1419

New and Convenient Synthesis of (Z)-Heneicos-6-en-11-one, the Douglas Fir Tussock Moth (*Orgyia pseudotsugata*) Sex Pheromone, and (Z)-Non-6-en-2one, the Immediate Precursor for the Synthesis of Brevicomin, the Sex Attractant of the Western Pine Beetle *Dentroctonus brevicomis*

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Convenient syntheses of (Z)-heneicos-6-en-11-one and (Z)-non-6-en-2-one were achieved from (Z)-1-nitrodec-4-ene and (Z)-1-nitrohept-4-ene. Solvent-free nitroaldol reaction of (Z)-1-nitroalkenes **1** with the aldehydes **2** on Amberlyst A-21, followed by *in situ* oxidation, gave the α -nitro ketones **3**. Denitration *via* p-tolylsulphonylhydrazones and removal of the protecting group gave the title compounds **6a** and **6b** in 60 and 53% overall yield.

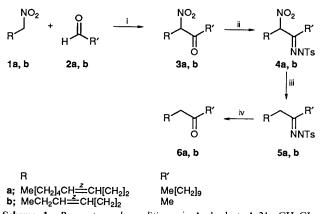
Aliphatic nitro compounds can be considered as versatile building blocks and intermediates in organic synthesis.^{1–7} Recently we have reviewed ⁸ the use of functionalized aliphatic nitro compounds in assembling carbon atoms, without the problems associated with the utilization of organometallic species. The denitration reaction is the key step in this procedure and makes the nitro alkanes useful and convenient reagents for alkyl anion synthons.

In exploring the application of functionalized nitro alkanes, we were attracted by the importance of two (Z)- δ - ϵ -alkenones, (Z)-heneicos-6-en-11-one **6a** and (Z)-non-6-en-2-one **6b**. (Z)-Heneicos-6-en-11-one **6a**, isolated ⁹ in 1975, is the sex pheromone of the Douglas Fir Tussock moth (*Orgyia pseudotsugata*). In contrast with other lepidopterous pheromones, which are unsaturated C₁₂-C₁₄ primary alcohols or acetates, this compound was found to be a C₂₁ (Z)- δ , ϵ -unsaturated ketone. The Douglas Fir Tussock moth is a severe defoliator of fir forests; consequently, considerable interest attends the synthesis of this pheromone. Although a number of syntheses have been reported, ¹⁰⁻¹² these procedures often exhibit some disadvantages such as low yields and the use of organometallic species and/or very low temperatures.

(Z)-Non-6-en-2-one **6b** is an important (Z)- $\delta_{,\varepsilon}$ -alkenone in which the thermal ¹³ or acid-calalysed ¹⁴ intramolecular opening of its epoxide **7** proceeds by carbonyl epoxide rearrangement in a stereoselective manner to yield *exo*-7-ethyl-5-methyl-6,8dioxabicyclo[3.2.1]octane **8** (brevicomin) (see Scheme 2) which has been identified as the principal component of the pheromone of the female western pine beetle, *Dentroctonus brevicomin*, which bores into ponderosa pine.¹⁵

We now report the syntheses of (Z)-heneicos-6-en-11-one **6a** and (Z)-non-6-en-2-one **6b**, starting from (Z)-1-nitrodec-4-ene **1a** and (Z)-1-nitrohept-4-ene **1b** (see Scheme 1). The nitro alkene **1a** can be easily obtained in good yield from commercial (Z)-dec-4-en-1-ol by conversion into the corresponding bromide and successive substitution with sodium nitrite in dimethylformamide (DMF), following the same procedure, previously reported by us,¹⁶ for the preparation of (Z)-1-nitrohept-4-ene **1b**.

Nitroaldol reaction of (Z)-1-nitro alkenes 1 with aldehydes 2 on Amberlyst A-21, in the absence of solvent, followed by oxidation of the resulting nitro alcohols with potassium dichromate in the presence of tetrabutylammonium hydrogen sulphate as phase-transfer catalyst,¹⁷ afforded the α -nitro ketones 3 in 70–78% yield. The conversion of compounds 3 into the corresponding (*p*-tolylsulphonyl)hydrazones 4 was performed in 90–94% yield. Treatment of compounds 4 in



Scheme 1 Reagents and conditions: i, Amberlyst A-21, CH₂CL₂, K₂Cr₂O₇ (70–78%); ii, TsNHNH₂–MeOH (90–94%); iii, LiAlH₄– THF, 0 °C (86–90%); iv, Amberlyst A-15, aq. acetone (93–95%)

tetrahydrofuran (THF) with lithium aluminium hydride¹⁸ at 0–10 °C produced the denitrated ketone (*p*-tolylsulphonyl)hydrazones **5** in 86–90% yield. Subsequent deprotection of compounds **5** carried out in acetone–water with Amberylst A-15 as catalyst¹⁹ gave (*Z*)-heneicos-6-en-11-one **6a** and (*Z*)-non-6-en-2-one **6b** in 95 and 93% yield, respectively. ¹³C NMR analyses indicated >99% isomeric purity.

