Dehydration of β-nitro alcohols catalyzed by Bu_2SnO

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β-Nitro alcohols (nitro aldols) in boiling benzene in the presence of Bu_2SnO (20—30 mol.%) under neutral conditions undergo dehydration leading to nitroalkenes.

Key words: β-nitro alcohols, nitro aldols, dehydration, nitroalkenes, dibutyltin oxide.

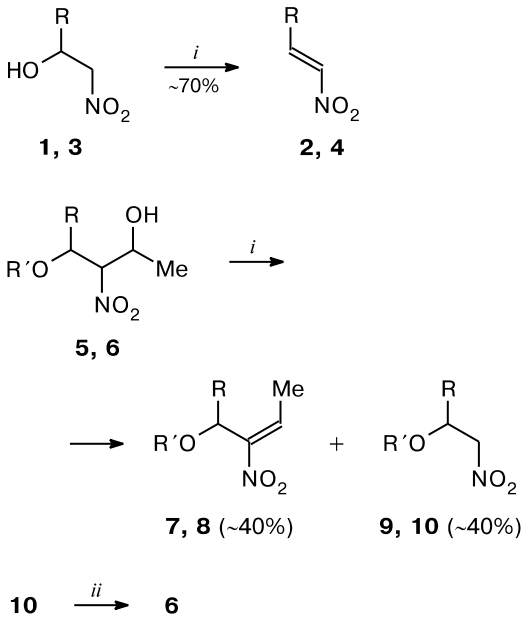
Dehydration of β-nitro alcohols (nitro aldols), which are products of the Henry reaction, is the most common route to valuable α,β-unsaturated nitro compounds.[1] Usually, this transformation is accomplished by heating with phthalic anhydride (140—180 °C) or by using such reagents as $MsCl/Et_3N$, $TFAA/Et_3N$, $Ac_2O/AcONa$, Ph_3P/CCl_4, or DCC.[1] Here we describe a novel dehydration of nitro aldols catalyzed by Bu_2SnO. For instance, we found that reflux of a solution of β-nitro alcohol **1** in benzene in the presence of a catalytic amount of Bu_2SnO (20—30 mol.%) with a Dean—Stark trap or with molecular sieves 4 Å (the latter is convenient in a scale less then 1 mmol) smoothly gives nitroalkene **2** (Scheme 1). The reaction is virtually stereospecific. Likewise, nitro alcohol **3** was transformed into *E*-nitroalkene **4**.

Reactions with β-nitro alcohols **5** and **6** containing secondary nitro groups occurred more ambiguously, giving not only dehydration products **7** and **8** but also nitro compounds **9** and **10** (**7** : **9** ≈ 1 : 1 and **8** : **10** ≈ 1 : 1). Apparently, the formation of the latter is due to a retro-nitroaldol decomposition as a side process. The dehydration of nitro alcohols **5** and **6** is also highly stereoselective: the resulting *E*-olefins **7** and **8** contain minor amounts (<10%) of *Z*-isomers (^{1}H NMR). Note that the dehydration of TBS derivative **5** we have done earlier[2] under the action of DCC gave a mixture of *E*- and *Z*-nitroalkenes in a ratio of 1 : 2.

An earlier undocumented mixture of diastereomers **6** was obtained by condensation of the known[3] MOM ether **10** with acetaldehyde in the presence of DBU and characterized by spectroscopic methods. The structure of novel compound **8** was also confirmed by ^{1}H NMR spectroscopy. Its spectrum contains a characteristic low-field (δ ≈ 7.2) quartet for the methine proton of the major compound (*E*-nitroalkene) and a low-intensity quartet at δ 6.04 for an impurity of the *Z*-isomer (*cf.* Ref. 2).

In conclusion, one can state that the discovered dehydration of β-nitro alcohols seems to be competitive for substrates containing a primary nitro group. Note that Bu_2SnO has never been employed earlier for dehydration of β-nitro alcohols.

Scheme 1



R = H_2C=$CHCH_2CH_2$ (**1**, **2**, **5**—**10**); *n*-C_7H_{15} (**3**, **4**)
R′ = TBS (**5**, **7**, **9**), MOM (**6**, **8**, **10**)

Reagents and conditions: *i*. Bu_2SnO (20—30 mol.%), PhH, reflux; *ii*. MeCHO, DBU (25 mol.%), hexane, 20 °C.

Experimental

Melting points were measured on a Kofler hot stage. IR spectra were recorded on a Bruker ALPHA-T instrument. ^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer in $CDCl_3$ at 298 K with reference to the signals of the solvent (δ 7.27). Mass spectra (ESI) were recorded on a Bruker

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micrOTOF II spectrometer (capillary potential 4500 V). A solution of a sample in methanol was syringed at a rate of 3 μL min^{-1} (positive ion mode, scan range from *m/z* 300 to *m/z* 2000, main nitrogen flow rate 4 L min^{-1}, 180 °C). Column chromatography was carried out on Silica gel 60 (0.04—0.06 mm, Fluka). For TLC, Silufol plates were used. Solvents (including light petroleum with b.p. 40—70 °C) were purified and dried according to standard procedures. Dibutyltin oxide, acetaldehyde, and DBU were purchased from Acros Organics. Compounds **1**,[3] **3**,[4] and **10** (see Ref. 3) and a mixture of diastereomers **5** (see Ref. 2) were prepared according to known procedures.

