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ABSOLUTE CONFIGURATION OF BIRKENAL, A *nor*-SESQUITERPENE ALDEHYDE FROM ESSENTIAL OIL OF *Betula pubescens* BUDS

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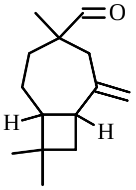
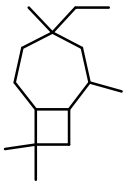
The absolute configuration of the nor-*sesquiterpene aldehyde birkenal isolated from essential oil of* Betula pubescens *(Betulaceae) buds was proved by chemical correlation with caryophyllene.*

Key words: *Betula pubescens*, Betulaceae, caryophyllene, isocaryophyllene, birkenal, Wittig reaction.

Essential oil from birch buds is a rich source of a variety of caryophyllene-type derivatives. Recently the observation of a new *nor*-sesquiterpene aldehyde in essential oil of birch was reported [1]. It was called birkenal (**1a**), the relative configuration of which was established based on NMR spectra [2]. However, the absolute configruation remained unknown. In this article, we established the absolute configuration of birkenal (**1a**) by chemical correlation with known caryophyllene-type derivatives.



1a



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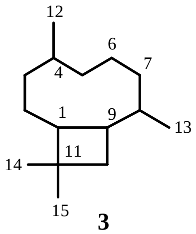

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Birkenal (**1a**) belongs to the 7(6→4) *abeo*-caryophyllane (**2**) type that is biogenetically related to caryophyllane (**3**).

Compounds of the *abeo*-carylphyllane (**2**) 7(6→4) structural type have not been isolated previously from natural sources. However, it was demonstrated that compounds with such a carbon skeleton are formed by thermal isomerization of caryophyllene and isocaryophyllene [3]. We used this feature to prove the absolute configuration of birkenal (**1a**) as follows. Caryophyllene (**4**) was isomerized to isocaryophyllene (**5**) upon heating with metallic selenium [4]. Then, isocaryophyllene was pyrolyzed to produce a mixture of two epimers of hydrocarbons **6** and **7**, the configuration of which had been proved reliably before [3]. Next we isolated birkenal (**1b**) from essential oil of buds of *Betula pubescens* Ehrh. (Betulaceae) growing extensively over western Siberia and produced a product identical to that in the literature [2]. Treatment of birkenal (**1b**) with trimethylmethylenephosphorane in a Wittig reaction gave a sesquiterpene hydrocarbon, the spectral properties and optical rotation of which agreed with those of the (4*S*)-epimer of **7**. Hydrocarbons **6** and **7** have practically identical mass spectra and similar NMR spectra but characteristic differences in the weak-field portion of the PMR spectra (signals for H atoms in double bonds) so that the synthesized compound could be reliably identified.

Thus, birkenal (**1b**) from essential oil of *Betula pubescens* buds is (1*S*,4*S*,7*R*)-4,8,8-trimethyl-2-methylenebicyclo[5.2.0]nonan-4-carbaldehyde.

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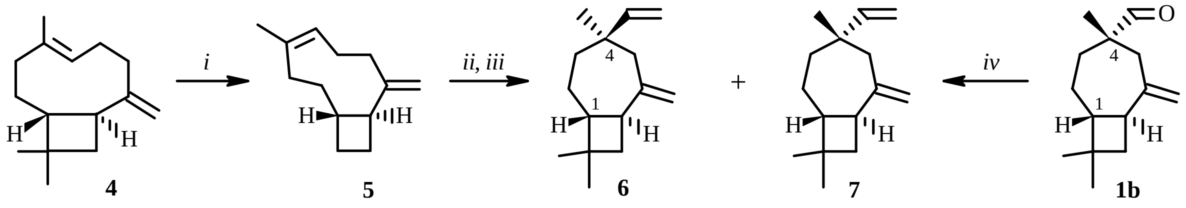

i. 200°C, Se; *ii.* 450°C, Ar; *iii.* preparative GC; *iv.* $Ph_3P^+CH_3I$/BuLi-THF

