New Fragmentation Process in Mass Spectrometry of Carbonyl Compounds with a δ-Silyl Group

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Electron-impact-induced fragmentations were performed in the gas phase on δ-silyl aldehydes, ketones, thioketones, carboxylic acids, and acetates. All of these compounds showed significant silyl migration through a transition state with a seven-membered ring. For ketones and acetates, this silyl migration process may overwhelm the McLafferty rearrangement, which involves a transition state with a six-membered ring.

Introduction

Organosilicon compounds are widely used in synthetic chemistry,[1] industry, and polymer science.[2,3] Functionalized silicon-containing compounds may possess special physical and chemical properties.[4] Their structural identification often involves mass spectrometry, in which one of the most important fragmentations is the McLafferty rearrangement.[5] It occurs to a molecule possessing an appropriately located heteroatom (e.g., O), a π system (usually a double bond), and an abstractable hydrogen atom γ to the hetero-functionality.

The McLafferty rearrangement may compete with other fragmentation paths in mass spectrometry. When a silyl group exists in organic compounds, it may exert an α-, β-, or γ-effect to stabilize or destablize intermediates of various types.[4,6−11] Weber et al.[12,13] reported that the γ-silyl group, instead of a γ-hydrogen atom, of methyl 4-trimethylsilylbutyrate migrates in the mass spectrometer. Thus one can envision that radical cation **1**, containing a carbonyl group and a δ-silyl group, may lead to different fragments as shown in Scheme 1. Through the McLafferty rearrangement, ketonic radical cation **1** should give **2** and **3** by path A, as well as afford **4** and **5** by path B. The favored path would depend on the balance of the steric[14,15] and the β-electronic[4] effects of the Me_3Si group. On the other hand, an unprecedented silyl migration could take place on **1** to give **6** and **7** by path C, which involves a seven-membered ring transition state.

To realize the fragmentation pattern of δ-silyl carbonyl compounds, we prepared a series of organosilicon compounds and studied their mass spectra.[16] Herein we report our findings on a new silyl migration in δ-silyl carbonyl compounds in the gas phase. The process could involve a transition state with a seven-membered ring.

Results and Discussion

Mass Spectra of Silicon-Containing Carbonyl Compounds and a Plausible Mechanism Involving a New Fragmentation Path. We synthesized silicon-containing acyclic ketones **8**−**11** and cyclic ketones **12**−**20** in good yields based on established procedures.[8,17] Furthermore, treatment of ketone **8** with the Lawesson's reagent[18] produced the corresponding thioketone **21** in 82% yield. To obtain a δ-silyl aldehyde and carboxylic acid, we allylated diethyl malonate with allyltrimethylsilane in the presence of MnO_2 and acetic acid at 160 °C.[8] Saponification followed by decarboxylation of the resultant 2-[3-(trimethylsilyl)propyl]malonic acid diethyl ester with KOH and then with HCl in methanol gave the carboxylic acid **23**. Reduction of δ-silyl acid **23** to the corresponding aldehyde **22** was accomplished by use of oxalyl chloride and then lithium tri-*tert*-butoxyaluminohydride[19] in the presence of a catalytic amount of

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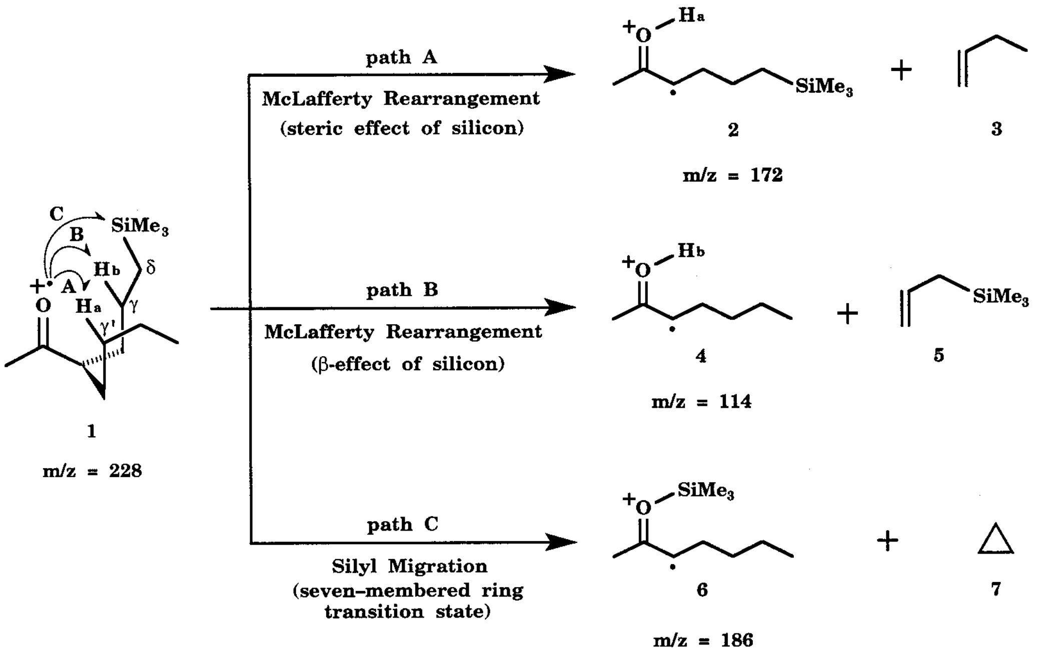
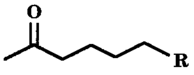
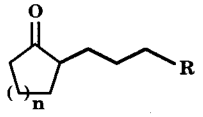
10.1021/om980804b CCC: $18.00

Scheme 1

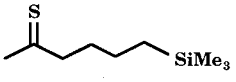




R =
8. $SiMe_3$
9. $SiMe_2Ph$
10. $SiMePh_2$
11. $SiMe_2F$



	n =	R =
12.	1	$SiMe_3$
13.	2	$SiMe_3$
14.	3	$SiMe_3$
15.	4	$SiMe_3$
16.	8	$SiMe_3$
17.	2	$SiMe_2Ph$
18.	2	$SiMePh_2$
19.	2	$SiPh_3$
20.	2	$SiMe_2F$



