A New Method for the Preparation of Silyl Enol Ethers from Carbonyl Compounds and (Trimethylsilyl)diazomethane in a Regiospecific and Highly Stereoselective Manner

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General Methods: Reactions requiring anhydrous conditions were performed in vacuum flame-dried glassware under nitrogen atmospheres. Air- and moisture-sensitive liquids and solutions were transferred *via* syringe or cannula into the reaction vessels through rubber septa. ^1H and ^{13}C NMR spectra were recorded at the specified field strength using a Jeol JNM-GX 270 or 400 FT spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm). Coupling constants are quoted in Hertz (Hz). Optical rotations were measured using a Perkin-Elmer 241 MC Polarimeter. $[\alpha]_{\text{D}}^{22}$ values are given in $10^{-1} \text{ deg cm}^2\text{mg}^{-1}$. Infrared spectra were recorded on a Perkin-Elmer Spectrum-One FT-IR spectrometer. Low resolution mass spectra (m/z) were recorded on either VG platform or VG Prospec spectrometers, with only molecular ions (M^+ or MH^+) and major peaks being reported with relative intensities quoted. High-resolution mass spectra were recorded on a VG Prospec spectrometer. ReactIR spectra were recorded on a ReactIR 1000 spectrometer fitted with an immersible zirconium tipped ATR probe. Analytical TLC was performed on Merck Kieselgel 60F₂₅₄ aluminium plates which were visualised using standard visualising agents: phosphomolybdic acid/ Δ , potassium permanganate/ Δ , *para*-anisaldehyde/ Δ . Flash chromatography was performed using Kieselgel 60F₂₅₄, 40-63 micron silica gel. Anhydrous THF and DCM were obtained from a purification column composed of activated alumina (A-2); see Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics*, **1996**, *15*, 1518. Liquid aldehydes and ketones were dried and purified by standard procedures, as specified in 'Purification of Laboratory Chemicals'. D. D. Perrin and W. L. F. Armarego, Pergamon Press, **1988**, 3rd Ed. $\text{Rh}_2(\text{OAc})_4$ was purchased from Strem Chemicals. (Trimethylsilyl)diazomethane was prepared according to the procedure described by Shioiri, T.; Aoyama, T.; Mori, S. *Org. Syntheses*, **1990**, *68*, 1-7. We found the commercially available aldrich material to work but it contains a substantial amount of unknown impurities which are difficult to remove after the reaction by Kugelrohr distillation. It is also necessary to thoroughly wash glassware prior to use with a solution of concentrated acid (80:20 HNO_3 : H_2O) (overnight), followed by a solution of base (KOH in *i*-PrOH) (overnight) since the reactions are catalytic in rhodium acetate dimer and are therefore sensitive to trace metals that are present.

Table 1. Formation of Silyl Enol Ethers from Carbonyl Compounds

Entry	Substrate	Product	Yield (%) ^a
1			84
2			81
3			71
4			74
5			77
6 ^c			70
7 ^c			83 ^b
8 ^{c,d}		+ (92 : 1 : 7) ^e	74
9 ^{c,d}		+ (96 : 4) ^e	75

^a Isolated yield after Kugelrohr distillation. ^b Yield calculated by ¹H NMR. ^c Intermediate diazo compound isolated prior to treatment with Rh₂(OAc)₄. ^d Reactions carried out at –100°C. ^e Ratios calculated by ¹H NMR of the crude reaction mixture.

General Procedure for the Preparation of Silyl Enol Ethers from Carbonyl Compounds (Table 1, entries 1-5).

To a stirred solution of (trimethylsilyl)diazomethane (2.40mmol) in anhydrous THF (5ml) under an atmosphere of nitrogen and at -78°C was added *n*-BuLi (1.54ml, 1.56M in hexanes, 2.4mmol) dropwise over 10 minutes. The solution went pale yellow and was allowed to stir for a further 1 hour at -78°C . The aldehyde (2.0mmol) was then added dropwise dissolved in THF (2ml) over 10 minutes and the reaction allowed to stir for a further 30 minutes. Methanol (122 μl , 3.0mmol) was then added and the reaction stirred for a further 10 minutes followed by addition of $\text{Rh}_2(\text{OAc})_4$ (10mg, 1mol%). The reaction went bright green and was allowed to warm to room temperature over 15 minutes (cooling bath removed) with evolution of nitrogen. Water (5ml) was added and the reaction extracted with diethyl ether (3 x 20ml). The combined organic extracts were dried over Na_2SO_4 , filtered, and evaporated under reduced pressure to give the crude silyl enol ethers as orange oils. Subsequent purification by Kugelrohr distillation gave the pure silyl enol ethers.

