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The conversion of the product of the ene reaction of PhSOC1 with geranyl acetate into racemic β -irone has been accomplished in seven steps, using highpressure techniques for the olefination of β -methylcyclocitral.

One of the principal components of oil of iris (Iris florentina), which is responsible for its unusual scent, has been identified as (+)- β -irone (Ia) [Ia]. A nonstereospecific synthesis of the racemic form of (Ia) has been reported, by the electrophilic cyclization of a mixture of pseudoirones, but without the requisite details [2]. There have also been reports of other methods for the preparation of (\pm) -(Ia) in admixture with its Δ^2 -isomer [3, 4]. We here describe a simple route to (\pm) - β -irone (Ia) from the allyl sulfoxide (II), which is the readily accessible product of the Lewis acid-catalyzed ene reaction of geranyl acetate with benzenesulfinyl chloride [5]. The choice of this compound as the starting point implied the necessity to synthesize the intermediate 5-methylcyclogeranyl derivative, and its subsequent linkage to the acetonyl fragment.



In accordance with the plan adopted, the allyl sulfoxide (II) was first converted by treatment with m-chloroperbenzoic acid (MCPBA) into the sulfone (III), which was then C-methylated to the precursor (IV) of the methylgeraniol (VII), a key compound in this scheme. Reductive desulfurization of (IV) gave a quantitative yield of the chromatographically readily separable mixture of the alcohol (VII) and its "head-to-head" dimer (VIII) in a ratio of -5:2, the allyl shift which is characteristic of sulfones and sulfonamides related to (IV) being, in this case, as shown by PMR spectroscopy, virtually complete.* The formation of the diol (VIII) characterized as its crystalline bisdinitrobenzoate, is easily explained (cf. [7]) by the partial recombination of the probable radical intermediate (V) prior to its reduction to the allyl carbanion (VI), protonation of which affords the known [8] tetra-substituted olefin (VII).



*Reduction of (IV) with Na/EtOH in THF at 10°C gave ~80% of a mixture of (VII) and its Δ^7 -isomer (~4:1 according to PMR), free from (VIII).

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The structures of the previously unreported compounds (III), (IV), and (VIII) were confirmed by their physicochemical characteristics and elemental analyses. Electrophilic cyclization of (VII) by treatment with fluorosulfuric acid under the conditions described earlier for geraniol [9] proceeded smoothly to give α -methylcyclogeraniol (IX) [3], oxidation of which afforded (±)- α -methylcyclocitral (X) [3]. Both these compounds exhibit compositions of approximately equal quantities of diastereomers which follows from a comparison of their PMR spectra relative to the integral intensities, for example, the doublet signal of CH₃-C⁵ in the region $\delta \approx 0.85$ ppm. Treatment of (x) with alcoholic alkali gave (±)- β -methylcyclocitral (XIa) quantitatively [3].



 $R = Me (XIa), H (XIb)_{\bullet}$

Conversion of the latter into the required (\pm) - β -irone (Ia) necessitates overcoming the reduced reactivity of the conjugated aldehyde group, which is also to some extent sterically hindered. It is probably for this reason that the simplest route, namely condensation of (XIa) with acetone, is unsatisfactory, affording mixtures of (Ia) and its α -isomer [3]. A related approach, based on the condensation of carbonyl compounds with trimethylsilyl isopropenyl ether [10], was unsuccessful in the present case, even when using as a model compound β -cyclocitral (XIb) [11], which is more accessible than (XIa). Both of the aldehydes (XI) were extremely inert under the conditions recommended for the Horner-Wittig olefination with diethyl 2-oxopropylphosphonate (cf. [12]) or acetylphosphorane [13]. Specifically, the reaction of the latter with (XIb) under severe conditions (boiling toluene, 50 h) gave β -ionone (Ib) in yields of less than 10%.

As expected, the use of high-pressure techniques, which are extremely effective for the Wittig olefination of carbonyl compounds [14], provided a simple route from the aldehydes (XI) to the conjugated ketones (I). It was found that acetylphosphorane reacted smoothly with (XIb) at 70°C and 14 kbar to give β -ionone (Ib) uncontaminated by isomers (PMR, 250 MHz). Similar olefination of (XIa) gave the required (±)- β -irone (Ia), the spectral characteristics of which were in good agreement with those reported previously [15] for the naturally occurring compound.

Geranyl acetate has thus been converted in eight steps into racemic β -irone, using high pressures in the Wittig olefination of the aldehyde group, which has reduced reactivity.

EXPERIMENTAL

IR spectra were obtained in chloroform on a UR-20 apparatus. PMR spectra of solutions in $CDCl_3$ were measured on a Bruker WM-250 spectrometer, relative to TMS. Mass spectra were obtained on Varian MAT CH-6 and Varian MAT 311A instruments, at 70 eV. R_f values are given for bound layers of Silufol, in the system hexane-ether (1:4).