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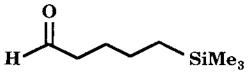

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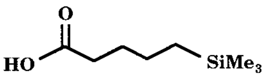

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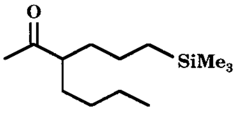

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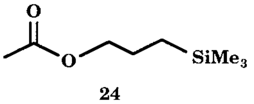


24

CuI in THF. Silicon-containing acetate **24** was prepared in 97% yield by acetylation of the corresponding 3-(trimethylsilyl)-1-propanol with acetyl chloride. Finally, allylation of 2-heptanone with allyltrimethylsilane in the presence of MnO_2 and acetic acid at 140 °C produced the desired δ-silyl ketone **25** in 53% yield.

We obtained the mass spectra of these δ-silyl carbonyl compounds at 70 eV electron energy and set the source temperatures between 175 and 190 °C. Through analysis of these spectra, we found that, in addition to the expected McLafferty rearrangement peaks, most of these spectra also showed significant peaks at $M^{•+} - 29$, $M^{•+} - 42$, and $M^{•+} - 57$ (see Table 1). These peaks may result from silyl migrations.

Our results from the fragmentation of silicon-containing ketones could be explained by a plausible mechanism shown in Scheme 2, in which the radical cation **26** is used as a representative example. Some of the fragments resulting from **26**, originated from compound **12** by electron beam, are indicated in Figure 1. The path A in Scheme 2 leads **26** ($m/z = 198$) to radical cation **28** ($m/z = 84$) via **27** through the well-established McLafferty rearrangement; yet the path B could lead **26** to intermediate **29** through a silyl migration with a seven-membered ring transition state. Further fragmentation took place on **29** to give radical cation **30** ($m/z = 156$), as observed in Figure 1, and cyclopropane (**7**). Loss of a methyl radical (**32**) from **30** produced the detected cation **31** ($m/z = 141$).

Meanwhile, a hydrogen migration occurring to **29** could generate **33**. It is then decomposed to afford oxonium species **34** ($m/z = 169$), as observed in Figure 1, and ethyl radical (**35**). The total relative abundance of the detectable species was 133.5%, which includes 51% from **30**, 2.5% from **31**, and 80% from **34**. All of them could originate from intermediate **29**. On the other hand, the relative abundance of intermediate **27** is reflected by the peak of **28** (22%). Consequently we obtained the ratio 1:6.1 for (path A)/(path B). Results from this type of analyses are summarized in Table 1 for ketones **8** and **12**−**16**.

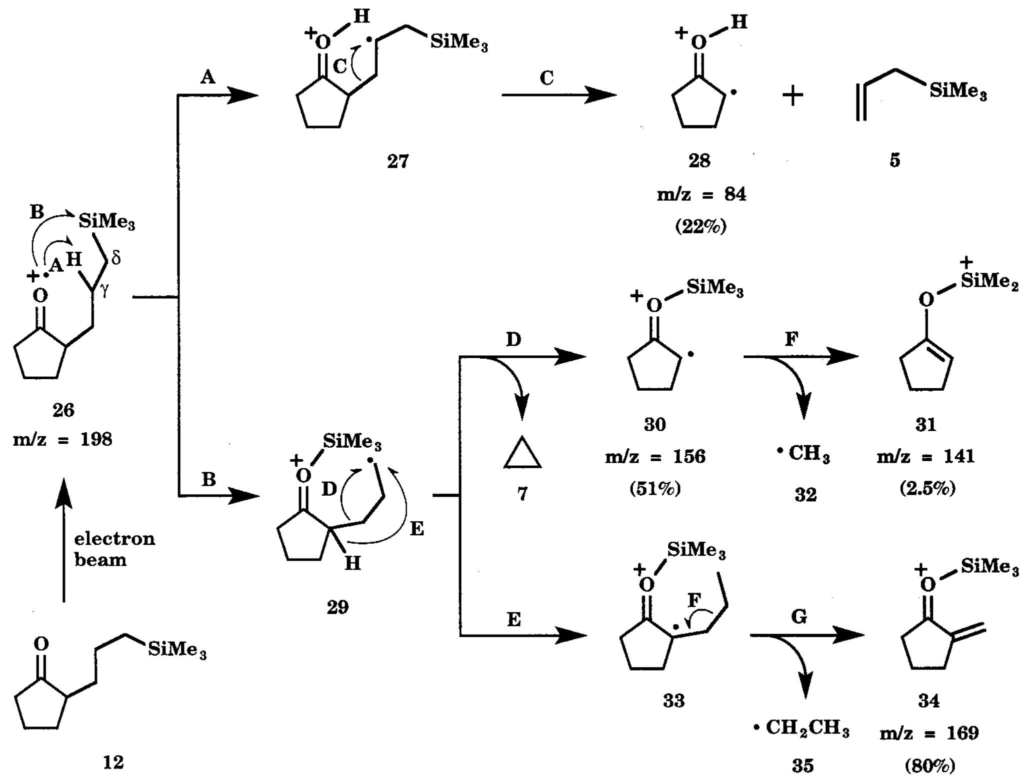
Furthermore, we confirmed the formula of the fragments resulting from the newly proposed silyl migration path by means of high-resolution mass spectroscopy. Satisfactory exact masses were obtained for all of the three crucial species, including $M^{•+} - 29$, $M^{•+} - 42$, and $M^{•+} - 57$, from silicon-containing cyclopentanone **12** (see Table 2). For acyclic ketone **8**, we were able to measure

