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Influence of Different Protecting Groups on the Regioselectivity of the Hydrotelluration Reaction of Hydroxy Alkynes

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GENERAL REMARKS

All reactions were conducted in flame dried glassware under nitrogen. All solvents were purified before use. THF was dried by distillation from sodium benzophenone ketyl. CH_2Cl_2 and DMF were dried by distillation from CaH_2. All other commercially available reagents and solvents were used as received.

^{1}H NMR data were recorded at 300 MHz using a Varian UNITY PLUS spectrometer. ^{1}H NMR chemical shifts are reported as delta (δ) units in parts *per* million (ppm) relative to residual $CHCl_3$ (7.26 ppm). Coupling constants (*J*) were reported in Hertz (Hz). ^{13}C NMR data were recorded at 75 MHz using a Varian UNITY PLUS spectrometer. ^{13}C NMR chemical shifts were reported as delta (δ) units in parts *per* million (ppm) relative to the central line of $CDCl_3$ (77.0 ppm). ^{125}Te NMR data were obtained at 94.6 MHz using diphenyl ditelluride as an external reference (422.0 ppm). Typical parameters were as follows: acquisition time equal to 0.64 second, pulse of 45°, spectral window of 43.9 kHz; and line broadening equal to 5.0 Hz; a good compromise value because although a greater line broadening would improve the signal-to-noise ratio of the tellurium spectra, which would also imply in less signal resolution.

Low resolution mass spectra were obtained using a Shimadzu QP-5050a Spectometer (70 eV) using helium 4.5 as a carrier gas and a DB-5 column (30 m × 0.25 μm).

Reactions were monitored by thin-layer chromatography on 0.25 mm E. Merck silica gel 60 plates (F254) using UV light and vanillin as visualizing agents. Column chromatographic purifications were performed using Silica Gel 60 (230 - 400 mesh) unless indicated otherwise.[1] All compounds purified by chromatography were sufficiently pure for use in further experiments, unless indicated otherwise.

Dibutylditelluride (BuTeTeBu)[11]

A 2 L round-bottomed flask was flamed dry and equipped with a 250 mL pressure equalized dropping funnel. Tellurium metal (40.2 g, 315 mmol, dried at 85 ºC prior to use in an oven) was suspended in dry THF (1 L) and cooled to 0 ºC. The addition funnel was charged with *n*-butyllithium (360 mmol, 144 mL of a 2.5 mol L^{-1} solution in hexanes). The *n*-butyllithium was added dropwise. After the addition was complete, the ice bath was removed and the reaction mixture was stirred at room temperature for 60 min. A saturated solution of ammonium chloride (450 mL) was then added slowly. The reaction was stirred at room temperature for about 3 h while open to the atmosphere (O_2). The organic layer was isolated and the aqueous layer was extracted with ethyl acetate (1 × 300 mL). The combined organic phases were dried over anhydrous magnesium sulfate and filtered through a pad of Celite. Concentration *in vacuo* provided 50.7 g (87%) of dibutylditelluride as a red oil which was used directly without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.10 (*t*, *J* 7.80Hz, 2H), 1.80 - 1.60 (*m*, 2H), 1.46-1.30 (*m*, 2H) , 0.92 (*t*, *J* 7.50 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.6; 24.5; 13.3; 4.21. IR (film) ν_{max}/cm^{-1}: 2955, 2921, 2868, 1457, 1175.

General Procedure for Protection of Propargyl Alcohol with R_3SiCl

To a round-bottomed flask under argon was added DMF (2 mL), imidazole (1.70 g, 25 mmol), and propargyl alcohol

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[1] Still, W. C.; Kahn, M.; Mitra, A.; *J. Org. Chem.* **1978**, *43*, 2923.

