

SILIPRAMINE AND RELATED DERIVATIVES

JOYCE Y. COREY* and ROBERTA L. FARRELL

Department of Chemistry, University of Missouri-St. Louis, St. Louis, Missouri 63121 (U.S.A.)

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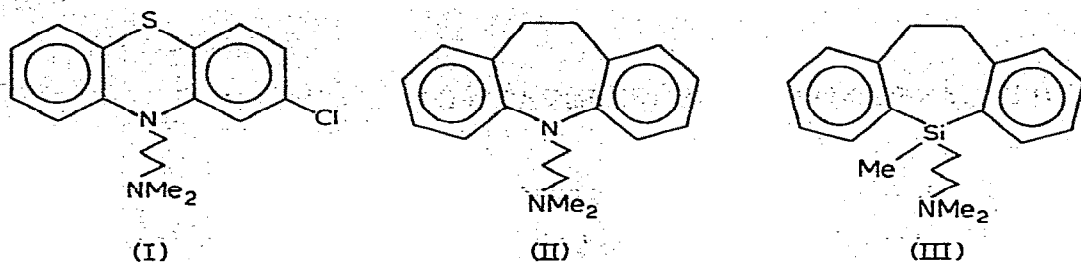
Summary

A series of new 10,11-dihydro-5*H*-dibenzo[*b,f*]silepins are prepared from the reaction *o,o'*-dilithiobibenzyl with the chlorosilanes HSiCl₃, ClCH₂CH₂CH₂SiCl₃, MeSiHCl₂ and MeSi(CH₂CH₂CH₂Br)Cl₂. The only isolated silepin product produced from HSiCl₃ is the spiro derivative. The silepin product produced from MeSiHCl₂ reacts with *N,N*-dimethylallylamine in the presence of H₂PtCl₆ to give silipramine, a tricyclic derivative which is related to the clinically effective antidepressant, imipramine. The silepin produced from (*o*-LiC₆H₄CH₂)₂ and MeSi(CH₂CH₂CH₂Br)Cl₂ was converted to the diethylaminopropyl derivatives as well as the unsaturated analog. 10-Bromo-5,5-dimethyl-10,11-dihydro-5*H*-dibenzo[*b,f*]silepin reacts with *N*-methylpiperazine to give the 10-(*N*-methylpiperazinyl)-substituted product but with competing dehydrobromination which is the predominant reaction with 2-dimethylaminoethanol.

Introduction

The discovery in 1952 of the therapeutic use of chlorpromazine (I) in the treatment of psychiatric disorders led to a series of investigations associated with structural modifications which could increase the potency of such antipsychotic agents and minimize the side effects of these drugs [1]. One such structural modification involved replacement of the S bridge in I by an ethano bridge to give the dibenzazepine, imipramine (II). Initial clinical tests of II demonstrated relatively little antipsychotic behavior but instead a specific value in treatment of depressive states. In general tricyclics with central six-membered rings exhibit antipsychotic behavior and those with central seven- and eight-membered rings exhibit antidepressant behavior. The introduction of an ethano or other 2 or 3 atom linkage between the benzo groups causes the benzo groups to twist relative to each other and we have developed a set of structural parameters to describe these ring systems [2,3]. In the study reported here the specific modification introduced into the tricyclic system is the inclusion of a silicon

heteroatom in the central ring. In the title compound, silipramine (III), an SiMe unit replaces the nitrogen in II. We have previously reported the synthesis and characterization of silicon analogs of phenothiazines [4], I, and thioxanthenes [5].

