

Short Note

6-Methyl-2-nitro-1-phenyl-hept-4-en-3-ol

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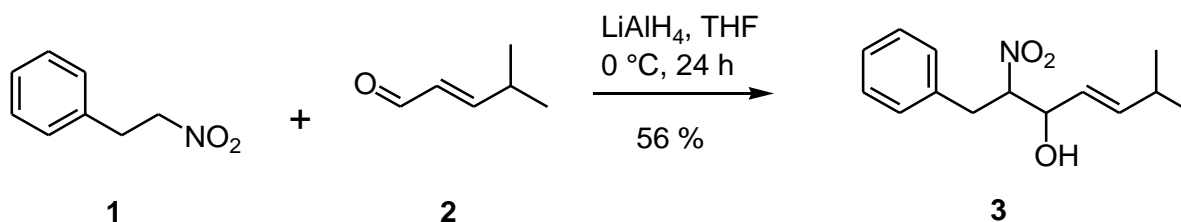
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Abstract: In this short note, we report the synthesis of 6-methyl-2-nitro-1-phenyl-hept-4-en-3-ol by a LiAlH_4 catalyzed nitroaldol reaction for carbon-carbon bond formation. The title compound was characterized by $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, MS, IR and elemental analysis.

Keywords: Henry reaction; nitroaldol reaction; carbon-carbon bond formation; LiAlH_4

The nitroaldol or Henry reaction is a well known powerful carbon-carbon bond forming reaction. It is the base catalyzed addition of a nitroalkane to a carbonyl compound and gives access to various substrates. The nitroaldol product, a 2-nitroalkanol, can be easily transferred into other substance classes like nitro alkenes, 2-amino alcohols and α -nitro ketones [1,2]. All these substance classes are highly functionalized organic molecules and thus very useful in natural product synthesis. In the course of a natural product synthesis we explored the nitroaldol reaction for 1-nitro-2-phenylethane (**1**) and 4-methyl-2-pentenal (**2**) as substrates for the synthesis of 6-methyl-2-nitro-1-phenyl-hept-4-en-3-ol (**3**) (Scheme 1).

Scheme 1. Synthesis of 6-Methyl-2-nitro-1-phenyl-hept-4-en-3-ol.



In this case, it is crucial to avoid elimination of water and 1,4-addition of the deprotonated nitroalkane to the α,β -unsaturated aldehyde. LiAlH_4 as catalyst achieves these requirements [3], because it is not basic enough for elimination of water and the coordination with Li^+ , that acts as Lewis acid, forms a transition state that avoids 1,4-addition. Because of the carefully controlled reaction conditions, including low temperature and high dilution of LiAlH_4 , the reduction of the nitro group could not be observed [4].

Experimental

General

$^1\text{H-NMR}$ was recorded on Bruker Avance 300 spectrometer and $^{13}\text{C-NMR}$ on Bruker Avance 400 spectrometer at 300 K, chemical shifts are reported in relation to Me_4Si ($\delta = 0$ ppm). The infrared spectrum was recorded on Bio-Rad FT-IR- FTS 155 spectrometer and for mass spectrometry a Finnigan MAT 95 spectrometer was used. LiAlH_4 and 4-methyl-2-pentenal (**2**) were used as purchased and 1-nitro-2-phenylethane (**1**) was synthesized according to common literature [5]. Solvents were purified and dried according to common procedures [6].

Synthesis of 6-methyl-2-nitro-1-phenyl-hept-4-en-3-ol (**3**)

The reaction was carried out under nitrogen atmosphere using standard schlenk techniques. 1-Nitro-2-phenylethane (3.8 g, 25 mmol) was added to a slurry of LiAlH_4 (27 mg, 0.7 mmol, 14 mol %) in dry THF (10 mL) at 0 °C. After 0.5 h 4-methyl-2-pentenal (0.50 g, 5.1 mmol) was added dropwise, subsequent stirring was continued for 24 h at 0 °C. The reaction mixture was quenched with HCl (1 M, 20 mL), allowed to warm to room temperature and extracted with dichloromethane (3×25 mL). The combined organic layers were dried with MgSO_4 and evaporated. The crude product was purified by flash chromatography (hexanes/ethyl acetate 9:1). Excess of 1-nitro-2-phenylethane (3.0 g, 20 mmol) was re-isolated for further reactions. 6-Methyl-2-nitro-1-phenylhept-4-en-3-ol was isolated as yellow oil in 56% yield. $^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 1.01$ (dd, $J = 6.7, 2.3$ Hz, 6H), 2.24 (d, $J = 5.8$ Hz, 1H), 2.28–2.41 (m, 1H), 3.10–3.37 (m, 2H), 4.44 (dd, $J = 13.4, 6.8$ Hz, 0.6H), 4.52 (dd, $J = 11.4, 4.5$ Hz, 0.4H), 4.66–4.77 (m, 1H), 5.37–5.48 (m, 1H), 5.80–5.91 (m, 1H), 7.15–7.34 (m, 5H) ppm. $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): $\delta = 22.0, 30.9, 36.6, 73.2, 93.5, 123.8, 127.4, 127.5, 128.5, 128.8, 128.9, 129.0, 135.1, 144.0$ ppm. **MS** (CI, NH_3): m/z (%) = 267.1 (100) [MNH_4^+]. **IR** [cm^{-1}]: $\nu = 699, 1017, 1548, 2962$. **Elemental analysis** calculated for $\text{C}_{14}\text{H}_{20}\text{NO}_3$: C, 67.18; H, 8.05; N, 5.60; O, 19.18; found: C, 66.92; H, 8.19; N, 5.51.

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