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EFFECT OF TRIMETHYLSILYL GROUPS ON BECKMANN REARRANGEMENTS AND FRAGMENTATIONS *

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Summary

Cyclic β-silyl ketones react with hydroxylamine-*O*-sulfonic acid in water to give as the major products olefinic nitriles resulting from silicon-directed Beckmann fragmentation reactions.

For some time we have been interested in using silyl groups to direct the course of carbon–carbon bond cleavage reactions. We have previously shown that Baeyer-Villiger reactions of β-trimethylsilyl ketones (γ-ketosilanes) are directed by the silicon to give esters of β-hydroxysilanes [1,2]. The mechanistic rationale for this observation was that the migrating group in a Baeyer-Villiger reaction is generally that group which can more readily support a positive charge, and that cations β to silicon in organosilicon compounds appear to be considerably stabilized by the silicon [3]. Using these reactions, we have converted cyclic β-silyl ketones into olefinic carbonyl compounds [1].

In the Beckmann rearrangement [4], the migrating group may also be that which can more readily support a positive charge; however, when one of the groups attached to the oxime carbon can support a positive charge sufficiently well, the Beckmann fragmentation reaction [4,5] frequently occurs. We have therefore studied Beckmann-type reactions of β-silyl ketones and oximes with a view toward preparing olefinic nitriles.

While this manuscript was in preparation, the trimethylsilyl triflate-induced fragmentation reactions of cyclic (*E*)-β-trimethylsilylketoxime acetates to give olefinic nitriles was reported [6].

Silyl ketone **1** was prepared from cyclohexanone by alkylation of the metalloenamine with Me_3SiCH_2Cl [1,7]. Silyl ketones **2** and **3** were prepared from

* Dedicated to Professor Makoto Kumada.

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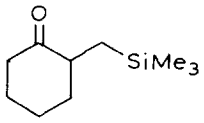
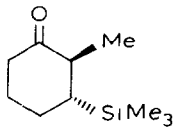
cyclohexenone by reaction with Me_3SiLi in THF/HMPA followed by alkylation with MeI or protonation, respectively [8] *.



(1)



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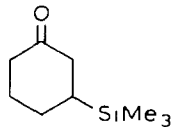
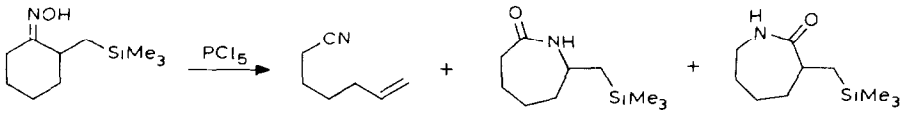


(3)

Initially, the oxime (**4**) of silyl ketone **1** was subjected to a variety of conditions expected to cause Beckmann rearrangement. Mixtures of a fragmentation product, olefinic nitrile **5**, and both isomeric rearrangement products, lactams **6** and **7**, were obtained. For example, treatment of **4** with PCl_5 in methylene chloride gave a mixture containing 24% of **5**, 28% of **6**, and 36% of **7** by VPC analysis. Under these conditions, therefore, the silicon appears to have little directing effect on the course of this reaction.



(4) (5) (6) (7)

In the Beckmann rearrangement, migration is generally believed to occur in an anti manner. With the oxime of an unsymmetrical ketone, relative migratory aptitudes can be expected to affect the direction of migration only if the oxime isomers are rapidly equilibrated under the reaction conditions. Isomerization of oximes is believed to be favored by the use of protonic acids in polar solvents [11]. The 200 MHz NMR spectrum of oxime **4** is consistent with its being a mixture of *syn*- and *anti*-oxime isomers. The above results are consistent with a reaction pathway in which the *E*-oxime gives rise to lactam **6**, while the *Z*-oxime is transformed to lactam **7**. (Nitrile **5** may also be formed from the *E*-oxime.)

