Synthetic Communications

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: http://www.tandfonline.com/loi/lsyc20

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To cite this article: Margarita Ortiz , Jose F. Cordero , Sheila Pinto & lleana Alverio (1994) A Convenient Method for the Synthesis of O-Tert-Butyldimethylsilyl Oximes, Synthetic Communications, 24:3, 409-415

To link to this article: http://dx.doi.org/10.1080/00397919408011200

SYNTHETIC COMMUNICATIONS, 24(3), 409-415 (1994)

A CONVENIENT METHOD FOR THE SYNTHESIS OF *O-TERT*-BUTYLDIMETHYLSILYL OXIMES

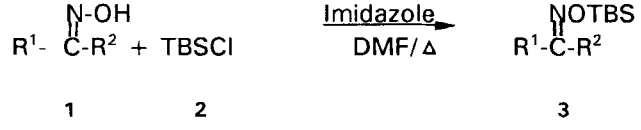
Margarita Ortiz*, José F. Cordero, Sheila Pinto, and Ileana Alverio
Department of Chemistry, University of Puerto Rico
Humacao, Puerto Rico 00791

Abstract. *Aromatic, aliphatic, cyclic and acyclic O-tert-butyldimethylsilyl oximes were prepared in 77 to 85% yield by the reaction of the corresponding aldoximes and ketoximes with tert-butyldimethylchlorosilane (TBSCl) using imidazole/DMF system.*

O-Silyl aldoximes and ketoximes are important intermediates in organic synthesis.[1] In our search to prepare large quantities of silyl ethers, we observed, that while the *O*-trimethylsilyl oximes are readily prepared,[2] they are very susceptible to hydrolysis.[3] The more stable *tert*-butyldimethylsilyl (TBS) derivatives are only available through the use of costly reagents and/or sophisticated techniques.[4] To our surprise, the Corey method for the TBS-protection of alcohols[5a] and amines[5b] has not been reported for the *O*-silyation of oximes except as an unrecommended derivatizing method for their GC-MS analysis[5c],

* To whom correspondence should be addressed

where the products were not isolated and characterized. We wish to report a simple and efficient method for the large scale preparation of a variety of *O*-*tert*-butyldimethylsilyl oximes employing this TBSCl, imidazole/DMF system.



1 2 3

Of the several methods available for the conversion of aldehydes and ketones to their oximes,[6a,b] we found that a modification of the Wieland method ($NH_2OH.HCl/Na_2CO_3/EtOH$),[6c] provides the best product yields. For the unsymmetrical aromatic oximes, the E isomer forms preferentially.[7] The standard procedure of the *O*-silylation of oximes,[2] namely the oxime with the corresponding chlorosilane in pyridine-benzene or in triethylamine-THF, failed for the TBS case. However, these silylated oximes (3) were obtained in high yields using two equivalents of imidazole in DMF after 6-8 h at 130 °C. The method can be generally applied to a variety of aldoximes and ketoximes as is illustrated in Table 1. For the unsymmetrical silyl oximes, the E isomer was the major product as determined by the E/Z ratios. As expected, the *O*-TBS oximes (3 a-f) were found to be remarkably stable toward hydrolysis.[1b] Further studies are in progress to investigate the chemistry of these interesting intermediates.

Table 1: Representative *O*-TBS oximes

Entry	3	R^1	R^2	bp(°C,Torr)	E/Z[a]	Yield[b] (%)
1	a	C_6H_5	H	96, 0.5[c]	92/4	80[d]
2	b	C_6H_5	CH_3	101, 0.5[c]	93/7	82
3	c	$pCH_3C_6H_4$	CH_3	93, 0.3	99/1	74[e]
4	d	CH_3	CH_3CH_2	37, 0.5	75/25	80[e]
5	e	$-(CH_2)_{-4-}$		60, 0.5[c]		82
6	f	$-(CH_2)_{5-}$		74, 0.6[c]		78

a)The E/Z isomer ratio was determined by GC, and the isomers were identified by ^1H and ^{13}C NMR.[7b] b)Isolated pure product of ≥ 95% purity by GC c)Unreported boiling point in reference 4d d)The mixture was heated at 100°C.[8] e)new compound

