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N-[(TRIORGANYLSILYL)ALKYL]ETHYLENEDIAMINES

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Summary

A series of *N*-organosilylalkyl-substituted ethylenediamines, $R_3Si(CH_2)_n$-$NHCH_2CH_2NH_2$ ($R = CH_3$, C_6H_5 or $4\text{-}CH_3C_6H_4$; $n = 1$ or 3), were prepared by the reaction of haloalkylsilanes with ethylenediamine. The cleavage of a methyl group from silicon by concentrated sulfuric acid was used for the preparation of 1,3-bis-[*N*-(2-aminoethyl)aminomethyl]-1,1,3,3-tetramethyldisiloxane. The proton and carbon-13 NMR spectra of these compounds are reported.

Introduction

The ability of *cis*-dichloro(diamino)platinum(II) and some related compounds to inhibit the growth of certain tumors is well known [1]. The antitumor activity of *cis*-platinum compounds with N-donor ligands and anions like chloride, sulfate or malonate has been established [2,3]. A large number of platinum compounds with a wide variety of N-donor ligands have been prepared and tested for their ability to cause regression of tumor cells [4–6]. However, no work has been done with silicon-containing N-donor ligands. As a first step in the synthesis and characterization of new antitumor organosilicon compounds, we have prepared a series of

$$\underset{(\mathbf{1})}{R_3Si[CH_2]_nNHCH_2CH_2NH_2} \qquad \underset{(\mathbf{2})}{R_3Si[CH_2]_nNHCH_2CH_2NH[CH_2]_nSiR_3}$$

($R = Me$, Ph or $p\text{-}MeC_6H_4$, $n = 1$ or 3)

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silicon-containing ethylenediamine ligands, **1** and **2**. The variation in the number of phenyls attached to silicon allows these compounds to serve as precursors to disiloxane and polysiloxane N-donor ligands through the selective strong acid cleavage of phenyls from silicon. This paper reports the synthesis and characterization of these organosilicon ethylenediamines.

Results and discussion

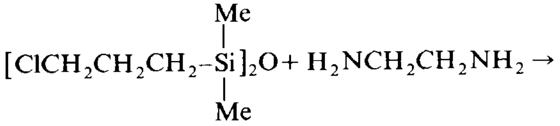
The most convenient method for the preparation of ethylenediamines **1** and **2** was the reaction of ethylenediamine with haloalkylsilanes [7,8]. The reaction of halomethylsilanes or halopropylsilanes with a three- to four-fold excess of ethylenediamine in refluxing toluene resulted in a 50 to 80% yield of N-substituted products contaminated with only small amounts of the *N,N'*-disubstituted amines (eq. 1).

$$\mathrm{R_3Si[CH_2]_\mathit{n}X + H_2NCH_2CH_2NH_2} \rightarrow \begin{cases} \mathrm{R_3Si[CH_2]_\mathit{n}NHCH_2CH_2NH_2} \quad (\mathbf{1}) \\ \mathrm{R_3Si[CH_2]_\mathit{n}NHCH_2CH_2NH[CH_2]_\mathit{n}SiR_3} \quad (\mathbf{2}) \end{cases} \qquad (1)$$

$(\mathrm{R = Me, Ph\ or\ } p\text{-}\mathrm{MeC_6H_4};\ \mathrm{X = Br\ or\ Cl};\ n = 1\ \mathrm{or}\ 3)$

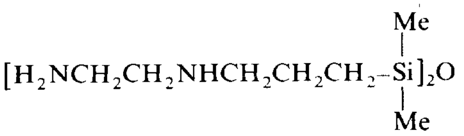
When equal molar ratios of reactants were employed, disubstituted ethylenediamines were formed as the main products. The synthesis and properties of these organosilicon ethylenediamines are summarized in Tables 1 and 2.

