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Note

Preparation of (−)-Periplanone D and Its Physical and Spectroscopic Properties

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(−)-Periplanones C and D were obtained in reproducible yields by modifying reported procedures. Our synthetic sample of (−)-periplanone D showed somewhat different physical and spectroscopic properties from those reported in the literature.

Key words: sex pheromone; periplanone; *Periplaneta fuliginosa*

In 1995, Takahashi *et al.* reported the isolation of the female-produced sex pheromone of the smoky brown cockroach (*Periplaneta fuliginosa* Serville), and identified the pheromone as periplanone D (**1**) by comparing its mass spectrum with that of authentic periplanone D.[1] Periplanone D itself had been identified as a minor sex pheromone component of the American cockroach (*Periplaneta americana*) and was synthesized as a racemate by Biendl *et al.*[2,3] Nishi *et al.* have recently reported the synthesis of the (−)-enantiomer of **1** and showed their synthetic pheromone to have potent biological activity toward *P. fuliginosa*.[4] Their study seems to confirm the correspondence of the smoky brown cockroach pheromone with periplanone D. However, Takahashi's structural assignment for the pheromone was carried out only by comparing the mass spectral data,[1] which made us feel the necessity for checking the correspondence by a direct GLC comparison. In this note, we describe a partially modified preparation of (−)-periplanone D, and the physical and spectroscopic properties of our synthetic pheromone, which showed somewhat different values from the data reported by Nishi *et al.*

Following the procedure developed originally by Shizuri *et al.*[5] and modified later by Nishi *et al.*,[4] (−)-germacrene D was converted in 6 steps to known alcohol **2a** {$[\alpha]^{19}_{\mathrm{D}}$ −122° (*c* 0.103, $CHCl_3$), lit.[4] $[\alpha]^{23}_{\mathrm{D}}$ −129.0° (*c* 0.1, $CHCl_3$)}, the ^{1}H-NMR spectrum of which was identical with the reported data.[4,5] The enantiomeric purity of **2a** was determined to be *ca.* 98% ee by analyzing the ^{1}H-NMR spectra of the corresponding (*R*)- and (*S*)-MTPA esters (**2b**). Oxidation of **2a** with activated manganese dioxide[4,5] in refluxing benzene did not give a reproducible yield of ketone **3**, probably due to the quality of the manganese dioxide used, but we could obtain **3** in a consistent yield (*ca.* 60%) by treating **2a** with tetrapropylammonium perruthenate and 4-methylmorpholine *N*-oxide according to Ley's procedure.[6] The ^{1}H-NMR spectrum of **3**, known as periplanone C which is also a minor sex pheromone component of the American cockroach,[2,3] was identical with that reported previously,[2,4,5] but our synthetic periplanone C showed a somewhat higher specific rotation value {$[\alpha]^{20}_{\mathrm{D}}$ −343° (*c* 0.154, $CHCl_3$)} than the literature values {$[\alpha]_{\mathrm{D}}$ −283° (*c* 0.1 ($CHCl_3$)[7] and $[\alpha]^{20}_{\mathrm{D}}$ −264° (*c* 0.15, $CHCl_3$)[4]}. Finally, conjugate reduction of (−)-periplanone C (**3**) with sodium dithionite[8] reproducibly afforded a *ca.* 50% yield of (−)-periplanone D (**1**), whose ^{1}H-NMR spectrum was identical with those reported by Biendl *et al.*[2] and Nishi *et al.*[4] Although the last reduction step had previously been performed with K-Selectride® in a 60% yield[2] and 36% yield[4] in two previous works, the reaction conditions were very rigorous and only a trace amount of **1** could be obtained in spite of our several attemps. The identity of the samples obtained under the two reduction conditions was confirmed by comparing their ^{1}H-NMR spectra. Our synthetic periplanone D was obtained as colorless needles after recrystallization from hexane, and showed a much higher specific rotation value {$[\alpha]^{20}_{\mathrm{D}}$ −712° (*c* 0.150, $CHCl_3$)} and melting point (mp 88–89°C) than the reported values {$[\alpha]^{23}_{\mathrm{D}}$