We were therefore interested in finding conditions which might be expected to favor equilibration of the oxime isomers. We found that treatment of silyl ketone **1** with hydroxylamine-*O*-sulfonic acid in water led to a much more selective reaction in which the olefinic nitrile (**5**) was the major product, isolated in 50–61% yield. The crude product contained 61% of **5** and 23% of lactam **6** by VPC analysis; lactam **7**

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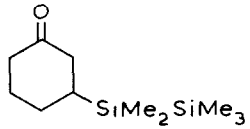
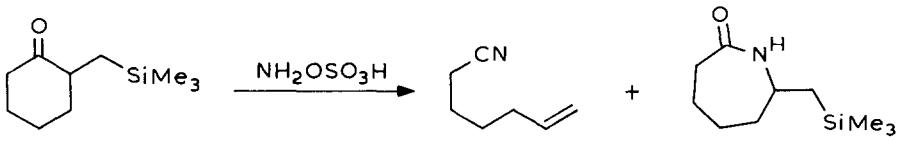
* Attempts to prepare silyl ketones **2** and **3** on a scale significantly larger than that reported [8] frequently led to little or none of the desired product [9]. On some occasions, the major product was silyl ketone *i*,



(i)

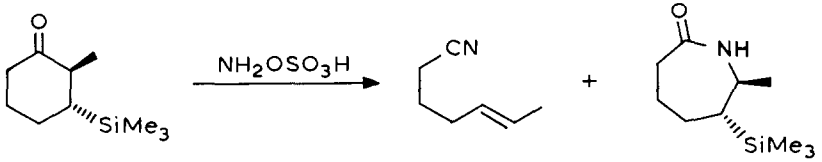
presumably formed via a conjugate addition reaction of $LiSiMe_2SiMe_3$ [10]. The disilyllithium reagent may have been formed in the course of the preparation of Me_3SiLi (from $Me_3SiSiMe_3$ and MeLi [8]) by reaction of Me_3SiLi with unreacted $Me_3SiSiMe_3$. Time and temperature control may be critical to the success of this reaction, and a modified procedure was developed in which up to 4–5 g of the ketones could be reproducibly prepared (see Experimental).

was not visible. Thus, the trimethylsilyl group appears to direct the course of the reaction under these conditions.

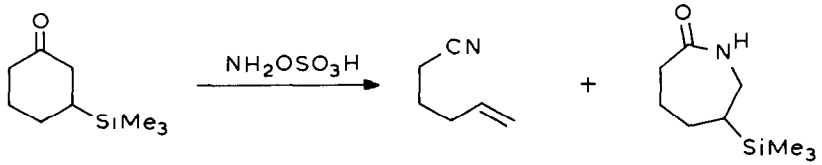


(1) (5) (6)

In a similar manner, treatment of silyl ketones **2** and **3** with NH_2OSO_3H led to olefinic nitriles **8** and **10**, respectively.



(2) (8) (9)

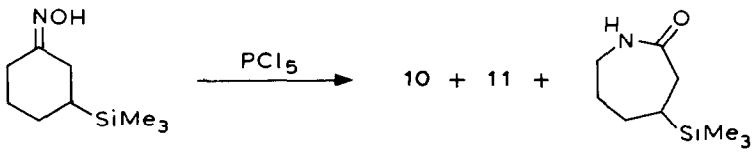


(3) (10) (11)

Nitrile **8** was isolated in 74% yield; in addition, a small amount of lactam **9** was isolated from the nonvolatile material. The regiospecificity of double bond formation (compare **1** → **5**) further demonstrates the controlling effect of silicon.

The reaction of ketone **3** with NH_2OSO_3H is particularly interesting since no configurational bias for the oxime would be expected. Olefinic nitrile **10** (80% of crude product by VPC, 43% isolated yield) was obtained together with lactam **11** (13% of crude product by VPC), the isomer resulting from silicon-directed migration. None of the isomeric lactam (**13**) (see below) was detectable.