1-Nitrohexa-1(*E*),5-diene (2). A suspension of Bu_2SnO (0.55 g, 2.2 mmol) and nitro alcohol **1** (1.6 g, 11.1 mmol) in benzene (10 mL) was refluxed with a Dean—Stark trap under argon for 30 min. (*Caution! The oil bath temperature should be maintained at no higher than 90 °C. Overheating can trigger an uncontrolled exothermic process leading to resinous products.*) Then the reaction mixture was cooled and chromatographed on SiO_2 pre-packed with light petroleum. Light petroleum followed by light petroleum—$MeOBu^t$ (5%) were used as eluents. Fractions containing the product were concentrated *in vacuo* (180 Torr, t_{bath} = 40—60 °C) in a distillation setup equipped with an efficient Vigreux column. The residue was distilled to give product **2** (1.02 g, 72%), colorless liquid, b.p. 38—40 °C (3 Torr). High-resolution MS (ESI), *m/z*: found 128.0704, calculated for $C_6H_9NO_5$, $[M + H]^+$ 128.0706; found 150.0518, calculated for $[M + Na]^+$ 150.0525. IR (thin film), ν/cm^{-1}: 637, 734, 839, 920, 958, 992, 1354, 1445, 1525, 1649, 2854, 2920, 2981, 3081, 3106. ^{1}H NMR (200.13 MHz), δ: 2.18—2.47 (m, 4 H, 2 CH_2); 5.08 (br.d, 1 H, HC(6), *J* = 10.3 Hz); 5.09 (br.d, 1 H, H´C(6), *J* = 17.3 Hz); 5.79 (m, 1 H, HC(5)); 6.99 (dt, 1 H, HC(1), *J* = 1.3 Hz, *J* = 13.3 Hz); 7.26 (dt, 1 H, HC(2), *J* = 6.7 Hz, *J* = 13.3 Hz).

1-Nitronon-1(*E*)-ene (4). A suspension of Bu_2SnO (82 mg, 0.33 mmol), molecular sieves 4 Å (0.1 g), and nitro alcohol **3** (284 mg, 1.5 mmol) in benzene (2 mL) was refluxed under argon for 2 h and concentrated *in vacuo*. The residue was chromatographed on SiO_2 with light petroleum followed by light petroleum—$MeOBu^t$ (10%) as eluents. The yield of nitroalkene **4** was 184 mg (72%), colorless oil. ^{1}H NMR (200.13 MHz), δ: 0.89 (t, 3 H, Me, *J* = 6.6 Hz); 1.18—1.64 (m, 10 H, 5 CH_2); 2.27 (dddd, 2 H, HC(3), *J* = 1.3 Hz, *J* = 7.3 Hz, *J* = 7.5 Hz, *J* = 7.5 Hz); 6.98 (dt, 1 H, HC(1), *J* = 1.3 Hz, *J* = 13.4 Hz); 7.28 (dt, 1 H, HC(2), *J* = 7.3 Hz, *J* = 13.4 Hz) (*cf.* Ref. 4).

(±)-5-[*tert*-Butyl(dimethyl)silyloxy]-6-nitrooct-1,6(*E*)-diene (7) and (±)-5-[*tert*-butyl(dimethyl)silyloxy]-6-nitrohex-1-ene (9) were obtained similarly from nitro alcohol **5** (100 mg, 0.33 mmol). The resulting product (120 mg) was chromatographed on SiO_2 with light petroleum followed by light petroleum—$MeOBu^t$ (10%) as eluents. The elution gave in sequence oily diene **7** (41 mg, 43%) and oily nitro compound **9** (36 mg, 43%).

Nitro diene **7**. ^{1}H NMR (200.13 MHz), δ: 0.09 (s, 6 H, 2 MeSi); 0.87 (s, 9 H, 3 Me); 1.80—2.24 (m, 4 H, 2 CH_2); 2.06 (d, 3 H, MeC=, *J* = 7.8 Hz); 4.44 (dd, 1 H, HC(5), *J* = 5.3 Hz, *J* = 7.8 Hz); 4.94—5.13 (m, 2 H, HC(1)); 5.81 (m, 1 H, HC(2)); 7.16 (q, 1 H, HC(Me)=, *J* = 7.8 Hz), *cf.* Ref. 2.