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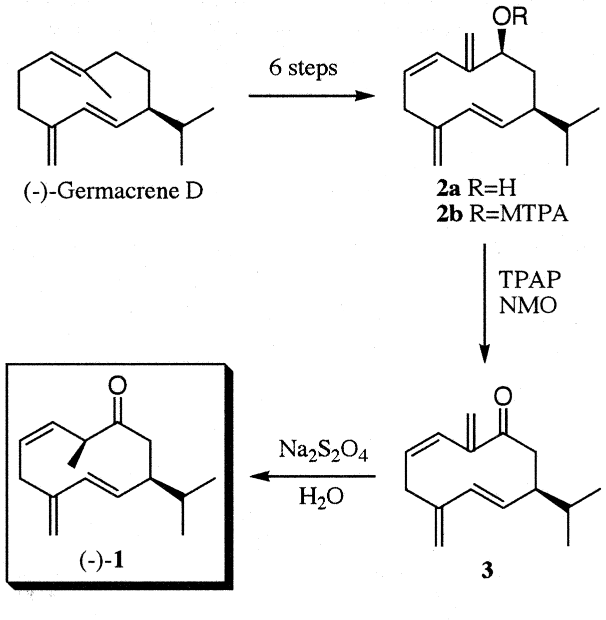
Abbreviations: MTPA, α-methoxy-α-(trifluoromethyl)phenylacetyl; TPAP, tetrapropylammonium perruthenate; NMO, 4-methylmorpholine *N*-oxide

−329.0° (c 0.15, $CHCl_3$) and mp 55–57°C for (−)-**1**[4]; mp 55–57°C for (±)-**1**[2]}. We think it is rather unusual that the melting point of (−)-**1** synthesized by Nishi *et al.* coincides with that of racemic **1** obtained by Biendl *et al.* Furthermore, the ^{13}C-NMR spectrum of our synthetic periplanone D did not coincide completely with that reported.[4] The ^{13}C-NMR spectrum of our synthetic sample showed just 15 peaks corresponding to the carbon number of periplanone D, while Nishi's data lacked the signal due to the carbonyl carbon (δ 215.05). In addition, we observed peaks at δ 17.45 and 144.70, instead of those of δ 28.90 and 128.78 reported by Nishi *et al.*,[4] although the other 12 peaks showed virtually the same chemical shifts (see the Experimental section). It is worth mentioning that, in the cases of periplanones A and C possessing analogous structures, the corresponding C-6 olefinic carbons resonated at δ 144.99[9] and 145.1,[4,7] respectively.

Experimental

IR spectra were measured with a JASCO FT/IR-5000 spectrometer. ^{1}H- (500 MHz) and ^{13}C-NMR (125 MHz) spectra were recorded with TMS as an internal standard in $CDCl_3$ by a JEOL JNM-A500 spectrometer. High-resolution mass spectra (70 eV) were measured with a Shimadzu GCMS 9020-DF spectrometer, and the optical rotation values were measured with a JASCO DIP-370 polarimeter. (−)-Germacrene D was obtained from R. C. Treatt & Co. Katayama Chemical silica gel 60 K 230 W was used for silica gel column chromatography.

Determination of the enantiomeric excess of **2a**. Allyl alcohol **2a** (2 mg) was converted to the corresponding (R)- and (S)-MTPA esters (**2b**) by treating overnight in pyridine (30 μl) with (S)- or (R)-MTPA chloride (5 μl), respectively. In the ^{1}H-NMR spectrum of the (R)-MTPA ester, the exomethylene protons γ to the ester function resonated at δ 5.12 and 5.25, while in the case of the (S)-MTPA ester, the corresponding exomethylene protons appeared at δ 5.20 and 5.40. Measurement of the peak areas revealed the enatiomeric purity of **2a** to be *ca.* 98% ee, in good agreement with Tanabe's data.[4,10]



Scheme. Preparation of (−)-Periplanones C and D.

