3-Methyl Navenone-B: Pheromone Synthesis and Stereochemical Assignment using $Fe(CO)_3$ Complexes

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3-Methyl navenone-B has been synthesised and the stereochemistry of the 3-methyl ene–one moiety established unambiguously using an $Fe(CO)_3$ complex.

The isolation[1] and structural identification[1,2] of the navenones is one of the classic parts of pheromone chemistry. When molested, the blind, carnivorous sea-slug, *Navanax inermis*, releases a photosensitive, bright yellow mixture of trail-breaking, alarm pheromones, the major components being identified by Fenical *et al.*, using chemical and spectroscopic methods, as the 10-aryldeca-3,5,7,9-tetraen-2-ones (**1a**—**c**, R = H). A subsequent synthesis[3] confirmed the structure of these natural products. Several (*E*,*Z*)-olefin isomers, and (**2**),[†] were tentatively identified among the minor components. This communication describes a synthesis which confirms the structure of (**2b**) and a novel, unambiguous method for determining the stereochemistry of the terminal ene–one and the *all-E*-configuration of the tetraene.

The reaction between 7-phenylhepta-2,4,6-trienal[4] (**3b**) and the phosphonate[5] (**4**, R = Me) gave, after chromatography and repeated recrystallisation, a bright yellow substance (**2b**), m.p. 113—114 °C [λ_{max} 355 nm, ϵ 5 8000 (EtOH)], identical[6] (i.r. and ^1H n.m.r. spectroscopy) with the trace metabolite. Further reaction between (**2b**) and excess of $Fe_3(CO)_{12}$ gave a mixture of iron carbonyl complexes from which the crystalline $Fe(CO)_3$ derivatives [(**5b**); orange, m.p. 127—128.5 °C] and [(**6b**); dark red, m.p. 137—138 °C] were separated and further converted into the orange-red crystalline di-iron derivatives [(**7b**); m.p. 122 °C (decomp.)] and [(**8b**); m.p. 127—127.5 °C (decomp.)]. All four complexes were easily identified spectroscopically as the thermodynamically most stable *syn*-(*E*)-isomers.[‡] Thus both (**7b**) and (**8b**) indicate that double bond C-3,C-4 is (*E*)-di-

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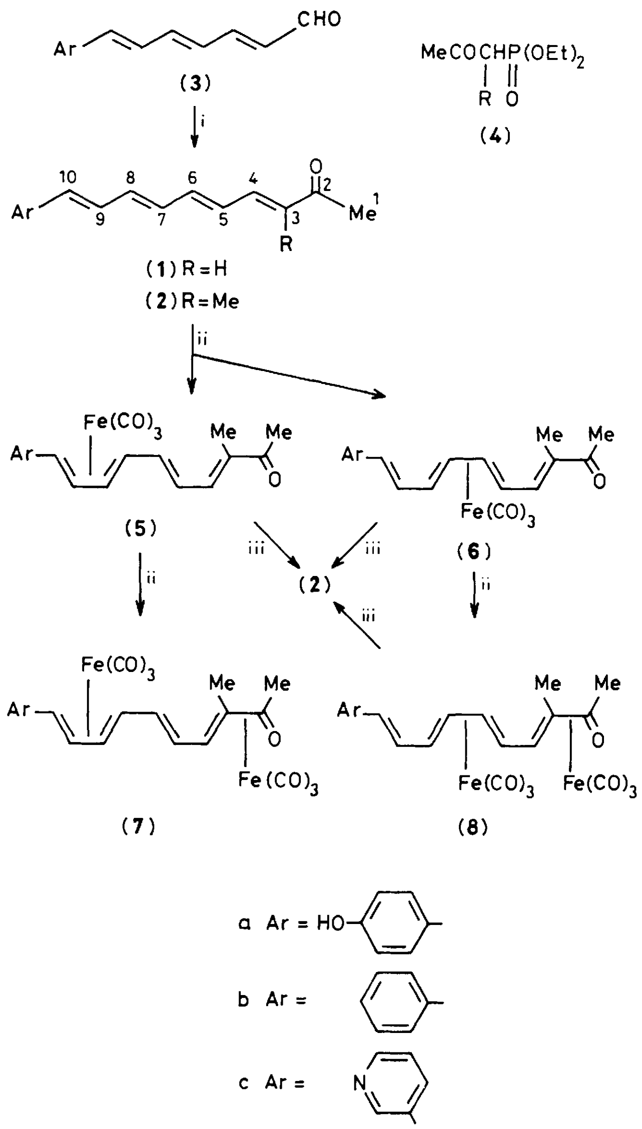
[†] 2 mg of this component was isolated (ref. 6).