EXPERIMENTAL

H-1 and C-13 NMR were obtained on a JEOL FX90Q and a General Electric 300 MHZ in $CDCl_3$ solution using TMS as internal reference. Mass spectra were recorded on a Hewlett-Packard 5996 G spectrometer at 70 eV. IR spectra were recorded on a Phillips PU 9700, and on a Perkin Elmer FT-1620 instruments. Purification of the *O*-TBS oximes was carried out on a B/R·8300 spinning band. GC analysis was performed on a Perkin Elmer 8500, flame ionization detector on a capillary column (25m X 0.33 mm bonded methylsilicone). Commercial grade reagents and solvents were used without further purification, except for THF distilled from sodium benzophenone ketyl and DMF distilled over CaH_2 and kept over 3 Å molecular sieves.

Representative Silylation Procedure: *Acetophenone O-(tert-Butyldimethylsilyl) oxime (3b)*

The oxime **1b**. (13.5 g, 100 mmol), TBSCl (15.9 g, 106 mmol) and dried DMF (10 mL) were placed in a three necked round bottomed flask, equipped with condenser, addition funnel, magnetic stirring bar and N_2 inlet.. A solution of imidazole (14.4 g, 212 mmol) in dried DMF (40 mL) was added dropwise and the reaction mixture was heated at 130 °C for 8 h. After the reaction was completed, as monitored by GC and IR, the mixture was allowed to cool at room temperature, and extracted with pentane (3 x 150 mL). The combined pentane layers were cooled at 0° C, washed first with $NaHCO_3$ (3 X 50 mL), then cold 1.5 M HCl (50 mL), followed by cold $NaHCO_3$ (50 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure (50 *ca* Torr) and the residue was fractionally distilled *under vacuum* to give 20.4 g (82%) of **3b** as a colorless liquid (bp 100-101 °C, 0.5 Torr). Analysis by GC indicated a E/Z ratio of 93/7, with a retention time of 4.92 min. and 3.56 min. respectively. The IR and ^1H NMR were similar to those reported in reference 4d.

C_{14} H23 NO Si (249.47): calc. C, 67.40; H, 9.29; N, 561.
found C, 67.27; H, 9.25; N, 5.64.

^{13}C NMR E isomer δ(ppm): - 5.09 (MeSi); 12.15 (MeC=N); 18.20 ($\underline{C}Me_3$); 26.18 ($\underline{Me}_3C$); 126.08, 128.26, 128.94 (Ar); 136.98 (C-C=N) 158.57 (C=N). The Z isomer was not observed.

MS Z isomer m/e (%): 234 (M^+-CH_3, 1); 192 (84); 151 (13); 118 (100); 103 (13); 77 (27); 75 (28). **E isomer**: 234 (1); 192 (40); 118 (100); 77 (46); 75 (34).

***O-tert-Butyldimethylsilylbenzaldoxime* (3a)**
Colorless liquid; GC retention time: 7.68 min. (Z) and 7.73 min. (E). The IR and ^{1}H NMR were identical to those reported in reference 4d.

^{13}C NMR E isomer δ(ppm): -5.13 (MeSi); 18.25 ($Me_3\underline{C}$); 26.17; ($\underline{Me}_3C$); 127.00, 128.57, 129.66, 132.77 (Ph); and 153.11 ($\underline{C}$=N).

MS E isomer: m/e (%): 235 (M^+, 0.49); 220 (M^+-Me, 0.7); 178 (55); 75 (100). The fragmentation pattern for the Z isomer was the same, except that the base peak was 178.

***4-Methylacetophenone O-(tert-Butyldimethylsilyl) oxime* (3c).**
Colorless liquid. GC retention time: 10:90 min. (E) and 10.43 min. (Z).

C_{15} H_{25} N O Si (263.22): calc. C, 68.44; H, 9.51; N, 5.32
found C, 68.56; H, 9.59; N, 5.56

IR (film) ν (cm^{-1}): 3080, 2950, 2920, 2850, 1635 (weak C=N), 1460, 1370, 1315, 1240 (Si:Me), 1000, 920 (very strong), 870, 840, 820, 780 cm^{-1}.