Table 1, entry 1: **1-(Trimethylsiloxy)-1-cyclohexylethene.**¹

Isolated as a clear, colorless oil at $50\text{--}70^\circ\text{C}$ (8.0mmHg), $\text{C}_{11}\text{H}_{22}\text{OSi}$, FW = 198.38, (333mg, 84%); IR ν_{max} (neat) / cm^{-1} 2924 (C-H), 2854 (C-H), 1619 (C=C); δ_{H} (400 MHz, CDCl_3) 0.20 (9H, s, $\text{Si}(\text{CH}_3)_3$), 1.08-1.31 (5H, m, 5 x CH), 1.61-1.69 (1H, m, CH), 1.71-1.89 (5H, m, 5 x CH), 3.99 (1H, d, $J = 1.0$ Hz, C=CHH), 4.02 (1H, broad s, C=CHH); δ_{C} (101 MHz, CDCl_3) 0.25 (3s), 26.3 (d), 26.4 (2d) 31.0 (2d), 44.4 (t), 87.4 (d), 164.2 (q); m/z (EI) 198 (M^+ , 22%), 183 (45), 143 (100); (Found $[\text{M}+\text{H}]^+$ 199.1516. $\text{C}_{11}\text{H}_{23}\text{OSi}$ requires m/z , 199.1518).

Table 1, entry 2: **2-(Trimethylsiloxy)non-1-ene.**²

Isolated as a clear, colorless oil at $75\text{--}90^\circ\text{C}$ (8.0mmHg), $\text{C}_{12}\text{H}_{26}\text{OSi}$, FW = 214.42, (347mg, 81%); IR ν_{max} (neat) / cm^{-1} 1625 (C=C); δ_{H} (270 MHz, CDCl_3) 0.20 (9H, s, $\text{Si}(\text{CH}_3)_3$), 0.83-0.92 (4H, m, 2 x CH_2), 1.19-1.51 (9H, m, CH_3 and 3 x CH_2), 2.00 (2H, t, $J = 7.4$ Hz, CH_2), 4.03 (2H, s, C=CHH); δ_{C} (101 MHz, CDCl_3) 0.20 (3s), 14.2 (s), 22.7 (d), 26.9 (d), 29.2 (d), 29.3 (d), 31.9 (d), 36.6 (d), 89.8 (d), 159.7 (q); m/z (CI) 215 ($[\text{M}+\text{H}]^+$, 51%), 199 (55), 143 (37), 85 (100); (Found $[\text{M}+\text{H}]^+$ 215.1840. $\text{C}_{12}\text{H}_{27}\text{OSi}$ requires m/z , 215.1831).

¹ Fleming, I.; Morgan, I. T.; Sarkar, A. K. *J. Chem. Soc., Perkin Trans. 1.* **1998**, 2749-2764.

² Sakakura, T.; Hara, M.; Tanaka, M. *J. Chem. Soc., Perkin Trans. 1.* **1994**, 283-288.

Table 1, entry 3: **2-(Trimethylsiloxy)hex-1-ene**.³

Isolated as a clear, yellow oil at 25-50°C (8.0mmHg), C₉H₂₀OSi, FW = 172.34, (245mg, 71%); IR ν_{max} (neat) / cm⁻¹ 2958 (C-H), 2933 (C-H), 2863 (C-H), 1678 (C=C); δ_{H} (270 MHz, CDCl₃) 0.21 (9H, s, Si(CH₃)₃), 0.90 (3H, t, *J* = 7.3 Hz, CH₃), 1.24-1.51 (4H, m, 2 x CH₂), 2.01 (2H, t, *J* = 7.3 Hz CH₂C), 4.03 (2H, s, C=CHH); δ_{C} (101 MHz, CDCl₃) 0.18 (3s), 13.9 (s), 22.2 (d), 29.1 (d), 36.3 (d), 89.8 (d), 159.7 (q); *m/z* (CI) 173 ([M+H]⁺, 25%), 157 (35).

Table 1, entry 4: **4-Phenyl-2-(trimethylsiloxy)but-1-ene**.⁴

Isolated as a clear, colorless oil at 100-120°C (0.3mmHg), C₁₃H₂₀OSi, FW = 220.38, (326mg, 74%); IR ν_{max} (neat) / cm⁻¹ 2957 (C-H), 2863 (C-H), 1635 (C=C); δ_{H} (270 MHz, CDCl₃) 0.15 (9H, m, Si(CH₃)₃), 2.20-2.32 (2H, m, PhCH₂CH₂), 2.66-2.75 (2H, m, PhCH₂CH₂), 3.96-3.99 (2H, m, C=CHH), 7.06-7.26 (5H, m, ArH); δ_{C} (101 MHz, CDCl₃) 0.29 (3s), 33.5 (d), 38.5 (d), 90.3 (d), 125.9 (2t), 128.3 (t), 128.5 (2t), 141.9 (q), 158.8 (q); *m/z* (EI) 220 (M⁺, 48%), 205 (54); (Found M⁺ 220.1284. C₁₃H₂₀OSi requires *m/z*, 220.1283).

Table 1, entry 5: **2-(Trimethylsiloxy)-3,3-dimethyl-but-1-ene**.⁵

Isolated as a clear, colorless oil at 25-50°C (8.0mmHg), C₉H₂₀OSi, FW = 172.34, (266mg, 77%); IR ν_{max} (neat) / cm⁻¹ 2959 (C-H), 2911 (C-H), 2871 (C-H), 1619 (C=C); δ_{H} (270 MHz, CDCl₃) 0.21 (9H, s, Si(CH₃)₃), 1.04 (9H, s C(CH₃)₃), 3.93 (1H, d, *J* = 1.3 Hz, C=CHH), 4.08 (1H, d, *J* = 1.3 Hz, C=CHH); δ_{C} (101 MHz, CDCl₃) 0.20 (3s), 28.2 (3s), 36.5 (q), 85.8 (d), 167.3 (q); *m/z* (EI) 172 (M⁺, 12%), 157 (100).

