ACTA CHEMICA SCANDINAVICA 22 (1968) 943–948

Thunbergol, a New Macrocyclic Diterpene Alcohol*

BJARNE KIMLAND and TORBJÖRN NORIN

Department of Wood Chemistry, Forest Products Research Laboratory, Stockholm Ö, Sweden

Thunbergol is a monocyclic diterpene alcohol which occurs in the oleoresin of Douglas fir, *Pseudotsuga menziesii* (Mirb.) Franco. Spectroscopic studies and dehydration to thunbergene (cembrene) *I* established the structure *II* (1-isopropyl-4,8 12-trimethyl-2,7,11-cyclotetradecatriene-4-ol) of thunbergol which is thus a new member of the diterpene series containing a fourteen-membered ring. The possible relationships between thunbergol (*II*) and cembrol previously isolated from *Pinus sibirica* R. Mayr. are discussed.

In the preceding paper relating to the constituents of pocket resin from Douglas fir, *Pseudotsuga menziesii* (Mirb.) Franco, the isolation of a new diterpene alcohol, $C_{20}H_{34}O$, was reported.[1] The alcohol was one of the main neutral constituents. The characterisation and structural elucidation of this alcohol, named thunbergol, will be discussed below.

Thunbergol was obtained in a crude state from the neutral fraction of the resin by chromatography on deactivated alumina. Rechromatography on silver nitrate impregnated silica gel gave pure thunbergol as a colourless oil, ($[\alpha]_D$ + 74.4°; *c* 6.3 in $CHCl_3$) which analysed for $C_{20}H_{34}O$. The molecular weight (290) was confirmed by a mass spectrometric determination. The infrared spectrum of the alcohol exhibited characteristic hydroxyl absorption (3350 and 1100 cm^{-1}) and its ultraviolet spectrum showed the absence of conjugated double bonds.

The alcohol, which on keeping readily underwent dehydration, polymerisation, and autoxidation to a sticky gum, could not be induced to crystallise. However, it could be characterised by catalytic hydrogenation to a crystalline hexahydro-derivative ($C_{20}H_{40}O$; MW 296, determined by mass spectrometry; m.p. 89—91°; $[\alpha]_D$ −14.0; *c* in chloroform 0.6). The formation of a saturated hexahydro-derivative also demonstrated the monocyclic nature of the alcohol.

Thunbergol exhibits spectroscopic properties (NMR and mass-spectra) similar to those of thunbergene (cembrene) which is also a constituent of Douglas fir pocket resin and of many other *Pinaceae* species (*cf.* Ref. 1).

* This is part 45 of the series *The Chemistry of the Order Pinales*. Part 44 appears in *Acta Chem. Scand.* **22** (1968) 938.

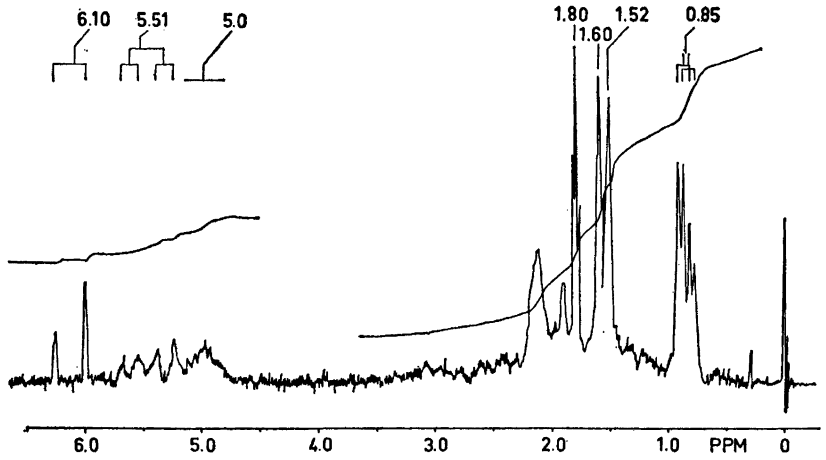


Fig. 1. NMR spectrum of thunbergene *I* (in $CDCl_3$; internal standard TMS).