Table 1. Relative Abundance (% Base) in Mass Spectra of Compound 8−24

	McLafferty (A)		silyl migration (B)						
carbonyl compound	*m*/*z*	relative abundance (%)	$M^{\bullet+} - 29$ (*m*/*z*)	relative abundance (%)	$M^{\bullet+} - 42$ (*m*/*z*)	relative abundance (%)	$M^{\bullet+} - 57$ (*m*/*z*)	relative abundance (%)	A:B
8	58	5.0	143	43	130	15	115	20	1:16
9	58	4.1	205	0.48	192	0.14	177	1.9	1.6:1
10	58	2.5	267	0.52	254	ND[a]	239	0.21	3.4:1
11	58	18	147	8.3	134	7.4	119	4.7	1:1.1
12	84	22	169	80	156	51	141	2.5	1:6.1
13	98	100	183	17	170	28	155	6.6	1.9:1
14	112	100	197	9.2	184	11	169	10	3.3:1
15	126	45	211	2.0	198	5.0	183	5.8	3.5:1
16	182	35	267	ND	254	4.8	239	ND	7.3:1
17	98	30	245	2.6	232	4.6	217	3.5	2.8:1
18	98	4.0	307	0.27	294	0.38	279	0.25	4.4:1
19	98	5.5	369	0.21	356	0.20	341	0.25	8.3:1
20	98	100	187	1.1	174	3.2	159	2.5	15:1
21	74	10	159	ND	146	ND	131	2.2	4.5:1
22	44	9.6	129	ND	116	ND	101	4.6	2.1:1
23	60	8.6	145	2.1	132	ND	117	ND	4.1:1
24	60	2.2	145	ND	132	ND	117	52	1:24

[a] ND: not detectable.

Scheme 2



the exact masses for the species $M^{\bullet+} - 29$ and $M^{\bullet+} - 57$; the intensity of the peak associated with the species $M^{\bullet+} - 42$ was too weak to be detected with accuracy. More solid evidence was obtained from the high-resolution mass spectrum of cyclohexanone **13** to support the species of $M^{\bullet+} - 29$ and $M^{\bullet+} - 42$ (Table 2).

To gain information on fragmentation from different silyl groups, we recorded electron-impact-induced fragmentation of ketones **9**−**11** and **17**−**20**. Significant silyl migrations were also observed, especially in **9** and **11**. To extend the scope of ketones to other types of compounds, we detected the fragmentation patterns of thioketone **21**, aldehyde **22**, carboxylic acid **23**, and acetate **24**. The new pattern of silyl migration through a transition state with a seven-membered ring was associated with each of them.

Among those compounds, the acetate **24** exhibited the most prominent ratio (i.e., 24:1) for the silyl migration to the McLafferty rearrangement. Its trend roughly follows the order acetate > ketone > aldehyde > carboxylic acid > thioketone, as indicated by the data associated with compounds **24**, **8**, **22**, **23**, and **21**, respectively.

Steric Effect of Silyl Groups on Their Migratory Aptitude Revealed by the CVFF Calculations. By analyzing the data in Table 1, we found that the silyl groups migrated easier in an acyclic ketone than in a cycloalkanone, as in comparison of the pairs **8** versus **12**−**16**, respectively, **9** versus **17**, and **11** versus **20**. To rationalize this phenomenon, we performed a series of graphic molecular modeling on a Silicon Graphics IRIS CRIMSON/Elan workstation. The program *Builder*

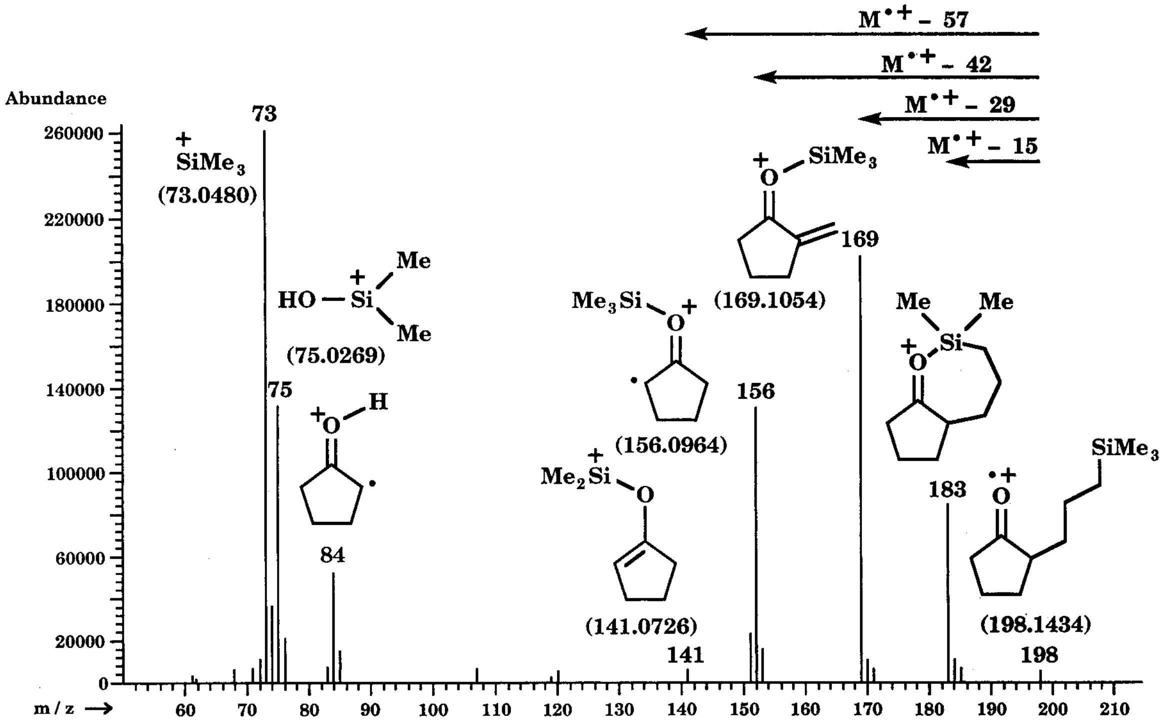


Figure 1. Analysis of the mass spectrum of 2-[3-(trimethylsilyl)propyl]cyclopentan-1-one (**12**). The values in parentheses are the detected high resolution mass associated with the structures.