[‡] The stereochemistry of a terminally substituted (diene)$Fe(CO)_3$ complex can be determined from ^1H n.m.r. measurements. In all cases when both *syn*-(*E*)- and *anti*-(*Z*)-isomers are available, each can be identified unambiguously from differences in J values [J_{trans} (*ca.* 7.5—10 Hz) > J_{cis} (*ca.* 6.5 Hz)] or δ values (ref. 7); when only one, thermodynamically stable isomer is obtained, J values alone have been a reliable guide to stereochemistry (ref. 10). ^1H n.m.r. data (250 MHz, decoupled spectra, $CDCl_3$), (**5b**): δ 2.22 (dd, 7-H, J_{7-8} 9.5, J_{6-7} 10.5 Hz), 2.46 (d, 10-H, J_{9-10} 9.1, J_{5-6} 15 Hz). (**6b**): 2.11 (dd, 5-H, J_{5-6} 7.4, J_{4-5} 10.5 Hz), 2.53 (dd, 8-H, J_{7-8} 7.7, J_{8-9} 10 Hz). (**7b**): 2.15—2.35 (m, 7-H, inc. 4-H), 2.84 (d, 10-H, J_{9-10} 10.6 Hz), 2.46 (s, $COCH_3$), 2.29 (s, CH_3). (**8b**): 1.47 (dd, 5-H, J_{5-6} 8.8, J_{4-5} 11 Hz), 2.14—2.23 (m, 8-H, inc. 4-H), 2.47 (s, $COCH_3$), 2.39 (s, CH_3).



i, (4)–NaH–dimethoxyethane; ii, $Fe_2(CO)_9$ or $Fe_3(CO)_{12}$; iii, Me_3NO.

substituted by the MeCO group§ and the Ph–C_6-unit, whilst (**6b**) and (**8b**) indicate [(*E*,*E*)-5,6,7,8] stereochemistry and (**5b**) and (**7b**) indicate [(*E*,*E*)-7,8,9,10] stereochemistry. Since complexes (**5b**), (**6b**), and (**8b**) were cleaved smoothly with trimethylamine *N*-oxide[9] (a reagent previously used for stereospecific pheromone synthesis)¶[10] and cleanly regenerated (**2b**) uncontaminated by any other isomer, it follows that the stereochemistry of the natural product, 3-methyl navenone-B, is unambiguously assigned the *all-E*-configuration (**2b**).

This complexation–decomplexation technique would appear to offer general potential for assigning stereochemistry to substituted ene–ones, *a priori*, a difficult process using spectroscopic methods alone.

Received, 27th June 1983; Com. 851

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§ Ene–ones ($R^1CH{=}CHCOR^2$) yield only the thermodynamically more stable [η^4-$Fe(CO)_3$] complex with a *syn*-(*E*)-R^1 group, *e.g.* ref. 8.

¶ An alternative synthesis of (**2b**) based upon Friedel–Crafts acylation of [η^4-$Ph(CH{=}CH)_4CH_3$]$Fe(CO)_3$, similar to the procedure successfully utilised for *lepidoptera* pheromone synthesis (ref. 10), was not satisfactory.