The linear disiloxane **4** was prepared through the reaction of bis(chloropropyl)disiloxane **3** with ethylenediamine in refluxing toluene (eq. 2). However, under the same conditions, the reaction of bis(chloromethyl)disiloxane (**5**) with ethylenediamine yielded the cyclic disiloxane **6** rather than a linear disiloxane (eq. 3). Intramolecular cyclization to form **6** occurs despite a 10/1 molar ratio of ethylenediamine to



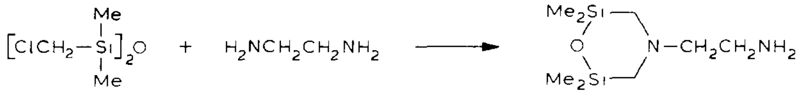
$$\mathrm{[ClCH_2CH_2CH_2{-}SiMe_2]_2O + H_2NCH_2CH_2NH_2} \rightarrow$$

(3)



$$\mathrm{[H_2NCH_2CH_2NHCH_2CH_2CH_2{-}SiMe_2]_2O} \qquad (2)$$

(4)



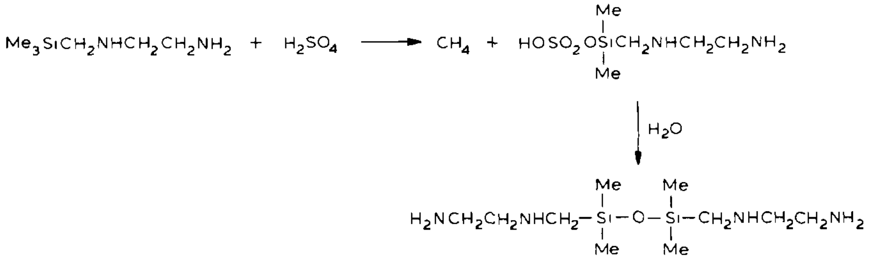
(3)

(5)

(6)

the chloromethyldisiloxane. Formation of **4** and **6** was confirmed with proton NMR spectra. The spectrum of **4** displays a multiplet at δ 2.70 corresponding to the four protons of the ethylenediamino group. In the spectrum of **6**, these methylene hydrogens are two triplets at δ 2.70 and 2.45 ppm. More importantly, the relative intensities for the ethylenediamino protons compared to the silicon methyl protons is 4/6 for **4** and 4/12 for **6**.

The linear disiloxane **7** which would have been formed if cyclization had not occurred may be prepared by acid cleavage (eq. 4) [7–11]. Exactly one mole of



$$\mathrm{Me_3SiCH_2NHCH_2CH_2NH_2 + H_2SO_4 \longrightarrow CH_4 + HOSO_2O\underset{Me}{\overset{Me}{Si}}CH_2NHCH_2CH_2NH_2}$$

$$\xrightarrow{\mathrm{H_2O}} \mathrm{H_2NCH_2CH_2NHCH_2{-}\underset{Me}{\overset{Me}{Si}}{-}O{-}\underset{Me}{\overset{Me}{Si}}{-}CH_2NHCH_2CH_2NH_2} \qquad (4)$$

(7)

methane is evolved for each trimethylsilyl group when trimethylsilylmethylethylenediamine is treated with concentrated sulfuric acid. These results strongly suggest that the best synthetic strategy for the preparation of disiloxanes and polysiloxanes containing ethylenediamine moieties is the preparation of phenylalkylsilyl derivatives of ethylenediamine followed by selective cleavage of phenyl groups from silicon by strong acids because phenyl groups are known to be easier to cleave than alkyl groups.

Experimental

Trimethylchlorosilane, dimethyldichlorosilane and methyllithium were obtained from Aldrich Chemical Co. Trimethyl(chloromethyl)silane, 3-chloropropyltrichlorosilane, 1,3-bis(3′-chloropropyl)-1,1,3,3-tetramethyldisiloxane and 1,3-bis-(chloromethyl)-1,1,3,3-tetramethyldisiloxane were purchased from Petrarch Systems, Inc., Levittown, PA. Bromobenzene was supplied by the American Drug and Chemical Co., Culver City, CA. Magnesium turnings were bought from MCB Manufacturing Chemists, Inc., Cincinnati, OH. Ethylenediamine from Fisher Scientific Co. was dried over potassium hydroxide and distilled before use. Dimethyl(bromomethyl)chlorosilane (b.p. 132–134°C) was obtained in 59% yield by bromination of trimethylchlorosilane [12].