Table 2. Exact Masses Obtained by Calculation and by High-Resolution Mass Spectrometer of δ-Silyl Carbonyl Compounds 8, 12, and 13

carbonyl compound	M•+ – 29		M•+ – 42		M•+ – 57	
	calcd	found	calcd	found	calcd	found
8	$C_7H_{15}SiO$		$C_6H_{14}SiO$		$C_5H_{11}SiO$	
	143.0892	143.0892	130.0814	ND[a]	115.0579	115.0578
12	$C_9H_{17}SiO$		$C_8H_{16}SiO$		$C_7H_{13}SiO$	
	169.1049	169.1054	156.0970	156.0964	141.0736	141.0726
13	$C_{10}H_{19}SiO$		$C_9H_{18}SiO$		$C_8H_{15}SiO$	
	183.1205	183.1212	170.1127	170.1124	155.0892	ND

[a] ND: not detectable.

(version 2.3.5) of Biosym Technologies was used for model building of the molecules and the program *Discover* (version 2.97) for energy minimization through CVFF calculations.[20] We minimized the energies for molecular conformations until the maximum derivative was less than 0.001 kcal/(mol Å).

The steric hindrance is not a concern in the McLafferty rearrangement, which involves an intramolecular transfer of a small hydrogen atom.[5] On the other hand, we obtained the lowest heat of formation (ΔH) for various conformations of ketones **8** and **13** with seven-membered-ring transition states, in which the steric hindrance associated with the trimethylsilyl group plays a prominent role. When the distance between the carbonyl oxygen and the silicon atom was fixed at 1.73 Å (cf. 1.66 Å for the standard O–Si bond[21]), the ΔH value was 73.028 kcal/mol for **8** and 87.202 kcal/mol for **13**. Their conformations are shown in Figure 2a,b.

Furthermore, the ΔH value was 2.195 kcal/mol for **8** and 14.399 kcal/mol for **13** by holding the most stable conformations[22] shown in Figure 2c,d. Thus the estimated activation energy was 70.833 kcal/mol for **8** and 72.803 kcal/mol for **13**. The difference between the two activation energies was 1.970 kcal/mol, which favors the acyclic compound (i.e., **8**) to form the seven-membered-ring transition state. According to the Arrhenius equation,[23] this energy difference would result in a ratio of 8.9:1 for **8**/**13** at 180 °C. Our estimation from computations accounts for the trend in favor of acyclic ketones as observed in our mass spectroscopic experiments.

We also found that it was more difficult for a bigger than a smaller silyl group to migrate through a seven-membered-ring transition state. The trend for the ratio of silyl migration to the McLafferty rearrangement decreased by following the order **8** > **9** > **10** and **13** > **17** > **18** > **19** (see Table 1).

Competition among Possible Fragmentation Paths. Electron-impact on δ-silyl ketone **25** gave radical cation **1**. We found that **1** was led to a mixture of **2** (1.1%), **4** (68%), and **6** (9.3%). The greater feasibility for H_b than H_a to migrate indicates that silicon exerts

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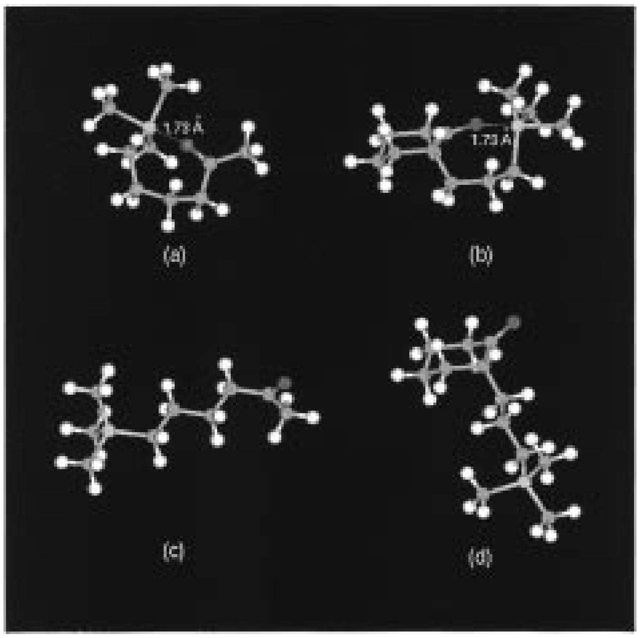

Figure 2. Structures and the lowest heats of formation (ΔH) were obtained by computer simulation and energy minimization with CVFF until the root mean square derivative reached 0.001 kcal/(mol Å): (a) the conformation of **8** with seven-membered-ring transition state (ΔH = 73.028 kcal/mol), (b) the conformation of **13** with seven-membered-ring transition state (ΔH = 87.202 kcal/mol), (c) the most stable conformation of **8** (ΔH = 2.195 kcal/mol), and (d) the most stable conformation of **13** (ΔH = 14.399 kcal/mol).

significant stabilizing effect on the β-carbo-radical intermediate (cf. **27**).[6−9]

Conclusions

A new fragmentation was established for δ-silyl carbonyl compounds in mass spectrometry. The molecular ions of aldehydes, ketones, thioketones, carboxylic acids, and acetates containing a δ-silyl group could undergo a silyl migration through a seven-membered-ring transition state. Its feasibility is greater for acyclic than cyclic carbonyl compounds. The migration proceeds easier for a smaller than a bigger silyl group.