(0.56 g, 0.58 mL, 10 mmol). The mixture was stirred and R_3SiCl [TBSCl, TIPSCl, TBDPSCl] (12 mmol) was slowly added. The mixture was stirred for 12 h, diluted with CH_2Cl_2 (20 mL) and quenched with water (20 mL). The organic phase was washed with 3% HCl (10 mL), saturated $NaHCO_3$ (20 mL) and finally water. The organic phase was then dried over $MgSO_4$, filtered and concentrated *in vacuo*. The pure silyl ether was distilled from the residue under reduced pressure.

*tert-butyldimethyl(prop-2-ynyloxy)silane (**2**)*

1.64 g (65%); (bp 40 °C, 8 mmHg) ^{1}H NMR (300 MHz, $CDCl_3$) δ 4,20 (*d*, *J* 1.8 Hz, 2H); 2,15 (*t*, *J* 2,7 Hz, 1H); 0,88-0,80 (*m*, 9H); 0,13-0,10 (*m*, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 81.0; 73.88; 53.01; 26.07; 18.23; −5.1.

*triisopropyl(prop-2-ynyloxy)silane (**3**)*

1.45 g (68%); (bp 110 °C, 20 mmHg) ^{1}H NMR (300 MHz, $CDCl_3$) δ 4,37 (*d*, *J* 2,4 Hz, 2H); 2,38 (*t*, *J* 2,7 Hz, 1H); 1,11-1,04, (*m*, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 81.40; 72.58; 51.72; 17.85; 11.90.

*tert-butyldiphenyl(prop-2-ynyloxy)silane (**4**)*

1.37 g (50%); ^{1}H NMR (300 MHz, $CDCl_3$) 7,80-7,35 (*m*, 10H); 4,32 (*d*, *J* 2,4 Hz, 2H); 2,39 (*t*, *J* 2,1 Hz, 1H); 1,07 (*s*, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.54; 134.78; 132.86; 129.54; 80.1; 73.02; 52.42; 26.08; 19.10.

*(but-3-yn-2-yloxy)triisopropylsilane (**9**)*

1.81 g (80%); ^{1}H NMR (300 MHz, $CDCl_3$) 4.60 (*dq*, *J* 6.5, 1.7 Hz, 1H); 2.38 (*d*, *J* 2.4 Hz, 1H); 1.46 (*d*, *J* 6.4 Hz, 3H); 1,07 (*m*, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.7, 71.2, 58.8, 25.5, 18.1, 17.8, 12.2.

*triisopropyl(pent-4-yn-2-yloxy)silane (**10**)*

1.90 g (80%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4,07 (*m*, 1H); 2,96 (*dd*, *J* 8.1 Hz, *J* 2.7 Hz, 2H); 1,98 (*t*, *J* 2.7 Hz, 1H); 1,29 (*d*, *J* 5.7 Hz, 3H); 1,07 (*m*, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 82.2; 73.1; 68.6; 31.4; 24.4; 18.5; 13.1.

*3-(2-methoxyethoxy)prop-1-yne (**5**)*

To a round-bottomed flask under argon was added diisopropylamine (5.0 mL, 35.7 mmol) and propargyl alcohol (0.84 g, 0.87 mL, 15 mmol). The mixture was stirred at room temperature and MEMCl (1.91 mL, 16.8 mmol) was slowly added. The mixture was stirred for 12 h, diluted with CH_2Cl_2 (20 mL) and quenched with water (20 mL). The organic phase was washed with 3% HCl (10 mL), saturated $NaHCO_3$ (20 mL) and finally water (3 × 20 mL). The organic phase was then dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was distilled under reduced pressure (bp 100 °C, 15 mmHg) to yield 0.68 g (50%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4,78 (*m*, 2H); 4,22 (*dd*, *J* 2.4 Hz, *J* 1.2 Hz, 2H); 3,69 (*m*, 2H); 3,53 (*m*, 2H); 3,36 (*t*, 3H); 2,41 (*dt*, *J* 7.2 Hz, *J* 2.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.53; 58.93; 66.69; 67.09; 74.52; 79.23; 95.55.

