxazoline, **4**, (2,5,6) and magnesium at reflux for 2 hours effected formation of the Grignard reagent which, upon addition of tetrahydrothiopyran-4-one, provided **5** (Scheme 1). Oxazoline **5** in aqueous hydrochloric acid at reflux hydrolyzed to the corresponding carboxylic acid, which cyclized to key intermediate lactone **6**. Addition of phenyllithium to lactone **6** in tetrahydrofuran provided lactol **7**. Reduction of **7** with lithium aluminum hydride in tetrahydrofuran gave diol **8**. Treatment of **8** in glacial acetic acid, with hydrochloric acid, effected cyclization to target compound **2a**, 1,2',3,3',5',6'-hexahydro-3-phenylspiro[isobenzofuran-1,4'-thiopyran].

Initial pharmacological screening indicated **2a** to be significantly less active as a CNS agent than the corresponding piperidine, **1a**. In an attempt to introduce a basic nitrogen approximately the same distance from the nuclear phenyl ring as in the piperidine series, **1**, we selected compounds **2b-d** as synthetic objectives.



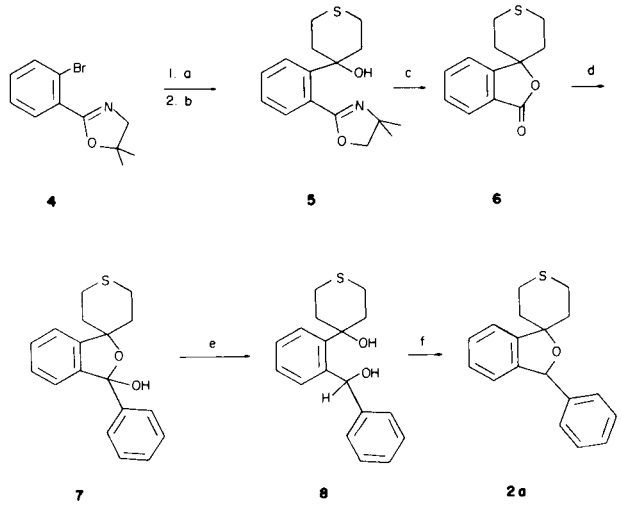
2
b, R = H, n = 3
c, R = phenyl, n = 3
d, R = phenyl, n = 2

Elaboration of lactone **6**, employing essentially the same synthetic sequence used for the preparation of **2a**, led to **2b** (Scheme 2). Thus, reaction of **6** with the Grignard reagent of 3-dimethylaminopropyl chloride provided lactol **9** (7). Reduction of **9** with lithium aluminum hydride yielded diol **10**, which upon treatment with hydrochloric acid in glacial acetic acid, cyclized to the desired dimethylaminopropylisobenzofuran **2b**.

Compounds **2c** and **2d** were prepared directly from 3-phenylisobenzofuranthiopyran **2a** (Scheme 3). Formation of 3-lithio **2a** was effected by treatment of **2a** with *n*-butyllithium at -10 to -20° (8). 3-Lithio **2a** was alkylated by addition of 2-dimethylaminoethyl chloride to afford **2d**. In a similar fashion, treatment of **2a** at -40 to -50° with *n*-butyllithium folowed by addition of 3-dimethylaminopropyl chloride provided **2c**.

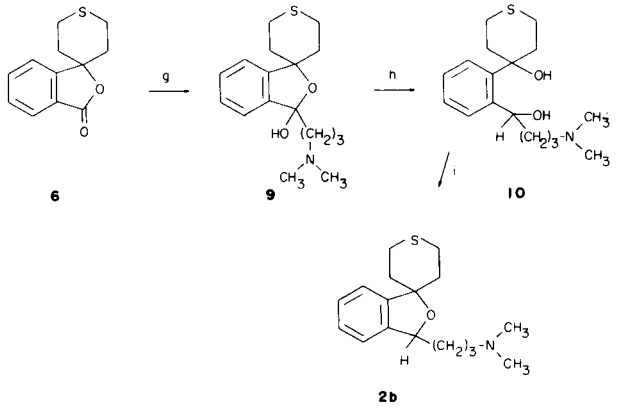
Pyrans **3** were prepared from 2-bromobenzhydrol methyl ether, **11** (2) (Scheme 4). Treatment of **11** with *n*-butyllithium effected formation of the 2-lithio compound to which was added 4-oxotetrahydropyran (9) to yield a mixture of 55% of the desired alcohol, **12**, and 45% of benzhydrol methyl ether. Compound **12** was isolated by chromatography and treated with hydrochloric acid in acetic acid to provide 1,2',3,3',5',6'-hexahydro-3-phenylspiro[isobenzofuran-1,4'-pyran], **3a**. Addition of *n*-butyl-