In order to confirm the structural assignment, the oxime (**12**) of silyl ketone **3** was prepared and treated with PCl_5 in methylene chloride. The crude product contained, by VPC analysis, 13% of olefinic nitrile **10**, 30% of the above lactam (**11**), and 48% of the isomeric lactam, **13**. The products were purified by preparative VPC, and their structures supported by spectra, in particular, the decoupled 200 MHz NMR spectra.

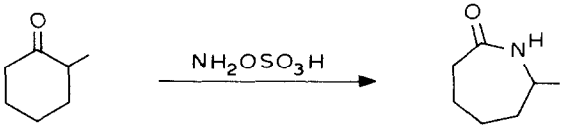


(12) (13)

Hydroxylamine-*O*-sulfonic acid has been used for a variety of reactions [12],

including the one-pot oximation and Beckmann rearrangement of certain ketones [12,13]; NH_2OSO_3H in water has been used for the conversion of aldehydes to nitriles [12,14].

To further establish the role of the trimethylsilyl group in Beckmann rearrangements and fragmentations, the reaction of 2-methylcyclohexanone with NH_2OSO_3H was carried out. 6-Methylcaprolactam was isolated in 60% yield; the olefinic nitriles **5** and **8** were not detectable in the crude product. Under these conditions, cyclohexanone was partially converted to the oxime; no rearrangement products were detected.



This work demonstrates that the presence of a β-trimethylsilyl group can direct the regiochemistry of the Beckmann rearrangement and Beckmann fragmentation, and can change the course of the reaction from rearrangement to predominantly fragmentation. The NH_2OSO_3H/water system seems to be one in which the *E* and *Z* oximes (or oxime sulfonates) are equilibrated, and migratory aptitudes can determine the product composition. Since the oximes need not be isolated (or purified), this reaction may be potentially useful as a one-pot conversion of cyclic β-silyl ketones to olefinic nitriles.

Experimental

Infrared (IR) spectra were taken using a Perkin–Elmer 1320 spectrometer. Proton nuclear magnetic resonance (NMR) spectra were obtained using a Nicolet NT-200 NMR spectrometer. Reported chemical shifts are in ppm (δ) relative to $CHCl_3$ ($\delta = 7.24$). Mass spectra were obtained using a Finnigan 3200-E automated GC-MS system. Vapor phase chromatographic (VPC) analyses were obtained on a Varian Aerograph Model 90-P instrument using helium as the carrier gas at the column temperature indicated. The retention time of a hydrocarbon standard under the conditions is included. Unless otherwise indicated, a 10 ft $\times$ 1/4 in. 10% SE-30 column was used for VPC analyses and a 10 ft $\times$ 1/4 in. 20% QF-1 column was used for preparative VPC. Exact mass determinations were carried out at the University of Nebraska. Elemental analyses were performed by Micro-Tech Laboratories, Inc., Skokie, Illinois.

Tetrahydrofuran (THF) was distilled from sodium and benzophenone. Hexamethylphosphoramide (HMPA) was distilled from CaH_2.

Preparation of silyl ketones 2 and 3

The following general procedure which is adapted from the published procedure [8] was used. A solution of 20 ml of HMPA and 10 ml (50 mmol) of hexamethyldisilane under argon and containing a magnetic stirrer was cooled in a Dry Ice-acetone bath. (The mixture becomes frozen.) Low-halide methyllithium (40 mmol) was added onto the frozen mixture followed by 100 ml of THF (in 10 ml portions). The Dry Ice-acetone bath was replaced with an ice bath. Within a minute or two, the solid

melted sufficiently so that stirring was possible. The mixture was stirred for 10–15 min (during which time it became bright red, indicating the formation of Me_3SiLi), then immediately cooled to −78°C, and a solution of 3.0 g (31 mmol) of 2-cyclohexen-1-one in 10–15 ml of THF was added. The resulting mixture was stirred for 5–10 min. Then methyl iodide (10 ml) or water (10–20 ml) was added, and stirring was continued for 5 min. The Dry Ice-acetone bath was replaced with an ice bath, and stirring was continued for 40 min. Pentane (250 ml) was added and the resulting mixture was poured into 400 ml of water and shaken vigorously. The pentane layer was washed with water (4 × 100 ml), dried ($MgSO_4$), concentrated, and distilled. The ketones were obtained in 70–85% yields.