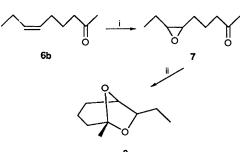
Epoxidation of (Z)-non-6-en-2-one **6b** with *m*-chloroperbenzoic acid afforded ¹⁰ the corresponding epoxy ketone **7** in quantitative yield, which with perchloric acid provided racemic *exo*-brevicomin **8** in 87% yield.

(Z)-Heneicos-6-en-11-one **6a** was obtained in 60% overall yield from (Z)-1-nitrodec-4-ene **1a**, while brevicomin **8** was obtained in 46% overall yield from (Z)-1-nitrohept-4-ene **1b**.

This procedure represents a very convenient and efficient synthesis of the target molecules which can be obtained in high yield and isomeric purity. In addition, only simple procedures and inexpensive chemicals are required.

Experimental

General Methods.—M.p.s were determined with a Büchi apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer 257 spectrophotometer. All 13 C and 1 H NMR spectra were recorded, in CDCl₃ as solvent, at 75 and 300 MHz respectively on a Varian VXR 300. Chemical shifts were recorded relative to internal SiMe₄, and J-values are given in Hz. Mass spectra were determined on a Hewlett-Packard



Scheme 2 Reagents: i, MCPBA (100%); ii, HClO₄ (85%)

GC/MS 5988A. The liquid products were monitored by GLC, performed on a Carlo Erba Fractovap 4160 using a capillary column of Duran glass (0.32 mm \times 25 m), stationary phase OV1 (film thickness 0.4–0.45 nm). Elemental analyses were performed using an Analyzer Model 185 from Hewlett-Packard. (Z)-Dec-4-en-1-ol was purchased from Alfa products.

(Z)-1-Nitrodec-4-ene **1a**.—To a mechanically stirred solution of (Z)-dec-4-ene-1-ol (10.92 g, 0.07 mol) and pyridine (2.66 cm³, 0.0282 mol), cooled in an ice–water-bath, was added, dropwise, phosphorus tribromide (1.8 cm³, 0.0234 mol) during 20 min. The mixture was stirred at room temperature for 2 h, water (25 cm³) was added and the product was extracted with diethyl ether (3×30 cm³). The organic layer was washed consecutively with HCl (2 mol dm⁻³; 15 cm³), sodium hydroxide (2 mol dm⁻³; 15 cm³), and finally with water (20 cm³). The ethered layer was dried (MgSO₄), then evaporated, and the residue was distilled under reduced pressure to give (Z)-1-bromodec-4-ene (10.57 g, 69%), b.p. 114 °C (0.6 mmHg).

The obtained bromide (4.8 g, 0.0219 mol) was added to a stirred solution of sodium nitrite (2.74 g, 0.0416 cm³) in DMF (50 cm³). The solution was stirred for 6 h, then quenched with cold water (80 cm³), and the mixture was extracted with diethyl ether (3 × 30 cm³). The combined extract was dried (MgSO₄), filtered through a bed of Florisil and evaporated at reduced pressure, and the residue was purified by column chromatography with hexane–ethyl acetate (90:10 v/v) to give (Z)-1-*nitrodec-4-ene* **1a** (2.55 g, 63%), b.p. 140 °C (0.03 mmHg) (Kugelrohr) (Found: C, 65.0; H, 10.5; N, 7.3. C₁₀H₁₉NO₂ requires C, 64.83; H, 10.34; N, 7.56%); $\delta_{\rm H}$ 0.88 (3 H, t, J 7.5), 1.18–1.41 (6 H, m), 1.93–2.22 (6 H, m), 4.37 (2 H, t, J 7.5), 5.23–5.38 (1 H, m) and 5.42–5.55 (1 H, m); v_{max}(film)/cm⁻¹ 1555.

x-Nitro Ketones 3a, b.—A 100 cm³, two-necked flask equipped with a mechanical stirrer was charged with a nitro compound 1 (0.01 mol) and cooled in an ice-water-bath. An aldehyde 2 (0.01 mol) was added and the mixture was stirred for 5 min. Amberlyst A-21 (3 g) was then added and the mixture was stirred for 7 h at room temperature before being extracted with dichloromethane $(3 \times 15 \text{ cm}^3)$. The filtered extract was poured into a 250 cm³, three-necked flask equipped with a mechanical stirrer. Tetrabutylammonium hydrogen sulphate (0.35 g, 0.001 mol) was added and the mixture was cooled to -10 °C. 30% Sulphuric acid (20 cm³) and potassium dichromate (3.9 g, 0.0132 mol) were added simultaneously and the mixture was stirred for 2 h at -10 °C. After this time 10% aq. iron(II) sulphate (20 cm³) was added and the layers were separated. The organic phase was dried $(MgSO_4)$ and passed through a bed of Florisil. The solvent was removed under reduced pressure to afford the crude nitro ketone 3a or 3b, which was used without further purification.

