報 文

Synthesis of *cis*-12-Nonadecen-9-one, *cis*-13-Icosen-10-one, the Pheromone of Peach Fruit Moth, and *cis*-5-Undecen-2-one, a Biologically Active Molecule from the Pedal Gland of the Bontebok

Tetsuo MIYAKOSHI

Department of Industrial Chemistry, Faculty of Engineering,
Meiji University (Higashimita, Tama-ku, Kawasaki)

A convenient synthesis of *cis*-12-nonadecen-9-one (**4a**), *cis*-13-icosen-10-one (**4b**), the pheromone of peach fruit moth, and *cis*-5-undecen-2-one (**4c**), the principal volatile component of the pedal gland exudate of the bontebok is described. (**4a**) was synthesized starting from 1-nitrononane (**1a**) and acrolein via three steps. The synthetic route is shown in **Scheme-1**.

(**4b**) was easily prepared starting from 1-nitrodecane (**1b**) in good yield.

Similarly, (**4c**) could be obtained by the Michael reaction of nitroethane (**1c**) with acrolein.

Scheme-1

1 Introduction

The sex pheromone emitted by the Japanese peach fruit moth (*Carposia niponensis* Walsingham), was identified as *cis*-12-nonadecen-9-one (**4a**), *cis*-13-icosen-10-one (**4b**) by Tamai and co-workers in 1977¹⁾. Since then, several methods for the synthesis of these pheromones have been reported^{1)~5)}.

cis-5-Undecen-2-one (**4c**) was isolated as the principal volatile component of the pedal gland exudate of the bontebok, *Damaliscus dorcas dorcas*⁶⁾. Since the above mentioned ketone (**4c**) has strong biological activity as a mammalian pheromone, various methods for its

synthesis have been reported^{7)~9)}.

However, an attempt to prepare these unsaturated ketones (**4a**)~(**4c**) by similar methods has not been reported. As an extension of our research on the synthesis of natural products using aliphatic nitro compounds, we report here a convenient synthesis of these pheromones by the Michael addition of nitroalkanes.

Aliphatic nitro compounds play important roles in the development of new synthetic methodology in organic synthesis^{10),11)}. We recently reported the Michael addition of nitroalkane to α, β -unsaturated ketones catalyzed by tertiary phosphine. This is convenient proce-

cedure for the preparation of γ -nitro ketones^{12)~14)}. In the present study, we demonstrate the synthetic applicability of this method, thus showing it to be a convenient synthesis of (**4 a**), (**4 b**), and (**4 c**) starting from readily available nitroalkanes (**1**) and acrolein.

2 Experimental

2.1 Analytical Apparatus

No correction was made for melting and boiling points. Melting points were taken on Yanagimoto micro melting point apparatus. The GLC analysis was carried out using a Hewlett Packard 5890 A research chromatograph (column 0.20 mm $\times$ 12.5 m, cross-linked methyl silicone). The IR spectra were recorded on a Shimadzu IR-27 G spectrophotometer. The ¹H-NMR spectra were recorded on a Varian EM-390 spectrometer at 90 MHz, using TMS (δ =0.00 ppm) as the internal standard; Abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and br=broad. Chemical shifts are given in ppm; spin-spin coupling constants *J* are given in Hz.

2.2 1-Nitrononane (**1 a**) and 1-nitrodecane (**1 b**)

1-Bromononane (20.7 g, 0.1 mol) was poured into a stirred mixture of 80 ml dimethyl sulfoxide (DMSO), 0.5 g of benzyltriethylammonium chloride as a catalyst, and 17.0 g of potassium nitrite (0.2 mol) contained in a 200 ml flask immersed in a water bath held at room temperature. Stirring was continued for 4 h. The reaction mixture was then poured into 200 ml of ice water and extracted with ethyl acetate.

The usual workup gave 1-nitrononane (**1 a**) (10.4 g, 60% yield) following distillation, bp 126°C/16 mmHg, IR (neat): 1545 cm⁻¹. ¹H-NMR(CCl₄): 0.97 (deformed t, 3 H, CH₃), 1.3~2.1 (m, 14 H, CH₂), 4.35 (t, *J*=6.8 Hz, 2 H, CH₂NO₂). Found: N, 8.15%. Calcd for C₉H₁₉O₂N: N, 8.09%.

1-Nitrodecane (**1 b**) was prepared from 1-bromodecane (22.1 g, 0.1 mol) and potassium nitrite (17.0 g, 0.2 mol) by a manner similar to that described above in a 62% yield, bp 136°C/16 mmHg (lit.¹⁵⁾ bp 107°C/2 mmHg).

