(*Z*)-1-Nitro-3-hexene as (*Z*)-3-Hexen-1-yl d^1-Reagent: Synthesis of (*Z*)-5-Octen-2-one and (*Z*)-1,8-Undecadien-5-one

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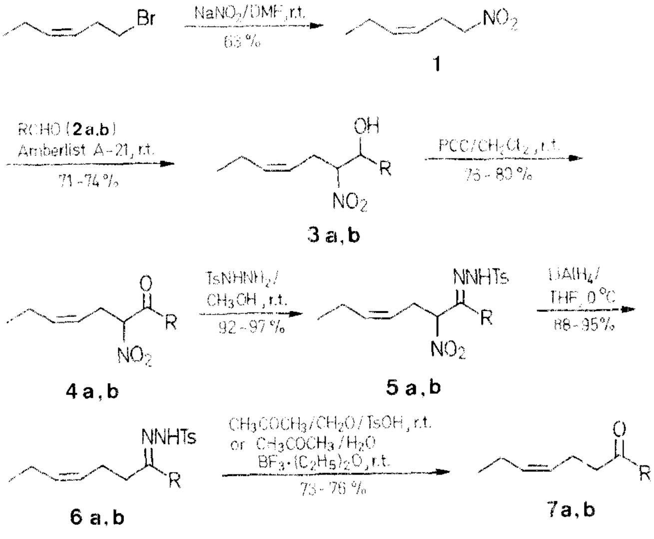
(*Z*)-1-Nitro-3-hexene is a versatile reagent corresponding to the (*Z*)-3-hexen-1-yl d^1-synthon. Nitroaldol addition, oxidation and denitration are the steps of a new methodology to conveniently prepare the title compounds, which are popular intermediates in the synthesis of (*Z*)-jasmololone and (*Z*)-jasmone.

The practical use of reagents for nucleophilic introduction of alkyl groups is subjected to three general conditions: firstly, that the anion precursor is an inexpensive and stable compound; secondly, that the carbon-carbon bond forming process is accomplished easily and mildly; thirdly, that anion stabilizing groups on the nucleophilic centre are removed or converted into other groups without interference of the other functionalities in the molecule. In this context the nitro group has found extensive use as an activating group for the formation of carbon-carbon bonds[1-2]. Moreover, the ease of replacement of a nitro group by hydrogen[3-6] as well its conversion into carbonyl[7-10], or other functional groups[11], have significantly increased the synthetic potential of nitroalkane derivatives as reagents for the nucleophilic introduction of functionalized alkyl groups in the synthesis of natural products[12-28].

In this paper we wish to describe a new synthetic procedure for the preparation of (Z)-5-octen-2-one **(7a)** and (Z)-1,8-undecadien-5-one **(7b)** using (Z)-1-nitro-3-hexene **(1)** as a reagent corresponding to the (Z)-3-hexen-1-yl d^1-synthon (Scheme). Compounds **7a** and **7b** are key intermediates in the syntheses of (Z)-jasmololone[29], [one of the ketoalcohols named rethrolones, components of the insecticidally active constituents of *Crysanthemum cinerariaefolium (pyrethrum)*[30]] and (Z)-jasmone[31] (an important naturally occurring substance widely used as a perfume ingredient[32]), respectively. (Z)-1-Nitro-3-hexene **(1)** was readily prepared in acceptable yield (63%) and purity (98% by GLC) from commercial (Z)-1-bromo-3-hexene and sodium nitrite in dimethylformamide. Nitroaldol addition (Henry reaction) of **1** to the aldehydes **2a** and **2b** was accomplished in presence of Amberlist A-21 without solvent. The nitroalkanols **3a** and **3b** were obtained in good yields and were converted into α-nitroketones **(4a, b)** by oxidation with pyridinium chlorochromate (PCC)[33]. The compounds **4a** and **4b**, when treated with *p*-toluenesulfonylhydrazine in methanol gave *p*-toluenesulfonylhydrazones **(5a, b)**, which were easily denitrated by reaction with lithium aluminium hydride[5] in tetrahydrofuran (THF) at 0°C. Subsequent acid catalyzed regeneration of the carbonyl group furnished (Z)-5-octen-2-one **(7a)** and (Z)-1,8-undecadien-5-one **(7b)**, in 39% and 33% overall yield from **6a** and **6b**, respectively. GC analysis of **7a** and **7b** indicated chemical purities above 98%.



