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# Unusual transformation of 5-methoxymethoxy-6-nitrohex-1-ene under the action of sodium methoxide

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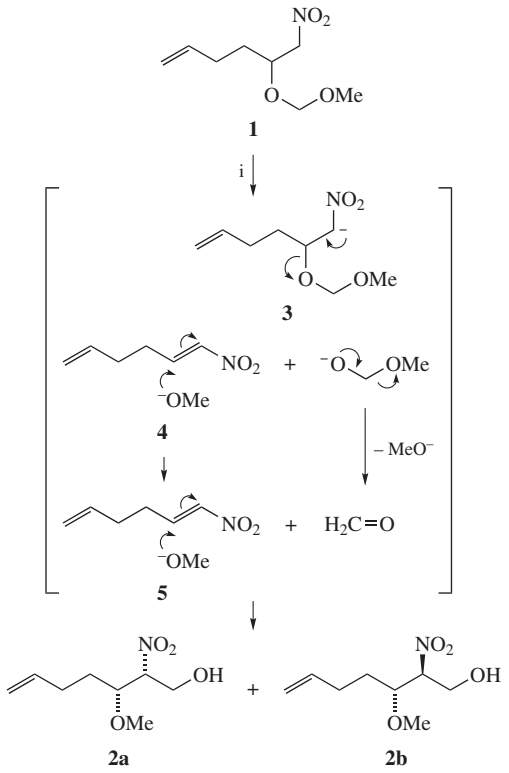
5-Methoxymethoxy-6-nitrohex-1-ene on treatment with sodium methoxide undergoes three cascade reactions to afford diastereomeric 3-methoxy-2-nitrohept-6-en-1-ols.

Condensation of nitroalkanes with carbonyl compounds (the Henry reaction) followed by β-elimination in the thus obtained nitroaldols is the principal access to valuable nitro olefins,[1] which serve as good substrates in the Michael addition.

Herein we describe an unusual transformation of 5-methoxymethoxy-6-nitrohex-1-ene **1** as a cascade of β-elimination, Michael addition and nitroaldol condensation within one operation. In fact, compound **1** on treatment with sodium methoxide in methanol is smoothly converted into a mixture of (2*R**,3*R**)- and (2*S**,3*R**)-3-methoxy-2-nitrohept-6-en-1-ols **2a** and **2b**, respectively (**2a**:**2b** ~ 7:5, 76%) (Scheme 1). The position of methoxy group in compounds **2** was confirmed by an HMBC experiment, which revealed $^1$H–$^{13}$C coupling between methyl group protons and the C-3 carbon atom.†

Evidently, the intermediate carbanion **3** undergoes β-elimination of methoxymethoxide anion (which is prone to decay to give formaldehyde and methoxide) with a formation of nitro olefin **4**. This substrate undergoes Michael addition of methoxide to form carbanion **5**. The latter upon addition to formaldehyde gives the ultimate nitroaldols **2a**,**b**.




**Scheme 1** *Reagents and conditions*: i, MeONa (1.2 equiv.), MeOH, 45 °C, 2 h, then AcOH (1.2 equiv.), 76%.

To the best of our knowledge, β-elimination leading to nitro olefins was not previously documented for β-methoxymethoxy nitroalkanes as well as for other β-alkoxy nitroalkanes. As for β-hydroxy nitroalkanes (nitroaldols), the preliminary transformation of their hydroxyl into a better leaving group, *e.g.*, methanesulfonyloxy one, is usually required.[1]

The starting nitro compound **1** was obtained by condensation of pent-4-enal with nitromethane under standard conditions[2] (Scheme 2). The MOM protection of the intermediate nitro alcohol **6**‡ was accomplished by the action of dimethoxymethane in the presence of excess of phosphorus pentoxide. Since the diastereomers **2** had almost identical chromatographic mobilities,

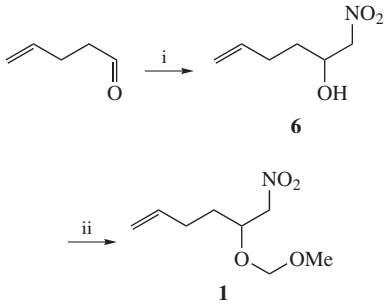
† *5-Methoxymethoxy-6-nitrohex-1-ene* **1**: colourless liquid, $R_f$ 0.68 ($SiO_2$ plate 'Silufol', Bu$^t$OMe–hexane, 1:1), bp 64–66 °C (0.1 Torr). IR (film, $\nu$/cm$^{-1}$): 920, 1032, 1108, 1156, 1212, 1384, 1420, 1556, 1640, 2828, 2840, 2936, 3080. $^1$H NMR (200.13 MHz, $CDCl_3$) $\delta$: 1.57–1.89 (m, 2H, HC-4), 2.17 (br. q, 2H, HC-3, *J* 7.7 Hz), 3.35 (s, 3H, MeO), 4.28 (m, 1H, HC-5), 4.43 (dd, 1H, HCN, *J* 4.2, 12.5 Hz), 4.52 (dd, 1H′, HCN, *J* 7.8, 12.5 Hz), 4.66 (s, 2H, $CH_2O_2$), 4.97–5.13 (m, 2H, $H_2C$=), 5.80 (dddd, 1H, HC=, *J* 6.6, 6.6, 10.1, 16.8 Hz). $^{13}$C NMR (50.03 MHz, $CDCl_3$) $\delta$: 28.84 and 31.42 (C-3, C-4), 55.74 (MeO), 74.38 (CHO), 78.90 ($CH_2N$), 96.32 ($CH_2O_2$), 115.56 ($H_2C$=), 136.99 (HC=). HRMS (ESI), *m*/*z*: found, 212.0889 [M+Na]$^+$; calc., 212.0893.