Experimental Section

General Procedures. Acetic acid, acetonitrile, ethyl acetate, and hexanes were purchased from Mallinckrodt Chemical Co. Ethyl acetate and hexanes were dried and distilled from CaH_2. Diethyl ether and THF from Mallinckrodt Chemicals Co. were dried by distillation from sodium and benzophenone under an atmosphere of nitrogen. Hydrofluoric acid was purchased from Merck Inc. Acetyl chloride, allyltrimethylsilane, 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide, diethyl malonate, *N*,*N*-dimethylformamide, lithium tri-*tert*-butoxyaluminohydride (1.0 M solution in THF), manganese dioxide, oxalyl chloride, pyridine, and 3-(trimethylsilyl)-1-propanol were purchased from Aldrich Chemical Co. Allyldimethylphenylsilane, allylmethyldiphenylsilane, and allyltriphenylsilane were prepared according to the procedure reported by Soderquist et al.[24] Compounds **8** and **12**−**19** were prepared by the established method.[8]

Analytical TLC was performed on precoated plates (Silica Gel 60 F_{254}) purchased from Merck Inc.; compounds were visualized by use of I_2 vapor or 2.5% phosphomolybdic acid in ethanol with heating. Mixtures of ethyl acetate and hexanes were used as eluants. Separations by medium-pressure liquid chromatography[25] (MPLC) were performed at a flow rate of 60 mL/h by use of a Waters Model M-45 metering pump or a Jasco Model 880-PU intelligent HPLC pump. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 Series II instrument equipped with a 25-m cross-linked methyl silicone gum capillary column (0.32 mm i.d.). The flow rate was set at 14 mL/min for nitrogen as the carrier gas. The retention time t_R was measured under the following conditions: injector temperature 260 °C, the initial temperature for column 50 °C, duration 2.00 min, increment rate 10 °C/min, and the final temperature for column 250 °C.

Gas chromatography−low resolution mass spectral analyses were performed on a Hewlett-Packard 5890 Series II instrument equipped with Hewlett-Packard 5971A mass selective detector and capillary HP-1 column. The mass spectra were recorded at 70 eV electron energy, and the source temperatures were set between 175 and 190 °C.

Infrared (IR) spectra were recorded on a Perkin-Elmer Model 882 spectrophotometer or a Bomem Michelson Series FT-IR. The wavenumbers reported are referenced to the polystyrene 1601 cm^{-1} absorption. Absorption intensities are recorded by the following abbreviations: s, strong; m, medium; w, weak; br, broad. Proton NMR spectra were obtained on a Gemini AC-300 (300 MHz) spectrometer or a Varian Unity-400 (400 MHz) spectrometer. Chloroform-*d* was used as solvent and internal standard. All NMR chemical shifts are reported as δ values in parts per million (ppm), and coupling constants (J) are given in hertz. Carbon-13 NMR spectra were recorded on a Gemini AC-300 (75 MHz) spectrometer or a Varian Unity-400 (100 MHz) spectrometer by use of chloroform-*d* as solvent. Carbon-13 chemical shifts are referenced to the center of the $CDCl_3$ triplet (δ 77.0 ppm). Multiplicities are recorded by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, unresolved multiplet. High-resolution mass spectra were obtained by means of a VG Analytical 70-250S mass spectrometer or a JEOL JMS-HX110 mass spectrometer. Elemental analyses were carried out on a Heraeus CHN-O RAPID element analyzer.

Standard Procedure for the Preparation of δ-Silyl Ketones 9, 10, and 25. A mixture containing ketone (10−20 equiv), allylsilane (1.0 equiv), MnO_2 (2.5 equiv), and acetic acid (0.050 mL) was added into a Pyrex combustion tube, which was then sealed by torch. The sealed tube was heated at 140 °C for 12−18 h. The reaction mixture was cooled to room temperature, and the metal oxides were filtered off over Celite and washed with Et_2O (15 mL × 3). The combined filtrates were washed with water and saturated aqueous NaCl. The mixture was then dried over $MgSO_4$(s), filtered, and concentrated under reduced pressure.

6-(Dimethylphenylsilyl)hexan-2-one (9). The standard procedure was followed by use of acetone (2.37 g, 40.8 mmol, 20 equiv), allyldimethylphenylsilane (0.360 g, 2.04 mmol, 1.0 equiv), MnO_2 (0.463 g, 5.33 mmol, 2.6 equiv), and acetic acid (0.050 mL). The reaction mixture was heated at 140 °C for 14 h and then worked up. The crude product was purified by MPLC (2% EtOAc in hexanes as eluant) to give pure ketone **9** (0.321 g, 1.37 mmol) as a colorless liquid in 67% yield: TLC R_f 0.28 (5% EtOAc in hexanes); GC t_R 15.52 min; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.30 (s, 6 H, $Si(CH_3)_2$), 0.74 (t, J = 8.0 Hz, 2 H, CH_2Si), 1.28−1.33 (m, 2 H, CH_2CH_2Si), 1.54−1.57 (m, 2 H, $COCH_2CH_2$), 2.01 (s, 3 H, $COCH_3$), 2.29 (t, J = 7.6 Hz, 2 H, $COCH_2$), 7.28−7.29 (m, 3 H, ArH), 7.48 (d, J = 7.6 Hz, 2 H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −3.58 ($SiCH_3$),

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15.05 (CH_2Si), 22.98, 26.97, 29.03, 42.59, 127.20, 128.26, 132.92, 138.54, 207.47 (CO); IR (neat) 2925 (s), 1715 (s, C═O), 1426 (m, Si−Ph), 1356 (m), 1248 (s, $Si-CH_3$), 1160 (m), 1112 (m), 998 (m), 834 (s, $Si-CH_3$), 730 (m), 700 (m) cm^{-1}; MS *m*/*z* (relative intensity) 234 (M^+, 1), 219 (3), 192 (0.2), 177 (2), 157 (13), 135 (75), 121 (7), 105 (18), 75 (41), 58 (5), 43 (100); exact mass calcd for $C_{14}H_{22}OSi$ 234.1440, found (70 eV) 234.1450. Its spectroscopic characteristics are consistent with those of the same compound reported.[26]

