Pergamon

Tetrahedron Letters, Vol. 35, No. 15, pp. 2291-2294, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0290-E

Synthesis of α–Trimethylsilylallenones

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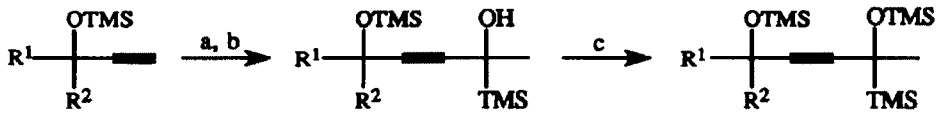
Summary: *Electrophilically initiated 1, 2-TMS group migration-elimination within bis(O-TMS) and 1-(O-TMS), 4-(O-mesyl) derivatives of 1-TMS-2-alkyn-1,4-diols affords α-TMS allenones.*

We have previously observed that silyl group migration is extremely facile in the acid-induced "silapinacol" rearrangement of 1, 2-(dihydroxyalkyl)silanes.[1] It appeared likely that this migratory aptitude could also prove fruitful in a "vinylogous"[2] setting possessing similar structural features. To this end, a number of 2-alkyn-1,4-diol derivatives (**1a-e; 2a,b**) have been investigated under electrophilic conditions to assess their ability to produce members of the scarce α-trimethylsilylallenone series (**3a-e**). To our knowledge, only two quite limited approaches to these species have been reported,[3,4] and their chemistry has been virtually unexplored. One notable exception is the recent use of an α-TMS allenone in an approach to enediynes.[5]

Schemes 1 and 2 indicate our synthetic approaches to these precursor diol derivatives.

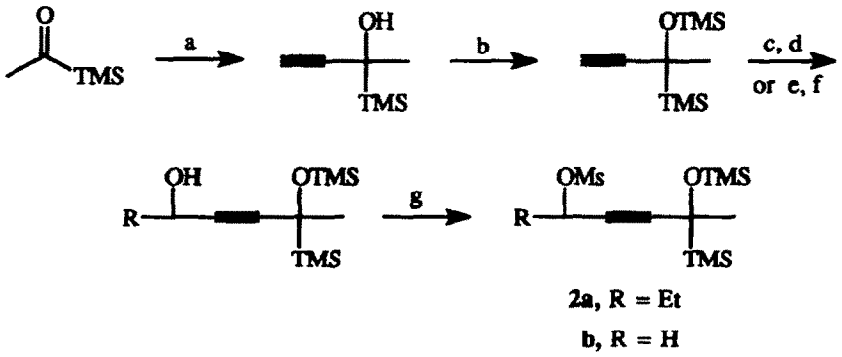
Scheme 1



1a, $R^1 = R^2 = Me$
b, $R^1 = H$; $R^2 = Ph$
c, $R^1 = H$; $R^2 = CH{=}CH_2$
d, $R^1 = H$; $R^2 = Et$
e, $R^1 = R^2 = H$

a) EtMgBr b) MeCOTMS c) 2 eq TMSCN, 60°C, 18h

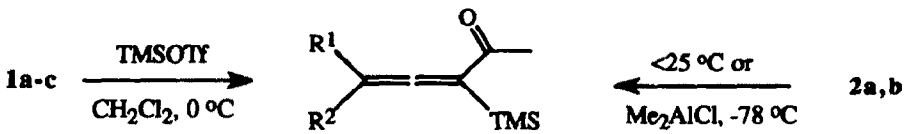
Scheme 2



a) ▬▬MgBr b) 2 eq TMSCN, 60 °C, 18h c) EtMgBr d) EtCHO e) LDA, -78 °C
f) $(CH_2O)_n$ g) MsCl, Et_3N, -78 °C

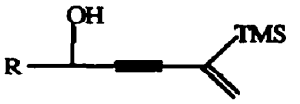
Treatment of **1a-c** with catalytic amounts of trimethylsilyltrifluoromethanesulfonate (TMSOTf) rapidly (< 5 min, 0 °C) afforded **3a-c** of 95-99% purity in good to excellent yields (Scheme 3). Attempted extension of this procedure to **1d,e**, however, led to partial or total formation of the elimination product **4** (O-desilylation accompanied elimination), and alternative protocols were sought. Resolution of this problem was found in the use of methanesulfonates (mesylates) **2a,b**. The mesylate **2a** could not be isolated, and underwent spontaneous conversion to **3d** below 25 °C. Mesylate **2b** was more robust, and suffered rearrangement at significant rates only above 60 °C. However, under any but the most stringently anhydrous conditions, thermal rearrangement was accompanied by partial desilylation of **2b**. Optimal yield and purity for **3e** were ultimately realized by treatment of **2b** with excess dimethylaluminum chloride at -78 °C.

