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SILICON-DIRECTED BECKMANN FRAGMENTATION. CATALYTIC CLEAVAGE OF CYCLIC β-TRIMETHYLSILYLKETOXIME ACETATES WITH TRIMETHYLSILYL TRIFLUOROMETHANESULFONATE

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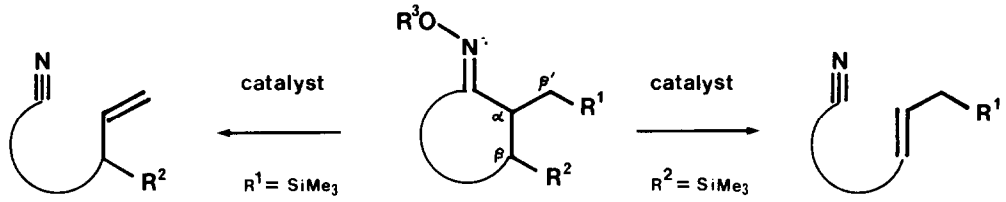
Abstract: Cyclic (E)-β-trimethylsilylketoxime acetates were effectively cleaved by a catalytic action of trimethylsilyl trifluoromethanesulfonate to give the corresponding unsaturated nitriles. The fragmentation in the Beckmann rearrangement is completely controlled and directed by trimethylsilyl group to lead regio- and stereospecific formation of the double bond.

Fragmentation in the Beckmann rearrangement has received much attention in the formation of ω-functional nitriles from certain cyclic ketoximes having α-substituents, such as hydroxy, alkoxy, carbonyl, amino, imino, sulfenyl, alkyl, or aryl groups.[1] Specifically, the fragmentation of cyclic α-di- or trialkylketoximes has been focused on introduction of an olefin in synthetic problems of natural products. However, the regio- and stereochemistry of the double bond has not been controllable due to random deprotonation.[2] We now report a regio- and stereospecific fragmentation of cyclic (E)-β-trimethylsilylketoximes strongly directed by a trimethylsilyl group.



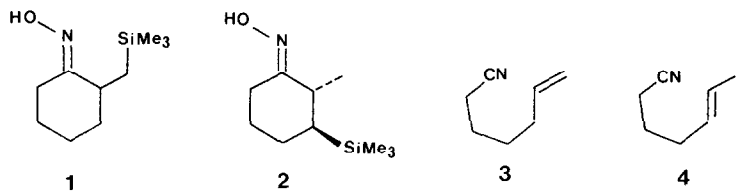
Cyclic
(E)-β-TMS-Oxime
R3=H, Ac

Recent interest in the utilization of the trialkylsilyl group as a selective leaving group, super proton[3], lies in highly selective formation of target olefins.[4] Therefore, the placement of a trimethylsilyl group on the β-carbon atom of the oximes should efficiently direct the formation of the double bond in the Beckmann fragmentation, which was rather unselective in the case of common α-trialkyl-substituted ketoximes.[2]

A series of cyclic (E)-β-trimethylsilylketoximes and their acetates were prepared by oximation ($HONH_2 \cdot HCl$, NaOAc, EtOH) of the corresponding β-silylketones, obtained by known

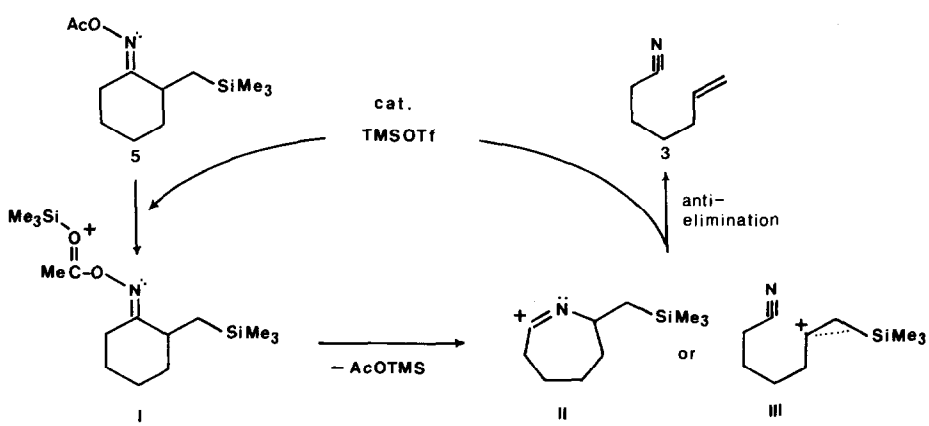
methods,[5] and subsequent acetylation (Ac_2O, pyridine, 0° C~room temp.). In each case the E-geometry of the oximes is indispensable for the desired rearrangement, and was confirmed on the basis of ^1H NMR studies.[6]

The β-silylketoximes 1 and 2 were subjected to reaction with common acid-catalysts for the Beckmann rearrangement to give the desired unsaturated nitriles 3 and 4, respectively: catalyst (yield, %); 3, PCl_5 (28%), P_2O_5 (73%), $POCl_3$ (48%), MsCl/Py (52%); 4, P_2O_5 (51%).[7] Under the extremely mild condition the Beckmann fragmentation directed by the trimethylsilyl group proved to be successfully promoted, however. It is desirable to think that the yields could be improved if experimental conditions were optimized or if any modifications were devised.



