© 1988 The Chemical Society of Japan NOTES Bull. Chem. Soc. Jpn., 61, 3368—3370 (1988) [Vol. 61, No. 9

Simple Synthesis of (*Z*)-12-Nonadecen-9-one, (*Z*)-13-Icosen-10-one, the Sex Pheromone of Peach Fruit Moth, and (*Z*)-5-Undecen-2-one, a Biologically Active Molecule from the Pedal Gland of the Bontebok1)

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(Received March 26, 1988)

Synopsis. A simple and convenient synthesis of (*Z*)-12-nonadecen-9-one, (*Z*)-13-icosen-10-one, the sex pheromone of the peach fruit moth, and (*Z*)-5-undecen-2-one, the pheromone from the pedal gland of the bontebok, is described. These pheromones were readily synthesized using successive alkylation of acetone dimethylhydrazone in one-pot.

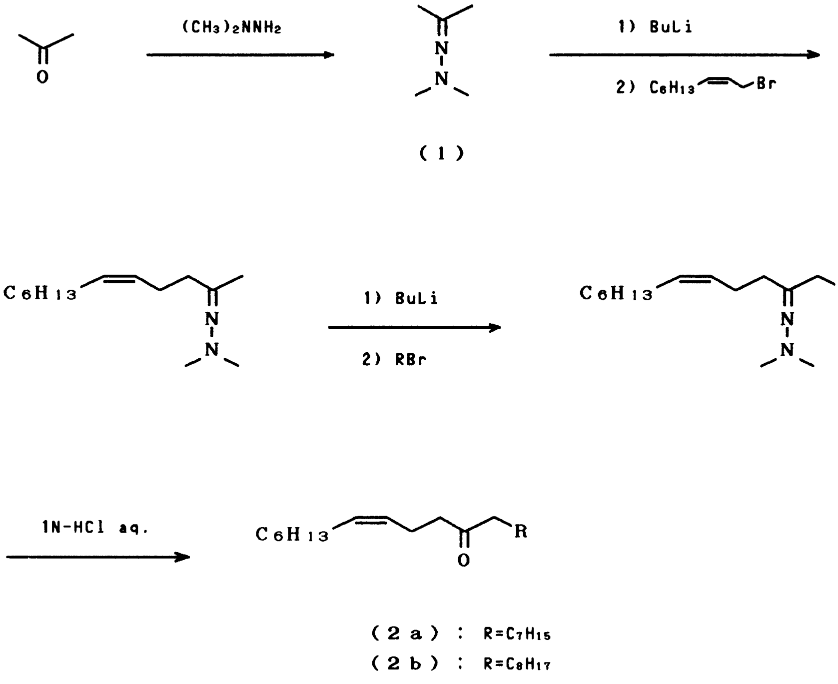
(*Z*)-12-Nonadecen-9-one (**2a**) and (*Z*)-13-icosen-10-one (**2b**) are the sex pheromones of the Japanese peach fruit moth (*Carposina niponensis* Walsingham), and have been isolated and identified by Tamaki et al. in 1977.2) Since these pheromones have attracted practical interest, several syntheses of these compounds have been reported.2,3)

On the other hand, we have previously reported a facile synthetic method of unsymmetrical ketones using acetone dimethylhydrazone (**1**) and the application of this method to the synthesis of jasmones.4)