^{1}H NMR E isomer δ(ppm): 0.4 (6H, s); 1.1 (9H, s); 2.20 (3H, s); 2.35 (3H, s); 7.0-7.6 (4H ,m).

^{13}C NMR E isomer δ(ppm): -5.09 (Si$\underline{Me}$); 12.11 ($\underline{Me}$C=N); 18.21 ($C\underline{Me}_3$); 21.21 ($\underline{Me}$-Ar); 26.19 (Si-$\underline{C}Me_3$); 126.00; 128.97; 134.24, 138.86, 158.51 ($\underline{C}$=N).

MS E isomer m/e (%): 248 (M^+-Me, 0.6); 206 (22); 132 (100), 91 (35); 75 (28). The Z isomer shows a similar fragmentation pattern.

2-Butanone O-(terbytyldimethylsilyl)oxime (3d).
Colorless liquid. GC retention time 1.78 min (E) and 1.71 min (Z)

$C_{10}H_{23}$ N O Si (201.39): calc. C, 59.64; H, 11.51; N, 6.95.
found C, 59.69; H, 11.58; N, 6.31

IR (film)γ (cm^{-1}): 2955; 2929, 2885; 2857; 1472, 1462, 1361; 1250; 922 (very strong); 872; 837; 805, 781, 674.

^{1}H NMR δ(ppm): 0.14 (6H, s); 0.93 (9H, s); 1.84 (3H, s) 2.19 (E) and 2.36 (Z), (2H, 2q).

^{13}C NMRδ (ppm): -5.28 (SiMe); 10.85 ($\underline{Me}$C=N, E); 13.53 (CH_2, Z); 18.05 (CMe_3); 18.14 ($\underline{CH_3}CH_2$, E); 19.2 ($\underline{C}H_3CH_2$; Z); 22.23 ($\underline{C}H_3C$=N, Z); 25.94 (Me_3C); 29.15 (CH_2, E); 162.42 (C=N, E); 163.13 (C=N, Z)

MS E isomer m/z (%): 186 (M^+-Me, 2); 144 (100); 75 (72); 70 (58); 42 (94). Z isomer: 186 (2); 144 (100); 75 (58); 70 (66); 42 (42).

Cyclopentanone O-(tert-Butyldimethylsilyl)oxime (3e)
Colorless liquid. IR and ^{1}H-NMR were similar to those reported in reference 4d.

^{13}C NMR δ(ppm): -5.21 ($\underline{Me}_2Si$); 18.02 ($\underline{C}Me_3$); 24.38, 25.31, 26.05 ($Me_3\underline{C}$); 27.76 ($\underline{CH}_2$-C=N, syn); 30.77 ($\underline{CH}_2$-C=N, anti), 171.30 (C=N).

MS m/e (%): 198 (M^+-Me, 1); 156 (92); 75 (100), 47 (24).

Cyclohexanone O-(tert-Butyldimethylsilyl)oxime (3f)
Colorless liquid. IR and ^{1}HNMR were similar to those reported in reference 4d.

^{13}C NMR δ(ppm): -5.29 ($\underline{Me}_2$-Si); 18.18 ($C\underline{Me}_3$) 24.93; 25.70; 25.84; 26.00, 26.12 ($\underline{C}$ Me_3); 27.11 ($\underline{CH}_2$-C=N, syn); 32.27 ($\underline{CH}_2$ - C=N, anti); 164.14 (C=N).

MS: m/e (%): 212 (M^+-Me, 2); 170 (100); 96 (43); 75 (75), 47 (20).

Acknowledgments

We wish to acknowledge our gratitude to Dr. John A. Soderquist (UPR-Río Piedras) for his encouragement and useful discussions. Thanks are also given to Dr. Marisa Bonilla for the GC/MS analysis and Mr. José Martínez from UPR-Río Piedras for the NMR spectra. This research was supported by NIH-MBRS (No. GM 08216), NSF-RCSE and UPR-Humacao.

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8- The *O*-TBS benzaldoxime, (3a), undergoes a facile 1,2 elimination, as inferred from the significant amount of benzonitrile obtained when the reaction mixture was allowed to heat at a higher temperature and/or longer reaction times.

(Received in the USA 14 May 1993)