6-(Methyldiphenylsilyl)hexan-2-one (10). The standard procedure was followed by use of acetone (2.33 g, 40.1 mmol, 20 equiv), allylmethyldiphenylsilane (0.479 g, 2.01 mmol, 1.0 equiv), MnO_2 (0.427 g, 4.91 mmol, 2.4 equiv), and acetic acid (0.050 mL). The reaction mixture was heated at 140 °C for 18 h and then worked up. The crude product was purified by MPLC (2% EtOAc in hexanes as eluant) to give pure ketone **10** (0.412 g, 1.39 mmol) as a colorless liquid in 69% yield: TLC R_f 0.28 (5% EtOAc in hexanes); GC t_R 21.53 min; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.55 (s, 3 H, $SiCH_3$), 0.95 (t, $J = 7.2$ Hz, 2 H, CH_2Si), 1.24−1.28 (m, 2 H, CH_2CH_2Si), 1.48−1.52 (m, 2 H, $COCH_2CH_2$), 1.96 (s, 3 H, $COCH_3$), 2.26 (t, $J = 7.2$ Hz, 2 H, $COCH_2$), 7.21−7.25 (m, 6 H, ArH), 7.38 (d, $J = 8.0$ Hz, 4 H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −4.57 ($SiCH_3$), 14.03 (CH_2Si), 23.44, 27.56, 29.74, 43.33, 127.76, 129.72, 134.35, 137.06, 209.12 (CO); IR (neat) 3068 (m), 2927 (m), 1714 (s, C═O), 1487 (m), 1428 (s, Si−Ph), 1355 (m), 1251 (m, $Si-CH_3$), 1112 (s), 832 (m, $Si-CH_3$), 787 (s), 699 (m) cm^{-1}; MS *m*/*z* (relative intensity) 296 (M^+, 1), 281 (2), 219 (54), 198 (34), 197 (100), 180 (9), 137 (17), 105 (9), 58 (3); exact mass calcd for $C_{19}H_{24}OSi$ 296.1596, found (70 eV) 296.1588. Anal. Calcd for $C_{19}H_{24}OSi$ C, 76.97; H, 8.16. Found: C, 77.01; H, 8.13.

6-(Fluorodimethylsilyl)hexan-2-one (11). Hydrofluoric acid (0.0210 g, 1.05 mmol, 1.0 equiv) was added to a solution containing **9** (0.241 g, 1.03 mmol, 1.0 equiv) in ethanol (15 mL). After the mixture was heated at reflux for 5.0 h, it was poured into water (1.0 mL). The aqueous layer was extracted with ether (15 mL × 4), and the combined organic layers were dried over $MgSO_4$(s). The crude products were purified by MPLC (1% EtOAc in hexanes as eluant) to give pure ketone **11** (0.160 g, 0.908 mmol) as a deep brown liquid in 88% yield: TLC R_f 0.34 (5% EtOAc in hexanes); GC t_R 8.23 min; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.24 (d, 6 H, $J = 3.2$ Hz, $Si(CH_3)_2$), 0.63 (t, $J = 7.2$ Hz, 2 H, CH_2Si), 1.32−1.34 (m, 2 H, CH_2CH_2Si), 1.53−1.57 (m, 2 H, $COCH_2CH_2$), 2.06 (s, 3 H, $COCH_3$), 2.37 (t, $J = 7.2$ Hz, 2 H, $COCH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −1.60 ($SiCH_3$), 16.29, 22.12, 26.98, 29.73, 43.20, 208.83 (CO); IR (neat) 2940 (s), 2865 (s), 1714 (s, C═O), 1463 (m), 1366 (m), 1246 (m, $Si-CH_3$), 1064 (m), 999 (m), 882 (s, $Si-CH_3$), 720 (m), 669 (s), 655 (m) cm^{-1}; MS *m*/*z* (relative intensity) 176 (M^+, 1), 147 (8), 134 (7), 119 (5), 118 (6), 82 (6), 81 (6), 77 (100), 62 (10), 58 (18); exact mass calcd for $C_8H_{17}OSiF$ 176.1033, found (70 eV) 176.1038. Anal. Calcd for $C_8H_{17}OSiF$: C, 54.50; H, 9.72. Found: C, 54.55; H, 9.63.

2-[3-(Fluorodimethylsilyl)propyl]cyclohexan-1-one (20). Hydrofluoric acid (0.0218 g, 1.09 mmol, 1.1 equiv) was added to a solution containing **17** (0.280 g, 1.02 mmol, 1.0 equiv) in ethanol (20 mL). After the mixture was heated at reflux for 5.0 h, it was poured into water (1.0 mL). The aqueous layer was extracted with ether (15 mL × 4), and the combined organic layers were dried over $MgSO_4$(s). The crude product was purified by MPLC (1% EtOAc in hexanes as eluant) to give pure ketone **20** (0.175 g, 0.809 mmol) as a deep brown liquid in 79% yield: TLC R_f 0.30 (5% EtOAc in hexanes); GC t_R 9.21 min; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.13 (d, $J = 3.2$ Hz, 6 H, $Si(CH_3)_2$), 0.48 (t, $J = 7.2$ Hz, 2 H, CH_2Si), 1.28−2.31 (m, 13 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ −1.51 ($SiCH_3$), 16.54 (CH_2Si), 20.24, 24.81, 27.95, 32.85, 33.84, 41.94, 50.37, 213.26 (CO); IR (neat) 2937 (s), 2862 (s), 1712 (s, C═O), 1459 (m), 1362 (m), 1054 (m), 999 (m), 882 (s), 720 (m), 669 (s), 655 (m) cm^{-1}; MS *m*/*z* (relative intensity) 216 (M^+, 1), 174 (3), 133 (5), 111 (5), 98 (100), 77 (46), 70 (23), 55 (9); exact mass calcd for $C_{11}H_{21}OSiF$ 216.1346, found (70 eV) 216.1352. Anal. Calcd for $C_{11}H_{21}OSiF$: C, 61.06; H, 9.78. Found: C, 61.12; H, 9.75.