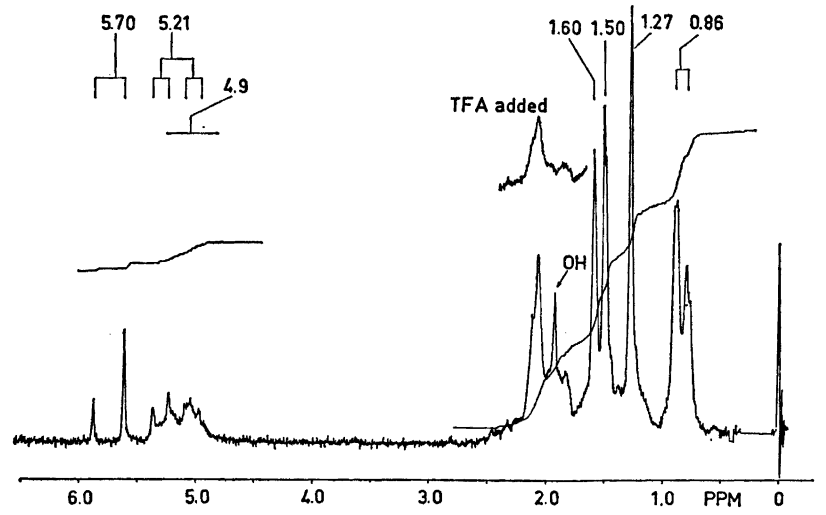
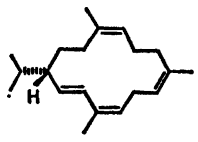


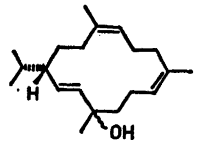
Fig. 2. NMR spectrum of thunbergol *II* (in $CDCl_3$; internal standard TMS).

Chemical and spectroscopic studies by two groups of investigators [2-4] have shown that thunbergene is a monocyclic fourteen-membered ring diterpene with structure *I*. The absolute configuration follows from a degradation to the known (—)-S-2-isopropyl-5-oxohexanoic acid.

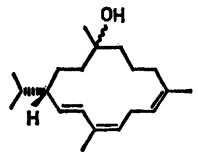
The NMR-spectra of thunbergene and thunbergol are shown in Figs. 1 and 2, respectively. The collected evidence from a comparison of the two spectra leaves little doubt that thunbergol must have structure *II*.



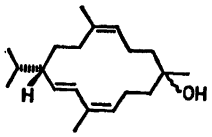
I



II



III



IV

In the spectrum of thunbergene the signals due to the methyl protons of the isopropyl group appear as two sets of doublets centered at 0.86 and 0.83 ppm ($J = 7$ cps). In the spectrum of thunbergol the corresponding signals appear as a slightly broadened doublet centered at 0.86 ppm ($J = 7$ cps). The two methyl groups attached to the non-conjugated trisubstituted double bonds exhibit slightly broadened singlets at 1.52 and 1.60 ppm in thunbergene and at 1.50 and 1.60 ppm in thunbergol. The triplet signal at 1.80 ppm ($J = 2$ cps) in the spectrum of thunbergene due to the methyl group attached to the conjugated double bond is absent in the thunbergol spectrum. Instead its spectrum exhibits a sharp methyl singlet at 1.27 ppm assigned to the methyl group on the carbon atom bearing the tertiary hydroxyl group.

A complex broad unresolved signal group centered around 5.0 ppm in the thunbergene spectrum integrates for three protons and is due to the olefinic protons attached to the three trisubstituted double bonds. In the spectrum of thunbergol a similar signal group corresponding to only two protons is centered around 4.9 ppm.

Thunbergene exhibits characteristic signals at 5.51 ppm ($J = 16$ and 8 cps) and 6.10 ppm ($J = 16$ cps) assigned to the protons of the *trans*-disubstituted double bond (*cf.* Ref. 4). A similar signal pattern appears in the thunbergol spectrum. However, the signals are shifted to a higher field, 5.21 ($J = 16$ and 8 cps) and 5.70 ppm ($J = 16$ cps) and do not exhibit significant long range couplings, all in agreement with the assigned structure.

The structure *II* of thunbergol was confirmed by a mild dehydration with phosphoryl chloride in pyridine to yield the crystalline thunbergene *I* in all respects identical with the natural hydrocarbon.