2.3 1, 1-Ethylenedioxy-4-nitrododecane (**2 a**), 1, 1-ethylenedioxy-4-nitrotridecane (**2 b**), and 1, 1-ethylenedioxy-

4-nitropentane (**2 c**)

To a stirred solution of acrolein (2.8 g, 50 mmol) and 1-nitrononane (**1 a**) (43.3 g, 0.25 mol) in benzene (50 ml), tributylphosphine (40 mg, 0.2 mmol) dissolved in benzene (1 ml) was added with moderately strong stirring. Following this addition the temperature reached 45~50°C and the mixture was cooled. Stirring was continued for 20 min followed by the addition of a solution of *p*-toluenesulfonic acid monohydrate (200 mg, 1 mmol) in ethylene glycol (3.7 g, 60 mmol) with stirring for 10 min. The mixture was then refluxed for 5 h, and washed with solution of 5% sodium hydrogen carbonate and saturated sodium chloride.

The organic solution was concentrated to give 1, 1-ethylenedioxy-4-nitrododecane (**2 a**). (**2 a**) was purified by column chromatography over silica gel (60~80 mesh) with benzene-hexane (30:1) as the eluent, giving 9.6 g (70% yield) of pure (**2 a**) as a colorless liquid.

IR (neat): 1540, 1140 cm⁻¹. ¹H-NMR(CCl₄): 0.95 (deformed t, 3 H, CH₃), 1.3~2.1 (m, 18 H, CH₂), 3.8 (m, 4 H, CH₂), 4.4 (m, 1 H, CH), 4.80 (t, *J*=4.2 Hz, 1 H, CH). Found: C, 61.63%; H, 9.99%. Calcd for C₁₄H₂₇O₄N: C, 61.51; H, 9.96%.

1, 1-Ethylenedioxy-4-nitrotridecane (**2 b**) was obtained from acrolein (2.8 g, 50 mmol) and 1-nitrotridecane (**1 b**) (46.8 g, 0.25 mol) by the same procedure in a 70% yield. IR (neat): 1540, 1140 cm⁻¹. ¹H-NMR(CCl₄): 0.97 (deformed t, 3 H, CH₃), 1.3~2.1 (m, 20 H, CH₂), 3.8 (m, 4 H, CH₂), 4.4 (m, 1 H, CH), 4.80 (t, *J*=4.2 Hz, 1 H, CH). Found: C, 62.81; H, 10.47%. Calcd for C₁₅H₂₉O₄N: C, 62.68; H, 10.17%.

1, 1-Ethylenedioxy-4-nitropentane (**2 c**) was obtained from acrolein (2.8 g, 50 mmol) and nitroethane (18.8 g, 0.25 mol) in a manner similar to the above in a 72% yield, bp 95~97°C/2 mmHg. IR (neat): 1540, 1140 cm⁻¹. ¹H-NMR(CCl₄): 1.53 (d, *J*=6 Hz, 3 H, CH₃), 1.7~2.3 (m, 4 H, CH₂), 3.9 (m, 4 H, CH₂), 4.6 (m, 1 H, CH), 4.82 (t, *J*=4.2 Hz, 1 H, CH). Found: C, 47.85; H, 7.59%. Calcd for C₇H₁₃O₄N: C, 47.99; H, 7.48%.

2.4 4-Oxododecanal (**3 a**), 4-oxotridecanal (**3 b**), and 4-oxopentanal (**3 c**)

Potassium acetate (0.5 g, 5 mmol) was added

to a stirred solution of 1,1-ethylenedioxy-4-nitrododecane (**2 a**) (2.7 g, 10 mmol) in methanol (40 ml) at 25°C. The mixture was electrolyzed in a Beaker type cell at a constant current (0.18 A, 8 V) using platinum electrodes (1 cm²) for 4 F/mol. The methanol was then removed on a rotary evaporator and the residue added to 4% hydrochloric acid (100 ml). The mixture was stirred at 40~45°C for 5 h under nitrogen, cooled and extracted with ethyl acetate (3×30 ml).

The combined organic layers were washed with 5% sodium hydrogen carbonate (50 ml) and dried with sodium sulfate. The solvent was evaporated and the residue purified by column chromatography over silica gel (60~80 mesh) with benzene-hexane (9:1) as the eluent, to give 1.6 g (81% yield) of pure 4-oxopentanal (**3 a**) as white crystals, mp 74°C, IR (KBr): 2710, 1715, 1705 cm⁻¹. ¹H-NMR (CCl₄): 0.90 (deformed t, 3H, CH₃), 1.3~1.8 (m, 12H, CH₂), 2.38 (t, *J*=7 Hz, 2H, CH₂), 2.55 (br s, 4H, CH₂), 9.70 (s, 1H, CHO). Found: C, 72.78; H, 11.31%. Calcd for C₁₂H₂₂O₂: C, 72.68; H, 11.18%.