Ts = *p*-tosyl

PCC = pyridinium chlorochromate

	R
a	CH_3
b	$-(CH_2)_2CH=CH_2$

The principle advantage of the methodology presented here is that the target molecules can be obtained in high purity by simple procedures using inexpensive chemicals.

^{1}H-NMR spectra were recorded at 90 MHz on a varian EM 390. IR spectra were recorded with a Perkin-Elmer 257 spectrophotometer. Microanalysis were performed by using a C,H,N Analyzer Model 185 from Hewlett-Packard Co. Gas chromatographic analyses were performed on a Carlo Erba Fractovap 4160 HRGC instrument using a capillary column (25 m, 0.3 mm) of fused silica (0.4–0.45 nm) with Carbowax 20 M. (Z)-1-Bromohex-3-ene, 4-pentenal, acetaldehyde. Amberlist A-21, pyridinium chlorochromate (PCC), p-toluenesulfonylhydrazine, lithium aluminium hydride, sodium nitrite and boron trifluoride etherate are commercial materials.

(Z)-1-Nitrohex-3-ene (1):
(Z)-1-Bromohex-3-ene (5.0 g, 30 mmol) is added dropwise to a stirred solution of sodium nitrite (3.73 g, 54 mmol) in dimethylformamide (60 ml). The solution is stirred for 7 h at room temperature, then cold water (100 ml) is added and the mixture is extracted with ether (3 × 50 ml). The combined extracts are dried with sodium sulfate, passed through a bed of Florisil, and concentrated to afford compound **1** as a yellow liquid that can be used without further purification; yield: 2,44 g (63%; b.p. 53°/1.6 torr.

$C_6H_{11}NO_2$ calc. C 55.79 H 8.58 N 10.85
(129.2) found 56.00 8.30 11.01

IR (neat): $\nu = 1555\ cm^{-1}$ (NO_2).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 0.98$ (t, 3H, $J = 7.5$ Hz); 1.85–2.30 (m, 2H); 2.55–2.95 (m, 2H); 4.35 (t, 2H, $J = 7.5$ Hz); 5.05–5.95 ppm (m, 2H).

2-Nitroalkanols 3a, b; General Procedure:
A 50 ml, two necked flask, equipped with a mechanical stirrer, is charged with compound **1** (5 g, 38.7 mmol) and cooled with an ice-water bath. The aldehyde **2a, b** (38.7 mmol) is added, and the mixture stirred during 5 min. Amberlist A-21 (10 g) is added and stirring continued for 16 h at room temperature. The mixture is then washed with dichloromethane (3 × 30 ml), and the filtered extract is concentrated under reduced pressure to give crude 2-nitroalkanols, which can be used without further purification (chromatography can be performed on a short column using silica gel and ethyl acetate/cyclohexane, 2:8, as eluent).

(Z)-2-Hydroxy-3-nitrooct-5-ene **(3a)**; yield: 4.96 g (74%).

$C_8H_{15}NO_3$ calc. C 55.47 H 8.73 N 8.09
(173.2) found 55.20 8.51 8.21

IR (neat): $\nu = 3400$ (OH), $1550\ cm^{-1}$ (NO_2).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 0.98$ (t, 3H, $J = 7.8$ Hz); 1.32 (d, 3H, $J = 6.3$ Hz); 1.72–3.16 (m, 5H); 4.00–4.60 (m, 2H); 5.00–5.88 ppm (m, 2H).

(Z)-5-Hydroxy-6-nitroundec-1,8-diene **(3b)**; yield: 5.86 g (71%).

$C_{11}H_{19}NO_3$ calc. C 61.94 H 8.98 N 6.57
(213.3) found 62.01 9.07 6.50

IR (neat): $\nu = 3440$ (OH), 1640 (C=C), $1550\ cm^{-1}$ (NO_2).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 0.93$ (t, 3H, $J = 7.5$ Hz); 1.65 (t, 2H, $J = 7.5$ Hz); 1.75–3.10 (m, 7H); 3.80–4.20 (m, 1H); 4.35–4.63 (m, 1H); 4.85–6.10 ppm (m, 5H).