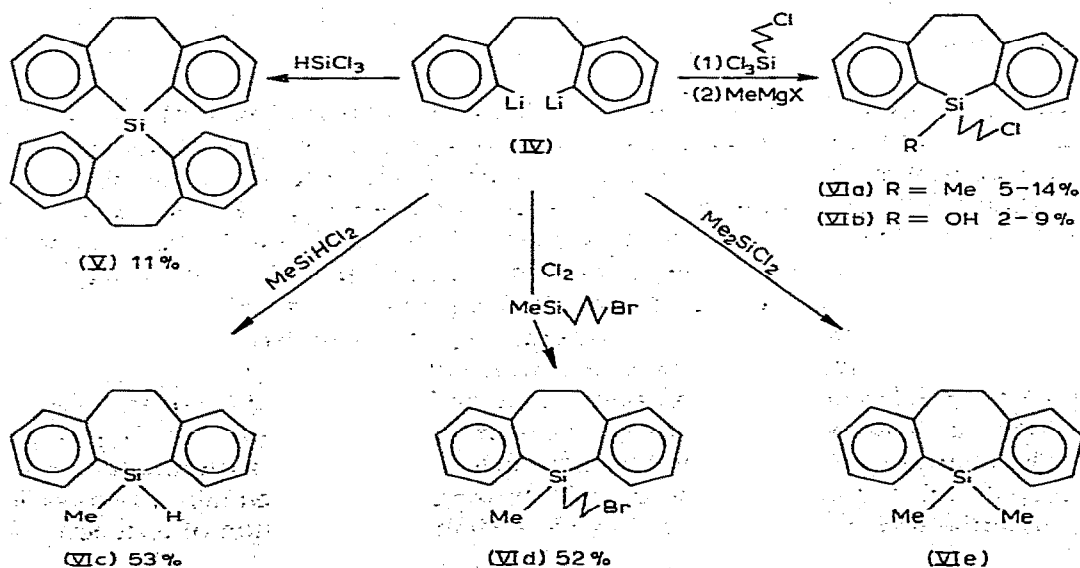


Those tricyclic derivatives which are in clinical use contain a three-atom side chain terminated by a nitrogen functional group. Several reactions of the silepin framework are described which result in the introduction of such a grouping either at silicon or the ethano linkage as well as reactions which introduce unsaturation at the 10,11-positions.

Results and discussion

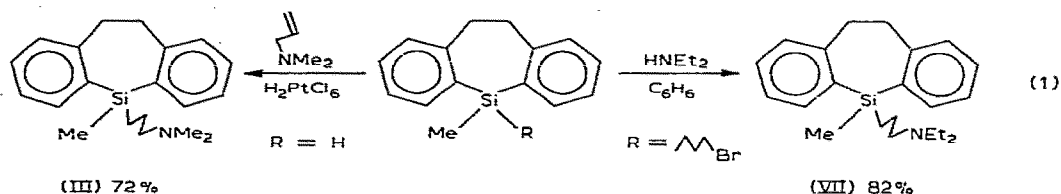
We have previously reported the synthesis of 10,11-dihydro-5H-dibenzo[*b,f*]-metalepins which include Si, Ge, Sn or Pb heteroatoms as well as the chemical reactions and spectroscopic properties of such systems [6]. The tricyclic metalepin framework is most efficiently generated by reaction of *o,o'*-dilithiobibenzyl (IV), with R_xMCl_{3-x} ($x = 0, 1$). The reaction of IV with a variety of chlorosilanes, chosen so that further substitution at silicon in the ring closed product should be possible, were originally investigated and the results are summarized in Scheme 1. The reaction of IV with other commercially available silanes,

SCHEME 1



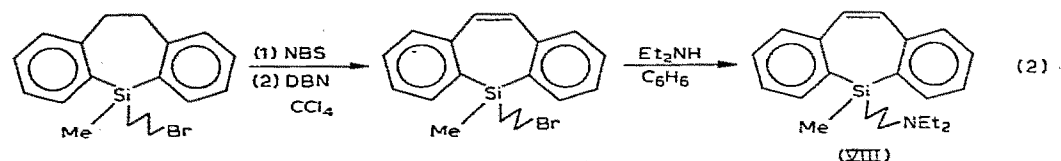
$\text{H}_2\text{NCH}_2\text{CH}_2\text{CH}_2\text{Si}(\text{Me})(\text{EtO})_2$ and $\text{MeSi}(\text{CH}_2\text{CH}_2\text{CN})\text{Cl}_2$ resulted in coupling but not ring closure for the former and formation of intractable gums with the latter.