Scheme 3



3a, $R^1 = R^2 =$ Me, 88%
b, $R^1 =$ H; $R^2 =$ Ph, 93%
c, $R^1 =$ H; $R^2 = CH{=}CH_2$, 75%
d, $R^1 =$ H; $R^2 =$ Et, 62%
e, $R^1 = R^2 =$ H, 84%

As the acylsilanes which initiate these synthetic sequences are now readily available,[6] the present method appears to offer a general entry into α-silyl allenones, species which will serve to broaden the scope of the rapidly-developing area of allenone chemistry itself.[7]



4, R = Et, H

Experimental[8]

The preparation of **1a** is typical of the synthesis of all bis(O-TMS) substrates. A solution of 0.78 g (5.0 mmol) of 3-methyl-3-(trimethylsilyloxy)-1-butyne[9] in 10 mL of THF was treated at 0 °C with 2.6 mL (5.5 mmol) of 2.0M EtMgCl. After 40 min at 25 °C, the solution was treated dropwise at 0 °C with 0.58 g (5.0 mmol) of acetyltrimethylsilane.[10] The cooling bath was removed and, after 12 min, the mixture was worked up. Distillation (80 °C, 0.1 mm) gave 0.81 g (60%) of the silyloxy alcohol, IR 3450 cm^{-1}. The silyloxy alcohol (0.59 g, 2.2 mmol) was combined with 0.44 g (4.4 mmol) of TMSCN and held at 60 °C for 5 h. After overnight at 25 °C (a total of 18 h at 60 °C for other **1**), distillation (80 °C, 0.1 mm) gave 0.66 g (87%) of **1a**, ^1H NMR: δ 0.04 (s, 9H); 0.14 (s, 9H); 0.16 (s, 9H); 1.39 (s, 3H); 1.46 (s, 3H); 1.47 (s, 3H).

1b: Bp 175 °C, 0.2 mm; 90% yield of diastereomers. ^1H NMR: δ 0.00, 0.06, 0.03, 0.09 (singlets, 18H); 0.18 (s, 9H); 1.40 (s, 3H); 5.51, 5.52 (singlets, 1H); 7.2-7.5 (m, 5H).

1c: Bp 90 °C, 0.1 mm; 78% yield of diastereomers. ^1H NMR: δ 0.03, 0.04, 0.12, 0.13 (singlets, 18H); 0.16 (s, 9H); 1.39 (s, 3H); 4.91 (m, 1H); 5.11 (d, J = 10 Hz, 1H); 5.33 (d, J = 17 Hz, 1H); 5.9 (m, 1H).

1d: Bp 90 °C, 0.1 mm; 90% yield of diastereomers. ^1H NMR δ 0.03 (s, 9H); 0.13 (s, 18H, coincident $SiMe_3$); 0.94 (t, J = 7 Hz, 3H); 1.38 (s, 3H); 1.66 (q, J = 7 Hz, 2H); 4.27, 4.29 (triplets, J = 7 Hz, 1H).

1e: Bp 100 °C, 0.3 mm; 96% yield. ^1H NMR: δ 0.03 (s, 9H); 0.13 (s, 9H); 0.14 (s, 9H); 1.38 (s, 3H); 4.33 (s, 2H).

The preparation of **3a** is typical of the synthesis of **3a-c**. A solution of 0.30 g (0.87 mmol) of **1a** in 3mL of anhydrous CH_2Cl_2 was treated at 0 °C with 9 μL (0.01 g, 0.05 mmol) of TMSOTf. After 5 min, the mixture was added to $NaHCO_3$ solution and worked up to give 0.14 g (88%) of **3a**, bp 50 °C, 0.9 mm. ^1H NMR: δ 0.09 (s, 9H); 1.76 (s, 6H); 2.19 (s, 3H). ^{13}C NMR: δ -1.1, 18.9, 27.9, 92.5, 103.2, 202.3, 215.1. IR: 1940, 1664, 1247 cm^{-1}. UV (hexane): nm(ε) = 220 (6240), 260 (163), 337 (74).

3b: Bp 100 °C, 0.1 mm. ^1H NMR: δ 0.19 (s, 9H); 2.29 (s, 3H); 6.28 (s, 1H); 7.2-7.4 (m, 5H). IR: 1916, 1668, 1600, 1249 cm^{-1}.