General Procedure for the Preparation of Silyl Enol Ethers from Carbonyl Compounds (Table 1, entries 6-9).

These silyl enol ethers were found to be very sensitive to the lithium methoxide generated from the MeOH quench and it was necessary to isolate the intermediate diazo compound initially before treating with Rh₂(OAc)₄ to give the required silyl enol ethers (by the method described below):

³ Camici, L.; Dembech, P.; Ricci, A.; Seconi, G.; Taddei, M. *Tetrahedron* **1988**, *44*, 4197-4206

⁴ Boehmer, J.; Hampel, F.; Schobert, R. *Synthesis* **1997**, *6*, 661-667.

⁵ Matano, Y.; Azuma, N.; Suzuki, H. *J. Chem. Soc., Perkin. 1.* **1994**, 1739-1748.

To a stirred solution of (trimethylsilyl)diazomethane (2.40mmol) in anhydrous THF (5ml) under an atmosphere of nitrogen and at -78°C was added *n*-BuLi (1.54ml, 1.56M in hexanes, 2.4mmol) dropwise over 10 minutes. The solution went pale yellow and was allowed to stir for a further 1 hour at -78°C . The aldehyde (2.0mmol) was then added dropwise dissolved in THF (2ml) over 10 minutes and the reaction allowed to stir for a further 30 minutes. Methanol (500 μl) was then added and the reaction stirred for a further 10 minutes and was then allowed to warm to room temperature over 15 minutes (cooling bath removed). Water (5ml) was added and the reaction extracted with diethyl ether (3 x 20ml). The combined organic extracts were dried over Na_2SO_4 , filtered, and evaporated under reduced pressure to give the crude diazo compounds as orange oils. The crude diazo compound was then dissolved in anhydrous THF (5ml) and cooled to -78°C under an atmosphere of nitrogen. $\text{Rh}_2(\text{OAc})_4$ (10mg, 1mol%) was added and the reaction went bright green and was allowed to warm to room temperature over 15 minutes (cooling bath removed) with evolution of nitrogen. The solvent was removed under reduced pressure to give the crude silyl enol ethers as orange oils. Subsequent purification by Kugelrohr distillation gave the pure silyl enol ethers.

For the reactions with benzaldehyde and acetophenone a lower temperature of -100°C was required for their addition to LTMSD to prevent elimination to the alkyne. The initial addition of *n*-BuLi to the TMSD was still however carried out at -78°C .

Table 1, entry 6: **(*S*)-1-(Trimethylsiloxy)-1-(2'-pyrrolidine-1-carboxylic acid tert-butyl ester)ethene.**

Isolated as a clear, colorless oil at $100\text{--}120^\circ\text{C}$ (0.1mmHg), $\text{C}_{14}\text{H}_{27}\text{NO}_3\text{Si}$, FW = 285.45, (400mg, 70%); IR ν_{max} (neat) / cm^{-1} 2975 (C-H), 2881 (C-H) 1693 (C=O); δ_{H} (270 MHz, CDCl_3) Doubling due to rotameric populations: 0.21 (9H, s, $\text{Si}(\text{CH}_3)_3$), 1.40-1.50 (9H, m, $\text{C}(\text{CH}_3)_3$), 1.81-2.10 (4H, m, 2 x CH_2), 2.95-3.48 (3H, m, CH_2N and CHN), 4.05-4.25 (2H, m, $\text{C}=\text{CHH}$); δ_{C} (101 MHz, CDCl_3) Doubling due to rotameric populations: 0.13 (3s), 22.8 (d), 28.3/28.5 (3s) 30.5 (d), 46.4/46.9 (d), 60.6 (t), 79.2 (q), 89.1/89.4 (d) 154.5 (q), 158.1/158.3 (q); $[\alpha]_{\text{D}}^{22} = -33.4^\circ$ (c = 1, CHCl_3). HPLC: Chiracel[®] OD Column., $t_{[\text{R}]}$ = 4.6 min, $t_{[\text{S}]}$ = 4.9 min (100% Hexane, 1.0ml min^{-1}), >98% ee. m/z (EI) 285 (M^+ , 1%), 229 (40), 185 (100); (Found $[\text{M}+\text{H}]^+ - \text{C}_4\text{H}_8$ 230.1204. $\text{C}_{10}\text{H}_{20}\text{NO}_3\text{Si}$ requires m/z , 230.1212).

Table 1, entry 7: **3-Phenyl-2-(trimethylsiloxy)propene.**⁶

This silyl enol ether was found to be very unstable and could not be purified by chromatography or by Kugelrohr distillation. The product also decomposed within hours at room temperature and therefore the yield for the preparation of this compound was calculated by ¹H NMR using 2,4-dimethoxybenzene as an internal standard.