Nitro compound **9**. ^{1}H NMR (200.13 MHz), δ: 0.06 (s, 3 H, MeSi); 0.11 (s, 3 H, MeSi); 0.92 (s, 9 H, Me_3C—Si); 1.54—1.75 (m, 2 H, $H_2C(4)$); 2.00—2.22 (m, 2 H, $H_2C(3)$); 4.29—4.50 (m, 3 H, CHOTBS, $CHNO_2$); 4.98—5.12 (m, 2 H, H_2C=); 5.81 (dddd, 1 H, HC=, *J* = 6.5 Hz, *J* = 6.5 Hz, *J* = 10.2 Hz, *J* = 16.8 Hz), *cf.* Ref. 2.

4-Methoxymethoxy-3-nitrooct-7-en-2-ols 6 (a mixture of diastereomers). A 1.76 *M* solution of acetaldehyde (1.7 mL, 3 mmol) in hexane and DBU (61 mg, 0.4 mmol) were successively added at 20 °C to a stirred solution of nitro compound **10** (see Ref. 3) (0.38 g, 2 mmol). The reaction mixture was stirred for 40 min and cooled to −5 °C. Then AcOH (32 mg, 0.53 mmol) and $MeOBu^t$ (15 mL) were added. The resulting solution was washed with brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on SiO_2 (gradient elution with light petroleum—$MeOBu^t$ up to 20% $MeOBu^t$ in the mixture). A mixture of diastereomers **6** (0.35 g, 75%) was obtained as a light yellow oil, R_f 0.30 (light petroleum—$MeOBu^t$, 2 : 1). High-resolution MS (ESI), *m/z*: found 234.1340, calculated for $C_{10}H_{19}NO_5$, $[M + H]^+$ 234.1336; found 256.1154, calculated for $[M + Na]^+$ 256.1155. IR (thin film), ν/cm^{-1}: 920, 952, 1032, 1096, 1144, 1380, 1448, 1552, 1616, 2936, 2980, 3076, 3450. ^{1}H NMR (200.13 MHz), δ: 1.27 (d, 3 H, Me, *J* = 6.2 Hz); 1.30 (d, 3 H, Me, *J* = 6.5 Hz); 1.58—1.96 (m, 2 H, HC(5)); 2.03—2.33 (m, 2 H, HC(6)); 3.44 (s, 3 H, MeO); 4.04—4.83 (m, HC(2), HC(3), HC(4), CH_2O_2); 4.94—5.13 (m, 2 H, HC(1)); 5.78 (m, 1 H, HC(2)).

(±)-5-Methoxymethoxy-6-nitrooct-1,6(*E*)-diene 8 and (±)-5-methoxymethoxy-6-nitrohex-1-ene (10) were obtained as oily products from nitro alcohol **6** (233 mg, 1 mmol) as described for TBS derivative **5**. The yields of compounds **8** and **10** were 84 mg (39%) and 67 mg (36%), respectively.

Nitro diene **8**. R_f 0.69 (light petroleum—$MeOBu^t$, 1 : 1). High-resolution MS (ESI), *m/z*: found 216.1232, calculated for $C_{10}H_{17}NO_4$, $[M + H]^+$ 216.1230; found 238.1047, calculated for $[M + Na]^+$ 238.1050. IR (thin film), ν/cm^{-1}: 726, 740, 778, 788, 920, 961, 997, 1030, 1100, 1123, 1152, 1215, 1289, 1335, 1377, 1446, 1522, 1556, 1642, 1666, 1728, 2780—2960, 3079. ^{1}H NMR (200.13 MHz), δ: 1.77—2.31 (m, 4 H, 2 CH_2); 2.02 (d, 3 H, Me, *J* = 7.7 Hz); 3.36 (s, 3 H, MeO); 4.57, 4.62 (both d, 1 H each, CH_2O_2, *J* = 5.9 Hz); 4.84 (dd, 1 H, HC(5), *J* = 5.7 Hz, *J* = 7.6 Hz); 4.97—5.13 (m, 2 H, HC(1)); 5.82 (m, 1 H, HC(2)); 7.26 (q, 1 H, HC(Me)=, *J* = 7.7 Hz).

Nitro compound **10**. ^{1}H NMR (200.13 MHz), δ: 1.57—1.89 (m, 2 H, HC(4)); 2.17 (br.q, 2 H, HC(3), *J* = 7.7 Hz); 3.35 (s, 3 H, MeO); 4.28 (m, 1 H, HC(5)); 4.43 (dd, 1 H, HCN, *J* = 4.2 Hz, *J* = 12.5 Hz); 4.52 (dd, 1 H, H´CN, *J* = 7.8 Hz, *J* = 12.5 Hz); 4.66 (s, 2 H, CH_2O_2); 4.97—5.13 (m, 2 H, H_2C=); 5.80 (dddd, 1 H, HC=, *J* = 6.6 Hz, *J* = 6.6 Hz, *J* = 10.1 Hz, *J* = 16.8 Hz), *cf.* Ref. 3.

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