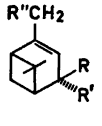
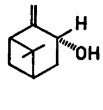
Perester Oxidation and NBS-Bromination of α-Pinene

H. HEIKMAN, P. BAECKSTRÖM and K. TORSSELL

Institute of Organic Chemistry, University of Stockholm, Box 6801, S-113 86 Stockholm, Sweden

α-Pinene is reported to give, on copper catalyzed perester oxidation,[1] a monobenzoate the structure of which was not determined. We repeated the reaction and found that a mixture of alcohols were formed, from which two alcohols, *trans*-verbenol, I, (30 %) and *trans*-pinocarveol, III, (19 %) were obtained in a pure form by column chromatography. A third fraction (9 %) was a mixture of myrtenol, IV, (major), *cis*- and *trans*-verbenol, II and I, and a fourth hydroxylic compound which had arisen *via* a sceletal rearrangement. The yields were calculated as percent of the crude alcohol fraction (80—100°/10 mm) which amounted to 30 % based upon α-pinene. The products were identified by comparison with authentic material (myrtenol, *trans*-pinocarveol) and published NMR data (*cis*- and *trans*-verbenol [2] and *trans*-pinocarveol [3]). The accepted radical mechanism for the reaction accounts for the products formed.



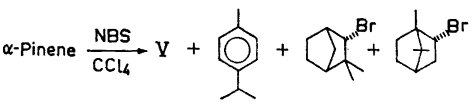


III

I R,R″ = H; R′ = OH
II R′,R″ = H; R = OH
IV R,R′ = H; R″ = OH
V R,R′ = H; R″ = Br

NBS-Bromination of α-pinene is reported to give a monobromo derivative [4,5] in a rather vigorous reaction [4] which, however, in our hands proceeded sluggishly. Distillation of the product gave a fraction, b.p. 55—75°C/9 mm, 50 %, which apart from some pinene contained at least 6 components in substantial amounts, four of which were separated by preparative GLC. Fraction 1 (11 %) was identified as *p*-cymene, VI by using spectral data and by comparison with authentic material. Fraction 2 (7 %), Mw. 216/218, 1:1 (mass spectrographically), is probably fenchyl bromide, VII. The NMR spectrum is closely related to the spectrum of fenchyl alcohol and is not in agreement with the pinane or camphane sceletons. Fraction 3 (48 %) consisted of bornyl bromide, VIII, proved by comparison with authentic material. The structure of the compound in fraction 4 (28 %) was proved to be myrtenyl bromide, V, using spectral data.

No verbenyl bromide, I, R′=Br, could be detected. Myrtenyl bromide is formed *via* allylic bromination; the fenchyl and bornyl bromides arise *via* sceletal rearrangement induced by the addition of hydrogen bromide.



VI VII VIII

Experimental. Perester oxidation of α-pinene. *t*-Butyl perbenzoate (4.0 g, 21 mmoles) was added over a period of 30 min to a stirred mixture of α-pinene (7.0 g, 51 mmoles), $[\alpha]_D = +34°$, and CuBr (40 mg, 0.035 mmoles) at 110°C under nitrogen. After 4 h at this temperature all perester had reacted. The mixture was extracted with sodium carbonate (3 × 50 ml, 2 M) and hydrolyzed with methanolic potassium hydroxide (15 ml, 3 M) for 18 h at 25°C. The free alcohols were precipitated with water, separated and distilled, 1.0 g, 30 %, b.p. 80—100°C/10 mm. The distillate was chromatographed on silica with isopropyl ether-petrol ether, 15:85, as eluent and three fairly well separated main fractions were collected. The first fraction (19 %, calculated as per cent of the distillate) is *trans*-pinocarveol which was gas chromatographically pure; IR: 3610, 3360—3500 cm^{-1}, OH; 3072, 1645, 899 cm^{-1}, C=CH_2; NMR: $\delta = 4.94$ (t), $J = 1.0$ cps, 1 H, and $\delta = 4.75$ (d), $J = 1.0$ cps, 1 H, C=CH_2; $\delta = 4.34$ (d, broad), $J = 6.8$ cps, C*H*OH; $\delta = 2.6 - 1.6$ (m), 6H + OH; $\delta = 1.28$ (s) and 0.64 (s), 2 CH_3. The NMR spectrum of a sample (impure) synthesized according to Schenck *et al.*[6] showed the same peaks.

The main component of the second fraction, 9 %, is myrtenol, NMR: $\delta = 5.41$ (m), 1 H; $\delta = 3.89$ (m) CH_2OH; $\delta = 1.31$ (s) and 0.85 (s) 2 CH_3. Inspection of the NMR spectrum revealed the presence of *trans*-verbenol and also small amounts of *cis*-verbenol. The third fraction, 28 %, is *trans*-verbenol, $[\alpha]_D = +72°$ ($c = 1.0$, $CHCl_3$, lit.[2] $[\alpha]_D^{22} = -124°$ from pure

(−)-α-pinene). The NMR spectrum agrees well with published data.[2]