Recently Pentegova *et al.*[5] reported the isolation of an oily diterpene alcohol, »cembrol» ($C_{20}H_{34}O$; $[\alpha]_D$ + 59.6°, *c* in chloroform 2.19) from the oleoresin of *Pinus sibirica* R. Mayr. Upon dehydration this alcohol gave thunbergene (cembrene) *I*. The alcohol exhibited an ultraviolet maximum at 244—246 mμ. The extinction coefficient was not given. A methyl signal centered at 1.32 ppm in its NMR spectrum indicates the presence of a methyl group attached to the same carbon atom as a hydroxyl group. This evidence

leads to the assignment of the two alternative structures *III* and *IV* for the alcohol. The presence of a signal group centered around 2.3 ppm assigned to a (=C—CH_2—C=)-group led Pentegova *et al.* to favour structure *III*.

The NMR data given [5] for cembrol are, however, confusing. Thus cembrol is reported to exhibit NMR signals at 1.60 and 1.50 ppm which are the same resonance positions as for the protons of the methyl groups attached to the non-conjugated double bonds in thunbergene *I* and thunbergol *II*. A compound with structure *III* or *IV* should lack one of these signals. In addition thunbergol *II* exhibits signals around 2.3 ppm in spite of the absence of a (=C—CH_2—C=)-group.

A direct comparison (m.p., mixed m.p., $[\alpha]_D$, IR and mass spectra) of the hexa-hydro-product from thunbergol with that of isocembrol, kindly put at our disposal by Dr. Pentegova, showed that the products were identical in all respects.

Dr. Pentegova has kindly informed us that the oleoresin of *P. sibirica* also contains a tertiary diterpene alcohol, which she names isocembrol. This alcohol possesses similar optical properties to that of cembrol; however, it lacks the ultraviolet absorption due to a conjugated diene system.

EXPERIMENTAL

Thin layer chromatographic examinations (TLC) were performed on silica gel G using an ether-benzene (1:10) solution. Gas-liquid chromatography (GLC) was performed on an Aerograph 204-1-B instrument using a deactivated silicon rubber column (1 % E 301 on Gas-Chrom P; 5′ × 1/8″) operating at 150°. GLC retention time data are given relative to thunbergene (R_t 1.00). NMR spectra were recorded on a Varian A-60 instrument (60 Mc/s) using deuterochloroform solutions. The chemical shifts are given in ppm from tetramethylsilane (internal standard). Mass spectra were recorded on an instrument with a heated all glass inlet system [7] (temp. 100°; 70 eV). Rotations were measured in chloroform. Light petroleum refers to the fraction b.p. 40—60°.

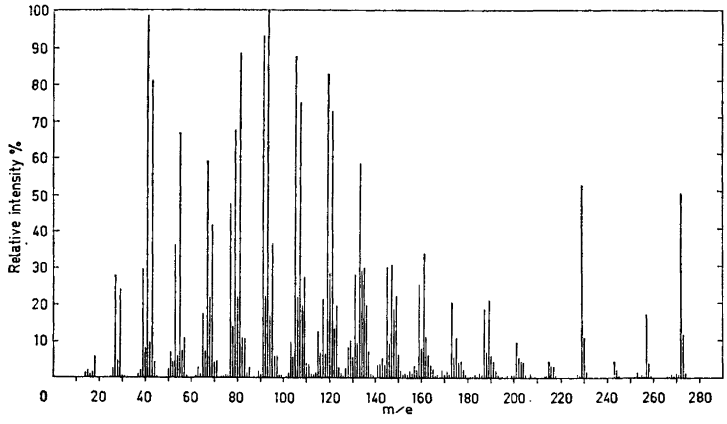


Fig. 3. Mass spectrum of thunbergene *I*.

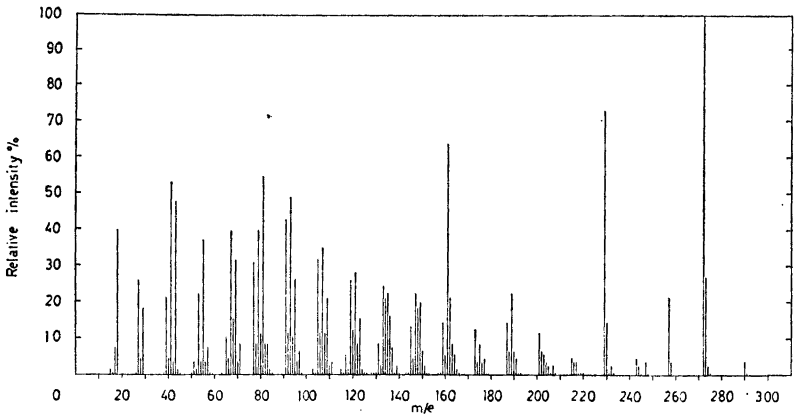


Fig. 4. Mass spectrum of thunbergol *II*.

