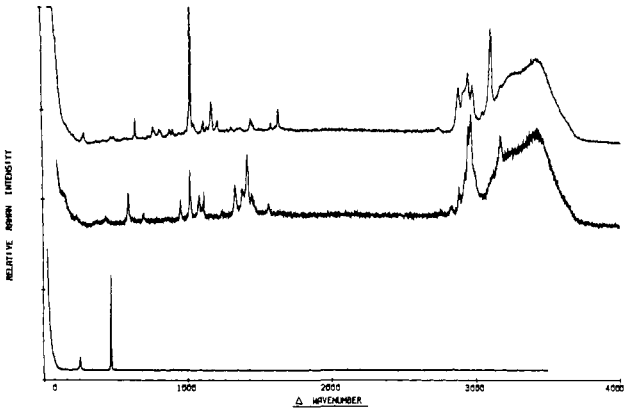


Figure 1. Raman spectra of BPC, (top), MEIC, (center) as aqueous solutions, and liquid BCl_3 (bottom).

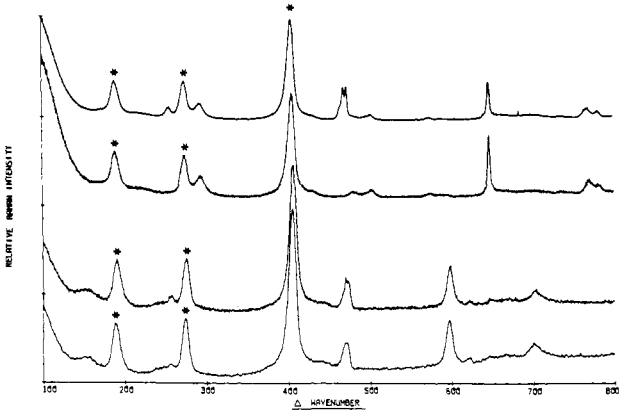


Figure 2. Raman spectra of room temperature tetrachloroborate melts: acidic BPC melt (molar ratio BCl_3:BPC = 2:1) (top); neutral BPC melt (BCl_3:BPC = 1:1) (second from top); acidic MEIC melt (BCl_3:MEIC = 2:1) (second from bottom); neutral MEIC melt (BCl_3:MEIC = 1:1) (bottom). Bands assigned to BCl_4^- are indicated by an asterisk. The composition of the neutral melt sample was nominally 1:1; however, some BCl_3 was present (peak near 470 cm^{-1}).

are formed at ~0 °C, one of which is BCl_3.

Raman spectra of aqueous solutions of BPC, MEIC and liquid BCl_3 are presented in Figure 1. Raman spectra of neutral (mole ratio BCl_3:organic chloride is approximately 1:1) and acidic (mole ratio approximately 2:1) melts prepared from BCl_3 and BPC or MEIC are presented in Figure 2. Three of the four modes of the tetrachloroborate anion are clearly seen for both the neutral and acidic melts; their positions are noted with an asterisk. The fourth mode (ν_3) is very weak and is obscured by a cation mode in the MEIC melt. The frequencies for BCl_4^- in the melts agree quite well with the tetrachloroborate frequencies reported by Bullock et al.[7] The melt frequencies and assignments are (with Bullock's frequency in parentheses) ν_1 405 (396), ν_2 188 (196), ν_3 696 (696), and ν_4 273 (275). No significant composition dependence was observed for the peak positions. In acidic melts, the spectra show the presence of dissolved BCl_3 in the melt phase; since these are saturated solutions, the intensity of the BCl_3 ν_1 peak, when compared to that of neat BCl_3, indicates that the solubility of BCl_3 in both BPC and MEIC melts is about 1 M.

Chloroaluminate melts with an excess of $AlCl_3$ are known to contain the $Al_2Cl_7^-$ ion.[8] All of the peaks in the spectra of acidic BCl_3 melts can be attributed to either the cation modes, BCl_3 modes, or BCl_4^- modes. There is no evidence for the presence of $B_2Cl_7^-$ ion in these systems, even when the melts are cooled to about 77 K.

(7) Bullock, J. I.; Taylor, N. J.; Parrett, F. W. *J. Chem. Soc., Dalton Trans.* **1972**, 1843.
(8) Torsi, G.; Mamantov, G. *Inorg. Chem.* **1972**, *11*, 1439. Brooker, M. H.; Papatheodorou, G. N. In *Advances in Molten Salt Chemistry*; Mamantov, G., Ed.; Elsevier: New York, 1983; Vol. 5, pp 26-184.