(Z)-10-*Nitroheneicos*-6-*en*-11-*one* **3a** (2.75 g, 78%); oil (Found: C, 71.6; H, 11.4; N, 4.1. $C_{21}H_{39}NO_3$ requires C, 71.34; H, 11.12; N, 3.96%); δ_H 0.82–0.92 (6 H, m), 1.18–1.65 (22 H, m), 1.9–2.19 (6 H, m), 2.42–2.65 (2 H, m), 5.1–5.18 (1 H, m), 5.21–

5.35 (1 H, m) and 5.40–5.57 (1 H, m); $v_{max}(film)/cm^{-1}$ 1730 and 1552.

(Z)-3-*Nitronon*-6-*en*-2-*one* **3b** (1.3 g, 70%); b.p. 105 °C (0.5 mmHg) (Kugelrohr) (Found: C, 58.5; H, 8.3; N, 7.3. C₉H₁₅NO₃ requires C, 58.36; H, 8.16; N, 7.56%); $\delta_{\rm H}$ 0.93 (3 H, t, *J* 7.3), 1.9–2.2 (6 H, m), 2.28 (3 H, s), 5.15 (1 H, m) and 5.18–5.60 (2 H, m); $v_{\rm max}$ (film)/cm⁻¹ 1735 and 1550.

 α -Nitro Ketone p-Tolylsulphonylhydrazones **4a**, **b**.—p-Tolylsulphonylhydrazine (1.4 g, 7.5 mmol) was added to a solution of an α -nitro ketone **3** (7-mmol) in methanol (6 cm³). The mixture was left for 12 h, then water was added to obtain, as a solid, the corresponding pure p-tolylsulphonylhydrazone **4**.

(Z)-10-*Nitroheneicos*-6-*en*-11-*one* p-*tolylsulphonylhydrazone* **4a** (3.28 g, 90%); m.p. 58–60 °C (from aq. MeOH) (Found: C, 64.7; H, 9.2; N, 8.3; S, 6.0. $C_{28}H_{47}N_3O_4S$ requires C, 64.46; H, 9.08; N, 8.06; S, 6.13%); δ_H 0.88 (6 H, t, *J* 7.5), 1.15–1.42 (24 H, m), 1.82–2.30 (8 H, m), 2.43 (3 H, s), 4.97–5.08 (1 H, m), 5.18–5.32 (1 H, m), 7.25 (s, 1 H) and 7.57 (4 H, AA'BB' pattern, *J* 8.0); ν_{max} (K Br)/cm⁻¹ 3220, 1610, 1555, 1335 and 1165.

(Z)-3-Nitronon-6-en-2-one p-tolylsulphonylhydrazone **4b** (2.32 g, 94%); m.p. 91–92 °C (from aq. MeOH) (Found: C, 54.55; H, 6.8; N, 12.0; S, 9.2. $C_{16}H_{23}N_3O_4S$ requires C, 54.38; H, 6.56; N, 11.89; S, 9.05%); δ_H 0.95 (3 H, t, J 7.5), 1.83 (3 H, s), 1.86–2.3 (6 H, m), 2.42 (3 H, s), 4.98–5.08 (1 H, m), 5.12–5.5 (2 H, m), 7.25 (s, 1 H) and 7.57 (4 H, AA'BB' pattern, J 8.0); ν_{max} (KBr)/cm⁻¹ 3210, 1540, 1330 and 1165.

Denitration of α -Nitro Ketone p-Tolylsulphonylhydrazones to give Compounds **5a**, **b**.—A solution of a nitro compound **4** (5 mmol) in dry THF (30 cm³) was added dropwise to a cooled (0 °C) mixture of lithium aluminium hydride (0.57 g, 15 mmol) in dry THF (40 cm³) under nitrogen. The mixture was stirred for 1.5 h, treated carefully with cold water, acidified with HCl (2 mol dm⁻³), and extracted with Et₂O (3 × 30 cm³). The combined ethereal layers were dried (MgSO₄), passed through a bed of Florisil and evaporated under reduced pressure to afford the tosylhydrazone **5a** or **5b**, pure by analytical data.