Several reaction conditions were explored in an effort to convert the chloropropyl group of VIa into a dimethylaminopropyl group and these were uniformly unsuccessful. The attempts included refluxing a solution of VIa and excess dimethylamine in hexane, heating VIa and Me_2NH in a sealed tube at $100^\circ\text{C}/24\text{ h}$ and stirring VIa and LiNMe_2 at room temperature for five days [7]. Such difficulties were not encountered in conversion of a bromopropyl group to a diethylaminopropyl group. Silipramine (III) was prepared in highest yields from hydride addition of VIc to *N,N*-dimethylallylamine (eq. 1). Both III and VII were successfully converted into crystalline hydrochloride salts by reaction with hydrogen chloride gas in an ether/chloroform mixture. Unlike imipramine hydrochloride, the hydrochloride salt of silipramine (III) is isolated as the hydrate and the struc-

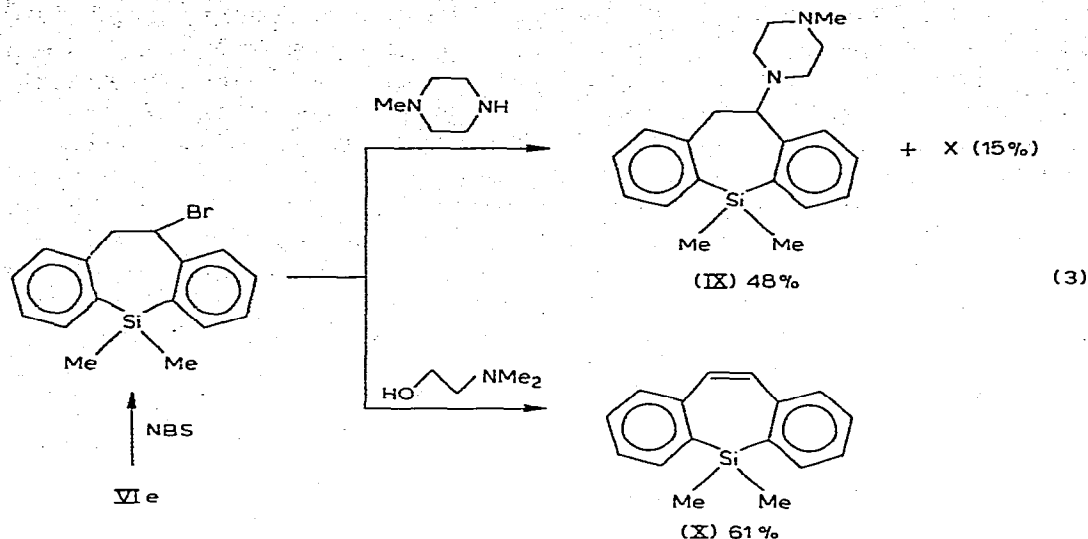


ture has been confirmed by a solid state structural study [3]. Attempts to prepare a crystalline fumarate salt of III was unsuccessful and reaction with gaseous HBr resulted in ring cleavage.

The antidepressant potency of iminostilbenes[1] corresponds closely to those of iminobibenzyls such as II, therefore methods were explored to introduce unsaturation in the 10,11-positions of III and VII. Direct reaction of VII with *N*-bromosuccinimide followed by addition of diazabicyclononene according to a previously established procedure[6a] did not result in formation of the desired products but a sequence of steps starting with VIId did prove to lead to VIII, albeit in low yields (eq. 2). A crystalline hydrochloride salt of VIII was obtained by the same method described for III.



Introduction of the side chain at a carbon atom of the ethano bridge should be possible via the 10-bromo derivative. These reactions tended to be complicated by a dehydrobromination reaction which produced the silepin X (eq. 3). In an attempt to introduce a $\text{Me}_2\text{NCH}_2\text{CH}_2\text{O}$ side chain at the 10-position, reaction of brominated VIe with 2-dimethylaminoethanol resulted in a $>50\%$ conversion to the silepin X. This dehydrobromination reaction produced higher yields of X than had previously been reported with diazabicyclononene[6a]. Preparation of IX was reported by Protiva and coworkers after our work had been completed [8].