Table I. Properties of Tetrachloroborate Melts

composition[a]	phases[b]	liquid temp[c]	density[d]	conductivity[e]	EC window[f] Pt	EC window[f] GC
1:1 BCl_3:BPC	1	+16.5	1.28	1.6×10^{-2}	1200	3300
2:1 BCl_3:BPC	2	-18	1.26	6.1×10^{-3}	900	
1:1 BCl_3:MEIC	1	+16.5	1.29	1.6×10^{-2}	1000	3300
2:1 BCl_3:MEIC	2	-12	1.23	1.6×10^{-2}	1000	

[a] Approximate mole ratio BCl_3:organic chloride. [b] Number of liquid phases present. [c] °C (±0.5 °C). [d] g/mL (±0.05 g/mL). [e] Ω^{-1} cm^{-1} (±10%). All measured near room temperature, except for the 1:1 BPC melt which was measured at 110 °C. [f] Electrochemical window width, mV. Pt refers to platinum working electrode; GC refers to glassy carbon working electrode.

Electrochemical and physical properties of the neutral and acidic melts are collected in Table I. The electrochemical measurements were made with a quasi-reference electrode;[9] hence only the width of the electrochemical window is reported. At the anodic limit a gaseous product, probably Cl_2, is formed; the cathodic limit corresponds to cation reduction, as suggested by the intense blue for BPC,[10] or orange for MEIC,[11] color formed at both platinum and glassy carbon (GC) electrodes. There is no evidence for boron deposition from these melts.

Acknowledgment. Support of the National Science Foundation, Grant CHE-8605166, and of the Air Force Office of Scientific Research, Grant 85-0321, is gratefully acknowledged. We wish to express sincere thanks to S. P. Zingg for her generous donation of a sample of MEIC.

(9) Fung, K. W.; Mamantov, G. In *Wilson & Wilson's Comprehensive Analytical Chemistry*; Volume III, Svehla, G., Ed.; Elsevier: New York, 1975; Vol. III, pp 305-370.
(10) Gale, R. J.; Osteryoung, R. A. *J. Electrochem. Soc.* **1980**, *127*, 2167.
(11) Hussey, C. L.; Sanders, R. J.; Oye, H. A. *J. Electrochem. Soc.* **1985**, *132*, 2156.

(Aminoalkyl)trimethylsilanes. A New Class of Monoamine Oxidase Inactivators

Richard B. Silverman* and Gregory M. Banik

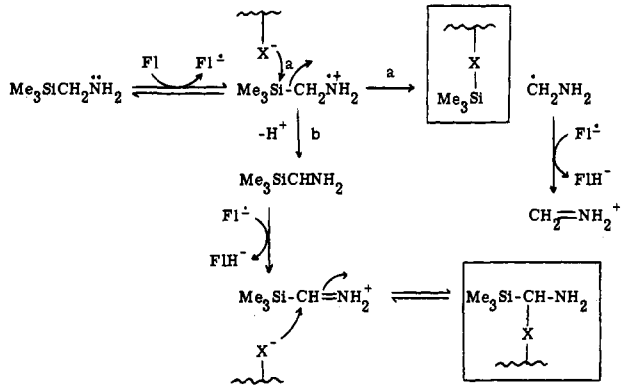
Department of Chemistry and Department of Biochemistry, Molecular Biology, and Cell Biology Northwestern University, Evanston, Illinois 60201
Received November 24, 1986

Inactivators of monoamine oxidase (MAO) have been shown to exhibit antidepressant activity.[1,2] Over the last several years we have investigated the mechanisms of inactivation of MAO by cyclopropylamines,[3-13] by a cyclobutylamine,[14] and by allylamine.[15] All of the evidence from these inactivation studies supports a radical mechanism for MAO-catalyzed amine oxidation.

(1) Kaiser, C.; Setler, P. E. In *Burger's Medicinal Chemistry*, 4th ed.; Wolffe, M. E., Ed.; Wiley: New York, 1981: Part III, pp 1000-1001.
(2) Berger, P. A.; Barchas, J. D. In *Psychotherapeutic Drugs*; Usdin, E., Forrest, I. S., Eds.; Marcel Dekker: New York, 1977; Part II.
(3) Silverman, R. B.; Hoffman, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 884-886.
(4) Silverman, R. B.; Hoffman, S. J.; Catus, W. B., III *J. Am. Chem. Soc.* **1980**, *102*, 7126-7128.
(5) Silverman, R. B.; Hoffman, S. J. *Biochem. Biophys. Res. Commun.* **1981**, *101*, 1396-1401.
(6) Silverman, R. B. *J. Biol. Chem.* **1983**, *258*, 14766-14769.
(7) Silverman, R. B.; Yamasaki, R. B. *Biochemistry* **1984**, *23*, 1322-1332.
(8) Silverman, R. B. *Biochemistry* **1984**, *23*, 5206-5213.
(9) Silverman, R. B.; Zieske, P. A. *Biochemistry* **1985**, *24*, 2128-2138.
(10) Silverman, R. B.; Zieske, P. A. *J. Med. Chem.* **1985**, *28*, 1953-1957.
(11) Vazquez, M. L.; Silverman, R. B. *Biochemistry* **1985**, *24*, 6538-6543.
(12) Yamasaki, R. B.; Silverman, R. B. *Biochemistry* **1985**, *24*, 6543-6550.
(13) Silverman, R. B.; Zieske, P. A. *Biochem. Biophys. Res. Commun.* **1986**, *135*, 154-159.
(14) Silverman, R. B.; Zieske, P. A. *Biochemistry* **1986**, *25*, 341-346.
(15) Silverman, R. B.; Hiebert, C. K.; Vazquez, M. L. *J. Biol. Chem.* **1985**, *260*, 14648-14652.