Scheme 1



Reagents: (a) Mg, THF; (b) Tetrahydrothiopyran-4-one; (c) 3*N* HCl; (d) 2*N* Phenyllithium in 70/30 benzene/ether, THF; (e) LAH, THF; (f) HCl, HOAc.

Scheme 2

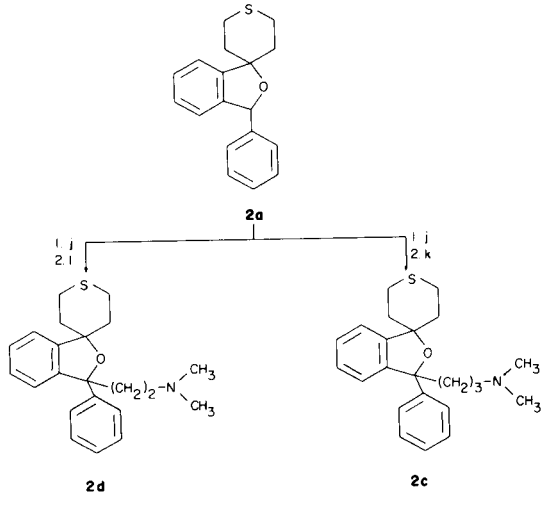


Reagents: (g) $(CH_3)_2N(CH_2)_3MgCl$; (h) LAH, THF; (i) HCl, HOAc.

lithium to **3a** effected formation of the 3-lithio salt which was alkylated with 2-dimethylaminoethyl chloride and 3-dimethylaminopropyl chloride to provide **3b** and **3c** respectively (Scheme 4).

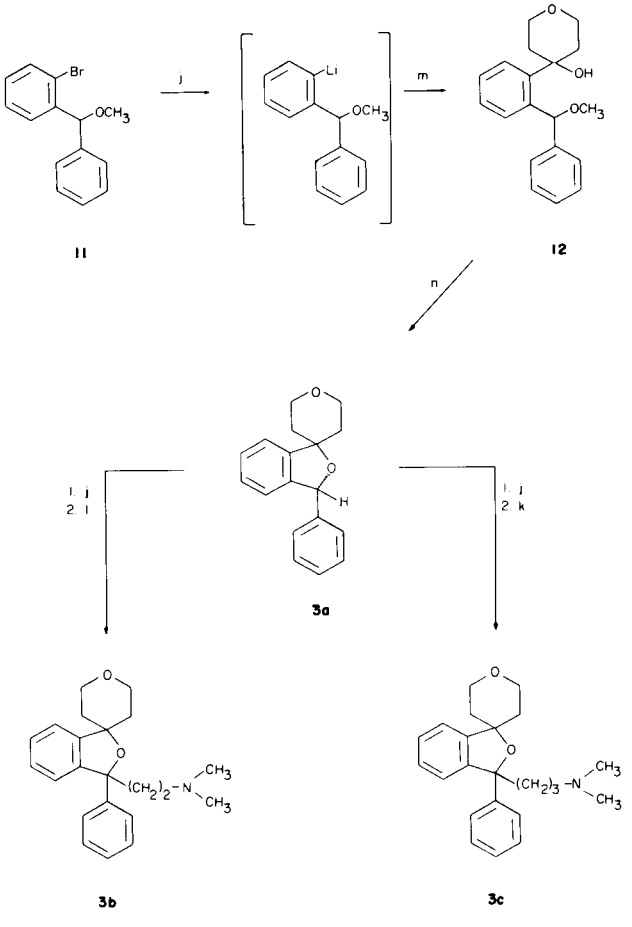
With respect to CNS activity: compounds **2a** and **3a** are less active than compounds **2b, 2c, 2d, 3b** and **3c** which are significantly less active than the series **1** compounds.