(Z)-Heneicos-6-en-11-one p-tolylsulphonylhydrazone **5a** (2.14 g, 90%); oil (Found: C, 70.3; H, 10.0; N, 5.6; S, 6.5. $C_{28}H_{48}N_2O_2S$ requires C, 70.55; H, 10.15; N, 5.88; S, 6.71%); δ_H 0.89 (6 H, t, J 7.0), 1.09–2.2 (32 H, m), 2.42 (3 H, s), 5.2–5.5 (2 H, m), 7.25 (s, 1 H) and 7.57 (4 H, AA'BB' pattern, J 8.0); v_{max} (KBr)/cm⁻¹ 3210, 1600, 1335 and 1165.

(Z)-*Non-6-en-2-one* p-*tolylsulphonylhydrazone* **5b** (1.34 g, 86%); m.p. 70–71 °C (from aq. MeOH) (Found: C, 62.6; H, 8.0; N, 8.9; S, 10.15. $C_{16}H_{24}N_2O_2S$ requires C, 62.31; H, 7.85; N, 9.09; S, 10.37%); δ_H 0.93 (3 H, t, J 7.5), 1.4–2.21 (8 H, m), 1.75 (3 H, s), 2.4 (3 H, s), 5.18–5.48 (2 H, m), 7.25 (s, 1 H) and 7.57 (4 H, AA'BB' pattern, J 8.0); ν_{max} (KBr)/cm⁻¹ 3215, 1163 and 1135.

Regeneration of Carbonyl Compounds **6a**, **b** from Tosylhydrazones **5a**, **b**.—A 100 cm³ flask, equipped with reflux condenser and magnetic stirrer, was charged with a tosylhydrazone **5** (2.5 mmol), acetone-water (10:1; 20 cm³) and Amberlyst A-15 (1 g). The mixture was stirred at 80 °C for 5 h. The acetone was removed by distillation. Extraction with pentane (3×10 cm³), filtration and distillation gave the pure ketone **6**.

(*Z*)-Heneicos-6-en-11-one **6a** (0.731 g, 95%); b.p. 240 °C (0.7 mmHg) (Kugelrohr) [lit.,²⁰ 161–162 °C (0.05 mmHg)] (Found: C, 81.9; H, 13.3. Calc. for C₂₁H₄₀O: C, 81.75; H, 13.07%); $\delta_{\rm H}$ 0.88 (6 H, t, *J* 7.5), 1.1–1.45 (22 H, m), 1.5–1.68 (2 H, m, *J* 7.2), 1.91–2.11 (4 H, m), 2.32–2.47 (4 H, m) and 5.25–5.48 (2 H, m); $\delta_{\rm c}$ 14.081, 14.120, 22.588, 22.69, 23.751, 23.902, 26.579, 27.214, 29.293, 29.322, 29.437, 29.494, 29,58, 31.527, 31.903, 42.091, 42.89, 128.64, 130.99 and 211.17; *m/z* 380 (M⁺, 2%), 251 (7), 237

(12), 167 (16), 169 (44), 124 (85), 82 (100) and 55 (61); $v_{max}(film)/cm^{-1}$ 1710.

(Z)-Non-6-en-2-one **6b** (0.325 g, 93%); b.p. 150 °C (45 mmHg) (Kugelrohr) [lit., ^{14c} 94–96 °C (20 mmHg)] (Found: C, 77.3; H, 11.3. Calc. for C₉H₁₆O: C, 77.09; H, 11.50%); $\delta_{\rm H}$ 0.95 (3 H, t, J 7.4), 1.55–1.70 (2 H, m), 1.92–2.08 (4 H, m), 2.12 (3 H, s), 2.37–2.45 (2 H, m) and 5.2–5.5 (2 H, m); $\delta_{\rm C}$ 23.578, 31.8455, 42.962, 128.11 and 209.169; m/z 140 (M⁺, 31%), 125 (37), 111 (57), 97 (43), 85 (34), 83 (43), 82 (93), 81 (56), 71 (50), 68 (35), 67 (100), 58 (37) and 55 (52); $\nu_{\rm max}({\rm film})/{\rm cm}^{-1}$ 1708.

(\pm)-exo-Brevicomin 8.---(\pm)-exo-Brevicomin 8 was obtained in 85% yield from compound 6b via its epoxidation with mchloroperbenzoic acid to give 7, then subsequent cyclization using perchloric acid, by the known method.¹⁰ B.p. 110 °C (20 mmHg) (Kugelrohr) [lit.,^{14c} 86–88 °C (50 mmHg)].

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