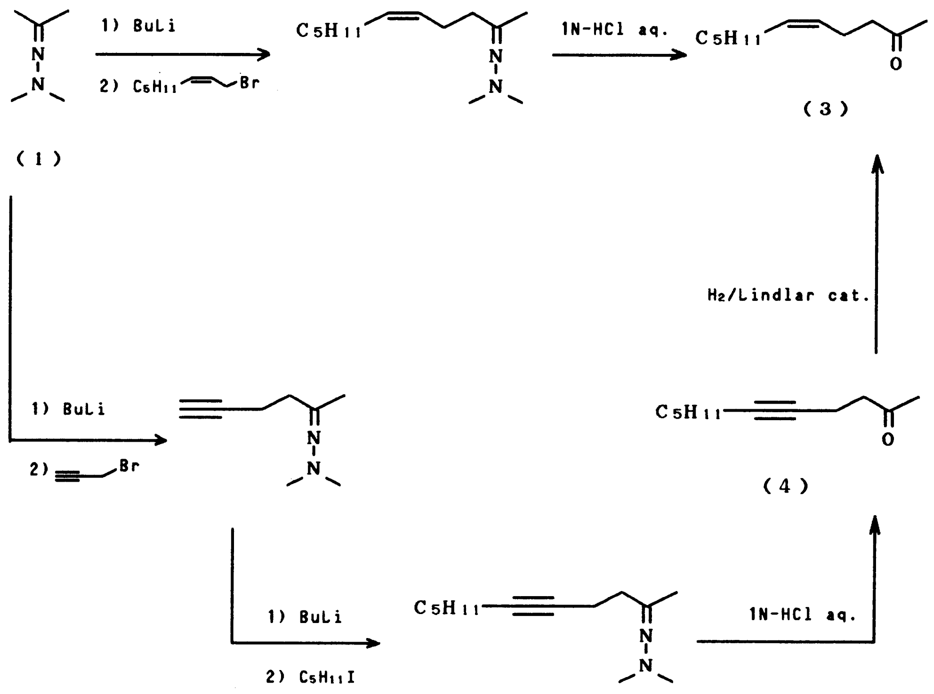
In this paper, we wish to report on a simple and convenient synthesis of the pheromones **2a** and **2b** via acetone dimethylhydrazone (**1**). Using this method, (*Z*)-5-undecen-2-one (**3**), which is known as a principal volatile component contained in the pedal gland exudate of the bontebok, *Damaliscus dorcas dorcas*,5) could also be synthesized.

The synthetic route of (*Z*)-12-nonadecen-9-one (**2a**) and (*Z*)-13-icosen-10-one (**2b**) from acetone as a starting material is described in Scheme 1. Acetone dimethylhydrazone (**1**), easily prepared from acetone and *N*,*N*-dimethylhydrazine in 80% yield, was allowed to react with 1 equiv. of butyllithium in tetrahydrofuran (THF) at −5 °C and then with (*Z*)-1-bromo-2-nonene to give the α-monoalkylated hydrazone. The hydrazone was then alkylated regioselectively at the α′ methyl carbon using 1 equiv. of butyllithium and 1-bromoheptane to afford the corresponding α,α′-dialkylated hydrazone, which was readily converted to the desired pheromone **2a** by hydrolysis under an acidic condition. These reactions were carried out successively in one-pot and the overall yield of the product **2a** was 70% from **1**. Similarly, after successive alkylation of the hydrazone **1** and hydrolysis of the product, (*Z*)-13-icosen-10-one (**2b**) was obtained in 62% overall yield from **1**.

The synthesis of (*Z*)-5-undecen-2-one (**3**) was carried out as follows. Acetone dimethylhydrazone (**1**) was treated successively with 1 equiv. of butyllithium and (*Z*)-1-bromo-2-octene, and the product was hydrolyzed to give the desired compound **3** in 98% yield (Scheme 2).6) The alternative synthetic route is also shown in Scheme 2, although the yield was low. Treatment of the hydrazone (**1**) with 1 equiv. of butyllithium at −5 °C, followed by the addition of 3-bromopropyne,



Scheme 1.



Scheme 2.

gave a monoalkylated hydrazone. To the hydrazone, without isolation, 1 equiv. of butyllithium was again added, followed by 1-iodopentane. The product was readily hydrolyzed by hydrochloric acid to afford 5-undecyn-2-one (**4**) in 14% yield from **1**. By partial hydrogenation of **4** over Lindlar catalyst, the expected pheromone **3** was obtained in 36% yield.

The corresponding (*E*)-isomers of **2a**, **2b**, and **3** were not detected by GC.

Experimental

The IR spectra were recorded on a Hitachi 260-10 Infrared Spectrophotometer. The NMR spectra were measured on a Hitachi R-600 FT-NMR Spectrometer at 60 MHz, using tetramethylsilane (δ=0.00) as an internal standard, and chemical shifts are given in ppm. The mass spectra (MS) were determined on a Hitachi RM-50 GC-MS spectrometer. The analytical gas chromatography was carried out on a Yanagimoto G-8 gas chromatograph with a column of 10% Silicone gum SE-30 on Chromosorb, and the column chromatography was performed on Merck silica gel 60 (230—400 mesh). All the boiling points were uncorrected, and all the yields were isolated ones.

