

Synthesis of (*Z*)-7-hexadecen-1-yl acetate and (*Z*)-7-hexadecenal

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MS received 6 August 1993; revised 30 November 1993

Abstract. Alkylation of 1-bromo-6-tetrahydropyranloxyhexane with the dianion of 4-pentyn-1-ol yielded 11-tetrahydropyranloxy-4-undecyn-1-ol (4) which upon catalytic hydrogenation and subsequent mesylation afforded (6). Li_2CuCl_4 catalysed the coupling of (6) with pentylmagnesium bromide gave 1-(tetrahydropyranloxy)-7(*Z*)-hexadecene (8) which on depyranylation resulted in (*Z*)-7-hexadecen-1-ol (9). The alcohol (9) was then converted into the corresponding target compounds, (*Z*)-7-hexadecen-1-yl acetate (1) and (*Z*)-7-hexadecenal (2).

Keywords. Pheromones; (*Z*)-7-hexadecen-1-yl acetate; (*Z*)-7-hexadecenal.

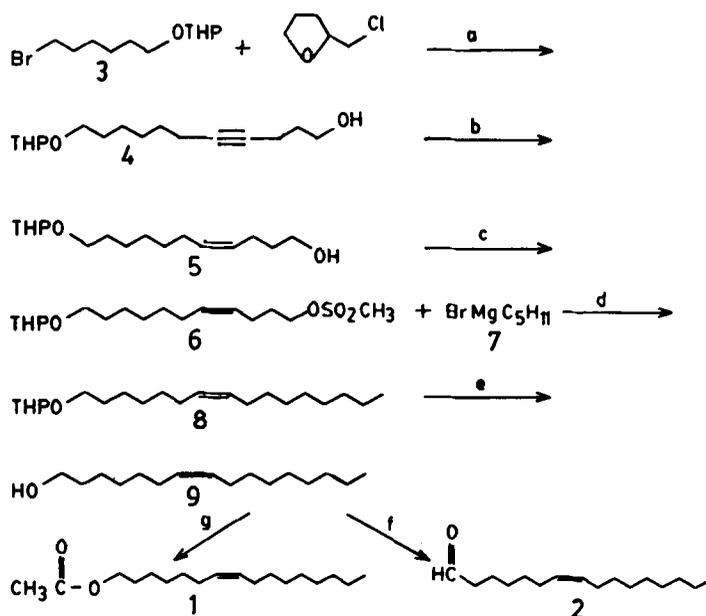
1. Introduction

Jacobson *et al* (1969) discovered and characterized (*Z*)-7-hexadecen-1-yl acetate (1) as the first sex attractant by an empirical approach. The molecule is an outstanding attractant for male pink bollworm moths, *Pectinophora gossypiella* (Jacobson *et al* 1969), a destructive pest of cotton. This has also been identified as the essential component of the sex pheromone of adult females of the dark-sided cutworm *Eoxoa messoria* (Byers and Struble 1987). (*Z*)-7-hexadecenal (2) is the major sex pheromone component of the old world bollworm moth, *Heliothis armigera* (Wang *et al* 1987) and a trail pheromone of the Argentine ant, *Iridomyrmex humilis* (Mayr) (Brown *et al* 1986). The literature (Yu *et al* 1987; Subramanian and Sharma 1988) records the synthesis of 1 and 2. We herein present a practical approach for the synthesis of 1 and 2 from a common precursor using easily available and inexpensive starting materials (scheme 1).

2. Result and discussion

The alkylation of (3) was carried out as reported in the literature (Yadav *et al* 1988) with the dianion of 4-pentyn-1-ol prepared *in situ* from tetrahydrofurfuryl chloride and lithium amide in liquid ammonia to give (4) in 70% yield, which was subjected to partial catalytic hydrogenation over Lindlar's (Lindlar and Dubws 1966) catalyst in dry hexane-ethanol (2:1) to yield the reduced alcohol (5). The structure of (5) was confirmed from the peak at 725 cm^{-1} in its IR spectrum and a multiplet at δ 5.4 in its PMR spectrum. The hydroxyl function in (5) was converted into the corresponding