Scheme 3



Reagents: (j) 2.1*N* *n*-Butyllithium/hexane; (k) $(CH_3)_2N(CH_2)_3Cl$; (ℓ) $(CH_3)_2N(CH_2)_2Cl$.

Scheme 4



Reagents: (j) 2.1*N* *n*-Butyllithium; (k) $(CH_3)_2N(CH_2)_3Cl$; (ℓ) $(CH_3)_2N(CH_2)_2Cl$; (m) 4-Oxotetrahydropyran; (n) HCl, HOAc.

EXPERIMENTAL

Melting points were determined by using a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded using a Perkin-Elmer 457 spectrophotometer. Nuclear magnetic resonance spectra were recorded at 50 MHz using a JEOL FX-60 spectrometer. Chemical shifts are given relative to internal tetramethylsilane. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Illinois. Solvents were reagent grade and were used without purification except that those specified as "dry" had been stored over molecular sieves. Unless otherwise indicated, organic compounds were obtained from Aldrich Chemical Company. Organolithium reagents were obtained from Alfa Chemical Company.

4-[2-(4,4-Dimethyl-2-oxazolin-2-yl)phenyl]-4-hydroxy-2,3,5,6-tetrahydrothiopyran (**5**).

To a stirred mixture of 1.0 g (0.041 mole) of magnesium shavings and 25 ml of dry tetrahydrofuran at reflux was added dropwise over 0.5 hour a solution of 8.6 g (0.03 mole) of 2-(2-bromophenyl)-4,4-dimethyl-2-oxazoline (**4**) (2,6) in 100 ml of dry tetrahydrofuran. The mixture was stirred 2 hours at reflux after which a solution of 3.5 g (0.03 mole) of tetrahydrothiopyran-4-one in 10 ml of tetrahydrofuran was added dropwise. The mixture was stirred at reflux for 0.5 hour and at room temperature for one hour. The mixture was allowed to cool to room temperature, poured into 500 ml of water and extracted twice with chloroform. The combined chloroform extracts were dried over potassium carbonate, filtered and concentrated under vacuum to provide 5.9 g of colorless crystals, mp 178-181°. Recrystallization from ethanol provided 5.0 g (0.017 mole, 57%) of colorless crystals, mp 181-182°; ir (potassium bromide): 3160, 1680, 1280, 1075 cm^{-1}; nmr (deuteriochloroform): δ 1.39 (s, 6, CH_3); 1.92-3.26 (m, 8, tetrahydrothiopyran CH_2); 3.22 (bs, 1, OH); 3.45 (d, 2, OCH_2), 7.32-7.92 (m, 4, aromatic H).

Anal. Calcd. for $C_{16}H_{21}NO_2S$: C, 65.96; H, 7.27; N, 4.81; S, 10.99. Found: C, 65.87; H, 7.25; N, 4.72; S, 11.08.

1,2',3,3',5',6'-Hexahydro-3-oxospiro[isobenzofuran-1,4'-thiopyran] (**6**).

To 70 ml of 3*N* hydrochloric acid was added 3.10 g (0.017 mole) of 4-[2-(4,4-dimethyl-2-oxazolin-2-yl)phenyl]-4-hydroxy-2,3,5,6-tetrahydrothiopyran (**5**). The solution was stirred at reflux for 1 hour. The reaction mixture was then cooled to 0°. White crystals were collected by filtration and washed with water to yield 2.27 g of material, mp 164-166°. Recrystallization from benzene provided 2.1 g (9.5 mmoles, 89%) of white crystals, mp 165-166°; ir (chloroform): 1755, 1470, 1270, 1110, 1040 cm^{-1}; nmr (deuteriochloroform): δ 1.96-3.55 (m, 8, CH_2), 7.32-8.11 (m, 4, aromatic H).

Anal. Calcd. for $C_{12}H_{12}O_2S$: C, 65.42; H, 5.49; S, 14.55. Found: C, 65.19; H, 5.47; S, 14.32.