Isolated crude as a clear, yellow oil, C₁₂H₁₈OSi, FW = 206.36 (343mg, 83%); δ_H (270 MHz, CDCl₃) 0.18 (9H, s, Si(CH₃)₃), 3.38 (2H, s, CH₂), 4.16 (1H, d, *J* = 0.9 Hz, C=CHH), 4.02 (1H, d, *J* = 0.9 Hz, C=CHH), 7.23-7.40 (5H, m, ArH); δ_C (101 MHz, CDCl₃) 0.04 (3s), 43.4 (d), 91.6 (d), 126.3 (t), 128.2 (2t), 129.3 (t), 138.5 (q), 158.7 (q) *m/z* (CI) 207 ([M+H]⁺, 23%), 193 (30), 183 (23).

Table 1, entry 8: **(*E*)- and (*Z*)-1-Phenyl-2-(trimethylsiloxy)ethene and 1-Phenyl-1-(trimethylsiloxy)ethene.**⁷

Isolated as a clear, colorless oil at 70-90°C (8.0mmHg), as a mixture of (*E*)- and (*Z*)-1-Phenyl-2-(trimethylsiloxy)ethene and 1-Phenyl-1-(trimethylsiloxy)ethene (92:1:7); C₁₁H₁₆OSi, FW = 192.33, (285mg, 74%); **(*E*)-1-Phenyl-2-(trimethylsiloxy)ethene:** δ_H (270 MHz, CDCl₃) 0.27 (9H, s, Si(CH₃)₃), 6.03 (1H, d, *J* = 12.5 Hz, PhCH=CH), 6.96 (1H, d, *J* = 12.5 Hz, PhCH=CH), 7.10-7.39 (5H, m, ArH); δ_C (101 MHz, CDCl₃) 0.17 (3s), 113.4 (t), 125.3 (2t), 125.9 (t), 128.6 (2t), 136.5 (q), 141.6 (t). **1-Phenyl-1-(trimethylsiloxy)ethene:** δ_H (270 MHz, CDCl₃) 0.27 (9H, s, Si(CH₃)₃), 4.43 (1H, d, *J* = 1.7 Hz, C=CHH), 4.91 (1H, d, *J* = 1.7 Hz, C=CHH), 7.10-7.39 (5H, m, ArH); δ_C (101 MHz, CDCl₃) 0.17 (3s), 91.1 (d), 125.3 (2t), 125.9 (t), 128.6 (2t), 136.5 (q), 187.7 (q). *m/z* (EI) 192 (M⁺, 63%), 177 (30).

Table 1, entry 9: **(*E*)- and (*Z*)-1-Phenyl-2-(trimethylsiloxy)propene.**⁸

Isolated as a clear, colorless oil at 75-100°C (8.0mmHg), as a mixture of diastereoisomers (96:4 *E*:*Z*); C₁₂H₁₈OSi, FW = 206.36, (309mg, 75%); IR ν_{max} (neat) / cm⁻¹ 3024 (C-H), 2959 (C-H), 2917 (C-H), 1651 (C=C); **(*E*)-isomer:** δ_H (270 MHz, CDCl₃) 0.28 (9H, s, Si(CH₃)₃), 1.98 (3H, s, CH₃), 5.84 (1H, s, PhCH), 7.09-7.41 (5H, m, ArH); δ_C (68 MHz, CDCl₃) 0.41 (3s), 19.6 (s), 110.4 (t), 125.4 (t), 128.1 (2t), 128.6 (2t), 137.7 (q), 151.2 (q); **(*Z*)-isomer:** δ_H (270 MHz, CDCl₃) 0.23 (9H, s, Si(CH₃)₃), 2.05 (3H, s, CH₃), 5.39 (1H, s, PhCH), 7.09-7.41 (5H, m, ArH); *m/z* (EI) 206 (M⁺, 62%), 191 (38).

⁶ Nakajima, T.; Segi, M.; Sugimoto, F.; Hioki, R.; Yokota, S.; Miyashita, K. *Tetrahedron* **1993**, *49*, 8343-8358.

⁷ Hippeli, C.; Basso, N.; Dammast, F.; Reissig, H.-U. *Synthesis* **1990**, *1*, 26-27

⁸ Bonafoux, D.; Bordeau, M.; Biran, C.; Cazeau, P.; Dunogues, J. *J. Org. Chem.* **1996**, *61*, 5532-5536.

General Procedure for the Preparation of Deuterium Labeled Silyl Enol Ethers

To a stirred solution of (trimethylsilyl)diazomethane (2.40mmol) in anhydrous THF (5ml) under an atmosphere of nitrogen and at -78°C was added *n*-BuLi (1.92ml, 1.56M in hexanes, 3.0mmol) dropwise over 10 minutes. The solution went pale yellow and was allowed to stir for a further 1 hour at -78°C . The aldehyde (2.0mmol) was then added dropwise dissolved in THF (2ml) over 10 minutes and the reaction allowed to stir for a further 30 minutes. CD_3OD (122 μl , 3.0mmol) was then added and the reaction stirred for a further 10 minutes followed by addition of $\text{Rh}_2(\text{OAc})_4$ (10mg, 1mol%). The reaction went bright green and was allowed to warm to room temperature over 15 minutes (cooling bath removed) with evolution of nitrogen. Water (5ml) was added and the reaction extracted with diethyl ether (3 x 20ml). The combined organic extracts were dried over Na_2SO_4 , filtered, and evaporated under reduced pressure to give the crude silyl enol ethers as orange oils. Subsequent purification by Kugelrohr distillation gave the pure silyl enol ethers.