α-Nitroketones 4a, b; General Procedure:
In a 100 ml two-necked round-bottom flask, equipped with a mechanical stirrer, pyridinium chlorochromate (PCC; 4.22 g, 19.6 mmol) is suspended in anhydrous dichloromethane (60 ml) in the presence of 3 Å molecular sieves (6). Nitroalkanol **3a, b** (13 mmol) is added all at once. The mixture is stirred at room temperature for 24 h and then another portion of PCC (2.1 g, 9.76 mmol) is added, and the mixture is stirred at room temperature for an additional 12 h. The solution is diluted with ether (60 ml) and the supernatant liquid passed through a pad of Florisil to give a clear solution. Evaporation of solvent gives α-nitroketone **4a, b**, which is purified by chromatography on a short column using silica gel and ethyl acetate/*n*-hexane; 2:8, as eluent.

(Z)-3-Nitrooct-5-en-2-one **(4a)**; yield: 1.69 g (76%).

$C_8H_{13}NO_3$ calc. C 56.12 H 7.65 N 8.18
(17.2) found 56.01 7.77 8.06

IR (neat): $\nu = 1730$ (C=O), $1555\ cm^{-1}$ (NO_2).

^{1}H-NMR ($CDCl_3$/TMS): $\delta = 1.00$ (t, 3H, $J = 7.8$ Hz); 1.8–2.28 (m, 2H); 2.36 (s, 3H); 2.60–3.20 (m, 2H); 5.05–5.88 ppm (m, 3H).

(Z)-6-Nitro-1,8-undecadien-5-one **(4b)**; yield: 2.19 g (80%).

$C_{11}H_{17}NO_3$ calc. C 62.54 H 8.11 N 6.63
(211.3) found 62.66 8.20 6.50

IR (neat): ν = 1730 (C=O), 1640 (C=C), 1555 cm^{-1} (NO_2).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.95 (t, 3 H, J = 7.5 Hz); 1.65–3.15 (m, 8 H); 4.80–6.10 ppm (m, 6 H).

α-Nitroketone *p*-Toluenesulfonylhyrazones (5a, b); General Procedure:

To a solution of α-nitroketone **4a, b** (8.53 mmol) in methanol (5 ml), p-toluenesulfonylhydrazine ($TSNHNH_2$, 1.65 g, 8.9 mmol) is added. The mixture is stirred for 10 h, then water is added to obtain the corresponding p-toluenesulfonylhydrazone **5a, b**, which was recrystallized from dichloromethane/*n*-hexane.

(Z)-3-Nitrooct-5-en-2-one p-Toluenesulfonylhydrazone **(5a)**; yield: 2.80 g (97 %); m. p. 77–78 °C.

$C_{15}H_{22}N_3O_4S$ calc. C 53.09 H 6.24 N 12.38
(339.3) found 53.11 6.17 12.21

IR (KBr): ν = 3230 (NH), 1600 (C=C), 1555 (NO_2), 1340, 1175 cm^{-1} (SO_2).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.9 (t, 3 H, J = 7.9 Hz); 1.56–3.24 (m, 5 H); 1.84 (s, 3 H); 2.44 (s, 3 H); 4.8–5.72 (m+t, 3 H, J = 7.9 Hz); 7.57 (AA'BB' pattern, 4 H, J = 8.0 Hz); 8.4 ppm (s, 1 H).

(Z)-6-Nitro-1,8-undecadien-5-one p-Toluenesulfonylhydrazone **(5b)**; yield: 2.97 g (92 %); m. p. 68–70 °C.

$C_{18}H_{25}N_3O_4S$ calc. C 56.98 H 6.64 N 11.08
(379.4) found 57.11 6.72 10.98

IR (KBr): ν = 3230 (NH), 1640, 1595 (C=C), 1545 (NO_2), 1340, 1165 cm^{-1} (SO_2).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.92 (t, 3 H, J = 7.5 Hz); 1.70–3.20 (m+s, 11 H); 4.75–6.00 (m, 6 H); 7.57 (AA'BB' pattern, 4 H, J = 8.0 Hz); 8.68 ppm (s, 1 H).