4-Oxotridecanal (**3 b**) was obtained from 1,1-ethylenedioxy-4-nitrotridecane (**2 b**) by the same procedure in an 85% yield, mp 67.0°C. IR (KBr): 2710, 1715, 1705 cm⁻¹. ¹H-NMR (CCl₄): 0.90 (deformed t, 3H, CH₃), 1.3~1.8 (m, 14H, CH₂), 2.38 (t, *J*=7 Hz, 2H, CH₂), 2.55 (br s, 4H, CH₂), 9.70 (s, 1H, CHO). Found: C, 73.71; H, 11.57%. Calcd for C₁₃H₂₄O₂: C, 73.53; H, 11.39%.

4-Oxopentanal (**3 c**) was synthesized from 1,1-ethylenedioxy-4-nitropentane (**2 c**) by a procedure similar to that described above in a 54% yield, bp 70°C/16 mmHg (lit.¹⁶) bp 64~65°C/11 mmHg). IR (neat): 2750, 1715, 1710 cm⁻¹. ¹H-NMR (CCl₄): 2.13 (s, 3H, CH₃), 2.63 (s, 4H, CH₂), 9.83 (s, 1H, CHO).

2.5 *cis*-12-Nonadecen-9-one (**4 a**), *cis*-13-icosen-10-one (**4 b**), and *cis*-5-undecen-2-one (**4 c**)

To a solution of heptyltriphenylphosphorane in benzene, prepared from heptyltriphenylphosphonium bromide (2.3 g, 5.2 mmol) and sodium amide (0.2 g, 5.3 mmol), was added solution of 4-oxododecanal (**3 a**) (1 g, 5.2 mmol) in benzene (70 ml) at room temperature with stirr-

ing. Stirring was continued at this temperature for 8 h followed by heating under reflux for 4 h. Benzene was evaporated under reduced pressure and hexane was poured onto the residue. The mixture was extracted with hexane and the extract washed with water and then dried over anhydrous sodium sulfate. The hexane was concentrated to give a crude product. This in turn was chromatographed over silica gel (60~80 mesh) with benzene-hexane (8:2) as the eluent to give a 0.87 g (60% yield) of *cis*-12-nonadecen-9-one (**4 a**) as a colorless liquid. IR (neat): 1710 cm⁻¹. ¹H-NMR (CCl₄): 0.90 (deformed t, 6H, CH₃), 1.1~1.7 (br s, 20H, CH₂), 1.9~2.15 (m, 2H, CH₂), 2.2~2.45 (m, 6H, CH₂), 5.1~5.4 (m, 2H, CH=CH). The product was identified by a comparison of the NMR spectrum with the one reported⁹.

cis-13-Icosen-10-one (**4 b**) was obtained in the same manner from 1,1-ethylenedioxy-4-nitrotridecane (**3 b**) in a 60% yield. IR (neat): 1710 cm⁻¹. ¹H-NMR (CCl₄): 0.90 (deformed t, 6H, CH₃), 1.1~1.7 (br s, 22H, CH₂), 1.9~2.15 (m, 2H, CH₂), 2.2~2.45 (m, 6H, CH₂), 5.1~5.4 (m, 2H, CH=CH). The product was identified by comparing its NMR spectrum with that in the literature⁴.

cis-5-Undecen-2-one (**4 c**) was obtained from 4-oxopentanal (**3 c**) using hexyltriphenylphosphonium ylide by the same procedure in a 58% yield, bp 80~81°C/2 mmHg (lit.⁹) bp 79~80°C/0.8 mmHg). IR (neat): 1710 cm⁻¹; ¹H-NMR (CCl₄): 0.90 (deformed t, 3H, CH₃), 1.1~1.7 (m, 6H, CH₂), 2.10 (s, 3H, CH₃), 2.2~2.45 (m, 6H, CH₂), 5.1~5.4 (m, 2H, CH=CH).

3 Results and Discussion

3.1 Michael reaction of nitroalkanes (1) with acrolein

Michael reactions of nitroalkanes (1) with acrolein were carried out using various tertiary phosphines as catalysts in benzene at room temperature. The results are shown in Table-1.