NBS-bromination of α-pinene. α-Pinene (6 g, $[\alpha]_D = +34°$), NBS (3 g), bis-azoisobutyronitrile (50 mg) and carbontetrachloride (18 ml) were refluxed for 16 h. The succinimide was filtered off and the solvent evaporated. Distillation *in vacuo* gave a fraction, 55−75°C/9 mm, 50 %, which, according to the GLC, contained at least six components. Four of them were separated by preparative GLC on a SE-52 column. Fraction 1, 11 %, was *p*-cymene, identified by NMR, IR, UV, and MS and by comparison with a reference sample. Fraction 2, 7 %, was probably fenchyl bromide, NMR: $\delta = 3.75$ (d), $J = 2.0$ cps, C*H*Br; $\delta = 1.88-1.25$ (m)~8 H; $\delta = 1.10$ (s) and 1.04 (s), 3 CH_3. Mw. 216/218, 1:1, calc. 217. The main fraction, 48 %, fraction 3, consisted of bornyl bromide, m.p. 76.5−78.0°C, $[\alpha]_D = +21.2°$ (lit.[7] m.p. 87−92°, $[\alpha]_D = -24.6°$, from (−)-α-pinene). NMR: $\delta = 4.25$ (m), $J = 10.5$, 5.0, and 2.5 cps, C*H*Br; $\delta = 2.7-1.0$ (m), 7H; $\delta = 0.99$ (s), 0.91 (s) and 0.87 (s), 3 CH_3. For comparison bornyl bromide was synthesized according to Wallach.[8] The fourth fraction, 27 %, was myrtenyl bromide, Mw. 214/216, 1:1, NMR: $\delta = 5.66$ (m) =CH; $\delta = 3.87$ (q), $J = 1.0$ cps, CH_2Br; $\delta = 2.7-1.9$ (m) 6 H; $\delta = 1.33$ (s) and 0.84 (s), 2 CH_3.

Acknowledgements. This work was supported by grants from *Statens Naturvetenskapliga Forskningsråd*. We would like to thank Prof. E. von Sydow for samples of myrtenol and fenchyl alcohol and Prof. T. Norin for (−)-α-pinene. Miss Lena Bäck has kindly run our spectra.

1. Kharash, M. S., Sosnovsky, G. and Yang, N. C. *J. Am. Chem. Soc.* **81** (1959) 5819.
2. Cooper, M. A., Salmon, J. R., Whittaker, D. and Scheidegger, U. *J. Chem. Soc.* **C 1967** 1259.
3. Arbusov, B. A., Isaeva, Z. G. and Sanitov, Yu.Yu. *Dokl. Akad. Nauk SSSR* **137** (1961) 589.
4. Buu-Hoi, Hiong-Ki-Wei, Lecomte, J. and Royer, R. *Bull. Soc. Chim. France* **1946** 148.
5. Ziegler, K., Späth, A., Schaaf, E., Schumann, W. and Winkelmann, E. *Ann.* **551** (1942) 80.
6. Schenck, G. O., Eggert, H. and Denk, W. Ann. **584** (1953) 177; Gollnick, K. and Schenck, G. O. *Pure Appl. Chem.* **9** (1964) 507.
7. Wallach, O. and Conrady, E. *Ann.* **252** (1889) 156.
8. Wallach, O. *Ann.* **239** (1887) 7.

Received June 28, 1968.

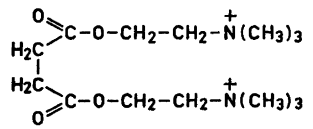
Crystal Data of Some Succinylcholine Salts

BIRTHE JENSEN

Chemical Laboratory C, The Royal Danish School of Pharmacy, Copenhagen, Denmark

As a part of an investigation of compounds acting as neuromuscular blocking agents, the following crystallographic data have been obtained.

The unit cell parameters have been determined from precession films (Mo$K\alpha$, $\lambda = 0.7107$ Å) and the estimated uncertainties are 0.2 % for the axes and 0.2−0.3° for the angles. The crystal structures of these salts are being studied. In the following the symbol Suc-chol^{2+} is used for the succinylcholinium ion,



Succinylcholine iodide, Suc-chol^{2+}, $2I^-$. Colourless crystals from a water-ethanol solution. M.p. 250−255° (decomp.).

$a = 12.9_0$ Å, $b = 8.24_2$ Å, $c = 9.65_7$ Å, $\beta = 98.0°$.

$\varrho_{obs.}$ 1.76 g/cm^3, $\varrho_{calc.}$ 1.778 g/cm^3. $Z = 2$. Space group $P2_1$.

Succinylcholine perchlorate, Suc-chol^{2+}, $2ClO_4^-$. Colourless crystals from a 50 % ethanol solution. M.p. 267−267.5°. A pronounced tendency to twin-formation was observed.

$a = 6.53_7$ Å, $b = 13.6_6$ Å, $c = 12.6_3$ Å, $\beta = 93.0°$.

$\varrho_{obs.}$ 1.43 g/cm^3, $\varrho_{calc.}$ 1.444 g/cm^3. $Z = 2$. Space group $P2_1/c$. Molecular symmetry $\bar{1}$.

Succinylcholine picrate, Suc-chol^{2+}, $2(NO_2)_3C_6H_2O^-$. Yellow needles from a water solution. M.p. 158.5−159°.

$a = 11.0_8$ Å, $b = 7.09_7$ Å, $c = 11.2_9$ Å, $\alpha = 101.7°$, $\beta = 108.9°$, $\gamma = 94.8°$.

$\varrho_{obs.}$ 1.51 g/cm^3, $\varrho_{calc.}$ 1.528 g/cm^3. $Z = 1$. Space group $P1$ or $P\bar{1}$.

Received June 18, 1968.