Reaction of ketone 1 with hydroxylamine-O-sulfonic acid

To a solution of 7.0 g (61 mmol) of NH_2OSO_3H in 20 ml of water was added 5.5 g (29.8 mmol) of ketone **1** [1,7]. The resulting mixture was stirred vigorously at room temperature for 1 h. The mixture was extracted with three portions of pentane, and the combined extracts were washed with two portions of saturated $NaHCO_3$ and with water, were dried ($MgSO_4$), and concentrated. VPC analysis (140°C, $C_{12}H_{26}$ = 1.8 min) showed peaks at 0.5 min (17%, $Me_3SiOSiMe_3$), 0.9 min (61%, **5**), and 8.6 min (22.5%, **6**). The crude product was distilled giving 1.62 g (50%) of nitrile **5**: b.p. 78–80°C (20 mmHg) (lit. 15 b.p. 82°C (20 mmHg). VPC analysis (140°C, C_6H_{14} = 0.5 min) showed the major peak at 0.9 min (99%, **5**).

The distillation residue was recrystallized from ether and subjected to preparative VPC giving 0.5 g of lactam **6**. An analytical sample was prepared by recrystallization from pentane giving white crystals: m.p. 75–76°C; IR (Nujol) 3200, 3080, 1660, 1250, 850 cm^{-1}; NMR ($CDCl_3$) δ 5.35 (1H, broad s), 3.44 (1H, m), 2.43 (2H, m), 0.81 (2H, d, *J* 8 Hz), 0.04 (9H, s); mass spectrum *m/z* 199 (M^+, 9), 184 (15), 170 (26), 157 (20), 116 (22), 112 (22), 100 (18), 75 (48), 73 (100). Anal. Found: C, 60.11; H, 10.44. $C_{10}H_{21}NOSi$ calcd.: C, 60.24; H, 10.62%.

Reaction of ketone 2 with hydroxylamine-O-sulfonic acid

Ketone **2** (5.5 g, 29.8 mmol) was treated with 6.75 g (59.7 mmol) of NH_2OSO_3H in 20 ml of water using the procedure used to convert **1** to **5** and **6**. Distillation of the crude product gave 2.4 g (74%) of nitrile **8**: b.p. 93–94°C (25 mmHg) (lit. 16 b.p. 78–81°C (19 mmHg)). The distillation residue was subjected to preparative VPC giving 64 mg of lactam **9**. Recrystallization from pentane gave white crystals: m.p. 71–72°C; IR (KBr) 3200, 3070, 2940, 1670, 1250, 830 cm^{-1}; NMR ($CDCl_3$) δ 5.5 (1H, broad s), 3.50 (1H, m), 2.45 (2H, m), 1.27 (3H, d, *J* 7 Hz), 0.80 (1H, m), 0.05 (9H, s); mass spectrum *m/z* 199.1404 (calcd for $C_{10}H_{21}NOSi$: 199.1392) (M^+, 2), 184 (16), 155 (25), 131 (20), 116 (19), 98 (15), 75 (66), 73 (100).

Reaction of ketone 3 with hydroxylamine-O-sulfonic acid

Ketone **3** (5.1 g, 30 mmol) was treated with 6.7 g (58 mmol) of NH_2OSO_3H in 20 ml of water using the procedure used to convert **1** to **5** and **6**. VPC analysis (140°C, $C_{12}H_{26}$ = 1.9 min) of the crude product showed peaks at 0.5 min (7%, $Me_3SiOSiMe_3$), 0.8 min (80%, **10**), and 8.5 min (12.5%, **11**). The crude product was distilled giving 1.2 g (42%) of nitrile **10**: b.p. 67°C (23 mmHg) (lit. 17 b.p. 54–59°C (16 mmHg)). VPC analysis (140°C, C_6H_{14} = 0.7 min) gave the major peak at 0.8 min (> 99%, **10**).