*2-(prop-2-ynyloxy)tetrahydro-2H-pyran (**6**)*

To a round-bottomed flask under argon was added PPTS (0.29 g, 0.9 mmol), propargyl alcohol (0.56 g, 0.58 mL, 10 mmol) and CH_2Cl_2 (10 mL). The mixture was stirred at room temperature and DHP (1,40 g, 1.68 mL, 10 mmol) was slowly added. The mixture was stirred for 3 h, diluted with CH_2Cl_2 (20 mL) and washed with water (3 x 20 mL). The organic phase was then dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was distilled under reduced pressure (bp 80 °C, 25 mmHg) to yield 1.54 (85%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4,73-4,70 (*m*, 1H); 4,26 (*dd*, *J* 2.7 Hz, *J* 1.2 Hz, 2H); 3,65–3,60 (*m*, 2H); 2,39 (*dt*, *J* 7.2 Hz, *J* 2.4 Hz, 1H); 1,62-1,60 (*m*, 2H); 1,56-1,50 (*m*, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.90; 25.33; 30.1; 53.88; 61.87; 73.93; 79.68; 96.71.

*Representative Procedure for the Hydrotelluration of Alkynes **1**-**10***

The appropriate alkyne (0.5 mmol) and dibutylditelluride (90 mg, 0.25 mmol) were dissolved in absolute ethanol (4.0 mL) at room temperature. Finely powdered sodium borohydride (26 mg, 0.7 mmol) was added in portions to the above solution. Additional sodium borohydride was added as necessary to maintain a yellow color (indicative of the butyltellurolate anion). The solution was heated to reflux for 5 h and cooled to room temperature. The reaction mixture was then poured into a saturated solution of sodium bicarbonate (20 mL) and diluted with EtOAc (20 mL). The organic layer was isolated and washed with water (50 mL) and brine (50 mL) before drying over anhydrous magnesium sulfate. The organic phase was filtered, concentrated *in vacuo*, and submitted to ^{1}H and ^{125}Te NMR analysis without further purification.

*Synthesis of 1-octanal (**12**)*

To a round-bottomed flask equipped with an addition funnel was added PCC (21.6 g, 100.2 mmol) and CH_2Cl_2 (100 mL). The solution was cooled to 0 °C and 1-octanol (**11**) (13 g, 100 mmol) was added dropwise over 1 h. After this period, the bath was removed and the solution stirred for an additional period of 3 h. The mixture was then filtered through a pad of Celite and the solvent was removed *in vacuo*. The residue was distilled under reduced

pressure (bp 90 °C, 80 mmHg) to yield 10 g (78%) of the title compound as a colorless oil. The data of the obtained compound match with the literature.

*Synthesis of (+/-)-dec-1-yn-3-ol (**13**)*

To a round-bottomed flask under argon and equipped with an addition funnel was added magnesium turnings (1.22 g, 51 mmol) and THF (30 mL). The mixture was stirred and 1-bromoethane (5.45 g, 50 mmol) was slowly added. In another flask under argon containing THF (20 mL) at −78°C dry acetylene gas was introduced through a gas-inlet tube (which reaches the bottom of the flask and is bent at the outer end for downward delivery) over 0.5 h period. The reaction was warmed up to room temperature and the solution of ethylmagnesium bromide was transferred *via* canula to this flask. The mixture was then cooled to 0 °C and **12** (3.20 g, 25 mmol) was added over a 45 min period. The mixture was then stirred for an additional 12 h and after this period slowly quenched with saturated NH_4Cl. Ethyl ether (100 mL) was added and the organic phase was washed with saturated NH_4Cl. The aqueous phase was extracted with ethyl ether (3 x 100 mL) and the combined organic phases were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was distilled under reduced pressure (bp 105 °C, 0.5 mmHg) to yield 1.88 g (49%) of the title compound as a colorless oil. The data of the obtained compound match with the literature.[2]