Materials. Tetrahydrofuran (THF) was dried over potassium–benzophenone under argon and distilled just before use. Benzene was also purified by distillation over sodium–benzophenone under argon, and stored over 4A Molecular Sieves. 3-Bromopropyne, 1-bromoheptane, 1-bromooctane, 1-iodopentane, acetone, *N,N*-dimethylhydrazine, and Lindlar catalyst were commercial products of the highest available purity, and were used without further purification. Butyllithium in hexane, also a commercial product, was titrated with *s*-butyl alcohol using 1,10-phenanthroline as an indicator just before use. (*Z*)-1-Bromo-2-octene was prepared by the hydrogenation of 2-octyn-1-ol[7] over Lindlar catalyst[8] followed by bromination. By the same procedure, (*Z*)-1-bromo-2-nonene was obtained from 2-nonyn-1-ol.[7]

Acetone Dimethylhydrazone (1). The hydrazone **1** was prepared by refluxing of acetone and *N,N*-dimethylhydrazine in 80% yield. IR (neat): 1660, 1170, 1090 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.93 (3H, s, CCH$_3$), 1.97 (3H, s, CCH$_3$), 2.04 (6H, s, N(CH$_3$)$_2$); MS *m/z* (%): 100 (M$^+$, 8), 44 (90), 42 (83), 28 (100).

(*Z*)-12-Nonadecen-9-one (2a). Butyllithium (3.0 mmol) was added via syringe at −5 °C with stirring under argon to a solution of acetone dimethylhydrazone (**1**) (0.30 g, 3.0 mmol) in THF (10 ml). After standing for 1 h, (*Z*)-1-bromo-2-nonene (0.61 g, 3.0 mmol) was added; the mixture was stirred for 20 h at room temperature. After cooling the mixture at −5 °C again, butyllithium (3.0 mmol) was added dropwise; 1 h later, 1-bromoheptane (0.47 ml, 3.0 mmol) was added, and the reaction mixture was stirred for 20 h at room temperature. After 1 mol dm^{-3} hydrochloric acid was added, the mixture was refluxed at 80 °C for 2 h, cooled to the room temperature, and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, filtered and concentrated. The residual liquid was distilled by Kugelrohr to give (*Z*)-12-nonadecen-9-one (**2a**) (0.59 g) in 70% yield, bp 210 °C/2 Torr (bath temp; Torr≈133.322 Pa). IR (neat): 2850, 1720, 1470 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.87 (6H, t, CH$_3$), 1.08—2.18 (20H, m, CH$_2$), 2.20—2.60 (8H, m, CH$_2$), 5.20—5.48 (2H, m, CH=CH); MS *m/z* (%): 280 (M$^+$, 6), 195 (7), 141 (100), 125 (15).

(*Z*)-13-Icosen-10-one (2b). In a manner similar to the above, (*Z*)-13-icosen-10-one (**2b**) was prepared by the successive alkylations of acetone dimethylhydrazone (**1**) using (*Z*)-1-bromo-2-nonene and 1-bromooctane and the hydrolysis in 62% yield. IR (neat): 2900, 1725, 1480 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.87 (6H, t, CH$_3$), 1.05—2.20 (22H, m, CH$_2$), 2.20—2.70 (8H, m, CH$_2$), 5.20—5.48 (2H, m, CH=CH) MS *m/z* (%): 294 (M$^+$, 10), 157 (100), 125 (22), 85 (18).

5-Undecyn-2-one (4). By the same procedure, using 3-bromopropyne and 1-iodopentane, successive alkylations of acetone dimethylhydrazone (**1**) and the hydrolysis were carried out. After the usual work up, column chromatography (hexane:ethyl acetate=9:1) gave 5-undecyn-2-one (**4**) in 14% yield. IR (neat): 1725 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.89

(3H, t, CH_3), 1.08—1.72 (6H, m, CH_2), 1.80—2.82 (6H, m, CH_2), 2.16 (3H, s, CH_3); MS m/z: 166 (M^+).

(*Z*)-5-Undecen-2-one (3). According to a manner similar to that described above, (*Z*)-5-undecyn-2-one (**3**) was obtained by the monoalkylation of acetone dimethylhydrazone (**1**) with (*Z*)-1-bromo-2-octene and the hydrolysis in 98% yield. On the other hand, the ketone **3** was also prepared by hydrogenation of 5-undecyn-2-one (**4**) over Lindlar catalyst[8] in 36% yield. IR (neat): 2930, 1735, 1360, 1160 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.90 (3H, t, CH_3), 1.06—1.70 (6H, m, CH_2), 2.14 (3H, s, CH_3), 1.80—2.75 (6H, m, CH_2), 5.20—5.50 (2H, m, CH=CH); MS m/z (%): 168 (M^+, 13), 109 (38), 81 (33), 43 (100).

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