(Z)- and (E)-2-Deuterio-1-(trimethylsiloxy)-1-cyclohexylethene (8).⁹

Isolated as a clear, colorless oil at $50\text{--}75^\circ\text{C}$ (8.0mmHg), as a mixture of diastereoisomers (98:2 *Z:E*); $\text{C}_{11}\text{H}_{21}\text{DOSi}$, FW = 199.38, (339mg, 79%); IR ν_{max} (neat) / cm^{-1} 2928 (C-H), 2854 (C-H), 1616 (C=C); (**Z**)-isomer: δ_{H} (270 MHz, CDCl_3) 0.20 (9H, s, $\text{Si}(\text{CH}_3)_3$), 1.04-1.41 (5H, m, 5 x CH), 1.59-1.97 (6H, m, 6 x CH), 4.00 (1H, s, C=CDH); δ_{C} (101MHz, CDCl_3) 0.19 (3s), 26.3 (d), 26.4 (2d), 31.0 (2d), 44.4 (t), 87.1 (t, $J = 23.6$ Hz), 164.1 (q); (**E**)-isomer: δ_{H} (270 MHz, CDCl_3) 0.20 (9H, s, $\text{Si}(\text{CH}_3)_3$), 1.04-1.41 (5H, m, 5 x CH), 1.59-1.97 (6H, m, 6 x CH), 3.97 (1H, s, C=CDH); m/z (EI) 199 (M^+ , 14%), 183 (16); (Found M^+ 199.1498. $\text{C}_{11}\text{H}_{21}\text{DOSi}$ requires m/z , 199.1503).

(Z)- and (E)-1-Deuterio-2-(trimethylsiloxy)-3,3-dimethylbut-1-ene.⁹

Isolated as a clear, colorless oil at $25\text{--}50^\circ\text{C}$ (8.0mmHg), as a mixture of diastereoisomers (68:32 *E:Z*); $\text{C}_9\text{H}_{19}\text{DOSi}$, FW = 173.35, (243mg, 70%); IR ν_{max} (neat) / cm^{-1} 2959 (C-H), 2909 (C-H), 2873 (C-H), 1614 (C=C); (**E**)-isomer: δ_{H} (270 MHz, CDCl_3) 0.21 (9H, s, $\text{Si}(\text{CH}_3)_3$), 1.05 (9H, s, $\text{C}(\text{CH}_3)_3$), 3.91 (1H, s, C=CHD); δ_{C} (101MHz, CDCl_3) 0.20 (3s), 28.1 (3s), 36.4 (q), 85.6 (t, $J = 24.7$ Hz), 167.2 (q); (**Z**)-isomer: δ_{H} (270 MHz, CDCl_3) 0.21 (9H, s, $\text{Si}(\text{CH}_3)_3$), 1.05 (9H, s, $\text{C}(\text{CH}_3)_3$), 4.07

⁹ Stereochemistry determined by NOE.

(1H, s, C=CHD); δ_C (101MHz, CDCl₃) 0.20 (3s), 28.1 (3s), 36.4 (q), 85.6 (t, $J = 24.7$ Hz), 167.2 (q); m/z (EI) 173 (M^+ , 12%), 158 (93); (Found $[M+H]^+$ 174.1420. C₉H₂₀DOSi requires m/z , 174.1424).

(E)- and (Z)-2-Deuterio-1-(trimethylsiloxy)-1-cyclohexylethene.

The experimental procedure was identical to that described above but using deuteriocyclohexane carboxaldehyde (226mg, 2.0mmol) and the reaction quenched with MeOH (122 μ l, 3.0mmol).

Isolated as a clear, colorless oil at 50-75°C (8.0mmHg), as a mixture of diastereoisomers (96:4 *E:Z*), C₁₁H₂₁DOSi, FW = 199.38, (337mg, 82%); IR ν_{max} (neat) / cm⁻¹ 2927 (C-H), 2854 (C-H), 1616 (C=C); (**E**)-isomer: δ_H (270 MHz, CDCl₃) 0.21 (9H, s, Si(CH₃)₃), 1.06-1.38 (5H, m, 5 x CH), 1.62-1.98 (6H, m, 6 x CH), 3.99 (1H, s, C=CDH); δ_C (101MHz, CDCl₃) 0.26 (3s), 26.4 (d), 26.7 (2d), 30.9 (2d), 44.4 (t), 87.2 (t, $J = 24.0$ Hz), 164.2 (q); (**Z**)-isomer: δ_H (270 MHz, CDCl₃) 0.21 (9H, s, Si(CH₃)₃), 1.06-1.38 (5H, m, 5 x CH), 1.62-1.98 (6H, m, 6 x CH), 4.02 (1H, s, C=CDH); m/z (EI) 199 (M^+ , 38%), 183 (43); (Found M^+ 199.1510. C₁₁H₂₁DOSi requires m/z , 199.1503).