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REAGENTS: a: Li, Liq. NH_3 , $\text{Fe}(\text{NO}_3)_3$, dry THF

e: PTS, Methanol

b: Lindlar's catalyst, H_2 , dry hexane-ethanol

f: PCC, dry CH_2Cl_2 , NaOAc

c: $\text{CH}_3\text{SO}_2\text{Cl}$, TEA, dry CH_2Cl_2

g: $(\text{CH}_3\text{CO})_2\text{O}$, Pyridine, DMAP

d: Li_2CuCl_4 , N_2 atm, -10°C , dry THF

Scheme 1.

mesylate (6) with methanesulphonyl chloride (Crossland and Serris 1970), and triethyl amine which was coupled with Grignard reagent (7) in the presence of Li_2CuCl_4 (Schlosser and Fouquet 1974) at -10° to give (8). The structure of 8 was confirmed from its IR and PMR spectra. Depyranylation (Grieco *et al* 1977) of coupled product (8) was effected using PTS in methanol to furnish alcohol (9). The presence of an IR signal at 3400 cm^{-1} confirmed the presence of the hydroxyl moiety. Treatment of alcohol (9) with PCC (Corey and Suggs 1975) in dry dichloromethane generated the title compound (2). Acetylation (Pattenden 1968) of enol (9) with acetic anhydride in dry pyridine using DMAP as catalyst afforded the desired compound 1.

3. Experimental

Boiling points are uncorrected. The petroleum ether used has the boiling point range $60-80^\circ$. IR spectra were recorded on a Perkin-Elmer 1430 spectrophotometer (wavenumber in cm^{-1}), and the PMR spectra in CCl_4 on a Varian EM-390 (90 MHz) spectrometer using tetramethylsilane as the internal standard. Chemical shifts are given in ppm (δ scale). Silica gel (Acme, 60-80 mesh) was used for column chromatography. Unless stated otherwise, all organic extracts were dried over anhydrous sodium sulphate.

3.1 [1]-(Tetrahydropyranyloxy)-undec-(4Z)-en-1-ol(5)

The alcohol 4 (8.0 g, 29 mmol) was subjected to partial catalytic hydrogenation over Lindlar's catalyst (200 mg) and quinoline (2 drops) in dry hexane-ethanol (2:1). A slight positive pressure was applied to the bottle and it was stirred mechanically. After 1 equivalent of hydrogen was taken up, the catalyst was filtered off. The solution was washed successively with dilute acetic acid and water, and then dried. Evaporation of the solvent furnished the reduced alcohol 5 (7.41 g, 92%). IR spectrum (neat): 3400, 1650, 925, 875, 810, 725 cm^{-1} . PMR spectrum: 5.4 δ (m, 2H, 2 \times H-C=C), 4.6 δ (s, 1H, H-2 of tetrahydropyranyloxy group), 3.5 δ (m, 7H, 3 \times OCH₂, OH), 2.1 δ (m, 4H, CH₂-C=C); 1.4 δ (m, 16H, 8 \times CH₂).

3.2 1-(Tetrahydropyranyloxy)-7(Z)-hexadecene (8)

To the well-cooled solution of 5 (5.0 g, 18 mmole), and triethyl amine (3.38 ml, 27 mmole) in dry CH₂Cl₂ (50 ml), methane sulphonyl chloride (1.71 ml, 22 mmol) was added slowly, over a period of 10 min. The reaction mixture was stirred for 2 h and the contents extracted with dichloromethane, washed successively with 5% HCl solution, 5% sodium hydrogen carbonate solution and water, and then dried over fused calcium chloride. Solvent evaporation yielded the mesylate 6 (5.44 g, 72%) which was used as such for the next reaction.

To the ice-cooled, stirred solution of the Grignard reagent (7), prepared from dry magnesium turnings (0.331 g, 13 mmol) and 1-bromopentane (2.03 g, 13 mmol) in anhydrous THF (15 ml) in an inert atmosphere, a solution of mesylate (6) (4.0 g, 11 mmole) in dry THF (20 ml) was added dropwise over 15-20 min. After stirring for 45 mins, Li₂CuCl₄ (2 ml) was added as a catalyst. The solution was cooled at -10° for another 3 h with stirring and the contents were left overnight at room temperature. The reaction mixture was decomposed with a saturated solution of ammonium chloride and the organic layer was separated. The aqueous phase was extracted with ether and the combined organic extracts dried. Solvent removal and purification by column chromatography over silica gel afforded 8 (2.23 g, 60%). IR spectrum (neat): 2950, 1650, 925, 875, 825, 730 cm^{-1} . PMR: 5.3 δ (m, 2H, 2 \times H-C=C); 4.5 δ (s, 1H, H-2 of tetrahydropyranyloxy group), 3.3-3.8 δ (m, 4H, 2 \times OCH₂); 2.1 δ (m, 4H, 2 \times CH₂-CH=C); 1.2-1.7 δ (m, 26H, 13 \times CH₂), 0.9 δ (t, 3H, CH₃).