EXPERIMENTAL

General Comments. TLC was performed on Silufol plates with an affixed SiO_2 layer. Compounds were developed by spraying with an alcoholic solution of vanillin (2 g vanillin + 5 mL conc. H_2SO_4 in 150 mL EtOH) and heating. Preparative column chromatography used Merck silica gel of particle size 0.063-0.100 mm. Mass spectra were obtained in a Finnigan MAT 8200 spectrometer (50-100°C, EI, 70 eV); PMR and ^{13}C NMR spectra, on a Bruker DRX-500 spectrometer (500.13 MHz for ^1H and 125.75 MHz for ^{13}C) for solutions in a mixture of CCl_4 and benzene-d_6 (4:1 v/v) at 5-40 mg/mL and 25°C with benzene-d_6 internal standard (δ_C = 128.00 ppm, δ_H = 7.19 ppm). Signals were assigned using ^{13}C NMR spectra recorded using J-modulation (proton decoupling, opposite phase for signals of atoms with even and uneven numbers of bound protons with tuning at J = 135 Hz). Optical rotation angles were measured on a Polamat A polarimeter.

Preparative GC was carried out in a Chrom-5 chromatograph refurbished for preparative work with a flame-ionization detector and N_2 carrier gas. Pyrolysis products were separated using steel columns: column 1 (4000 × 5 mm, 15% OV-101 on Chromaton N-AW-DMCS support of particle size 0.315-0.400 mm); column 2 (4000 × 5 mm, 15% Carbowax 6000 on Chromaton N-AW-DCMS support of particle size 0.200-0.300 mm). The purity of the resulting fractions was monitored by analytical GC on a Biochrom-1 chromatograph (capillary column 11000 × 0.1 mm, SE-30 stationary phase) with a flame-ionization detector and N_2 carrier gas.

Isolation of Birkenal (1b). Essential oil of *Betula pubescens* buds (1.800 g) was separated by column chromatography using gradient elution (petroleum ether, bp 40-70°C:diethylether) to isolate a mxiture of slightly polar compounds (1.050 g, ethers and esters, carbonyl compounds). A portion (570 mg) of the mixture was rechromatographed to afford a fraction (340 mg) enriched in aldehydes from which preparative GC (column 2, isothermal regime, +200°C) isolated an aldehyde (30 mg), $[\alpha]_{573}^{23}$ +55° (*c* 1.64, EtOH), the PMR and ^{13}C NMR and mass spectra of which agreed with those published [2] for birkenal with $[\alpha]_D^{23}$ +25° (*c* 0.006, EtOH).

Isocaryophyllene (**5**), $[\alpha]_{578}^{19}$ -24°, was prepared as before [4].

Pyrolysis of Isocaryophyllene [3]. Isocaryophyllene (**5**, 1.79 g) was added under a stream of Ar to a quartz tube (40 × 2 cm) and heated to 450°C for 8 min. Products (1.67 g) were collected in a receiver cooled with liquid nitrogen and separated first by preparative GC over column 1 (isothermal regime, +220°C) to remove unreacted isocaryophyllene (980 mg) from the mixture of diastereomeric hydrocarbons (232 mg). The latter mixture was rechromatographed (column 2, isothermal regime, +150°C) to afford **6** (3 mg) and **7** (26 mg).

(1*S*,4*R*,7*R*)-4,8,8-Trimethyl-2-methylen-4-vinylbicyclo[5.2.0]nonane (6). PMR spectrum (δ, ppm, J/Hz): 0.932 (3H, s), 0.937 (3H, s), 0.945 (3H, s), 1.31 (1H, m), 1.38-1.48 (2H, m), 1.50-1.55 (2H, m), 1.62 (1H, td, J = 11.3 and 5.3), 1.71 (1H, dd, J = 10.2 and 7.6), 2.01 (1H, d, J = 14.8), 2.38 (1H, d, J = 14.8), 2.48 (1H, q, J = 9.5, $W_{1/2}$ = 7 Hz), 4.45 (1H, s, $W_{1/2}$ = 5 Hz), 4.61 (1H, s, $W_{1/2}$ = 6 Hz), 4.78 (1H, dd, J = 10.8 and 1.3), 4.89 (1H, dd, J = 17.6 and 1.3), 5.75 (1H, dd, J = 17.6 and 10.8).