The possibility of introduction of an exocyclic double bond in the 10-position of VIe was also explored by reaction of the phosphonium salt prepared from brominated VIe with BuLi and trapping the Wittig reagent with cyclohexanone. Although the color characteristic of the Wittig reagent was observed and decolorization occurred on addition of cyclohexanone the only product that could be identified were X and Ph₃PO. Attempts to oxidize the 10-position of VIe with CrO₃ in acetic acid under conditions reported for oxidation of 9,9-dimethyl-9,10-dihydro-9-silaanthracene [9] were unsuccessful as was the attempt to convert the 10-brominated derivative of VIe to the alcohol with AgNO₃/H₂O in methyl cellosolve, followed by oxidation with CrO₃.

The structural relationship between silipramine and imipramine has been discussed in detail [3]. Insertion of the larger sized silicon atom relative to *sp*³-C or to *sp*³-N in the 5-position (as a one-atom bridge) tends to decrease the twist of the benzo groups relative to each other and to increase the distance between the benzo group centers. A crystal structure analysis of IX has been completed and the piperazinyl group is found to occupy the pseudoequatorial position in the boat conformation in contrast to the analogous sulfur heterocycle (S in the 5-position) in which the piperazinyl substituent occupies the pseudoaxial position. Attempts to obtain solid state data from the crystalline hydrochloride salt of VIII have thus far been hampered by the lack of suitable crystals.

Experimental

All reactions which involved organolithium reagents and chlorosilanes were carried out under an atmosphere of dry N₂ in flame-dried glassware.

The commercial reagents, Me₂SiCl₂, Cl₂SiCl₃, HSiCl₃, MeSiHCl₂, Me₂NCH₂CH=CH₂, HNEt₂, MeN-C₆H₁₀-NH, diazabicyclononene, Ph₃P and HOCH₂-CH₂NMe₂ were used as supplied. *N*-Bromosuccinimide [10] was recrystallized from water prior to use.

The 5,5-dimethyl-10,11-dihydro-5*H*-dibenzo[*b,f*]silepin [6e], *o,o'*-dibromobi-

benzyl [11] and methyl(3-bromopropyl)dichlorosilane [12] were prepared by published procedures.

Proton NMR spectra were recorded in CCl_4 or CDCl_3 on a Varian T-60 spectrometer (internal TMS as a reference unless otherwise specified). Mass spectral data were collected at 70 eV on an AEI MS-1201B mass spectrometer.

Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

Reaction of *o,o'*-dilithiobibenzyl with chlorosilanes

(a) HSiCl_3 . The general procedure has been described in detail [6a]. A solution of trichlorosilane (4.2 ml, 0.040 mol) was added to a solution of *o,o'*-dilithiobibenzyl prepared from *o,o'*-dibromobibenzyl (15 g, 0.040 mol) and *n*-butyllithium (0.097 mol, 1.2 *M*). After the mixture had been heated at reflux for 1 h a solution of phenyllithium prepared from bromobenzene (6.7 ml, 0.063 mol) and lithium (0.91 g, 0.13 mol) was added and the mixture heated again at reflux for 1/2 h. After hydrolysis and evaporation of the ether the insoluble solid which separated was removed and the residue distilled to give an oil, b.p. 125–210°C/0.01 mmHg, 4 g. From the viscous oil which remained another 0.3 g sample of crystalline solid was obtained which was combined with the previously isolated solid. Two recrystallizations from hexane/chloroform gave 0.82 g (11%) of pure spiro derivative V, m.p. 173.4–174.5. (Found: C, 86.21; H, 6.05. $\text{C}_{28}\text{H}_{24}\text{Si}$ calcd.: C, 86.60; H, 6.19%.) ^1H NMR (CCl_4) δ (ppm) (external TMS): 7.6–6.7 (m, 16, Ar); 3.2 (s, 8.0, CH_2CH_2). *m/e* 388.

Attempts to separate 5-phenyl-10,11-dihydro-5*H*-dibenzo[*b,f*]silepin comparable to an authentic sample [6c] from the distilled oil were unsuccessful.