The proton NMR spectra were obtained in deuterochloroform with a Varian Associates EM-390 spectrometer and are referenced to internal tetramethylsilane. For the proton shifts presented in Tables 1–4, phenyl shifts are for the center of multiplets. For $CH_2CH_2CH_2$ groups, the three shifts are for the center of a triplet, complex multiplet, and triplet. The carbon-13 spectra were obtained in deuterochloroform with a JEOL JNM-PS-100/Nicolet 1080 Fourier Transform Spectrometer. The spectra were proton-noise decoupled at an observed frequency of 25.0335 MHz and a sweep width of 5,000 Hz. The chemical shifts are referenced to internal tetramethylsilane.

(Continued on p. 36)

TABLE 1

SYNTHESIS AND PROPERTIES OF *N*-[(TRIORGANYLSILYL)ALKYL]ETHYLENEDIAMINES, $R_2R'Si(CH_2)_nNHCH_2CH_2NH_2$

R	R′	*n*	Reflux (h)	Yield (%)	B.p. (°C (Torr))	Analysis (Found (calcd.) (%))		^{1}H chemical shifts					^{13}C chemical shifts			
						C	H	CH_3	Ph	$(CH_2)_n$	CH_2CH_2	NH,NH_2	CH_3	Ph	$(CH_2)_n$	CH_2CH_2
Me	Me	1	5	60	104 (50)	48.95 (49.26)	12.34 (12.40)	0.10		2.10	2.77	1.49	−2.7		39.8	56.8 41.0
Me	Me	3	12	71	75–77 (0.9)	55.28 (55.11)	12.52 (12.72)	0.02		2.63 1.50 0.48	2.75	1.57	−2.0		52.3 24.2 13.8	53.0 41.6
Me	Ph	1	12	55	127 (0.8)	63.12 (63.40)	9.59 (9.67)	0.33	7.38	2.30	2.70	1.13	−4.1	133.5 128.9 127.7	38.8	56.6 40.9
Me	Ph	3	48	39	153–155 (1.2)	66.31 (66.04)	10.33 (10.23)	0.30	7.38	2.60 1.50 0.73	2.70	1.45	−3.5	133.1 128.4 127.3	51.9 24.0 12.9	52.7 41.3
Me	4-MeC_6H_4	1	24	72	135–138 (0.6)	64.68 (64.80)	10.03 (9.97)	0.30	7.38	2.27	2.70	1.20	−4.0	133.5 128.5	38.8	56.7 40.8
Ph	Me	1	24	53	193–195 (1.5)	71.33 (71.06)	8.01 (8.20)	0.60	7.38	2.60	2.70	1.13	−5.2	134.4 129.3 127.8	37.4	56.7 40.8
Ph	Me	3	48	68	183–185 (0.4)	72.56 (72.43)	8.85 (8.78)	0.53	7.38	2.60 1.55 1.03	2.68	1.23	−4.7	134.2 128.9 127.6	52.3 24.3 11.6	52.9 41.6
Ph	Ph	1	48	60	m.p. 80	75.65 (75.85)	7.37 (7.28)		7.40	2.90	2.73	1.48		135.6 129.6 127.8	36.7	56.9 40.9

TABLE 2

PROPERTIES OF *N*,*N*′-BIS[(TRIMETHYLSILYL)ALKYL]ETHYLENEDIAMINES, **2**, AND DISILOXANES **4**, **6**, AND **7**

Compound	Yield (%)	B.p. (°C (Torr))	Analysis (Found (calcd.) (%))		^{1}H chemical shifts				^{13}C chemical shifts		
			C	H	CH_2	$(CH_2)_n$	CH_2CH_2	NH,NH_2	CH_3	$(CH_2)_n$	CH_2CH_2
2, *n* = 1	33	90–92 (1.0)	51.79 (51.66)	12.08 (12.14)	0.09	2.10	2.77	1.32	−2.7	39.9	53.0
2, *n* = 3	16	117.9 (0.3)	58.37 (58.26)	12.49 (12.57)	0.01	2.60 1.50 0.50	2.73	1.37	−1.8	49.4 24.4 14.4	53.3
4	31	167–71 (0.3)	50.41 (50.25)	11.60 (11.45)	0.07	2.60 1.51 0.33	2.73	1.48	0.1	52.3 23.6 15.6	52.8 41.6
6	62	74–75 (0.7)	43.76 (43.99)	10.34 (10.15)	0.15	1.82	2.70 2.45	1.60	−0.3	48.3	69.2 39.3
7	54	147–150 (0.8)	42.99 (43.12)	10.69 (10.86)	0.17	2.07	2.71	1.30	−1.1	40.5	56.1 40.2