General Procedure for the Preparation of the Intermediate Diazo Compounds from Aldehydes.

To a stirred solution of (trimethylsilyl)diazomethane (2.40mmol) in anhydrous THF (5ml) under an atmosphere of nitrogen and at -78°C was added *n*-BuLi (1.54ml, 1.56M in hexanes, 2.4mmol) dropwise over 10 minutes. The solution went pale yellow and was allowed to stir for a further 1 hour at -78°C. The aldehyde (2.0mmol) was then added dropwise dissolved in THF (2ml) over 10 minutes and the reaction allowed to stir for a further 30 minutes. Methanol (500 μ l) was then added and the reaction stirred for a further 10 minutes and was then allowed to warm to room temperature over 15 minutes (cooling bath removed). Water (5ml) was added and the reaction extracted with diethyl ether (3 x 20ml). The combined organic extracts were dried over Na₂SO₄, filtered, and evaporated under reduced pressure to give the crude diazo compounds as orange oils.

For the reaction with benzaldehyde a lower temperature of -100°C was required for its addition to LTMSD to prevent elimination to the alkyne. The initial addition of *n*-BuLi to the TMSD was still however carried out at -78°C.

(1-Diazomethyl-2,2-dimethyl-propoxy)-trimethyl-silane.

Isolated as a clear, colorless oil, $C_9H_{20}N_2OSi$, FW = 200.35, (309mg, 77%); IR ν_{max} (neat) / cm^{-1} 2957 (C-H), 2870 (C-H), 2064 (C=N=N); δ_H (270 MHz, $CDCl_3$) 0.21 (9H, s, $Si(CH_3)_3$), 0.89 (9H, s, $C(CH_3)_3$), 3.63 (1H, d, $J = 6.9$ Hz, CHN_2), 3.93 (1H, d, $J = 6.9$ Hz, OCH); δ_c (101 MHz, $CDCl_3$) 0.14 (3s), 26.1 (3s), 38.1 (q), 39.8 (t), 78.5 (t); m/z (EI) 172 ($[M-N_2]^+$, 12%), 157 (100); (Found $[M+H]^+-N_2$ 173.1363. $C_9H_{21}OSi$ requires m/z , 173.1362).

(2-Diazo-1-phenyl-ethoxy)-trimethyl-silane.

Isolated as a clear, yellow oil, $C_{11}H_{16}N_2OSi$, FW = 220.34, (350mg, 79%); IR ν_{max} (neat) / cm^{-1} 3065 (C-H), 3030 (C-H), 2957 (C-H), 2899 (C-H), 2065 (C=N=N); δ_H (270 MHz, $CDCl_3$) 0.15 (9H, s, $Si(CH_3)_3$), 3.92 (1H, d, $J = 6.3$ Hz, CHN_2), 5.54 (1H, d, $J = 5.9$ Hz, $PhCH$), 7.21-7.51 (5H, m, ArH); δ_c (101 MHz, $CDCl_3$) 0.13 (3s), 44.1 (t), 71.5 (t), 125.8 (2t), 127.7 (t), 128.4 (2t), 142.7 (q); m/z (EI) 192 ($[M-N_2]^+$, 73%), 177 (37).

General Procedure for the Preparation of Silyl Enol Ethers from the Intermediate Diazo Compounds.

To a stirred solution of the crude diazo compound (1.0mmol) in THF (5ml) under an atmosphere of nitrogen and at $-78^\circ C$ was added rhodium acetate dimer (5mg, 0.5mol%). The resulting bright green solution was allowed to stir for 5 minutes and then allowed to warm to room temperature over 15 minutes (cooling bath removed) with evolution of nitrogen. The solvent was removed under reduced pressure to give the crude silyl enol ethers as orange oils. Subsequent purification by Kugelrohr distillation gave the pure silyl enol.

Table 1, entry 5: 2-(Trimethylsiloxy)-3,3-dimethyl-but-1-ene.

Isolated as a clear, colorless oil at $25-50^\circ C$ (8.0mmHg), $C_9H_{20}OSi$, FW = 172.34, (155mg, 90%);

Compound characterization data as earlier.

Table 1, entry 8: **(E)- and (Z)-1-Phenyl-2-(trimethylsiloxy)ethene and 1-Phenyl-1-(trimethylsiloxy)ethane.**

Isolated as a clear, colorless oil at 70-90°C (8.0mmHg), C₁₁H₁₆OSi, FW = 172.34, (161mg, 94%);

Compound characterization data as earlier.

General Procedure for the Preparation of Substituted Silyl Enol Ethers from Aldehydes.