The distillation residue solidified giving 1.89 g of lactam **11**. Recrystallization

from ether gave 1.04 g of **11**: m.p. 91–92°C; an analytical sample had m.p. 91.5–92°C; IR (Nujol) 3280, 1660, 1620, 1245, 850 cm^{-1}; NMR ($CDCl_3$) δ 6.5 (1H, broad s), 3.13 (2H, crude t), 2.44 (2H, m), 0.78 (1H, m), −0.03 (9H, s); mass spectrum *m/z* 185 (M^+, 8), 184 (7), 170 (14), 131 (30), 116 (24), 75 (55), 73 (100). Anal. Found: C, 58.60; H, 10.25. $C_9H_{19}NOSi$ calcd.: C, 58.32; H, 10.33%.

Reaction of 2-methylcyclohexanone with hydroxylamine-O-sulfonic acid

To a solution of 6.0 g (57 mmol) of NH_2OSO_3H in 20 ml of water was added 3.0 g (26 mmol) of 2-methylcyclohexanone. The resulting mixture was stirred vigorously at room temperature for 30 min. The mixture was extracted with three portions of CH_2Cl_2. The combined extracts were washed with three portions of $NaHCO_3$ and with two portions of water, were dried ($MgSO_4$), and concentrated giving 2.74 g (83%) of crude 6-methylcaprolactam: m.p. 82–88°C. The crude product showed no evidence of nitriles **5** or **8** by VPC analysis. Recrystallization from ether gave 2.0 g (60%) of the lactam as colorless needles: m.p. 90–90.5°C (lit. 18 m.p. 90–91°C).

Reaction of the oxime (4) of silyl ketone 1 with PCl_5

Oxime **4** was prepared from 10 g (54 mmol) of ketone **1** using $NH_2OH \cdot HCl$ and NaOH in aqueous MeOH [19]. Extraction and distillation of the crude product gave 9.2 g (85%) of **4**: b.p. 88–92°C (0.6 mmHg); IR (film) 3250, 2940, 1654w, 1450, 1248, 850 cm^{-1}; NMR ($CDCl_3$) δ 9.07 (1H, s), 2.47 (2H, m), 2.18 (1H, m), 1.9–1.3 (7H, m), 1.1–0.5 (2H, m), 0.00 (9H, s); mass spectrum *m/z* 199 (M^+, 1), 198 (3), 184 (27), 168 (33), 126 (13), 110 (53), 75 (43), 73 (100). VPC analysis (140°C, $C_{12}H_{26}$ = 1.1 min) showed the major peak at 2.1 min (99%).

To an ice-cooled suspension of 6.85 g (32.9 mmol) of PCl_5 in 50 ml of CH_2Cl_2 under nitrogen was added 3.34 g (16.8 mmol) of oxime **4** in 10 ml of CH_2Cl_2. The resulting mixture was stirred for 1 h at ice temperature, then poured into 50 ml of ice cold saturated NaCl and stirred for 5 min. The layers were separated, and the aqueous layer was extracted with two portions of CH_2Cl_2. The organic extract was washed with two portions of saturated $NaHCO_3$ and with water, dried ($MgSO_4$), and concentrated. VPC analysis (140°C, $C_{12}H_{26}$ = 1.1 min) showed the major peaks at 0.9 min (24%, **5**), 6.8 min (28%, **6**), and 7.7 min (36%, **7**). The three major components were purified by bulb-to-bulb distillation and by preparative VPC (QF-1 and SE-30). Nitrile **5** and lactam **6** had spectra consistent with those obtained above for these compounds. Lactam **7** had IR (film) 3300, 3220, 2940, 1660, 840 cm^{-1}; NMR ($CDCl_3$) δ 6.0 (1H, broad s), 3.24 (2H, m), 2.55 (1H, m), 1.21 (1H, dd, *J* 6, 15 Hz), 0.61 (1H, dd, *J* 8, 15 Hz), 0.05 (9H, s); mass spectrum *m/z* 199.1392 (calcd for $C_{10}H_{21}NOSi$: 199.1392) (M^+, 5), 198 (6), 184 (100), 170 (23), 156 (16), 110 (23), 75 (39), 73 (65). Anal. Found: C, 59.89; H, 10.68. $C_{10}H_{21}NOSi$ calcd.: C, 60.24; H, 10.62%.