TABLE 3

SYNTHESIS AND PROPERTIES OF TRIORGANYL(HALOMETHYL)SILANES, $R_2R'SiCH_2X$

R	R′	X	Reagents (mol)	Yield (%)	B.p. (°C(Torr)) B.p. (lit.)	^1H chemical shifts		
						CH_3	CH_2	Ph
Me	Ph	Br	$BrCH_2Me_2SiCl$ (0.30) PhMgBr (0.33)	76	93–95(2) 78(0.6) [13]	0.43	2.60	7.37
Me	Ph	Cl	$ClCH_2Me_2SiCl$ (0.35) PhMgBr (0.38)	90	59–61(1)	0.42	2.94	7.45
Me	4-MeC_6H_4	Cl	$ClCH_2Me_2SiCl$ (0.34) 4-MePhMgBr (0.37)	60	95–96(1) 80(1) [14]	0.40	2.91	7.37
Ph	Me	Cl	$ClCH_2MeSiCl_2$ (0.33) PhMgBr (1.02)	71	134–138(0.3) 100–102(0.01)	0.70	3.20	7.45
Ph	Ph	Cl	$ClCH_2SiCl_3$ (0.20) PhMgBr (0.72)	32	m.p. 112–114		3.50	7.40

Triorganyl(halomethyl)silanes. The preparation of dimethyl(chloromethyl)phenylsilane is described as an example. The other halomethylsilanes listed in Table 3 were synthesized similarly. Phenylmagnesium bromide was obtained from bromobenzene (90.0 g, 0.57 mol) and magnesium turnings (12.2 g, 0.50 mol) in anhydrous diethyl ether (230 ml) under a dry nitrogen atmosphere. Dimethyl(chloromethyl)-chlorosilane (50.1 g, 0.35 mol) was added dropwise over a period of 30 min to the stirred Grignard solution contained in a 500 ml, three-necked flask equipped with a reflux condenser. The mixture was then refluxed for 16 h and subsequently poured into ice water (300 ml). The mixture was extracted with diethyl ether (2 × 200 ml) and the extract washed with three 250 ml portions of water and then dried over sodium sulfate. The ether was distilled and the residue was fractionated in vacuo to give dimethyl(chloromethyl)phenylsilane (57.9 g, 0.31 mol, 90% yield).

Triorganyl(halopropyl)silanes. In the preparation of dimethylphenyl- and methyldiphenyl-(3-chloropropyl)silanes, it is important to add the phenyl organometallic first followed by the methyl organometallic. If methyl Grignard were added first followed by phenylmagnesium bromide or phenyllithium, the last phenyl–silicon bond formed with difficulty and much hexaorganyldisiloxane was isolated upon workup. For the preparation of triphenyl(3-chloropropyl)silane, an excess of phenylmagnesium was used but still the yield was low. The preparation of dimethylphenyl(3-chloropropyl)silane is described as an example. The other halopropylsilanes listed in Table 4 were synthesized similarly. A solution of 3-chloropropyltrichlorosilane (84.2 g, 0.40 mol) in diethyl ether (200 ml) was placed in a nitrogen-purged, 2 l three-necked flask equipped with a stirrer and a reflux condenser. Phenylmagnesium bromide (0.40 mol) in diethyl ether (200 ml) was added to the stirred silane solution during 1 h. Methyllithium (0.80 mol) in diethyl ether (615 ml) was added dropwise to the reaction mixture over a period of 6 h. The mixture was refluxed for 32 h and then poured into ice water (1000 ml). The ether layer was washed with water (6 × 500 ml) and dried with magnesium sulfate. The solvent was evaporated and the residue was fractionated in vacuo to give dimethylphenyl(3-chloropropyl)silane (52.7 g, 0.25 mol, 62% yield).