0002-7863/87/1509-2219$01.50/0

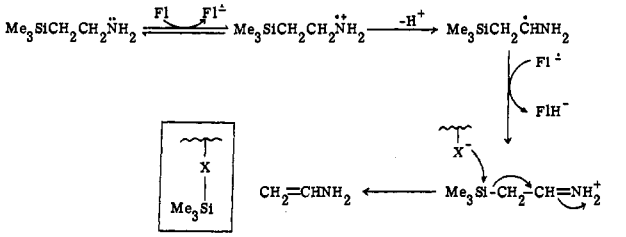
Scheme I. Proposed Mechanism of Inactivation of Monoamine Oxidase by (Aminomethyl)trimethylsilane[a]



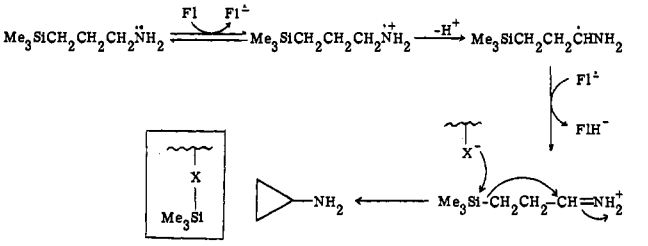
[a] Fl is oxidized flavin; $Fl^{\cdot -}$ is flavin semiquinone; FlH^- is reduced flavin.

On the basis of the work of Mariano and co-workers[16-19] indicating that a radical cation β to a silicon atom activates the molecule for C–Si bond cleavage and the known high electrophilicity of silicon when β to a resonance stabilizing group,[20] we have designed and synthesized[21] (aminoalkyl)trimethylsilanes ($Me_3Si(CH_2)_nNH_2$ (**1**), n = 1–3) as potential inactivators of MAO. All three of the silicon compounds **1** were found to be pseudo-first-order time-dependent inactivators of homogeneous beef liver MAO.[26] A Kitz and Wilson[27] replot of the data indicated that saturation was attained. The K_I values for **1** (n = 1–3) are 2.11, 30.8, and 47.6 mM, respectively, and the k_{inact} values are 0.64, 0.35, and 0.12 min^{-1}, respectively. All inactivations were carried out at pH 7.0 and 25 °C except for **1** (n = 2), which was at pH 7.0 and 0 °C. The substrate, benzylamine, protects the enzyme from inactivation. β-Mercaptoethanol (5 mM) has no significant effect on the rate of inactivation, suggesting that the species responsible for inactivation is not released from the active site. Concomitant with inactivation is the conversion of the flavin spectrum to its reduced form; however, denaturation gives reoxidized flavin. This sugests that either attachment is to the protein or that denaturation releases the adduct. These possibilities will be differentiated with the use of radioactive inactivator. The stabilities of the inactivated enzyme adducts that result from the reactions with the three compounds were different. Upon dialysis at pH 7.0 (40 mM potassium phosphate buffer) and 25 °C of MAO completely inactivated by **1** (n = 1 and 2), enzyme activity returned in a unimolecular reaction with a $t_{1/2}$ of 5.5 days (relative to native enzyme under the same conditions); enzyme inactivated by **1** (n = 3) became reactivated by dialysis at pH 7.0 also in a unimolecular reaction with a $t_{1/2}$ of 13 h. The reactivation experiments were terminated prior to compete return of enzyme activity because of the loss of activity in the control enzyme over this time period. However, this indicates that at least two different adducts are formed. On the basis of previous mechanistic work[3-15] and that of Mariano and co-workers,[16-19] potential inactivation mechanisms are proposed in Schemes I–III for the three organosilicon compounds; the speculated inactivated enzyme adducts are enclosed in boxes. In Scheme I one-electron transfer would produce an amine radical cation that may have two fates. Pathway a depicts the chemistry of Mariano and co-workers,[16-19] namely, nucleophilic attack at the electrophilic silicon atom, leading to trimethylsilation of the enzyme. Pathway b depicts further proton and electron transfer via the proposed[3-15] normal catalysis to give the immonium ion of formyltrimethylsilane; the corresponding acylsilanes are highly electrophilic.[20] It is known that the silicon of α-silyl carbonyl compounds is highly electrophilic;[28] consequently, trimethylsilation of MAO as shown in Scheme II is well precedented. The cyclopropanation of trimethylsilylpropyl cationic species also is well precedented,[29-31] supporting the plausibility for the mechanism in Scheme III.