3-Hydroxy-1,2',4,4',5',6'-hexahydro-3-phenylspiro[isobenzofuran-1,4'-thiopyran] (**7**).

To a stirred solution of 23 ml (0.045 moles) of 2*N* phenyllithium in 70/30 benzene/ether was added dropwise a solution of 3.40 g (0.0154 moles) of 1,2',3,3',5',6'-hexahydro-3-oxospiro[isobenzofuran-1,4'-thiopyran] (**6**) in 200 ml of tetrahydrofuran. Following addition, the solution was stirred three hours at room temperature. The reaction mixture was poured into 900 ml of water and extracted twice with ethyl acetate. The solvent was evaporated and the resulting crystals triturated with benzene to yield 3.45 g (0.0116 moles, 75%) of colorless needles. Recrystallization from ethanol provided analytically pure material, mp 155-157°; ir (potassium bromide): 3320, 1430, 1005 cm^{-1}; nmr (deuteriochloroform): δ 2.00-3.71 (m, 8, CH_2); 3.38 (s, 1, OH); 7.19-8.10 (m, 9, aromatic H).

Anal. Calcd. for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08; S, 10.74. Found: C, 72.32; H, 6.24; S, 10.89.

4-Hydroxy-4-[2-(1-hydroxy-1-phenylmethyl)phen-1-yl]-2,3,5,6-tetrahydrothiopyran (**8**).

To a stirred suspension of 6.2 g (0.0160 mole) of lithium aluminum hydride in 200 ml of dry tetrahydrofuran was added dropwise a solution of 26 g (0.087 mole) of 3-hydroxy-1,2',3,3',5',6'-hexahydro-3-phenylspiro-[isobenzofuran-1,4'-thiopyran] (**7**) in 200 ml of tetrahydrofuran. The mixture was stirred at room temperature for 0.5 hour and at reflux for one hour. The suspension was allowed to cool to room temperature and subsequently quenched very slowly by addition of water. The mixture was extracted with chloroform, and the organic phase dried over magnesium sulfate, filtered and concentrated to an oil. Crystallization from benzene provided 15.0 g (0.0499 mole, 57%) of colorless crystals, mp 129-132°; ir (potassium bromide): 3650, 3400, 1390, 770 cm^{-1}; nmr (deuteriochloroform): δ 2.00-3.93 (m, 10, CH_2, 2×OH), 6.48 (d, 1, CH), 7.35 (m, 9, aromatic H).

Anal. Calcd. for $C_{18}H_{20}O_2S$: C, 71.97; H, 6.71; S, 10.67. Found: C, 71.93; H, 6.72; S, 10.80.

1,2',3,3',5',6'-Hexahydro-3-phenylspiro[isobenzofuran-1,4'-thiopyran] (**2a**).

In 55 ml of hot glacial acetic acid was dissolved 12.0 g (39.9 mmoles) of 4-hydroxy-4-[2-(1-hydroxy-1-phenylmethyl)phenyl-1-yl]-2,3,5,6-tetrahydrothiopyran (**8**). To the stirred solution, which had been cooled to 40°, was added 13.5 ml of concentrated hydrochloric acid and 60 ml of glacial acetic acid. The mixture was stirred at reflux for five minutes and subsequently allowed to cool to room temperature. Filtration provided 9.8 g (34.8 mmoles, 87%) of needles. Recrystallization from cyclohexane provided colorless cyrstals, mp 148-149°; ir (potassium bromide): 2905, 1010, 760 cm^{-1}; nmr (deuteriochloroform): δ 1.85-3.58 (m, 8, CH_2), 6.17 (s, 1, CH), 6.82-7.55 (m, 9, aromatic H).

Anal. Calcd. for $C_{18}H_{18}OS$: C, 76.56; H, 6.42; S, 11.35. Found: C, 76.24; H, 6.34; S, 11.53.

4-[2-(1-Hydroxy-4-dimethylaminobutyl)phen-1-yl]-4-hydroxy-2,3,5,6-tetrahydrothiopyran (**10**).