To a stirred solution of (trimethylsilyl)diazomethane (2.40mmol) in anhydrous THF (5ml) under an atmosphere of nitrogen and cooled to -78°C was added *n*-BuLi (1.91ml, 1.56M in hexanes, 3.0mmol) dropwise over 10 minutes. The solution went pale yellow and was allowed to stir for a further 1 hour at -78°C. The aldehyde (2.0mmol) was then added dropwise dissolved in THF (2ml) over 10 minutes and the reaction allowed to stir for a further 30 minutes. MeI (249μl, 4.0mmol) was then added dissolved in THF (2ml) over 5 minutes and the reaction stirred for a further 2 hours followed by addition of Rh₂(OAc)₄ (10mg, 1mol%). The reaction went bright green and was allowed to warm to room temperature over 15 minutes (cooling bath removed) with evolution of nitrogen. Water (5ml) was added and the reaction extracted with diethyl ether (3 x 20ml). The combined organic extracts were dried over Na₂SO₄, filtered, and evaporated under reduced pressure to give the crude silyl enol ethers as orange oils. Subsequent purification by Kugelrohr distillation gave the pure silyl enol ethers.

(Z)-1-Cyclohexyl-1-(trimethylsiloxy)propene.¹⁰

Isolated as a clear, colorless oil at 50-75°C (8.0mmHg), C₁₂H₂₄OSi, FW = 212.40, (246mg, 58%); IR ν_{max} (neat) / cm⁻¹ 2926 (C-H), 2854 (C-H), 1673 (C=C); δ_H (270 MHz, CDCl₃) 0.19 (9H, s, Si(CH₃)₃), 1.01-1.36 (5H, m, 5 x CH), 1.51 (3H, dd, *J*¹ = 6.6 Hz, *J*² = 1.0 Hz, CH₃), 1.60-1.91 (6H, m, 6 x CH), 4.49 (1H, dq, *J*¹ = 6.6 Hz, *J*² = 1.0 Hz, C=CH); δ_c (101 MHz, CDCl₃) 0.75 (3s), 10.9 (t), 26.6 (d), 26.7 (2d), 31.3 (2d), 44.6 (s), 99.6 (t), 156.1 (q); *m/z* (EI) 212 (M⁺, 25%), 197 (12), 183 (35); (Found M⁺ 212.1594. C₁₂H₂₄OSi requires *m/z*, 212.1596).

(Z)-3-(Trimethylsiloxy)hept-2-ene.

¹⁰ Kato, M.; Mori, A.; Oshino, H.; Enda, J.; Kobayashi, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, 106, 1773-1778.

Isolated as a clear, colorless oil at 40-50°C (8.0mmHg),, C₁₀H₂₂OSi, FW = 186.37, (337mg, 85%); IR $\nu_{\max}$ (neat) / cm⁻¹ 2958 (C-H), 2933 (C-H), 2863 (C-H), 1678 (C=C); δ_{H} (270 MHz, CDCl₃) 0.19 (9H, s, Si(CH₃)₃), 0.89 (3H, t, *J* = 7.3 Hz, CH₂CH₃), 1.24-1.48 (4H, m, 2 x CH₂), 1.50 (3H, dt, *J*¹ = 6.6 Hz, *J*² = 1.3 Hz, CHCH₃), 1.99 (2H, t, *J* = 7.3 Hz, CCH₂), 4.51 (1H, q, *J* = 6.6 Hz, C=CH); δ_{C} (101 MHz, CDCl₃) 0.67 (3s), 10.7 (s), 14.0 (s), 22.3 (d), 29.2 (d), 36.3(d), 102.0 (t), 151.3 (q); *m/z* (CI) 187 ([M+H]⁺, 15%), 171 (18), 100 (100); (Found [M+H]⁺ 187.1516. C₁₀H₂₃OSi requires *m/z*, 187.1518).

Dideuterio-cyclohexylmethanol.¹¹

To a stirred partial solution of lithium aluminium deuteride (4.0g, 95.3mmol) in anhydrous THF (250ml) under an atmosphere of nitrogen and cooled to 0°C was added dropwise methyl cyclohexanecarboxylate (6.77g, 47.6mmol) dissolved in anhydrous THF (50ml) over 15 minutes. Once the addition was complete the reaction was allowed to warm to room temperature and was heated at reflux for 2 hours. The reaction was cooled again to 0°C and quenched by the sequential addition of water (4ml), 15% NaOH (4ml), and then water (12ml). The solids were removed by filtration through a pad of celite and washed several times with EtOAc. The combined organics were dried over MgSO₄, filtered, and evaporated under reduced pressure to yield the product as a clear, colorless oil, C₇H₁₂D₂O, FW = 116.20, (5.42g, 98%); IR $\nu_{\max}$ (neat) / cm⁻¹ 3318 (O-H), 2923 (C-H), 2851 (C-H); δ_{H} (400 MHz, CDCl₃) 0.94 (2H, dt, *J*¹ = 12.1 Hz, *J*² = 3.3 Hz, 2 x CH) 1.12-1.32 (3H, m, 3 x CH) 1.41-1.51 (1H, m, CH) 1.63-1.82 (5H, m, 5 x CH), 2.07 (1H, broad s, OH); δ_{C} (101 MHz, CDCl₃) 25.9 (2d), 26.7 (d), 29.6 (2d), 40.3 (t), 67.9 (q, *J* = 21.5 Hz); *m/z* (EI) 116 (M⁺, 1%), 98 (26), 83 (100).