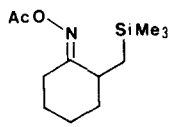
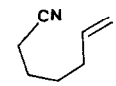
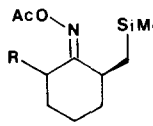
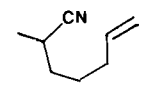
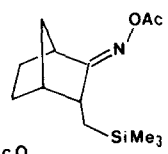
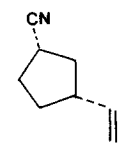
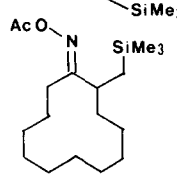
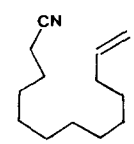
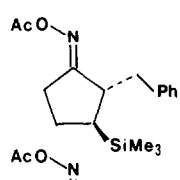
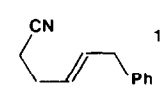
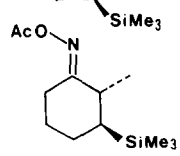
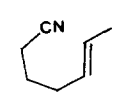
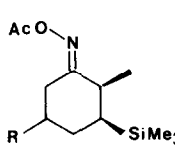
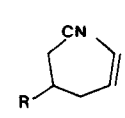
1 2 3 4

We reasoned that as a design of the fragmentation, *the combination of β-trimethylsilylketoxime acetates and trimethylsilyl trifluoromethanesulfonate (TMSOTf)*[8] makes the reaction catalytic to afford the unsaturated nitriles. The obvious advantages of the results lead the specific formation of the desired nitriles in high yields under control of the regio- and stereochemistry of the double bond (Table I). The stereospecificity in the olefin formation can be accounted for the anti-elimination of the silyl group and the nitrilium center as shown in the following scheme.[9,10]

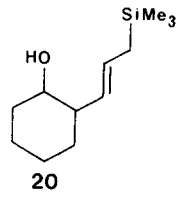


Dienonitrile 22 was obtained by the same procedure [89%, TMSOTf (10 mol%), CH_2Cl_2, room temp., 12 hr] from δ-silyl β,γ-unsaturated ketoxime 21, which was prepared from the alcohol 20[11] in three steps: oxidation with CrO_3-Py (76%), oximation (91%), and acetylation (82%).

Table I. Beckmann Fragmentation of β-Trimethylsilylketoxime Acetates with a Catalytic Amount of Trimethylsilyl Trifluoromethanesulfonate.[a]

Entry	β-Trimethylsilylketoxime Acetate	Product	Yield (%)
1	 5	 3	89
2	 6 R = —Me	 7	95
3	8 R = ---Me		82
4	 9	 10	94
5	 11	 12	81
6	 13	 14	93
7	 15	 4	94
8	 16 R = H	 17 R = H	90
9	18 R = 	19 R = 	94

[a] To a solution of the oxime acetate (ca. 0.5-1.0 mmol) in anhydrous CH_2Cl_2 (2-4 mL) was added dropwise TMSOTf (10 mol%) at 0°C. The mixture was stirred for 1-4 hr (monitored by TLC), was treated with triethylamine (0.1 mL) and aqueous sodium bicarbonate, and was quickly extracted with ether (10 mL). The extract was concentrated, and the residual oil was purified by silica gel column chromatography to give the corresponding nitrile. Satisfactory ^1H and ^{13}C NMR, IR, and mass spectra were obtained for the products.



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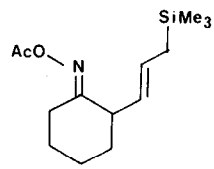

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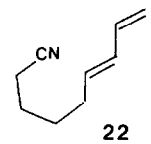

22

Thus we have found a new Beckmann fragmentation directed by a silyl group. Active investigation on the synthetic application is under progress.

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(7) CH_2Cl_2, room temp., for 1 day; by product, the corresponding lactum (ca. 5-35% yield).

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(9) $BF_3 \cdot Et_2O$ is also a good catalyst for the fragmentation of the β-TMS-oxime acetates; $BF_3 \cdot Et_2O$ (1.1 eq.), CH_2Cl_2, room temp., 30 min., 3 (80% from 5). $TiCl_4$ and $AlCl_3$ gave the nitriles in low yields.

(10) Under the same reaction condition, (Z)-isomers of the β-TMS-oxime acetates were almost recovered (~90%).

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