

Short Note

Synthesis of Bis (1-Methyl-2-octynyl) Ether

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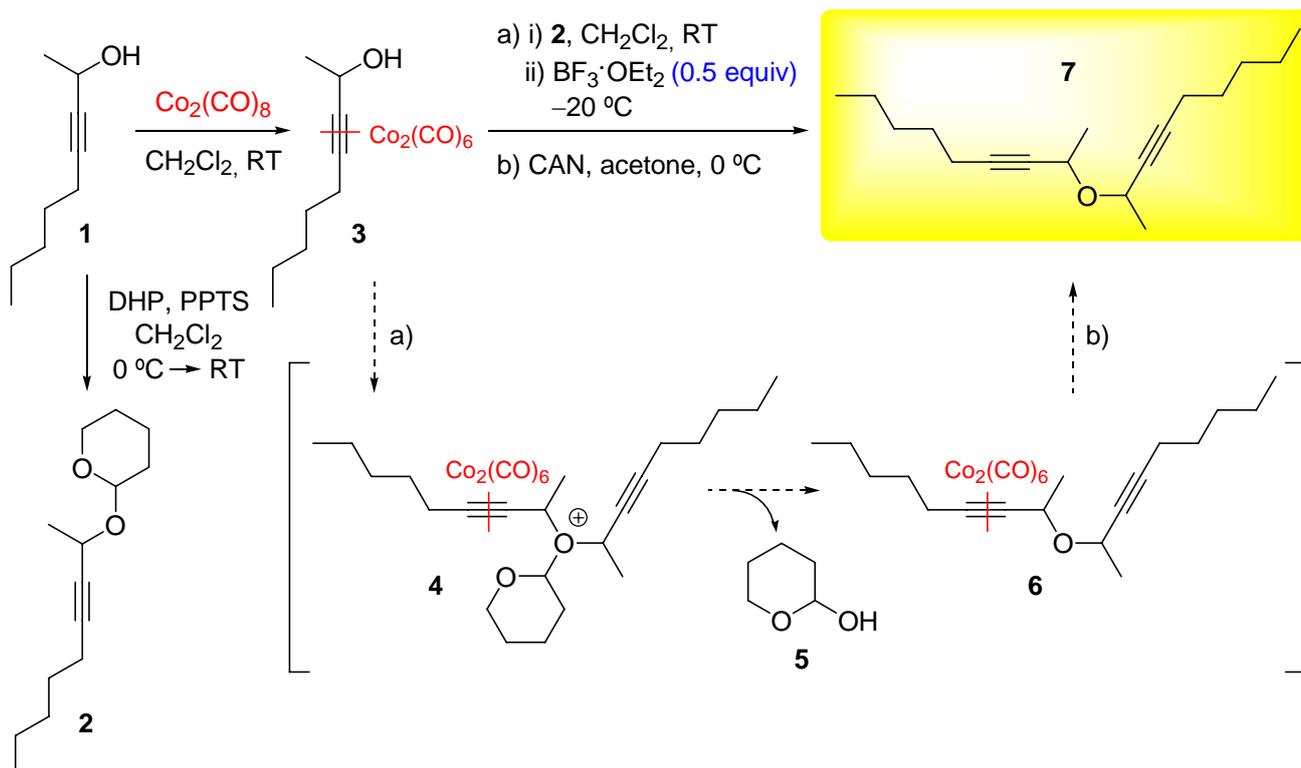
Abstract: The synthesis of bis (1-methyl-2-octynyl) ether using two secondary alcohols under Nicholas reaction conditions is reported. The reaction is possible due to a catalytic participation of the Lewis acid when the nucleophilic alcohol is protected as a THPO-ether.

Keywords: Nicholas reaction; cobalt; alkyne complexes

The reaction of a dicobalt octacarbonyl-stabilized propargylic cation with a nucleophile, followed by oxidative demetallation to yield propargylated products (Nicholas reaction) has been proved to be a versatile synthetic tool in organic synthesis [1–4]. This process has been used to prepare both symmetrical and unsymmetrical propargylic ethers [5], which are particularly important due to the wide range of functional group interconversions that the triple bond permits [6]. Nevertheless, when the propargylic cation is formed using a secondary alcohol, only primary alcohols are effective as nucleophiles to yield the corresponding ethers and avoid competitive elimination reactions [5].

Herein, we report the synthesis of bis (1-methyl-2-octynyl) ether (**7**) using only the secondary alcohol **1** as electrophile and its O-protected derivative **2** as nucleophile under Nicholas reaction conditions (Scheme 1). The overall reaction is possible due to a catalytic participation of the Lewis acid when the nucleophilic alcohol is protected as a THPO-ether **2**, generating the desired ether **7** and tetrahydropyran-2-ol (**5**) as by-product, which is in agreement with previous observations [7].

Scheme 1.



Experimental Section

General

^1H and ^{13}C NMR spectra were recorded at 25°C on Bruker Avance-300 spectrometer in CDCl_3 as solvent, and chemical shifts are reported relative to Me_4Si . Low- and high-resolution mass spectra were obtained by using a Micromass Autospec spectrometer. Elemental analysis was performed on a Fisons Instrument EA 1108 CHNS-O analyzer. Infrared spectra were recorded on a Bruker IFS 55 spectrophotometer on compounds dispersed on a CaF_2 disc (20×2 mm). Column chromatographies were performed on Merck silica gel, 60 \AA and $0.2\text{--}0.5$ mm. Methylene chloride was dried by distillation over calcium hydride prior to use. Compound 3-nonyn-2-ol (**1**) was prepared as previously described in the literature and displayed spectroscopic data identical to those reported therein [8].