To a stirred suspension of 0.75 g (0.02 mole) of lithium aluminum hydride in 25 ml of dry tetrahydrofuran was added dropwise a solution of 3.07 g (0.01 mole) of 3-(3-dimethylaminopropyl)-1,2',3,3',5',6'-hexahydro-3-hydroxyspiro[isobenzofuran-1,4'-thiopyran] (**9**) (7) in 25 ml of tetrahydrofuran. The mixture was stirred for 0.5 hour at room temperature, one hour at reflux and one hour at room temperature. The excess lithium aluminum hydride was destroyed by slow, dropwise addition of water. The mixture was poured into water, extracted with chloroform, dried over magnesium sulfate, filtered and the solvent evaporated to provide an oil. Crystallization from benzene-hexane and recrystallization from cyclohexane provided 2.09 g of white crystals, mp 111-114°; ir (potassium bromide): 3480, 1200, 1010, 760 cm^{-1}; nmr (deuteriochloroform): δ 2.35 (s, 6, NCH_3), 1.55-3.75 (m, 16, $(CH_2)_3N$, tetrahydrothiopyran CH_2, 2×OH), 5.10 (m, 1, CH), 7.07-7.60 (m, 4, aromatic H).

Anal. Calcd. for $C_{17}H_{27}NO_2S$: C, 65.98; H, 8.80; N, 4.52; S, 10.36. Found: C, 66.26; H, 8.94; N, 4.44; S, 10.19.

3-(3-Dimethylaminopropyl)-1,2',3,3',5',6'-hexahydrospiro[isobenzofuran-1,4'-thiopyran]oxalate (**2b**).

A solution of 1.0 g (0.0032 mole) of 4-[2-(1-hydroxy-4-dimethylaminobutyl)phenyl]-4-hydroxy-2,3,5,6-tetrahydrothiopyran (**10**), 1.2 ml of concentrated hydrochloric acid, and 10 ml of acetic acid was stirred at reflux for 0.5 hour, cooled to room temperature, diluted with water, made basic with 10*N* sodium hydroxide, and extracted with chloroform. The chloroform solution was dried over magnesium sulfate and concentrated to an oil which was converted to its oxalate salt. Three recrystallizations from 2-propanol provided 0.83 g (68%) of colorless crystals, mp 146-149°; ir (potassium bromide): 1610, 1400, 1190 cm^{-1}; nmr (DMSO-d_6): δ 2.73 (s, 6, $^+N\,CH_3$), 1.48-3.38 (m, 14, $(CH_3)_3N^+$, tetrahydrothiopyran CH_2), 5.15 (m, 1, CH), 7.30 (m, 4, aromatic H).

Anal. Calcd. for $C_{19}H_{27}NO_5S$: C, 59.82; H, 7.14; N, 3.67; S, 8.40. Found: C, 59.95; H, 7.12; N, 3.62; S, 8.40.

3-(3-Dimethylaminopropyl)-1,2',3,3',5',6-hexahydro-3-phenylspiro[isobenzofuran-1,4'-thiopyran] (**2c**).

A solution of 1.41 g (0.005 mole) of 1,2',3,3',5',6'-hexahydro-3-phenylspiro[isobenzofuran-1,4'-thiopyran] (**2a**) in 25 ml of tetrahydrofuran was

cooled to -40°. To the solution was added dropwise 2.9 ml (0.0061 mole) of 2.1*M* *n*-butyllithium in hexane. The dark solution was stirred under nitrogen at -40 to -50° for 0.5 hour after which 668 mg (0.0055 mole) of 3-dimethylaminopropyl chloride in 15 ml of tetrahydrofuran was added over five minutes. Stirring was continued at room temperature overnight. The mixture was poured into water and extracted with chloroform. The combined organic fractions were dried over sodium sulfate, filtered and the solvent evaporated to provide 1.1 g (60%) of colorless prisms, mp 78-80°. Three recrystallizations from petroleum ether (30-60°) provided an analytical sample, mp 79-80°; ir (chloroform): 2950, 1280, 1040 cm^{-1}; nmr (deuteriochloroform): δ 2.16 (s, 6, NCH_3), 1.09-3.71 (m, 14, $(CH_2)_3N$, tetrahydrothiopyran CH_2), 7.09-7.23 (m, 9, aromatic H).