<u>6-Benzoylsulfonyl-3,7-dimethylocta-2E,7-dimethylocta-2E,7-dimethylocta-2E,7-dimethylocta-2E,7-dimethyloctate (III)</u>. To a solution of 6.8 g (21.2 mmoles) of (II) [5] in 80 ml of ether was added portionwise, with stirring under argon at -40°C over 10 min, 4.39 g (25.4 mmoles) of MCPBA. The mixture was kept at -20°C for 1 h, then poured into 200 ml of saturated aqueous sodium bicarbonate. The mixture was stirred vigorously at 25°C for 2 h, and the aqueous layer separated and extracted with ether. The combined organic layers were washed with water, dried over magnesium sulfate, evaporated under reduced pressure, and the residue (~7 g) chromatographed on 100 g of silica. Gradient elution from hexane to ether gave 5.64 g (79%) of (III) as a colorless oil, R_f 0.66. IR spectrum (v, cm⁻¹): 910, 960, 1030, 1090, 1150, 1235, 1315, 1370, 1385, 1450, 1590, 1650, 1675, 1745, 2860, 2960, 3075. PMR spectrum (δ , ppm; J, Hz): 1.63 and 1.78 br. s (6H, CH₃), 1.9-2.3 m (4H, CH₂), 2.04 s (3H, CH₃CO), 3.50 (1H, HCS), 4.55 d (2H, CH₂O, J = 6), 4.70 and 5.05

br. s (2H, $H_2C=C$), 5.30 br. t (1H, HC=C, J = 6), 7.5-7.9 m (5H, C_6H_5). Found, %: C 63.97, H 7.47, S 9.49. $C_{18}H_{24}O_4S$. Calculated, %: C 64.26, H 7.19, S 9.53.

<u>6-Phenylsulfonyl-3,6,7-trimethylocta-2E,7-dien-1-ol (IV).</u> To a stirred solution of 5.6 g (16.6 mmoles) of (III) in 60 ml of THF and 3 ml of DMF was added over 20 min at -70°C under argon 29.1 ml of a 2 M solution of n-BuLi in hexane (58.2 mmoles). After 20 min, the mixture was treated over 10 min with a solution of 8.28 g (58.3 mmoles) of MeI in 10 ml of THF, and after 1 h it was warmed to 25°C and further diluted with ether and water. The aqueous layer was separated, neutralized with 50% sulfuric acid, and extracted with ether. The combined extracts were worked up in the usual way to give ~6 g of product, which was chromatographed on 100 g of silica. Gradient elution from hexane to ether gave 4.83 g (94%) of (IV) as a colorless oil, Rf 0.29. IR spectrum (ν , cm⁻¹): 910, 1000, 1070, 1150, 1310, 1385, 1450, 1540, 1635, 1670, 2880, 2930, 3060, 3530, 3610. PMR spectrum (δ , ppm; J, Hz): 1.44 s, 1.61 and 1.70 br. s (9H, CH₃), 1.8-2.3 m (4H, CH₂), 4.16 d (2H, CH₂O, J = 6.5), 4.76 and 5.18 br. s (2H, H₂C=C), 5.44 br. t (1H, HC=C, J = 6.5), 7.5-7.8 m (5H, C₆H₅). High-resolution mass spectrum for m/z 167 (M-PhSO₂)⁺: found, 167.14389; calculated, 167.14357. For C_{1.7}H_{2.4}O₃S, mol. mass 308.4.

<u>Methylgeraniol (VII) and 3,6,7,10,11,14-Hexamethylhexadeca-2E,6E,10E,14E-tetraene-1,16-</u> <u>diol (VIII).</u> To a stirred solution of 0.84 g (2.72 mmoles) of (IV) in 40 ml of ammonia and 5 ml of THF was added portionwise under argon at -70 °C over 10 min 0.3 g (13.1 mg-atom) of sodium. The mixture was kept at -70 °C for 15 min, decomposed with an excess of ammonium chloride, the ammonia evaporated, and the residue treated with ether and water. The aqueous layer was separated, extracted with ether, and the combined organic layers washed with water, dried over magnesium sulfate, evaporated under reduced pressure, and the residue (-0.5 g) chromatographed on 15 g of silica. Gradient elution from hexane to ether gave 0.3 g (66%) of (VII) and 0.12 g (26%) of (VIII).

<u>Methylgeraniol (VII)</u> was a colorless liquid, bp 72-73°C (2.5 mm), n_{D}^{20} 1.4793 [8]. PMR spectrum (δ , ppm; J, Hz): 1.64 and 1.70 br. s (12H, CH₃), 2.0-2.2 m (4H, CH₂), 4.15 d (2H, CH₂0, J = 7.5), 5.42 br. t (1H, HC=C, J = 7.5).

<u>Diol (VIII)</u>. Colorless oil, R_f 0.32. IR spectrum (v, cm⁻¹): 900, 950, 1000, 1160, 1220, 1305, 1385, 1450, 1640, 1670, 2870, 2935, 3350, 3630. PMR spectrum (δ , ppm; J, Hz): 1.63 and 1.67 br. s (18H, CH₃), 2.1-2.2 m (12H, CH₂), 4.11 d (4H, CH₂O, J = 7.5), 5.38 br. t (2H, HC=C, J = 7.5).