^{13}C NMR spectrum (δ, ppm): 22.38 (q), 24.63 (t), 27.31 (q), 30.74 (q), 35.02 (s), 38.45 (t), 40.00 (s), 40.42 (t), 40.65 (d), 50.01 (t), 50.17 (d), 108.20 (t), 110.38 (t), 148.65 (d), 151.62 (s).

Mass spectrum (EI, 70 eV, *m/z*, I_{rel}, %): 204 (3) $[M]^+$, 189 (16), 175 (7), 161 (33), 148 (15), 133 (59), 119 (29), 105 (48), 93 (100), 79 (58), 69 (75), 55 (38), 41 (86), 27 (20).

(1*S*,4*S*,7*R*)-4,8,8-Trimethyl-2-methylen-4-vinylbicyclo[5.2.0]nonane (7). $[\alpha]_{578}^{23}$ +90° (*c* 0.62, hexane), lit. [3] $[\alpha]_D^{20}$ +88°. PMR spectrum (δ, ppm, J/Hz): 0.928 (3H, s), 0.932 (6H, s), 1.23 (2H, m), 1.34-1.41 (2H, m), 1.47 (1H, dd, J = 10.0 and 9.7), 1.53 (1H, td, J = 11.1 and 4.9), 1.71-1.79 (2H, m), 2.36 (2H, s), 2.55 (1H, q, J = 9.5, $W_{1/2}$ = 6 Hz), 4.38 (1H, s, $W_{1/2}$ = 5 Hz), 4.60 (1H, s, $W_{1/s}$ = 6 Hz), 4.88 (1H, dd, J = 11.0 and 1.4), 4.92 (1H, dd, J = 17.8 and 1.4), 5.73 (1H, dd, J = 17.8 and 11.0).

^{13}C NMR spectrum (δ, ppm): 22.39 (q), 26.32 (t), 30.71 (q), 34.18 (q), 34.87 (s), 39.48 (t), 40.36 (s), 41.12 (d), 42.33 (t), 48.48 (t), 50.63 (d), 107.03 (t), 112.39 (t), 146.42 (d), 152.52 (q).

Mass spectrum (EI, 70 eV, *m/z*, I_{rel}, %): 204 (4) $[M]^+$, 189 (14), 175 (7), 161 (24), 148 (19), 133 (57), 119 (28), 105 (45), 93 (100), 79 (56), 69 (76), 55 (37), 41 (85), 27 (20).

Methylenation of Birkenal (1b) by a Wittig Reaction. Birkenal (**1b**, 30 mg, 0.15 mmol) in THF (0.5 mL) and an excess of triphenylmethylenephosphorane [1.5 mmol, prepared from PPh_3CH_3I and *n*-BuLi (2 M) in hexane] were mixed at 0°C, stirred at room temperature for 1.5 h and then for another 1.5 h at 65°C. Solvent was removed in vacuo. The solid was extracted with hexane (3 × 5 mL). The combined extracts were evaporated in vacuo. The crude product (15 mg) was purified by chromatography over silica gel to afford **7** (6.9 mg), $[\alpha]_{578}^{23}$ +81° (*c* 0.38, hexane), the mass spectrum and PMR and ^{13}C NMR spectra of which agreed completely with those of the 4*S*-epimer of 4,8,8-trimethyl-2-methylenevinylbicyclo[5.2.0]nonane prepared by pyrolysis of isocaryophyllene.

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REFERENCES

1. a) R. Hiltunen, L. Vaisanen, K. Forsen, and M. Von Schantz, *Acta Pharm. Fenn.*, **92**, No. 2, 137 (1983);
   b) D. N. Vedernikov, Yu. V. Migunova, and V. I. Roshchin, in: Abstracts of the First All-Russian Conference "Chemistry and Technology of Plant Substances," Syktyvkar (2000), Sect. 1, Paper No. 19.
2. K. D. Klika, B. Demirci, J.-P. Salminen, V. V. Ovcharenko, S. Vuorela, K. H. C. Baser, and K. Pihlaja, *Eur. J. Org. Chem.*, 2627 (2004).
3. G. Ohloff, G. Uhde, and K. H. Schulte-Elte, *Helv. Chim. Acta*, **50**, 561 (1967).
4. R. Stanley, Ger. Pat. No. DE 2044018 (1971), *Chem. Abstr.*, **75**, 49364 (1971).