Reaction of the oxime (12) of silyl ketone 3 with PCl_5

Oxime **12** was prepared from 3.0 g (17.6 mmol) of silyl ketone **3** using $NH_2OH \cdot HCl$ and NaOH in aqueous MeOH [19]. Extraction and distillation of the crude product gave 2.6 g (79%) of **12**: b.p. 89.5–91.5°C (1.95 mmHg); IR (film) 3240, 2940, 1660w, 1450, 1250, 830 cm^{-1}; NMR ($CDCl_3$) δ 9.3 (1H, broad s), 3.29 1H, t), 2.36 (1H, t), 2.1–1.1 (6H), 0.9–0.6 (1H, m), −0.02, −0.04 (total 9H); mass spectrum *m/z* 185 (M^+, 1), 168 (21), 154 (20), 141 (13), 126 (26), 96 (22), 75 (22), 73 (100).

VPC analysis (140 °C, $C_{12}H_{26}$ = 1.1 min) showed the major peak at 3.5 min (99%).

To an ice-cooled suspension of 3.3 g (15 mmol) of PCl_5 in 20 ml of CH_2Cl_2 under nitrogen was added 1.5 g (8.1 mmol) of oxime **12** in 8 ml of CH_2Cl_2. The resulting mixture was stirred for 2 h at ice temperature, then poured into 20 ml of ice cold saturated NaCl and stirred for 5 min. The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with two portions of saturated $NaHCO_3$ and with water, dried ($MgSO_4$), and concentrated. VPC analysis (140 °C, $C_{12}H_{26}$ = 1.1 min) showed the major peaks at 0.7 min (13%, **10**), 7.2 min (48%, **13**), and 7.8 min (30%, **11**). The three major components were purified by bulb-to-bulb distillation and by preparative VPC. Nitrile **10** and lactam **11** had spectra consistent with those obtained above for these compounds. Lactam **13** had IR (Nujol) 3440, 3280, 3200, 1640, 1250, 850 cm^{-1}; NMR ($CDCl_3$) δ 6.12 (1H, broad s), 3.17 (2H, m), 2.33 (2H, m), 0.82 (1H, m), −0.15 (9H, s); mass spectrum *m/z* 185.1221 (calcd. for $C_9H_{19}NOSi$: 185.1236) (M^+, 12), 184 (24), 170 (55), 142 (19), 75 (19), 73 (100).

The assigned structures for lactams **11** and **13** were supported by the following NMR ($CDCl_3$) decoupling experiment. For lactam **13**, irradiation at δ 0.82 collapsed the doublet at δ 2.3 to a singlet, irradiation at δ 2.3 collapsed the multiplet at δ 0.82 to a doublet, and irradiation at δ 3.2 did not affect the multiplet at δ 0.82. For lactam **11**, irradiation at δ 0.78 collapsed the triplet at δ 3.13 to a doublet, irradiation at δ 3.16 collapsed the multiplet at δ 0.83 to a doublet, and irradiation at δ 2.4 did not affect the triplet at δ 3.13 or the multiplet at δ 0.78.

Acknowledgments

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