6-(Trimethylsilyl)hexane-2-thione (21). A solution containing **8** (0.495 g, 2.87 mmol, 1.0 equiv) and 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide[18] (0.582 g, 1.44 mmol, 0.50 equiv) was heated at 75 °C under nitrogen. After 5.0 min, benzene (20 mL) was added, and the mixture was heated at reflux for 2.0 h. Then it was cooled to room temperature. The benzene was removed by rotary evaporator, and the resultant yellow slurry was distilled under reduced pressure. The crude product was purified by MPLC (1% EtOAc in hexanes as eluant) to give pure thioketone **21** (0.444 g, 2.36 mmol) as a light yellow liquid in 82% yield: TLC R_f 0.42 (5% EtOAc in hexanes); GC t_R 10.45 min; ^1H NMR ($CDCl_3$, 400 MHz) δ −0.36 (s, 9 H, $Si(CH_3)_3$), 0.51 (t, $J = 8.8$ Hz, 2 H, CH_2Si), 1.23−1.34 (m, 2 H, CH_2CH_2Si), 1.53−1.56 (m, 2 H, $CSCH_2CH_2$), 1.80 (s, 3 H, $CSCH_3$), 1.89 (t, $J = 8.4$ Hz, 2 H, $CSCH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −6.38 ($SiCH_3$), 12.29, 15.05, 23.97, 27.95, 35.53, 171.24 (CS); IR (neat) 2939 (s), 2883 (s), 1698 (s, C═S), 1463 (m), 1361 (m), 1164 (m), 997 (m), 880 (s), 740 (m), 689 (s), 615 (m) cm^{-1}; MS *m*/*z* (relative intensity) 188 (M^+, 4), 173 (2), 147 (7), 114 (24), 91 (22), 82 (9), 74 (10), 73 (100), 59 (10); exact mass calcd for $C_9H_{20}SSi$ 188.1055, found (70 eV) 188.1048. Anal. Calcd for $C_9H_{20}SSi$ C, 57.38; H, 10.70. Found: C, 57.42; H, 10.73.

5-(Trimethylsilyl)pentanal (22). To a solution of *N*,*N*-dimethylformamide (85.9 mg, 1.18 mmol, 1.0 equiv) in CH_2Cl_2 (2.0 mL) at 0 °C was added oxalyl chloride (0.375 g, 2.95 mmol, 2.5 equiv). After the mixture was stirred for 1.0 h, the solvent was removed under reduced pressure. The residue was redissolved in a mixture of acetonitrile (1.5 mL) and THF (2.5 mL), to which was added a solution containing **23** (0.206 g, 1.18 mmol, 1.0 equiv), pyridine (93.5 mg, 1.18 mmol, 1.0 equiv), and THF (2.0 mL) at −30 °C. After the solution was stirred at −30 °C for 1.0 h, a suspension of CuI (22.5 mg, 0.118 mmol, 0.10 equiv) in THF (2.0 mL) and a solution of lithium tri-*tert*-butoxyaluminohydride[19] (1.0 M solution in THF, 2.36 mL, 2.36 mmol, 2.0 equiv) were added into the reaction mixture at −78 °C. After being stirred for 10 min, the reaction mixture was quenched by aqueous HCl solution (2 N, 1.5 mL) and extracted with ether (20 mL × 3). The combined organic layers were washed with saturated $NaHCO_3$ solution (5.0 mL), dried over $MgSO_4$(s), and concentrated under reduced pressure. The crude product was purified by MPLC (5% EtOAc in hexanes as eluant) to give pure aldehyde **22** (0.136 g, 0.859 mmol) as a slightly yellow liquid in 73% yield: TLC R_f 0.45 (20% EtOAc in hexanes); GC t_R 5.54 min; ^1H NMR ($CDCl_3$, 400 MHz) δ −0.06 (s, 9 H, $Si(CH_3)_3$), 0.46 (t, $J = 8.8$ Hz, 2 H, CH_2Si), 1.24−1.28 (m, 2 H, CH_2CH_2Si), 1.54−1.58 (m, 2 H, $COCH_2CH_2$), 2.39 (t, $J = 7.6$ Hz, 2 H, $COCH_2$), 9.75 (s, 1 H, HCO); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −1.67 ($SiCH_3$), 16.83 (CH_2Si), 23.57, 29.72, 33.57, 195.65 (CO); IR (neat) 2940 (s), 2865 (s, HCO), 2745 (s, HCO), 1714 (s, C═O), 1463 (m), 1366 (m), 1064 (m), 999 (m), 832 (s, $Si-CH_3$), 720 (m), 669 (s), 655 (m) cm^{-1}; MS *m*/*z* (relative intensity) 158 (M^+, 1), 143 (12), 100 (5), 75 (96), 99 (100), 71 (15), 59 (25), 44 (10); exact mass calcd for $C_8H_{18}OSi$ 158.1127, found (70 eV) 158.1132. Anal. Calcd for $C_8H_{18}OSi$: C, 60.69; H, 11.46. Found: C, 60.72; H, 11.41.

5-(Trimethylsilyl)pentanoic Acid (23). A mixture containing diethyl malonate (6.58 g, 41.1 mmol, 20 equiv), allyltrimethylsilane (0.234 g, 2.05 mmol, 1.0 equiv), MnO_2 (0.363 g, 4.18 mmol, 2.0 equiv), and acetic acid (0.050 mL) was added into a Pyrex combustion tube, which was then sealed by torch. The sealed tube was heated at 160 °C for 14 h. The reaction mixture was cooled to room temperature and the metal oxides were filtered off over Celite and washed with Et_2O (15 mL × 3). The combined filtrates were washed with water and saturated aqueous NaCl. The mixture was then dried over

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[26] Eaborn, C.; Ghose, B. N.; Walton, D. R. M. *J. Organomet. Chem.* **1974**, *65*, 169.