(b) $\text{Cl}_3\text{SiCH}_2\text{CH}_2\text{CH}_2\text{Cl}$ and MeMgX . A solution of *o,o'*-dilithiobibenzyl prepared from *o,o'*-dibromobibenzyl (30 g, 0.088 mol) and *n*-butyllithium (0.18 mol, 1.6 *M*) and a solution of 3-chloropropyltrichlorosilane (13.5 ml, 0.088 mol) in 200 ml ether were added simultaneously to 100 ml ether. After addition the mixture was heated for 12 h and MeMgBr (0.088 mol, 2.5 *M*) added and heating continued for an additional 2 h. After hydrolysis and evaporation of the ether the residue was distilled to give 13 g oil, b.p. 125–175°C/0.01 mmHg. The solid which precipitated from the distilled oil was removed and was shown to be unreacted *o,o'*-dibromobibenzyl (4.0 g). The remaining oil was eluted over silica gel, and the silepin VIa, was collected in 50% C_6H_6 /hexane, 1.44 g (6.3%). (Found: C, 70.70; H, 6.82. $\text{C}_{18}\text{H}_{21}\text{ClSi}$ calcd.: C, 71.64; H, 7.02%.) ^1H NMR (CCl_4) δ (ppm) (external TMS): 7.6–6.8 (m, 7.3, Ar); 3.2–2.9 (t + s, 5.5, CH_2Cl + $\text{ArCH}_2\text{CH}_2\text{Ar}$); 1.8–0.7 (m, 5.4, $\text{CH}_2\text{CH}_2\text{Si}$); 0.45 (s, 2.9, SiMe). *m/e* 300 (based on ^{35}Cl). Another fraction which eluted with 45% $\text{EtOAc}/\text{C}_6\text{H}_6$ was consistent with the silanol VIb, 2.02 g (8.8%). ^1H NMR (CCl_4) δ (ppm) (external TMS): 7.8–6.9 (m, 7.5, Ar); 3.2–2.8 (overlap of t, s, br s, 6.2, SiOH, CH_2Cl + $\text{ArCH}_2\text{CH}_2\text{Ar}$); 2.0–0.9 (m, 5.2, $\text{CH}_2\text{CH}_2\text{Si}$). *m/e* 302 (based on ^{35}Cl).

When the reaction was repeated with the exception that the 3-chloropropyltrichlorosilane was added to the dilithiobibenzyl followed by addition of freshly prepared MeMgI the yields of VIa and VIb were 5.3% and 1.7% respectively. If the MeMgBr was added to the $\text{Cl}_3\text{Si} \wedge \wedge \text{Cl}$ prior to the addition to the dilithiobibenzyl, 14% yield of VIa was obtained and no VIb.

(c) MeSiHCl_2 . To a solution of dilithiobibenzyl prepared from *o,o'*-dilithiobibenzyl (10.0 g, 0.0294 mol) and *n*-butyllithium (0.060 mol, 2.0 *M*) was added

MeSiHCl₂ (3.0 g, 0.029 mol) dissolved in ether, and the mixture stirred for 48 h at room temperature. After hydrolysis and workup, distillation gave 3.5 g (53%) VIc, an oil, b.p. 105–120°C/0.07 mmHg. ¹H NMR (CCl₄) δ (ppm): 7.7–6.8 (m, 8.2, Ar); 5.2–4.9 (q, 0.8, SiH); 3.15 (s, 3.8, CH₂CH₂); 0.60–0.58 (d, 3.2, SiMe). *m/e* 224. The oil was used without further purification for reactions with *N,N*-dimethylallylamine.

(d) BrCH₂CH₂CH₂Si(Me)Cl₂: To a solution of the dilithiobibenzyl prepared from *o,o'*-dibromobibenzyl (9.5 g, 0.027 mol) and *n*-butyllithium (0.054 mol, 2.0 M) was added methyl(3-bromopropyl)dichlorosilane (6.4 g, 0.027 mol). After hydrolysis and workup, Kugelrohr distillation gave 4.9 g (52%) VID. ¹H NMR (CCl₄) δ (ppm): 7.65–6.7 (m, 8.1, Ar); 3.35–2.8 (overlapping t + s, 5.9, CH₂Br and CH₂CH₂); 2.0–0.8 (m, 4.5, CH₂CH₂Si); 0.55 (s, 2.5, SiMe). *m/e* 344 (based on ⁷⁹Br). The product was used without further purification for reaction with diethylamine.