TABLE 4

SYNTHESIS AND PROPERTIES OF TRIORGANYL(3-CHLOROPROPYL)SILANES, $R_2R'Si(CH_2)_3Cl$

R	R′	Reagents (mol)	Yield (%)	B.p. (°C(Torr)) B.p. (lit.)	CH_3	¹H chemical shifts			
						$ClCH_2$	CH_2	CH_2Si	Ph
Me	Me	$Cl(CH_2)_3Si(OEt)_3$ (0.08) MeLi (0.30)	58	149–150 66(43) [16]	0.01	3.45	1.75	0.57	
Me	Ph	$Cl(CH_2)_3Si(OEt)_3$ (0.08) PhMgBr (0.08), MeLi (0.20)	56	105–107(1.6) 110(2) [17]	0.28	3.45	1.75	0.83	7.37
Ph	Me	$Cl(CH_2)_3SiCl_3$ (0.40) PhMgBr (0.80), MeLi (0.40)	33	163–165(0.3) 179–180(3) [17]	0.57	3.45	1.83	1.17	7.38
Ph	Ph	$Cl(CH_2)_3SiCl_3$ (0.25) PhMgBr (1.00)	19	m.p. 82–85		3.54	1.94	1.50	7.40

N-[(Triorganylsilyl)alkyl]ethylenediamine (1). Ethylenediamine was dissolved in toluene (150 ml) and heated to reflux. The chloroalkyl(triorganyl)silane, approximately 0.25 times the molar amount of diamine, was added dropwise to the stirred, refluxing diamine solution. The mixture was refluxed for several hours after the addition was completed. The precipitated salts were removed by filtration, the solvent evaporated and the residue fractionated in vacuo. Details for the synthesis of each (triorganylsilyl)alkylethylenediamine are presented in Table 1.

N,N′-Bis[(trimethylsilyl)methyl]ethylenediamine (2, n = 1). Chloromethyltrimethylsilane (12.3 g, 0.10 mol) and ethylenediamine (6.0 g, 0.10 mol) were refluxed in toluene (150 ml) in the presence of potassium carbonate (13.8 g) for 24 h. After evaporation of the solvent, vacuum fractionation of the residue gave **2**, ($n = 1$) (7.7 g, 0.033 mol, 66% yield, b.p. 90–92 °C/1 Torr).

N,N′-Bis[(trimethylsilyl)propyl]ethylenediamine (2, n = 3). This compound was formed as a higher boiling component in the synthesis of (trimethylsilylpropyl)ethylenediamine (16% yield, b.p. 117–119 °C/0.3 Torr).

1,-3-Bis[N-(2-aminoethyl)-3-aminopropyl]tetramethyldisiloxane (4). Ethylenediamine (18.0 g, 0.30 mol) was dissolved in toluene (50 ml) and 1,3-bis(3-chloropropyl)tetramethyldisiloxane (14.4 g, 0.052 mol) was added with stirring. The soluton was refluxed for 24 h, the salts removed by filtration and the solvent evaporated. The residue was fractionated in vacuo to give **4** (5.2 g, 0.016 mol, 31% yield, b.p. 167–171 °C/0.3 Torr).

1,1,3,3-Tetramethyl-5-(2-aminoethyl)-1,3-disila-2-oxa-5-azacyclohexane (6). Ethylenediamine (24.0 g, 0.40 mol) was dissolved in toluene (80 ml) and 1,3-bis(chloromethyl)tetramethyldisiloxane (9.2 g, 0.040 mol) was added dropwise with stirring. The solution was refluxed for 24 h, the salts removed by filtration and the solvent evaporated. The residue was fractionated in vacuo to give **6** (5.4 g, 0.025 mol, 62% yield, b.p. 74–75 °C/0.7 Torr).

1,3-Bis[N-(2-aminoethyl)aminomethyl]tetramethyldisiloxane (7). *N*-(Trimethylsilylmethyl)ethylenediamine (5.8 g, 0.044 mol) was added slowly to concentrated sulfuric acid (25 ml) cooled in an ice bath. The solution was then heated at 100 °C for 6 h. Methane (897 ml at STP, 0.044 mol) evolved during this time. The solution was poured into ice water (100 ml), made alkaline with potassium hydroxide and filtered. The water was evaporated to give a viscous residue. Distillation of the residue in vacuo gave disiloxane **7** (3.0 g, 0.011 mol, 54% yield. b.p. 147–150 °C/0.8 Torr).

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