$MgSO_4$(s), filtered, and concentrated under reduced pressure to give 2-[3-(trimethylsilyl)propyl]malonic acid diethyl ester. This ester was hydrolyzed by refluxing with a solution of KOH (0.235 g) in methanol (20 mL) for 2.0 h. The mixture was evaporated to dryness on a oil bath. The residue was redissolved in hot water (5.0 mL), to which was added concentrated hydrochloric acid until the solution was slightly acidic. After being boiled for 20 min, the solution was extracted with ether (15 mL × 3), dried over $MgSO_4$(s), and then distilled on a oil bath to give pure acid **23** (0.326 g, 1.87 mmol) as a slightly brown liquid in 91% yield: TLC R_f 0.05 (5% EtOAc in hexanes); GC t_R 9.21 min; ^{1}H NMR ($CDCl_3$, 400 MHz) δ −0.05 (s, 9 H, $Si(CH_3)_3$), 0.48 (t, $J = 8.4$ Hz, 2 H, CH_2Si), 1.30−1.32 (m, 2 H, CH_2CH_2Si), 1.33−1.65 (m, 2 H, $COCH_2CH_2$), 2.33 (t, $J = 7.4$ Hz, 2 H, $COCH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −1.73 ($SiCH_3$), 16.32 (CH_2Si), 23.49, 28.39, 33.77, 180.06 (CO); IR (neat) 3265 (br, OH), 2944 (s), 2875 (s), 1710 (s, C=O), 1460 (m), 1368 (m), 1164 (m), 989 (m), 842 (s, Si−CH_3), 730 (m), 699 (s), 655 (m) cm^{-1}; MS *m/z* (relative intensity) 174 (M^+, 1), 159 (2), 145 (2), 129 (9), 76 (8), 75 (100), 60 (9), 59 (19); exact mass calcd for $C_8H_{18}O_2Si$ 174.1076, found (70 eV) 174.1081. Anal. Calcd for $C_8H_{18}O_2Si$: C, 55.12; H, 10.41. Found: C, 55.20; H, 10.48.

3-(Trimethylsilyl)propyl Acetate (24). To a solution containing 3-(trimethylsilyl)-1-propanol (0.266 g, 2.01 mmol, 1.0 equiv) and acetyl chloride (0.244 g, 3.11 mmol, 1.5 equiv) in dry CH_2Cl_2 (20 mL) was added triethylamine (0.103 g, 1.02 mmol, 0.51 equiv) at room temperature. The solution was stirred for 2.0 h under a nitrogen atmosphere. Saturated aqueous NH_4Cl (0.50 mL) was added to the reaction mixture, and the solution was extracted with CH_2Cl_2 (20 mL × 3). The combined organic layers were dried over $MgSO_4$(s) and concentrated to give a crude product. The crude product was purified by MPLC (1% EtOAc in hexanes as eluant) to give pure acetate **24** (0.340 g, 1.95 mmol) as a colorless liquid in 97% yield: TLC R_f 0.46 (5% EtOAc in hexanes); GC t_R 4.53 min; ^{1}H NMR ($CDCl_3$, 300 MHz) δ −0.03 (m, 9 H, $Si(CH_3)_3$), 0.46 (t, $J = 8.4$ Hz, 2 H, CH_2Si), 1.53−1.64 (m, 2 H, CH_2CH_2Si), 2.02 (s, 3 H, $COCH_3$), 3.99 (t, $J = 8.4$ Hz, 2 H, $COOCH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −1.87 ($SiCH_3$), 12.38 (CH_2Si), 20.97, 23.19, 67.11, 170.85 (CO); IR (neat) 2946 (s), 2855 (s), 1728 (s, C=O), 1460 (m), 1356 (m), 1061 (m), 989 (m), 862 (s), 728 (m), 659 (s), 653 (m) cm^{-1}; MS *m/z* (relative intensity) 174 (M^+, 1), 159 (4), 131 (2), 117 (52), 76 (8), 75 (100), 73 (94), 60 (2); exact mass calcd for $C_8H_{18}O_2Si$ 174.1076, found (70 eV) 174.1073. Anal. Calcd for $C_8H_{18}O_2Si$: C, 55.12; H, 10.41. Found: C, 55.22; H, 10.34.

2-[3-(Trimethylsilyl)propyl]heptan-2-one (25). The standard procedure was followed by use of 2-heptanone (4.66 g, 40.8 mmol, 20 equiv), allyltrimethylsilane (0.233 g, 2.04 mmol, 1.0 equiv), MnO_2 (0.443 g, 5.10 mmol, 2.5 equiv), and acetic acid (0.050 mL). The reaction mixture was heated at 140 °C for 14 h and then worked up. The crude product was purified by MPLC (2% EtOAc in hexanes as eluant) to give ketone **25** (0.246 g, 1.08 mmol) as a colorless liquid in 53% yield: TLC R_f 0.38 (5% EtOAc in hexanes); GC t_R 13.25 min; ^{1}H NMR ($CDCl_3$, 400 MHz) δ −0.06 (s, 9 H, $Si(CH_3)_3$), 0.42 (t, $J = 8.4$ Hz, 2 H, CH_2Si), 0.84 (t, $J = 7.2$ Hz, 3 H, CH_2CH_3), 1.16−1.69 (m, 10 H), 2.07 (s, 3 H, $COCH_3$), 2.29 (m, 1 H, COCH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −1.72 ($SiCH_3$), 13.86 (CH_2Si), 16.85, 21.86, 22.75, 28.58, 29.62, 31.38, 35.64, 53.13, 213.18 (CO); IR (neat) 2955 (s), 2930 (s), 2872 (m), 1712 (s, C=O), 1459 (w), 1378 (m), 1247 (s, Si−CH_3), 1067 (w), 860 (s), 836 (s, Si−CH_3), 689 (m), 668 (m) cm^{-1}; MS *m/z* (relative intensity) 228 (M^+, 1), 213 (13), 199 (2), 186 (9), 172 (1), 143 (100), 114 (68), 75 (39), 73 (99), 59 (16); exact mass calcd for $C_{13}H_{28}OSi$ 228.1909, found (70 eV) 228.1917. Anal. Calcd for $C_{13}H_{28}OSi$: C, 68.35; H, 12.35. Found: C, 68.44; H, 12.27.

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