5-Methyl-5-(3-dimethylaminopropyl)-10,11-dihydro-5H-dibenzo[b,f]silepin · hydrochloride · hydrate, silipramine (III)

A sample of VIc (2.33 g, 0.0104 mol) and 4 ml of *N,N*-dimethylallylamine to which two drops of H₂PtCl₆/*t*-BuOH had been added were heated at reflux for 18 h. After stripping the volatiles, Kugelrohr distillation gave III, an oil, b.p. 130–140°C/0.1 mmHg, 2.31 g (72%). ¹H NMR (CCl₄) δ (ppm): 7.7–6.7 (m, 8.1, Ar); 3.03 (s, 4.2, CH₂CH₂); 2.2–1.7 (overlapping t + s, 7.2, CH₂N, CH₂CH₂); 1.7–0.67 (m, 4.7, SiCH₂CH₂); 0.42 (s, 2.7, SiMe). *m/e* 309.

The free base III was dissolved in ether which contained 10% CHCl₃ and gaseous HCl added until the solution became cloudy. Additional CHCl₃ was added until the solution became clear. The HCl salt of III crystallizes slowly (1.5 g). An analytical sample was obtained after two recrystallizations from xylene/chloroform, m.p. 160–161.5°C as the hydrate. (Found: C, 6.21; H, 8.35. C₂₀H₂₇NSi · HCl · H₂O calcd.: C, 66.02; H, 8.25%.) ¹H NMR (CDCl₃) δ (ppm): 7.5–6.7 (m, 8.7, Ar); 3.1 (s, 3.9, CH₂CH₂); 3.0–2.4, 2.6 (overlapping m + s, 8.0, CH₂NHMe₂⁺); 2.0–0.7 (m, 4.6, CH₂CH₂); 0.57 (s, 2.8, SiMe).

Attempts to prepare the fumarate salt of III in EtOH produced oils which could not be included to crystallize and addition of HBr to III caused ring cleavage.

5-Methyl-5-3-diethylaminopropyl)-10,11-dihydro-5H-dibenzo[b,f]silepin · hydrochloride

A solution of VID (3.0 g, 0.0083 mol) and 5 ml anhydrous diethylamine in 30 ml dry benzene were heated at reflux for 16 h. The precipitated Et₂NH₂⁺Br⁻ (1.17 g) was removed, the filtrate stripped, and the residue distilled on a Kugelrohr to give an oil, VII, b.p. 145–160°C/0.2 mmHg (2.4 g, 82%). ¹H NMR (CCl₄) δ (ppm): 7.6–6.4 (m, 7.2, Ar); 3.0 (s, 4.3, ArCH₂CH₂Ar); 2.6–1.7 (overlapping t + g, 5.8, CH₂N(CH₂CH₃)₂); 1.2–0.56 (overlapping m + t, 11, CH₂CH₂Si and N(CH₂CH₃)₂); 0.43 (s, 2.7, SiMe). *m/e* 337.

Gaseous HCl was bubbled into a solution of VII (1.5 g) in 40 ml 15% CHCl₃ in ether to give a crystalline solid, VII · HCl, m.p. 124–125°C. (Found: C, 70.38; H, 8.66. C₂₂H₃₁NSi · HCl calcd.: C, 70.68; H, 8.57%.)

5-Methyl-5-(3-dimethylaminopropyl)-5H-dibenzo[b,f]silepin · hydrochloride

A slurry of VID (8.0 g, 0.023 mol) and *N*-bromosuccinimide (3.9 g, 0.022 mol) was heated to reflux and irradiated with a GE sunlamp until all the insoluble solid had become less dense than CCl_4 . After removal of succinimide (2.2 g, 100%) the volatiles were stripped and the oil residue redissolved in fresh CCl_4 (50 ml) and a solution of diazabicyclononene (4.0 g, 0.032 mol) in 20 ml CCl_4 added dropwise. The solution was heated at reflux for 1.5 h during which time it turned a dark green. The reaction mixture was hydrolyzed with water and extracted with 400 ml ether. After the volatiles were removed the residue was distilled to give crude 5-methyl-5-(3-dimethylaminopropyl)-5H-dibenzo[b,f]-silepin, 3.6 g, b.p. 185–200°C/0.3 mmHg. A sample was purified by elution of 1.5 g over 50 g silica gel. The purified silepin (0.88 g) eluted with 30% benzene in hexane. $^1\text{H NMR}$ (CCl_4) δ (ppm): 7.4–6.8 (m, 9, Ar); 6.67 (s, 1.9, HC=CH); 3.2–2.8 (t, 2.1, CH_2Br); 1.4–0.6 (m, 4.3, $\text{CH}_2\text{CH}_2\text{Si}$); 0.55 (s, 2.8, SiMe). *m/e* 270 (based on ^{79}Br).