Scheme II. Proposed Mechanism of Inactivation of Monoamine Oxidase by (Aminoethyl)trimethylsilane



Scheme III. Proposed Mechanism of Inactivation of Monoamine Oxidase by (Aminopropyl)trimethylsilane



These are the first organosilicon inactivators of MAO; however, Nagahisa et al.[32] prepared a trimethylsilyl analogue of a steroid and showed that it was a mechanism-based inactivator of cytochrome $P\text{-}450_{scc}$. In this case a cation mechanism was suggested to result in a trimethylsilylated enzyme. Neither this inactivated enzyme nor MAO inactivated by **1** (n = 1–3) is reactivated by fluoride ion (100 equiv). However, fluoride ion is highly solvated in aqueous solutions, so it may not be an effective desilylating agent under these conditions.

We are currently attempting to elucidate the mechanisms of inactivation of MAO by each of these inactivators and to identify the adducts produced.

Acknowledgment. We are grateful to the National Institutes of Health (Grant GM 32634) for financial support. R.B.S. is a National Institutes of Health Research Career Development Awardee (1982–1987).

(16) Brumfield, M. A.; Quillen, S. L.; Yoon, U. C.; Mariano, P. S. *J. Am. Chem. Soc.* **1984**, *106*, 6855–6856.
(17) Lan, A. J. Y.; Quillen, S. L.; Heuckeroth, R. O.; Mariano, P. S. *J. Am. Chem. Soc.* **1984**, *106*, 6439–6440.
(18) Ohga, K.; Yoon, U. C.; Mariano, P. S. *J. Org. Chem.* **1984**, *49*, 213–219.
(19) Chen, S. F.; Ullrich, J. W.; Mariano, P. S. *J. Am. Chem. Soc.* **1983**, *105*, 6160–6162.
(20) Fleming, I. In *Comprehensive Organic Chemistry*; Barton, D., Ollis, W. D., Eds.; Pergamon: Oxford, 1979: Vol. 3, pp 541–686.
(21) Compound **1** (n = 1) was prepared as described by Sommer and Rockett.[22] Compound **1** (n = 2) was made[23] by lithium aluminum hydride reduction (refluxing ether, 24 h) of (trimethylsilyl)acetonitrile (Petrarch Systems, Inc.) followed by extraction of an ethereal solution of the amine with dilute HCl. Compound **1** (n = 3) was synthesized by conversion of 3-(trimethylsilyl)-1-propanol (Aldrich) to *N*-[3-(trimethylsilyl)propyl]phthalimide with phthalimide, triphenyl phosphine, and diethyl azodicarboxylate[24] followed by hydrazinolysis. All of the compounds had melting points that corresponded to literature values;[22] **1** (n = 1) mp = 245–246.5 °C (lit. 242–243 °C); **1** (n = 2) mp = 296–298 °C (lit. 300 °C); **1** (n = 3) mp 190–192 °C (lit. 183–184 °C). NMR spectral data also were consistent with those reported previously.[25]
(22) Sommer, L. H.; Rockett, J. *J. Am. Chem. Soc.* **1951**, *73*, 5130–5134.
(23) Fialova, V; Bazant, V.; Chvalovsky, V. *Coll. Czech. Chem. Commun.* **1973**, *38*, 3837–3844.
(24) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679–680.
(25) Schraml, J.; Nguyen, D.C.; Chvalovsky, V. *Org. Magn. Reson.* **1975**, *7*, 379–385.
(26) Salach, J. I. *Arch. Biochem. Biophys.* **1979**, *192*, 128–137.
(27) Kitz, R.; Wilson, I. B. *J. Biol. Chem.* **1962**, *237*, 3245–3249.
(28) Brooke, A. G. *Acc. Chem. Res.* **1974**, *7*, 77–84.
(29) Sommer, L. H.; van Strien, R. E.; Whitmore, F. C. *J. Am. Chem. Soc.* **1949**, *71*, 3056–3060.
(30) Calas, R.; Valade, J. *Bull. Soc. Chim. Fr.* **1958**, 919.
(31) Batuev, M. I.; Petrov, A. D.; Ponomarenko, V. A.; Matveeva, A. D. *Zh. Obshch. Khim.* **1956**, *26*, 2336–2346; *Chem. Abstr.* **1957**, *51*, 4979a.
(32) Nagahisa, A.; Orme-Johnson. W. H.; Wilson, S. R. *J. Am. Chem. Soc.* **1984**, *106*, 1166–1167.