Denitration of α-Nitroketone *p*-Toluenesulfonylhydrazones 5a, b; General Procedure:

Lithium aluminium hydride (0.3 g, 7.92 mmol) is added to dry tetrahydrofuran (THF, 30 ml) in a dried, nitrogen-flushed, 100 ml flask, fitted with a septum inlet and stirrer. The mixture is cooled to 0 °C, and a solution of **5a, b** (2.64 mmol) in dry THF (20 ml) is added dropwise. The mixture is stirred for 0.5 h, treated carefully with cold water, acidified with 2 normal sulfuric acid and extracted with ether (2 × 50 ml). The ether layer is dried with sodium sulfate and passed through a bed of Florisil; the solvent is removed under reduced pressure to afford **6a, b**.

(Z)-5-Octen-2-one p-Toluenesulfonylhydrazone **(6a)**; yield: 2.21 g (95 %); m. p. 66 °C.

$C_{15}H_{22}N_2O_2S$ calc. C 61.20 H 7.53 N 9.52
(294.3) found 61.00 7.45 11.01

IR (KBr): ν = 3220 (NH), 1600 (C=C), 1340, 1165 cm^{-1} (SO_2).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.9 (t, 3 H, J = 7.9 Hz); 1.64–2.52 (m, 6 H); 1.74 (1, 3 H); 4.94–5.64 (m, 2 H); 7.57 ppm (AA'BB' pattern, 4 H, J = 8.0 Hz).

(Z)-1,8-Undecadien-5-one p-Toluenesulfonylhydrazone **(6b)**; Yield: 2.33 g (88 %), as an oil.

$C_{18}H_{26}N_2O_2S$ calc. C 64.65 H 7.84 N 8.38
(334.4) found 64.51 7.75 8.50

IR (neat): ν = 3225 (NH), 1640, 1600 (C=C), 1340, 1160 cm^{-1} (SO_2).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.9 (t, 3 H, J = 7.5 Hz); 1.65–2.32 (m, 10 H); 2.40 (s, 3 H); 4.78–5.95 (m, 5 H); 7.57 (AA'BB' pattern, 4 H, J = 8.0 Hz); 7.62 ppm (s, 1 H).

(*Z*)-5-Octen-2-one (7a):

Compound **6a** (2.30 g, 7.80 mmol) is dissolved in a mixture of acetone (75 ml) and water (10 ml), and boron trifluoride etherate (0.9 ml, 6.9 mmol) is added. The mixture is stirred at room temperature for 10 h, then diluted with pentane and washed with water (2 × 20 ml), and 2 normal sodium hydroxide (2 × 10 ml) to remove acetone p-toluenesulfonylhydrazone. After drying with sodium sulfate, solvent is removed by distillation, and compound **7a** is obtained; yield: 0.745 g, (76 %); b. p. 68–70 °C/20 torr (lit.[29] b. p. 54–57 °C/10 torr). Chemical purity: 98 % by GC.

$C_8H_{14}O$ calc. C 76.14 H 11.18
(126.2) found 76.10 11.02

IR (neat): γ = 1720 cm^{-1} (C=O).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.90 (t, 3 H, J = 7.9 Hz); 1.72–2.64 (m, 6 H); 2.08 (s, 3 H); 5.00–5.6 ppm (m, 2 H).

(*Z*)-1,8-Undecadien-5-one (7b):

Compound **6b** (2.5 g, 7.5 mmol) is dissolved in a mixture of acetone (75 ml) and water (10 ml). Paraformaldehyde (2.25 g, 75 mmol) and p-toluenesulfonic acid (TsOH, 1.02 g, 4.6 mmol) are added. The mixture is stirred at room temperature for 2 h and then concentrated under reduced pressure. The residue is diluted with ether (100 ml), washed with 10 % aqueous sodium carbonate solution, water and finally dried with sodium sulfate. Solvent is removed under reduced pressure, and the crude product is purified by column chromatography on silica gel using ethyl acetate/*n*-hexane, 2:8, as eluent. Product **7b** is obtained as an oil; yield: 0.410 g (73 %); b. p. 75 °C/1.7 torr (lit[31] b. p. 120 °C/2 torr).

$C_{11}H_{18}O$ calc. C 79.46 H 10.92
(166.3) found 79.40 10.95

IR (neat) ν = 1715 (C=O), 1640 cm^{-1} (C=C).

^{1}H-NMR ($CDCl_3$/TMS): δ = 0.86 (t, 3 H, J = 7.5 Hz); 1.70–2.60 (m, 10 H); 4.78–5.10 (m, 2 H); 5.10–5.45 (m, 2 H); 5.45–6.00 ppm (m, 1 H).

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