The crude silepin (2 g) and diethylamine (4 ml) were dissolved in 20 ml benzene and heated at reflux for 4 h. After removal of $\text{Et}_2\text{NH}_2^+\text{Br}^-$ (0.44 g) the filtrate was stripped to give a yellow oil which was eluted over 70 g basic alumina. 5-Methyl-5-[3-diethylaminopropyl]-5H-dibenzo[b,f]silepin (0.99 g) was eluted with 20% MeOH in benzene.

The oil was dissolved in 15% CHCl_3 in Et_2O and gaseous HCl added. The precipitated solid (0.66 g) was recrystallized from xylene/chloroform to give VIII · HCl, m.p. 174–174.5°C. (Found: C, 70.51; H, 8.20. $\text{C}_{22}\text{H}_{29}\text{NSi} \cdot \text{HCl}$ calcd.: C, 71.06; H, 8.08%.) $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.3–6.8 (m, 8.5, Ar), 6.55 (s, 2.0, CH=CH); 3.0–2.3 (br. m, 6.5, $\text{CH}_2\text{N}(\text{H})(\text{CH}_2\text{CH}_3)_2$); 1.8–0.62 (overlapping m + t, 9.8, SiCH_2CH_2 and $\text{N}(\text{CH}_2\text{CH}_3)_2$); 0.75 (s, 3.6, SiMe).

5,5-Dimethyl-10-(*N*-methylpiperazinyl)-10,11-dihydro-5H-dibenzo[b,f]silepin · fumarate

A slurry of 5,5-dimethyl-10,11-dihydro-5H-dibenzo[b,f]silepin (3.7 g, 0.016 mol) and *N*-bromosuccinimide (2.8 g, 0.016 mol) in CCl_4 (25 ml) was heated to reflux and irradiated with a GE sunlamp until succinimide formed. After removal of succinimide and removal of the CCl_4 the oil residue was heated with *N*-methylpiperazine (5.5 ml) in 25 ml toluene for 10 h. After removal of *N*-methylpiperazinium bromide (2.7 g) the solvent was stripped and the residue distilled on a Kugelrohr apparatus to give an oil, b.p. 145–170°C/0.2 mmHg, 3.5 g. Elution of the product over 75 g basic alumina gave 0.84 g of a mixture of starting material and 5,5-dimethyl-5H-dibenzo[b,f]silepin (X) (approximate ratio 1 : 2), which was eluted with 25–50% hexane in benzene and IX (2.55 g) which was eluted in benzene and 10% MeOH in benzene. The oil IX, crystallized slowly on standing, m.p. 64–66°C. $^1\text{H NMR}$ (CDCl_3) δ (ppm): 7.9–6.8 (m, 7.7, Ar); 3.7–3.1 (m, 2.7, ArCH_2CHAr); 2.8–1.7 (m, 11.5, $(\text{CH}_2\text{CH}_2)_2\text{NMe}$); 0.47 (s, 6.1, SiMe₂). *m/e* 336.

To a boiling solution of IX (0.748 g, 0.00223 mol) in 5 ml EtOH was added fumaric acid (0.258 g, 0.0023 mol) in 5 ml boiling EtOH. Slow precipitation occurred to give 0.863 g IX · fumarate, m.p. 201–203°C. (Found: C, 66.21; H, 7.49. $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_4\text{Si}$ calcd.: C, 66.21; H, 7.06%.)