3.3 (Z)-7-hexadecen-1-ol (9)

To 8 (2.23 g, 6 mmol) in distilled methanol (25 ml) was added *p*-toluenesulphonic acid (200 mg) and the mixture was stirred at room temperature for 4 h. The completion of the reaction was checked by tlc. Methanol was removed under reduced pressure, and the residue extracted with diethyl ether and washed with 5% aqueous NaHCO₃ solution, water and brine, and then dried. Evaporation of the solvent followed by chromatographic purification yielded 9 (1.28 g, 78%). IR spectrum (neat): 3400, 1650, 1050, 725 cm^{-1} . PMR spectrum: 5.4 δ (m, 2H, 2 \times H-C=C); 3.5 δ (m, 3H, -OCH₂, OH); 2.1 δ (m, 4H, CH₂-C=C); 1.4 δ (m, 20H, 10 \times CH₂), 3.9 δ (t, 3H, *J* = 6.9 Hz, CH₃).

3.4 (Z)-7-hexadecen-1-yl acetate (1)

The alcohol 9 (1 g, 4 mmol) was taken in pyridine (5 ml, 63 mmol) and a catalytic

amount of DMAP was added, the mixture was cooled in an ice bath, acetic anhydride (1.506 g, 14 mmol) was added and the whole stirred at room temperature for 2 h. The reaction was quenched with ice and extracted with ethyl acetate, washed with 5% HCl, 5% aq. NaHCO₃, water and brine, and then dried. Concentration of the solvent afforded (**1**, 1.05 g) in almost quantitative yield: IR spectrum (neat): 2960, 1740, 1650, 1050, 720 cm⁻¹; PMR spectrum: 5.4 (*m*, 2H, 2 × H-C=C), 4.0 (*t*, 2H, -OCH₂); 2.1 (*m*, 4H, CH₂-CH=C); 2.0 (*m*, 3H, CH₃CO), 1.2-1.5 (*m*, 20H, 10 × CH₂); 0.9 (*t*, 3H, *J* = 6.9 Hz, CH₃). ¹³C NMR: 170.2, 130.0, 129.7, 64.5, 31.9, 29.9, 29.5, 29.0, 27.4, 26.0, 22.8, 20.8, 13.9δ (Found: C, 76, H, 12.0%. C₁₈H₃₄O₂ requires C, 76.5, H, 12.1%).

3.5 (Z)-7-hexadecenal (**2**)

The alcohol **1** (**2**, 8 mmol) was oxidised to the aldehyde (**2**) using PCC (2.70 g, 12 mmol) and sodium acetate (a pinch) in dry dichloromethane (20 ml). The reaction was followed through tlc and anhydrous ether was added after the completion of the reaction. The supernatant layer was decanted from the black gummy residue. The organic solution was passed through a short column of alumina, the solvent was removed and the residue chromatographed over a neutral alumina column for further purification to procure pure **2** (1.34 g, 68%). IR (neat): 2945, 1750, 1650, 1465, 720 cm⁻¹. PMR spectrum: 9.7δ (*s*, 1H, CHO); 5.3δ (*m*, 2H, 2 × H-C=C); 2.1-2.5δ (*m*, 6H) 1.4δ (*m*, 18H, 9 × CH₂); 0.8δ (*t*, 3H, *J* = 6.9 Hz, CH₃). ¹³C NMR: 199.3, 129.5, 129.0, 43.2, 31.70, 29.60, 29.30, 29.1, 28.6, 27.0, 26.8, 22.5, 21.6, 13.7δ (Found: C, 79.6, H, 12.5%. C₁₆H₃₀O requires C, 80.6, H, 12.6%).

Acknowledgement

Financial support from the Council of Scientific and Industrial Research, New Delhi is gratefully acknowledged.

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