Anal. Calcd. for $C_{23}H_{29}NOS$: C, 75.15; H, 7.95; N, 3.81; S, 8.72. Found: C, 75.08; H, 8.12; N, 3.55; S, 8.63.

3-(3-Dimethylaminoethyl)-1,2′,3,3′,5′,6′-hexahydro-3-phenylspiro[isobenzofuran-1,4′-thiopyran]hydrochloride (**2d**).

A solution of 1.7 g (0.006 mole) of 1,2′,3,3′,5′,6′-hexahydro-3-phenylspiro[isobenzofuran-1,4′-thiopyran] (**2a**) in 25 ml of tetrahydrofuran was cooled to -10°. To the solution was added dropwise 3.3 ml (0.0069 mole) of 2.1*M* *n*-butyllithium in hexane. The dark red solution was stirred under nitrogen at -10° to -20° for 0.5 hour after which 713 mg of freshly distilled 2-dimethylaminoethyl chloride in 10 ml of tetrahydrofuran was added dropwise over five minutes. The reaction mixture was stirred overnight at room temperature, poured into water and the resultant suspension extracted four times with ether. The ether extract was dried over sodium sulfate, filtered and the solvent evaporated to provide an oil (1.5 g), the hydrochloride (1.3 g, 56%) of which was recrystallized from acetone-ether to yield prisms, mp 245-246°; ir (potassium bromide): 2980, 2350, 1480, 1040 cm^{-1}; nmr (deuteriochloroform): δ 2.75 (s, 6, $^+N\ CH_3$), 1.72-3.55 (m, 12, tetrahydrothiopyran CH_2, $(CH_2)_2N^+$), 7.10-7.91 (m, 9, aromatic H).

Anal. Calcd. for $C_{22}H_{28}ClNOS$: C, 67.72; H, 7.23; N, 3.59; Cl, 9.08; S, 8.22. Found: C, 67.44; H, 7.34; N, 3.36; Cl, 8.87; S, 7.98.

1,2′,3,3′,5′,6′-Hexahydro-3-phenylspiro[isobenzofuran-1,4′-pyran] (**3a**).

A stirred solution of 11.08 g (0.040 mole) of 2-bromobenzhydrol methyl ether (**11**) (2) in 23 ml of dry tetrahydrofuran and 7 ml of hexane under nitrogen was cooled to -50°. To the reaction mixture was added dropwise 22 ml of 2.2*N* *n*-butyllithium such that the temperature remained below -50°. Strirring was continued at -60 to -70° for two hours. To the gray suspension was then added dropwise 5.0 g (0.0499 mole) of 4-oxotetrahydropyran (9) in 5 ml of dry tetrahydrofuran. The mixture was stirred at -60° for three hours and at room temperature overnight. To the solution was then added slowly 20 g of ice.

The organic layer was separated and the aqueous layer extracted four times with chloroform. The combined organic fractions were dried over sodium sulfate, filtered and the solvent evaporated to provide an oil. The nmr analysis indicated the oil to be 55% of the desired 4-hydroxy-4-[2-(1-methoxy-1-phenylmethyl)phen-1-yl]-2,3,5,6-tetrahydropyran (**12**) and 45% of benzhydrol methyl ether. Compound **12** was isolated by column chromatography on 300 g of alumina (Fisher, absorption). Elution of the mixture with benzene removed the benzhydrol methyl ether. Subsequent elution with ether provided, after evaporation of solvent from the eluent, 6.3 g of **12**. A solution of 6.3 g of **12**, 60 ml of glacial acetic acid and 15 ml of concentrated hydrochloric acid was stirred at reflux for thirty minutes. Evaporation of solvent provided 4.4 g (0.0165 mole, 38%) of **3a**. Recrystallization from hexane provided analytically pure material, mp 132-134°; ir (chloroform): 3050, 1460, 1100, 1050 cm^{-1}; nmr (deuteriochloroform): δ 1.50-2.62 (m, 4, CH_2-C-CH_2), 4.04 (dd, 4, CH_2-O-CH_2), 6.28 (s, 1, CH), 6.99-7.64 (m, 9, aromatic H).