*Synthesis of (+/-)-(dec-1-yn-3-yloxy)triisopropylsilane (**14**)*

To a round-bottomed flask under argon was added DMF (1 mL), imidazole (0.17 g, 2.5 mmol), and **13** (0.154 g, 1 mmol) the mixture was stirred and TIPSCl (0.23 g, 1.2 mmol) was slowly added. The mixture was stirred for 24 h, diluted with CH_2Cl_2 (20 mL) and quenched with water (20 mL). The organic phase was washed with 3% HCl (10 mL), saturated $NaHCO_3$ (20 mL) and finally water. The organic phase was then dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexanes) to yield 0.27 g (88%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4,54 (*td*, *J* 4.5 Hz, *J* 2.1, 1H); 2,33 (*d*, *J* 2.1 Hz, 1H); 1,71 (*q*, *J* 7.5 Hz, *J* 4.5 Hz, 2H); 1,45-1,20 (*m*, 10H); 1,10 (*m*, 21H); 0,90 (*t*, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 84.43; 72.65; 65.42; 46.96; 29.66; 28.72; 26.90; 23.05; 22.15; 17.81; 14.09; 12.27. GC/MS *m/z* (rel. Int. %) 267 (100); 225 (8) 211 (10); 169 (81); 157 (9); 131 (39); 103 (46); 75 (34); 61 (17); 59 (13); 57 (9); 43 (8); 41 (9).

*Synthesis of (+/-)-(Z)-(1-(butyltellanyl)dec-1-en-3-yloxy) triisopropylsilane (**15**)*

Compound **14** (0.31 g, 1 mmol) and dibutylditelluride (0.18 g, 0.5 mmol) were dissolved in degassed ethanol (5.0 mL) at room temperature. Finely powdered sodium borohydride (53 mg, 1.4 mmol) was added in portions to the above solution. Additional sodium borohydride was added as necessary to maintain a yellow color (indicative of the butyltellurolate anion). The solution was heated to reflux for 12 h and cooled to room temperature. The reaction mixture was then poured into a saturated solution of sodium bicarbonate (30 mL) and diluted with EtOAc (20 mL). The organic layer was isolated and washed with water (50 mL) and brine (50 mL) before drying over anhydrous magnesium sulfate. The organic phase was filtered, concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexanes) to yield 0.44 g (90%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.62 (*d*, *J* 9.6 Hz, 1H); 6.23 (*dt J* 9.6 Hz, *J* 1.8 Hz, 1H); 4.22-4.16 (*m*, 1H); 2.71-2.58 (*m*, 2H), 1,80-1,68 (*m*, 2H), 1,44-1.34 (*m*, 2H), 1.44-1.27 (*m*, 10H), 1.35-1.25 (*m*, 2H), 1.20-1.00 (*m*, 21H), 0,95-0.85 (*m*, 6H).^{13}C NMR (75 MHz, $CDCl_3$) 143.53; 101.49; 75.73; 38.00; 34.09; 31.82; 29.79; 24.90; 24.86; 22.65; 18.11; 14.10; 13.40; 12.36; 7.03. ^{125}Te NMR (94.6 MHz, $CDCl_3$) 274.3. GC/MS *m/z* (rel. Int. %) 498 (M^+) (5); 455 (17); 397 (9); 323 (5); 311 (11); 267 (100); 157 (15); 131 (32); 115 (30); 103 (29); 95 (25); 87 (28); 81 (31); 75 (79); 73 (41); 67(35); 61 (50); 59 (66); 57 (52); 55 (39); 45 (16); 43 (35); 41 (60).

[2] Skattebol, L.; Jones, E. R. H.; Whiting, M. *Org. Syn*. **1963**, *4*, 793; Rinaldi, P. L.; Levy, G. C.; *J. Org. Chem*. **1980**, *45* , 4348.