(3Z,7E,9S)-9-Isopropyl-2,6-bis(methylene)-3,7-cyclodecadien-1-one (**3**). To a stirred mixture of **2a** (132 mg, 0.605 mmol) and powdered 4A molecular sieves (306 mg) in dichloromethane (1.2 ml) were successively added a solution of 4-methylmorpholine N-oxide (216 mg, 1.84 mmol) in dichloromethane (1.2 ml) and tetrapropylammonium perruthenate (21.6 mg, 0.0614 mmol) at room temperature under a nitrogen atmosphere. After 25 min, the mixture was filtered through a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was chromatographed over silica gel (10 g; hexane-ethyl acetate, 40:1), and the resulting product was further purified by preparative TLC (Merck silica gel 60 F_{254} 5744-1M) to give 78.6 mg (60.1%) of **3** as an oil, $[\alpha]^{20}_{D}$ −343° (c 0.154, $CHCl_3$). IR (film) ν_{max} cm^{-1}: 3082 (w), 3020 (w), 2962 (s), 2936 (s), 2874 (m), 1686 (vs), 1613 (m), 1468 (m), 1441 (m), 1386 (m), 1369 (m), 1305 (m), 1048 (m), 971 (m), 891 (m), 754 (m), 685 (m). ^{1}H-NMR δ: 0.89 (3H, d, J=6.7 Hz, 9-CH-CH_3), 0.94 (3H, d, J=6.7 Hz, 9-CH-CH_3), 1.57–1.66 (1H, m, 9-CH), 2.06-2.14 (1H, m, 9-H), 2.45 (1H, dd, J=10.3, 5.2 Hz, 10-H), 2.60 (1H, dd, J=12.2, 6.8 Hz, 5-H), 3.00 (1H, dd, J=11.1, 10.3 Hz, 10-H), 3.40 (1H, dd, J=12.2, 9.6 Hz, 5-H), 4.73 (1H, t, J=1.5 Hz, 6-methylene), 4.92 (1H, br s, 6-methylene), 5.45 (1H, br s, 2-methylene), 5.56 (1H, dd, J=16.3, 10.5 Hz, 8-H), 5.58 (1H, ddd, J=11.4, 9.6, 6.8 Hz, 4-H), 5.76 (1H, s, 2-methylene), 5.80 (1H, d, J=16.3 Hz, 7-H), 6.22 (1H, d, J=11.4 Hz, 3-H). HRMS m/z (M$^+$): calcd. for $C_{15}H_{20}O$, 216.1513; found, 216.1530.

(2S,3Z,7E,9S)-9-Isopropyl-2-methyl-6-methylene-3,7-cyclodecadien-1-one (**1**). To a stirred solution of **3** (38.0 mg, 0.176 mmol) in benzene (3.5 ml) was added a solution of sodium dithionite (85% purity, 332 mg, 1.62 mmol), trioctylammonium chloride (21.8 mg, 0.054 mmol) and sodium bicarbonate (272 mg, 3.24 mmol) in water (3.5 ml) under a nitrogen atmosphere, and the mixture was stirred at 80°C for 1.2 h. The mixture was diluted with water and extracted with ether. The extract was successively washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed over silica gel (10 g; hexane-ethyl acetate, 70:1), and the resulting product was further

purified by preparative TLC (Merck silica gel 60 F_{254} 5744-1M) to give 19.1 mg (49.8%) of **1** as crystals, which gave colorless needles when recrystallized from hexane, mp 88–89°C (measured with a Yanaco MP-S3 instrument), $[\alpha]_D^{20}$ $-712°$ (c 0.150, $CHCl_3$). IR (KBr disc) ν_{max} cm^{-1}: 3082 (w), 3016 (m), 2960 (s), 2930 (s), 2880 (s), 1702 (vs), 1659 (w), 1618 (w), 1473 (m), 1452 (m), 1334 (m), 1122 (m), 1054 (m), 978 (m), 897 (s), 733 (s). ^{1}H-NMR δ: 0.91 (3H, d, $J=6.8$ Hz, 9-CH-CH_3), 0.93 (3H, d, $J=6.8$ Hz, 9-CH-CH_3), 1.14 (3H, d, $J=6.9$ Hz, 2-CH_3), 1.57–1.66 (1H, m, 9-CH), 2.11-2.18 (1H, m, 9-H), 2.38 (1H, dd, $J=10.2$, 5.0 Hz, 10-H), 2.55 (1H, dd, $J=11.7$, 10.2 Hz, 10-H), 2.63 (1H, dd, $J=12.3$, 6.2 Hz, 5-H), 3.19 (1H, dd, $J=12.3$, 9.0 Hz, 5-H), 3.53–3.60 (1H, m, 2-H), 4.75 (1H, s, 6-methylene), 4.97 (1H, s, 6-methylene), 5.40 (1H, ddd, $J=11.0$, 9.0, 6.2 Hz, 4-H), 5.44 (1H, dd, $J=11.0$, 9.5 Hz, 3-H), 5.67 (1H, dd, $J=16.0$, 10.5 Hz, 8-H), 5.90 (1H, d, $J=16.0$ Hz, 7-H). ^{13}C-NMR δ: 17.45, 20.06, 20.19, 32.35, 36.62, 46.41, 47.16, 49.87, 112.86, 127.39, 131.08, 131.33, 134.77, 144.70, 215.05 (lit.:[4] 20.05, 20.16, 28.90, 32.32, 36.55, 46.35, 47.12, 49.84, 112.88, 127.42, 128.78, 131.00, 131.24, 134.77). HRMS m/z (M^+): calcd. for $C_{15}H_{22}O$, 218.1670; found, 218.1668.

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