The Michael reaction products of nitroalkane with α , β -unsaturated aldehydes have been reported to decompose on heating^{17), 18)}. The conversion of γ -nitro aldehyde into ethylenedioxy acetale in the present research was thus carried out using ethylene glycol. In so doing, γ -ethylenedioxy nitroalkanes (2) were obtained by

Table-1 Preparation of 1, 1-ethylenedioxy-4-nitroalkane (2)

R ¹ CH ₂ NO ₂ (1) R ¹	Molar ratio of (1)/ acrolein	Catalyst mmol	Time (min)	Solvent	Yield of (2) (%)
a C ₈ H ₁₇	3	TPP 0.4	20	Benzene	52
a C ₈ H ₁₇	3	TBP 0.2	20	Benzene	60
a C ₈ H ₁₇	3	TBP 0.6	20	Benzene	42
a C ₈ H ₁₇	3	TBP 0.2	60	Benzene	35
a C ₈ H ₁₇	5	TBP 0.2	20	Benzene	70
a C ₈ H ₁₇	3	TCP 0.2	20	Toluene	61
b C ₉ H ₁₉	5	TBP 0.2	20	Benzene	70
c CH ₃	5	TBP 0.2	20	Benzene	72

TCP: Tricyclohexylphosphine

TBP: Tributylphosphine

TPP: Triphenylphosphine.

distillation. Whenever the nitroalkane (1) possess more than one hydrogen on the carbon α of the nitro group, multiple Michael additions can occur, leading to undesirable products. To prevent the occurrence of such reactions as much as possible, a reactant ratio of 5~3:1 of (1) to acrolein was used. When (1a) and acrolein reacted in benzene in the presence of tributylphosphine (TBP), the primary product was 1, 1-ethylenedioxy-4-nitrododecane (2a). The yield of product (2a) was found to be influenced by the concentrations of TBP, corresponding to the type of tertiaryphosphine [*e.g.*, tricyclohexylphosphine, TBP, triphenylphosphine (TPP)], and to relative concentration of (1a) corresponding to acrolein and time. The yields were best at lower concentrations of TBP (0.004 equivalents) and with stronger base (TBP in place of TPP). The yields varied from 52~70% and were not optimal.

Similarly, 1, 1-ethylenedioxy-4-nitrotridecane (2b) and 1, 1-ethylenedioxy-4-nitropentane (2c) were obtained from 1-nitrotridecane (1b) and nitroethane (1c) in 70 and 72% yields, respectively.

3.2 Synthesis of *cis*-12-nonadecen-9-one (4a), *cis*-13-icosen-10-one (4b), and *cis*-5-undecen-2-one (4c)

The Michael reaction of 1-nitrononane (1a) with acrolein catalyzed by TBP in benzene followed by acetalization gave 1, 1-ethylene-dioxy-4-nitrododecane (2a) in a 70% yield. (2a) was subjected to the Nef reaction with the electrochemical oxidation in methanol in the presence of potassium acetate. The product, without being isolated, was then acid hydrolyzed so as to undergo deacetalization to 4-oxododecanal (3a) in good yield, 81%. 4-Oxotridecanal (3b) was also prepared in the same manner from 1, 1-ethylenedioxy-4-nitrotridecane (2b). 4-Oxopentanal (3c) was obtained by the same procedure from 1, 1-ethylenedioxy-4-nitropentane (2c) in a low yield, 54%.

The salt-free Wittig reagent prepared from heptyltriphenylphosphonium bromide and sodium amide was added to a solution of (3a) in benzene to give *cis*-12-nonadecen-9-one (4a) in a 60% yield. *cis*-13-icosen-10-one (4b) was synthesized from (3b) by the same procedure. Similarly, *cis*-5-undecen-2-one (4c) was obtained by the Wittig reaction of hexyltriphenylphosphonium ylide with (3c). The resulting products, (4a), (4b), and (4c) showed no infrared absorption bands in the neighborhood of 970 cm⁻¹ due to disubstituted *trans*-alkene. The structures of these products were identified by a comparison of their IR and NMR spectra with those reported^{(4), (5), (7)}.

In conclusion, the methods described above were found to be convenient procedures for easily preparing (4a), (4b) and (4c). Particularly, γ -oxoaldehydes (3) are obtainable from 1, 1-ethylenedioxy-4-nitroalkanes (1). The utilization of 1, 1-ethylenedioxy-4-nitroalkanes (2) and γ -oxoaldehydes (3) for the synthesis of perfumes and insect pheromones is now under further investigation.

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ニトロアルカンを用いる昆虫フェロモン *cis*-12-ノナデセン-9-オン, *cis*-13-イコセン-10-オン及び *cis*-5-ウンデセン-2-オンの簡便な合成

宮腰哲雄

明治大学工学部工業化学科 (川崎市多摩区東三田 1-1-1)

cis-12-ノナデセン-9-オン (**4a**), *cis*-13-イコセン-10-オン (**4b**) 及び *cis*-5-ウンデセン-2-オン (**4c**) の簡便な合成を報告する。**(4a)** は 1-ニトロノナン (**1a**) とアクロレインの Michael 反応を利用して三段階で、目的のフェロモンを合成することができた。**(4b)** は 1-ニトロデカン (**1b**) を出発物質にして、収率よく得ることができた。同様に **(4c)** はニトロエタンとアクロレインの Michael 反応を利用して合成することができた。