3c: Bp 50 °C, 0.1 mm. ^1H NMR: δ 0.14 (s, 9H); 2.25 (s, 3H); 5.01 (d, J = 10 Hz, 1H); 5.23 (d, J = 17 Hz, 1H); 5.96 (d, J = 10 Hz, 1H); 6.11 (dt, J = 10 Hz, 17 Hz, 1H); 6.20 (dt, J = 10 Hz, 17 Hz, 1H). IR: 1903, 1675, 1618, 1253 cm^{-1}. UV (hexane): nm(ε) = 219 (31,400), 239.5 (20,300), 327 (196).

The preparations of **1d,e** were similar, but only **1e** could be isolated. A solution of 24 mL of 0.5N ethynyl magnesium bromide (12 mmol) in 20 mL THF was treated dropwise at 25 °C with a solution of

1.16 g (10 mmol) of acetyltrimethylsilane in 20 mL THF over 44 min. After workup, 0.79 g (52%) of alcohol was obtained, bp 50 °C, 0.5 mm. A 1.0 g sample of alcohol was treated with 2 equivalents of TMSCN (60 °C, 15 h), freed of excess TMSCN (25 °C, 6.5 mm, 25 min) and distilled (50 °C, 0.7 mm) to give 0.98 g (64%) of the O-TMS acetylene. ^{1}H NMR: δ 0.06 (s, 9H); 0.15 (s, 9H); 1.41 (s, 3H); 2.60 (s, 1H). A solution of this acetylene (0.77 g, 3.6 mmol) in 3.5 mL THF was then added dropwise to LDA prepared from 1.00 g (7.1 mmol) of diisopropylamine and 3.0 mL (7.5 mmol) of 2.5N nBuLi in 9 mL THF at -78 °C. After 25 min at -78 °C, 0.33 g (11 mmol) of dry paraformaldehyde was added at once. After 10 min at -78 °C and 40 min at 25 °C, workup with aqueous NH_4Cl and dilute HCl was followed by chromatography on silica gel (15% ether-hexane) to give 0.59 g (67%) of silyloxy alcohol. ^{1}H NMR: δ 0.04 (s, 9H); 0.14 (s, 9H); 1.39 (s, 3H); 1.4 (s, 1H); 4.31 (d, J = 6 Hz, 2H). IR: 3340 cm^{-1}. The silyloxy alcohol (0.22 g, 0.90 mmol) in 3 mL CH_2Cl_2 was treated sequentially at -78 °C with Et_3N (0.10 g, 1.0 mmol) and methanesulfonyl chloride (0.11 g, 1.0 mmol). The cooling bath was removed and the mixture worked up 40 min later. After solvent removal (1mm), 0.27 g (93%) of **2b** was obtained. ^{1}H NMR: δ 0.07 (s, 9H); 0.14 (s, 9H); 1.43 (s,3H); 3.09 (s, 3H); 4.94 (s, 2H).

A solution of 0.115 g (0.356 mmol) of **2b** in 3 mL CH_2Cl_2 was treated dropwise at -78 °C with 0.54 mL (0.54 mmol) of 1M Me_2AlCl in hexane. After 3 min, the mixture was allowed to warm to ca. 20 °C and poured into aqueous $NaHCO_3$. Workup gave 0.046 g (84%) of **3e**, bp 50 °C, 5 mm. ^{1}H NMR: δ 0.14 (s, 9H), 2.28 (s, 3H); 4.80 (s, 2H). IR: 1927, 1669, 1250 cm^{-1}. UV (hexane): nm(ε) = 220 (5,600), 305 (125), 337 (63).

3d was isolated from chromatography of the mesylation reaction. ^{1}H NMR: δ 0.15 (s, 9H); 1.06 (t, J = 7 Hz, 3H); 2.13 (q, J = 7 Hz, 2H); 2.26 (s, 3H) 5.30 (t, J = 7 Hz, 1H). IR: 1916, 1673, 1256 cm^{-1}.

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8. All **1** and **3** displayed satisfactory C, H analyses. NMR spectra were determined in $CDCl_3$ ($CHCl_3$ taken as δ 7.24). Unless otherwise indicated, all workup procedures involved hydrolysis with dilute NH_4Cl, pentane extraction, and dessication with $MgSO_4$. Distillations employed a kugelrohr apparatus.
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(*Received in USA* 19 *November* 1993; *revised* 18 *January* 1994; *accepted* 3 *February* 1994)