Bisnitrobenzoate. Colorless crystals, mp 133-135°C (ether-hexane). Found, %: N 7.95. C₃₆H₄₂N₄O₁₂. Calculated, %: N 7.75.

<u>a-Methylcyclogeraniol (IX).</u> To a vigorously stirred solution of 8 g (79.9 mmoles) of freshly distilled HSO_3F in 80 ml of i-PrNO, at -90°C was added under argon over 10 min a solution of 2 g (11.9 mmoles) (VII) in 10 ml i-PrNO₂ and subsequently, over 5 min, -25 g (247.1 moles) of triethylamine in 50 ml of ether. The mixture was treated at 0°C with ether and water, the ether layer separated and extracted with ether, and the combined organic layers worked up in the usual way to give ~2 g of product, which was chromatographed on 50 g of silica. Gradient elution from hexane to ether (up to 20% of the latter) gave 1.7 g (85%) of (IX) as a colorless liquid, bp 84-86°C (3.5 mm), n_D^{20} 1.4913. Literature values [3], bp 108° (11 mm), n_D^{22} 1.4862. PMR spectrum (δ , ppm; J, Hz): 0.72, 0.76, 0.99, and 1.02 s (6H, CH₃-C⁶), 0.81 and 0.84 d (3H, CH₃-C⁵, J = 7.5), 1.4-2.1 m (4H, HC¹, HC⁴, HC⁵), 1.72 and 1.78 br. s (3H, CH₃-C²), 3.75 m and 3.86 d.d (2H, CH₂O, J = 13 and 4.5), 5.50 and 5.55 m (1H, HC³).

<u>a-Methylcyclocitral (X)</u>. To a stirred solution under argon of 8.48 g (107.2 mmoles) of pyridine and 5.35 g (53.5 mmoles) of CrO₃ in 80 ml of dichloromethane was added at 25°C over 5 min a solution of 1.5 g (8.9 mmoles) of (IX) in 5 ml of dichloromethane. After 30 min, the mixture was filtered through a layer (~5 cm) of silica. The filtrate was evaporated under reduced pressure, and the residue (~2 g) chromatographed on 60 g of silica. Gradient elution from hexane to ether (up to 20% of the latter) gave 1.2 g (81%) of (X) as a colorless liquid, bp 28-29°C (2 mm), n_D^{20} 1.4757, cf. [3]. PMR spectrum (δ , ppm; J, Hz): 0.79, 0.90, 0.97, and 0.99 s (6H, CH₃-C⁶), 0.86 and 0.88 d (3H, CH₃-C⁵, J = 7), 1.4-2.2 m (3H, CH₂, HC⁵), 1.53 and 1.59 br. s (3H, CH₃-C²), 2.3 and 2.5 m (1H, HC¹), 5.6 m (1H, HC³), 9.51 and 9.60 d (1H, CHO, J = 6).

 (\pm) - β -Methylcyclocitral (XIa). To a stirred solution under argon of 1.2 g (7.2 mmoles) of (X) in 5 ml of methanol at 25°C was added 10 ml of 8.5% methanolic KOH. The mixture was kept

at 25°C for 2 h, then treated with ether and water. The aqueous layer was separated, neutralized with 20% sulfuric acid, and extracted with ether. The combined organic layers were worked up in the usual way to give 1.3 g of material, which was chromatographed on 30 g of silica. Gradient elution from hexane to ether gave 1.14 g (95%) of (XIa) as a colorless liquid, bp 56-58°C (3.5 mm), $n_D^{2^0}$ 1.4983, cf. [3]. PMR spectrum (δ , ppm; J, Hz): 0.89 d (3H, CH₃-C⁵, J = 7), 1.05 and 1.20 s (6H, CH₃-C⁶), 1.5 and 2.1 m (5H, CH₂, HC⁵), 2.07 s (3H, CH₃-C²), 10.11 s (1H, CHO).

<u> β -Ionone (Ib)</u>. A solution of 0.17 g (1.11 mmoles) of β -cyclocitral (XIb) [11] and 1.06 g (3.33 mmoles) of acetyltriphenylphosphorane [13] in 2.2 ml of dichloromethane was kept in a Teflon ampul at a pressure of 14 kbar and a temperature of 70°C for 5 h, then treated with hexane. The hexane extract was separated from the oily residue, evaporated under reduced pressure, and the residue (~0.2 g) chromatographed in 10 g of silica. Gradient elution from hexane to ether (up to 20% of the latter) gave 50 mg of the starting (XIb), and 90 mg (59%) of (Ib) as a colorless liquid, bp 60-61°C (0.07 mm), n_D^{20} 1.5189, cf. [1b].

 (\pm) - β -Irone (Ia). Similarly, from 0.19 g (1.14 mmoles) of (XIa) and 1.07 g (3.36 mmoles) of acetyltriphenylphosphorane, following chromatography as in the preceding preparation, there were obtained 45 mg of the starting (XIa) and 70 mg (39%) of (Ia) as a colorless liquid, bp 68-69°C (0.085 mm), $n_D^{2^0}$ 1.5175, cf. [1a]. The PMR spectrum of (Ia) was the same as that given in [15].

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