Reaction of 5,5-dimethyl-10,11-dihydro-5H-dibenzo[b,f]silepin with NBS and 2-dimethylaminoethanol

A slurry of silepin (2.38 g, 0.010 mol) and *N*-bromosuccinimide (1.78 g, 0.010 mol) were heated at reflux in CCl_4 and irradiated with a GE sun lamp until succinimide formed. After removal of succinimide (0.96 g) the CCl_4 was removed and the residue dissolved in toluene (25 ml) and 2 ml 2-dimethylaminoethanol added. The mixture was stirred for 48 h then heated at reflux for 6 h. The toluene was stripped and 5% NaOH added to the residue followed by extraction with ether. After removal of the ether the residue was eluted over 50 g silica gel and the fraction which eluted with 50% benzene in hexane was identical to an authentic sample of 5,5-dimethyl-5H-dibenzo[b,f]silepin[6a] (1.46 g, 61%).

Reaction of 5,5-Dimethyl-10,11-dihydro-5H-dibenzo[b,f]silepin with NBS and triphenylphosphine

A slurry of silepin (2.70 g, 0.0113 mol) and *N*-bromosuccinimide (2.01 g, 0.0113 mol) was heated to reflux in CCl_4 until succinimide formed. After removal of the succinimide (1.06 g) the CCl_4 was removed, the residue dissolved in xylenes (50 ml) and triphenylphosphine (3.0 g, 0.011 mol) added. The solution was heated at reflux for 20 h and then the solvent removed to give an oil which slowly crystallized. The semi-solid was slurried with ether and *n*-butyllithium added (0.012 mol, 2.4 M) to give a red-brown solution. The solution decolorized when cyclohexanone (1.5 ml) was added. The solution was hydrolyzed with water and extracted with ether. After removal of the ether the residue was eluted over 50 g silica gel. The fraction which eluted with 60% benzene in hexane (0.40 g) exhibited spectroscopic properties identical to a sample of authentic X. A total of 0.46 g of Ph_3PO was recovered from the methanol eluant.

Biological testing

The HCl salts of III, VII and VIII as well as the fumarate salt of IX have been tested for CNS activity and exhibit similar patterns of activity; however, the potency is less than that of standard pharmacological agents used for comparison*.

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References

- 1 C. Kaiser and C.L. Zirkle, in A. Burger (Ed.), *Medicinal Chemistry*, Pt. II, Chap. 55, Wiley-Interscience, New York, 1970.
- 2 E.R. Corey, J.Y. Corey and M.D. Glick, *J. Organometal. Chem.*, 101 (1975) 177.
- 3 E.R. Corey, J.Y. Corey and M.D. Glick, *Acta Crystallogr.*, B, 32 (1976) 2025.
- 4 J.Y. Corey, J.P. Paton and D.M. Rankin, *J. Organometal. Chem.*, 139 (1977) 1.
- 5 J.Y. Corey, M.J. Dye, R.L. Farrell and M.V. Mitchell, *J. Organometal. Chem.*, in press.
- 6 (a) J.Y. Corey, M. Dueber and B. Bichlmeir, *J. Organometal. Chem.*, 26 (1970) 167; (b) J.Y. Corey, M. Dueber and M. Malaidza, *ibid.*, 36 (1972) 49; (c) J.Y. Corey, *Synth. Inorg. Metal.-Org. Chem.*, 2 (1972) 85.
- 7 J.Y. Corey and R.L. Farrell, 8th Midwest Regional Meeting Amer. Chem. Soc., Lawrence, Kansas, Oct. 1973.
- 8 K. Sindelar, J.O. Jilek, V. Bartl, J. Metysova, B. Kakac, J. Holubek, E. Svatek, J. Pomykacek and M. Protiva, *Coll. Czech. Chem. Commun.*, 41 (1976) 910.
- 9 P. Jutzi, *Chem. Ber.*, 104 (1971) 1455.
- 10 H.J. Dauben, Jr. and L.L. McCoy, *J. Amer. Chem. Soc.*, 81 (1959) 4863.
- 11 R.L. Letsinger and I.H. Skoog, *J. Amer. Chem. Soc.*, 77 (1955) 576.
- 12 V. Bzant, V.C. Chvalovsky and J. Rathousky, *Organosilicon Compounds*, Vol. 2, Pt. I, 1965, p. 91.