Synthesis of 1-methyl-2-octynyl tetrahydro-2H-pyran-2-yl ether (**2**)

To a stirred solution of 3-nonyn-2-ol (**1**) (200 mg, 1.43 mmol) in dry CH_2Cl_2 (8 mL) was added dihydropyran (0.20 mL, 2.15 mmol) and pyridinium *p*-toluenesulfonate (25 mg, 0.01 mmol) under an argon atmosphere at 0°C . The reaction was allowed to continue at room temperature for 1 hour, after which time the mixture was poured into 20 mL of ice-water and extracted with CH_2Cl_2 (3×15 mL). The combined organic phases were washed with brine, dried (MgSO_4), concentrated, and the crude purified by silica gel column chromatography yielding **2** (285 mg, 89% yield) as a yellowish oil: ^1H NMR (300 MHz, CDCl_3) $\delta/\text{ppm} = 0.87$ (m, 3H), 1.29–1.31 (m, 6H), 1.41 (d, $J = 7.4$ Hz, 3H),

1.45–1.67 (m, 6H), 2.03 (m, 2H), 3.49–3.61 (m, 1H), 3.62–3.76 (m, 1H), 4.47–4.50 (m, 1H), 4.91 (br s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ/ppm = 13.9 (q), 18.5 (t), 19.5 (t), 22.0 (t), 22.2 (q), 25.4 (t), 28.3 (t), 30.6 (t), 33.9 (t), 61.1 (d), 62.2 (t), 81.3 (s), 85.2 (s), 98.8 (d); FT-IR (thin film) ν_{max} (cm^{-1}) 2875, 1458, 1310, 1115, 1091; FAB-MS m/z (relative intensity %) 224 $[\text{M}]^+$ (11), 223 $[\text{M}-1]^+$ (24), 153 $[\text{M}-\text{C}_5\text{H}_{11}]^+$ (30), 85 (100). HMRS calculated for $\text{C}_{14}\text{H}_{24}\text{O}_2$ $[\text{M}]^+$ 224.177630, found 224.177120.

Synthesis of bis (1-methyl-2-octynyl) ether (7)

To a solution of alcohol **1** (100 mg, 0.71 mmol) was added dicobalt octadecarbonyl (297 mg, 0.86 mmol) in dry CH_2Cl_2 (7 mL) at room temperature. The reaction was stirred for 1 h, after which time the mixture was filtered through a pad of silica and the solvent evaporated to yield $\text{Co}_2(\text{CO})_6$ -propargylic ether **3** as a reddish oil. Complex **3** was dissolved in dry CH_2Cl_2 (7 mL) and THPO-protected propargylic alcohol **2** (302.4 mg, 1.35 mmol) was added. Then, $\text{BF}_3 \cdot \text{OEt}_2$ (29 μL , 0.23 mmol) was slowly added and the reaction mixture stirred for 1 h at -20°C . The mixture was poured with vigorous stirring into a saturated solution of NaHCO_3 (15 mL) and extracted with CH_2Cl_2 (2×15 mL). The combined organic phases were washed with brine, dried (MgSO_4), and concentrated to obtain the crude $\text{Co}_2(\text{CO})_6$ -propargylic ether **6** as a reddish oil, which was used in the next step without further purification. The crude **6** was dissolved in acetone (5 mL) and the mixture cooled to 0°C . Then, $\text{Ce}(\text{NO}_3)_6(\text{NH}_4)_2$ (480 mg, 0.88 mmol) was added in one portion and the mixture stirred for 5 min. The reaction mixture was concentrated and the resulting residue extracted with Et_2O (3×10 mL). The combined organic phases were dried (MgSO_4), concentrated, and the residue purified by silica gel column chromatography to yield **7** (83 mg, 45% overall yield) as a yellowish oil: ^1H NMR (300 MHz, CDCl_3) δ/ppm = 0.88 (t, J = 11.0 Hz, 6H), 1.27–1.37 (m, 6H), 1.40 (d, J = 6.5 Hz, 6H), 1.46–1.60 (m, 6H), 2.20 (ddd, J = 7.1, 7.1, 1.9 Hz, 4H), 4.43 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ/ppm = 13.9 (q), 18.7 (t), 20.0 (q), 22.2 (t), 28.3 (t), 31.0 (t), 62.8 (d), 80.2 (s), 89.0 (s); FT-IR (thin film) ν_{max} (cm^{-1}) 2875, 1458, 1310, 1172, 1091; FAB-MS m/z (relative intensity %) 262 $[\text{M}]^+$ (0.1), 247 $[\text{M}-\text{CH}_3]^+$ (34), 243 (14), 221 (17), 191 $[\text{M}-\text{C}_5\text{H}_{11}]^+$ (5), 71 (100). Elemental analysis: Calculated for $\text{C}_{18}\text{H}_{30}\text{O}$: C, 82.38; H, 11.52. Found: C, 82.51; H, 11.80.

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References and Notes

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