Thunbergol (II, 1-isopropyl-4,8,12-trimethyl-2,7,11-cyclotetradecatriene-4-ol). The isolation of thunbergol from the resin of *Pseudotsuga menziesii* (Mirb.) Franco is described in the previous paper.[1] Thunbergol is characterised by the following properties: TLC R_F-value 0.31; GLC relative retention time 1.57; $[\alpha]_D$ + 75.4° (*c* 0.63); IR bands at (thin film) 3350, (strong = s), 2960 (s), 2920 (s), 2870 (s), 2850 (inflexion), 1655, 1460 (s), 1445 (s), 1385 (s), 1375 (inflexion), 1370 (s), 1230, 1180, 1165, 1115 (s), 1100 (s), 1035 (s), 980 (s), 945, 915, 900, 870, 850 cm^{-1}; NMR spectrum, see Fig. 2; mass spectrum, see Fig. 4.

Catalytic hydrogenation of thunbergol. Hydrogenation of thunbergol in acetic acid using a platinum catalyst (Adams) afforded two crystalline tetrahydro products *A* and *B* in the approximate proportions 1:1. The two products were separated by repeated chromatography on silver nitrate impregnated silica gel [6] using benzene for the elution. *Tetrahydro-product A:* m.p. 60.5—63°; TLC R_F-value 0.29; GLC relative retention time 1.57; mass spectrum M^+ 294 *m/e*. *Tetrahydro-product B:* m.p. 88—90°; TLC R_F-value 0.24; GLC relative retention time 1.57; mass spectrum, very similar to that of product *A*, M^+ 294 *m/e*.

Upon prolonged hydrogenation with the same catalyst and solvent the two tetrahydro-products gave the same *hexahydro-product:* m.p. 89—91°; $[\alpha]_D$ −14.0° (*c* 0.6); TLC R_F-value 0.23; GLC relative retention time 1.80; mass spectrum, M^+ 296. (Found: C 81.1; H 13.5. Calc. for $C_{20}H_{40}O$; C 81.0; H 13.6). This product was found to be identical in all respects with the hexahydro-product (m.p. 88—90°) obtained in the same manner from isocembrol kindly put at our disposal by Dr. Pentegova.

Dehydration of thunbergol. Thunbergol (0.11 g) was dissolved in pyridine (6 ml) and the solution cooled in ice-water. Phosphoryl chloride (0.35 ml) was added dropwise to the solution. After 48 h in a refrigerator the reaction mixture was poured with stirring into a large volume of ice-water. The water solution was extracted with light petroleum (3 × 50 ml). The combined solutions were filtered through alumina and the light petroleum evaporated. The residue was then chromatographed on silver nitrate impregnated silica [6] with benzene and benzene/ether yielding crystalline thunbergene (*I*). The compound was found to be identical in all respects (m.p.; mixed m.p.; IR, UV, NMR, see Fig. 1; mass spectrum, see Fig. 3; TLC; GLC) with an authentic sample of thunbergene.

Acknowledgements. We thank Dr. K. I. Dahlquist for recording the NMR spectra and Drs. C. Enzell and R. Ryhage for the mass spectra. We are also indebted to Dr. V. A. Pentegova for a gift of material.

REFERENCES

1. Erdtman, H., Kimland, B., Norin, T. and Daniels, P. J. L. *Acta Chem. Scand.* **22** (1968) 938.
2. Kobayashi, H. and Akiyoshi, S. *Bull. Chem. Soc. Japan* **35** (1962) 1044.
3. Kobayashi, H. and Akiyoshi, S. *Bull. Chem. Soc. Japan* **36** (1963) 823.
4. Dauben, W. G., Thiessen, W. F. and Resnick, P. R. *J. Org. Chem.* **30** (1965) 1693.
5. Lisina, A. I., Rezvukhin, A. I. and Pentegova, V. A. *Khim. Prirodn Soedin., Akad. Nauk Uz. SSR.* **1965** 250; see also *Chem. Abstr.* **64** (1966) 5144.
6. Norin, T. and Westfelt, L. *Acta Chem. Scand.* **17** (1963) 1828.
7. Ryhage, R. *Arkiv Kemi* **16** (1960) 19.

Received October 18, 1967.