*(2R*,3R*)-3-Methoxy-2-nitrohept-6-en-1-ol* **2a** *and (2S*,3R*)-3-methoxy-2-nitrohept-6-en-1-ol* **2b**, a mixture of diastereomers (**2a**:**2b** ~ 7:5, $^1$H NMR): colourless liquid, $R_f$ 0.44 ($SiO_2$ plate 'Silufol', Bu$^t$OMe–hexane, 1:1), bp 82–85 °C (0.15 Torr). IR (film, $\nu$/cm$^{-1}$): 868, 916, 1000, 1050, 1096, 1188, 1360, 1456, 1556, 2840, 2940, 2980, 3080, 3430. HRMS (ESI), *m*/*z*: found, 212.0893 [M+Na]$^+$; calc., 212.0893.

**2a**: $^1$H NMR (600.13 MHz, $CDCl_3$) $\delta$: 1.55–1.75 (m, 2H, HC-4)*, 2.11–2.26 (m, 2H, HC-5)*, 2.53 (br. s, 1H, OH), 3.41 (s, 3H, MeO), 3.88 (ddd, 1H, HC-3, *J* 4.7, 4.7, 7.7 Hz), 4.01 (dd, 1H, HC-1, *J* 3.1, 12.8 Hz), 4.27 (dd, 1H, H′C-1, *J* 7.7, 12.8 Hz), 4.57 (ddd, 1H, HC-2, *J* 3.1, 4.7, 7.7 Hz), 5.00–5.10 (m, 2H, $H_2C$=)*, 5.79 (tdd, 1H, HC=, *J* 6.6, 10.2, 16.9 Hz)*. $^{13}$C NMR (150.03 MHz, $CDCl_3$) $\delta$: 29.09 and 30.40 (C-4, C-5), 58.70 (MeO), 59.83 (C-1), 79.35 (*C*–OMe), 90.18 (C–N), 115.69 (C-7), 136.98 (C-6).

**2b**: $^1$H NMR (600.13 MHz, $CDCl_3$) $\delta$: 1.55–1.75 (m, 2H, HC-4)*, 2.11–2.26 (m, 2H, HC-5)*, 2.42 (br. s, 1H, OH), 3.39 (s, 3H, MeO), 3.80 (ddd, 1H, HC-3, *J* 3.9, 7.6, 7.6 Hz), 3.96 (dd, 1H, HC-1, *J* 3.0, 12.6 Hz), 4.11 (dd, 1H, H′C-1, *J* 7.6, 12.6 Hz), 4.69 (ddd, 1H, HC-2, *J* 3.0, 7.6, 7.6 Hz), 5.00–5.10 (m, 2H, $H_2C$=)*, 5.79 (tdd, 1H, HC=, *J* 6.6, 10.2, 16.9 Hz)*. $^{13}$C NMR (150.03 MHz, $CDCl_3$) $\delta$: 28.46 and 29.32 (C-4, C-5), 58.50 (MeO), 60.28 (C-1), 78.58 (*C*–OMe), 91.34 (C–N), 115.53 (C-7), 137.16 (C-6).

Asterisks denote the overlapped signals of protons of the diastereomers.




**Scheme 2** *Reagents and conditions*: i, $MeNO_2$ (1 equiv.), EtOH, dropwise aq. NaOH (10 M, 1 equiv.), 25 °C, then AcOH (1 equiv.), ~60%; ii, $CH_2(OMe)_2$ (1.5 equiv.), $P_2O_5$ (2 equiv.), portionwise, $Et_2O$, 20 °C, ~70%.

our attempts to separate them either by chromatography on $SiO_2$ or by HPLC failed. Hence, these products were characterized by the spectra of their mixture.

The relative configuration of the substituents in diastereomers **2** was assigned in accordance with observations by Seebach and coworkers,[3] who investigated NMR spectra of the representative series of nitroaldols and their *O*-silyl ethers. In particular, they established that the differences of $^{13}C$ chemical shifts of C(N) and C(O) atoms within a pair of diastereomers are characteristic of the (*R**,*R**) and (*S**,*R**) configurations. The C(O) signals of the (*R**,*R**)-isomers lay at the higher field (by 0.2–0.6 ppm) and the C(N) signals are observed at the lower field (by 0.4–1.4 ppm) than those of the (*S**,*R**)-isomers. In our case, these differences are 0.77 and 1.16 ppm, respectively.

In conclusion, the unprecedented behaviour of the methoxymethoxy moiety in the transformation under consideration has been revealed, this moiety being not only a leaving group but also a source of *in situ* generated formaldehyde. The search for new manifestations of this phenomenon is to be of synthetic interest.

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‡ *(±)-1-Nitrohex-5-en-2-ol* **6**: colourless liquid, $R_f$ 0.55 ($SiO_2$ plate 'Silufol', $Bu^tOMe$–hexane, 1:1), bp 56–59 °C (0.1 Torr). $^1H$ NMR (200.13 MHz, $CDCl_3$) $\delta$: 1.45–1.75 (m, 2H, HC-3), 2.04–2.39 (m, 2H, HC-4), 2.95 (br. s, 1H, OH), 4.24–4.47 (m, 3H, HCO, $CH_2N$), 4.96–5.13 (m, 2H, $H_2C$=), 5.80 (dddd, 1H, HC=, *J* 6.7, 6.7, 10.2, 16.9 Hz) (*cf.* ref. 4). HRMS (ESI), *m/z*: found, 168.0781 $[M+Na]^+$; calc., 168.0788.