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.15; H, 6.88. Found: C, 81.22; H, 6.87.

3-(3-Dimethylaminopropyl)-1,2′,3,3′,5′,6′-hexahydro-3-phenylspiro[isobenzofuran-1,4′-pyran]hydrochloride (**3c**).

To a stirred solution of 1.33 g (0.0050 mole) of 1,2′,3,3′,5′,6′-hexahydro-3-phenylspiro[isobenzofuran-1,4′-pyran] (**3a**) in 20 ml of dry tetrahydrofuran at -10° was added dropwise 4 ml of 2.1*M* *n*-butyllithium in hexane. Stirring was continued for 1 hour under nitrogen after which 800 mg (0.00656 mole) of freshly distilled dimethylaminopropyl chloride in 5 ml of dry tetrahydrofuran was added over 1-2 minutes. The reaction mixture was stirred at -10° for one hour and at room temperature overnight. To the reaction mixture was added 20 g of ice. The organic layer was separated and the aqueous extracted four times with ether. The organic solution was dried over sodium sulfate, filtered and the solvent evaporated to provide 1.05 g of an oil which was converted to its hydrochloride salt (0.96 g, 0.0025 mole, 50%), mp 234-235.5°. The hydrochloride was recrystallized four times from acetone-ether to provide analytically pure material, mp 234-235.5°; ir (potassium bromide): 3450, 1475, 1240, 980 cm^{-1}; nmr (deuteriochloroform): δ 1.18-3.22 (m, 10, CH_2-C-CH_2, $(CH_2)_3$-N^+), 2.67 (s, 6, N-CH_3), 3.82-4.27 (m, 4, CH_2-O-CH_2), 7.01-7.92 (m, 9, aromatic H).

Anal. Calcd. for $C_{23}H_{30}ClNO_2$: C, 71.20; H, 7.79; N, 3.61; Cl, 9.14. Found: C, 70.96; H, 7.76; N, 3.58; Cl, 9.19.

3-Dimethylaminoethyl-1,2′,3,3′,5′,6′-hexahydro-3-phenylspiro[isobenzofuran-1,4′-pyran]hydrochloride (**3b**).

To a solution of 1.33 g (0.0050 mole) of 1,2′,3,3′,5′,6′-hexahydro-3-phenylspiro[isobenzofuran-1,4′-pyran] (**3a**) in 20 ml of tetrahydrofuran at -10° was added dropwise 4.5 ml of 2.2*N* *n*-butyllithium in hexane. The solution was stirred at -10° for one hour after which 1.07 g (0.0099 mole) of freshly distilled dimethylaminoethyl chloride in 5 ml of tetrahydrofuran was added over 1-2 minutes. The reaction mixture was subsequently stirred for 1 hour at -10° and overnight at room temperature. To the solution was added 20 g of ice. The organic layer was separated and the aqueous phase extracted four times with ether. A solution of the combined organic fractions was dried over sodium sulfate, filtered and the solvent evaporated to provide an oil which was converted to its hydrochloride salt (1.70 g, 0.0045 mole, 90%). Recrystallization from ethanol-ether yielded analytically pure material, mp 273-274° dec; ir (potassium bromide): 2460, 1450, 1280, 980 cm^{-1}; nmr (deuteriochloroform + DMSO-d_6): δ 1.52-3.15 (m, 8, CH_2-C-CH_2, $(CH_2)_2$-N^+), 2.77 (s, 6, N-CH_3), 3.88-4.20 (m, 4, CH_2-O-CH_2), 7.19-7.92 (m, 9, aromatic H).

Anal. Calcd. for $C_{22}H_{28}ClNO_2$: C, 70.66; H, 7.54; N, 3.74; Cl, 9.48. Found: C, 70.44; H, 7.54; N, 3.75; Cl, 9.58.

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REFERENCES AND NOTES

(1) Presented in part at the first Chemical Congress of the North American Continent, Mexico City, Mexico, Nov. 30-Dec. 5, 1975, BMPC section.

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