α -Deuterio-cyclohexanecarboxaldehyde.¹²

To a stirred partial solution of pyridinium dichromate (16.2g, 43.1mmol) in anhydrous DCM (200ml) under an atmosphere of nitrogen was added dropwise the deuterated cyclohexyl alcohol (4.0g, 34.5mmol) dissolved in anhydrous DCM (100ml) *via* cannula over 10 minutes. The reaction was allowed to stir for 16 hours and filtered through a pad of silica. The solvent was dried over MgSO₄, filtered, and evaporated under reduced pressure to give the product as a pale yellow oil. The product was purified by flash chromatography (10 % ethyl acetate in petroleum ether) to yield the aldehyde as a clear, colorless oil, C₇H₁₁DO, FW = 113.18, (976mg, 25%); R_f = 0.50 (30 % ethyl acetate in petroleum ether), IR $\nu_{\max}$ (neat) / cm⁻¹ 2927 (C-H), 2854 (C-H),

¹¹ Wells, A. P.; Kitching, W. J. *Chem. Soc. Perkin Trans., 1*. **1995**, 527-536.

¹² Yamashita, M.; Miyoshi, K.; Nakazono, Y.; Suemitsu, R. *Bull. Chem. Soc. Jpn.* **1982**, 55, 1663-1664.

1710 (C=O); δ_{H} (270 MHz, CDCl_3) 1.17-1.48 (4H, m, 4 x CH), 1.60-1.80 (4H, m, 4 x CH), 1.85-1.97 (2H, m, 2 x CH), 2.18-2.32 (1H, m, CHCDO); δ_{C} (101 MHz, CDCl_3) 25.0 (2d), 25.9 (d), 26.0 (2d), 49.8 (t, $J = 3.5$ Hz), 204.7 (q, $J = 25.8$ Hz); m/z (EI) 113 (M^+ , 7%), 95 (19), 83 (43); (Found $[\text{M}+\text{H}]^+$ 114.1037. $\text{C}_7\text{H}_{12}\text{DO}$ requires m/z , 114.1029).

ReactIR Data

ReactIR was employed to unravel the sequence of events as shifts in the diazo stretching frequency provide characteristic information on the reaction intermediates. The studies were carried out with cyclohexane carboxaldehyde, resulting in the formation of the corresponding silyl enol ether 1-cyclohexyl-1-(trimethylsiloxy)ethene (Scheme 1).

Scheme 1. Silyl Enol Ether Formation from Cyclohexane Carboxaldehyde for ReactIR Investigation

From this analysis we concluded that the mechanism for silyl enol ether formation shown below was operative (Scheme 2).

Scheme 2. Mechanism of Silyl Enol Ether Formation

Start of Reaction

As shown in the ReactIR spectrum (Figure 1), addition of *n*-BuLi to TMSD (species **A**) to produce LTMSD (species **B**) resulted in a substantial change in stretching frequency of the diazo group from 2064cm^{-1} to 2043cm^{-1} . The deprotonation required about 20 minutes at -78°C .

Figure 1. Start of the Reaction

Subsequent addition of the aldehyde resulted in no change in the shape or peak maximum of the diazo stretch, indicating that a lithiated diazo species is present. It is highly likely that the addition adduct **C** is in equilibrium with the lithiated diazo species **D** which is the predominant species. Interestingly, quenching the reaction at this stage with AcOH furnished the protonated form of **C** whilst quenching with MeOH furnished the protonated form of **D** (**E**). The stretching band for the lithiated diazo species **D** is broad probably due to the presence of a number of aggregated structures present in solution. No aldehyde C=O stretch was observed indicating that it was consumed immediately upon addition.

End of Reaction (Reverse Angle)

As shown in the ReactIR spectrum (Figure 2), addition of the rhodium acetate catalyst at low temperature does not cause decomposition of species **D**, as the diazo stretch remains unchanged over a period of 20 minutes. Upon addition of methanol, the diazo group stretch moves from 2043cm^{-1} to 2064cm^{-1} which is consistent with the formation of the neutral species **E**.

Figure 2. End of the Reaction

Upon complete protonation of species **D** to give species **E**, there is still no reaction with the rhodium acetate catalyst at -78°C over 15 minutes. However, upon warming to room temperature, species **E** underwent decomposition to give silyl enol ether **G** (*via F* presumably). This is seen by the disappearance of the diazo stretch at 2064cm^{-1} and can be seen more clearly from the 2D plot below.

Disappearance of the Diazo Peak at 2064cm^{-1} with Increasing Temperature

The decomposition of the diazo intermediate **E** was very slow at low temperature. Only upon warming to around -10°C was there any substantial reduction in the intensity of the diazo stretch of **E**.

Figure 3. Disappearance of the Diazo Peak at 2064cm^{-1} with Increasing Temperature

Further 2D plots showing a clearer and more simplified view of the shift in the diazo stretching frequencies during the course of the reaction are shown below (Figures 4 and 5).

Figure 4. Changes in the Diazo Stretch During the Progress of the Reaction

Position of C=N=N Stretching Band During the Progress of the Reaction

Figure 4. Position of the Diazo Stretching Band During the Progress of the Reaction