

A NEW SYNTHESIS OF EGONOL

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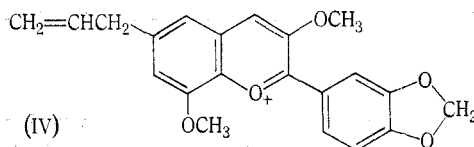
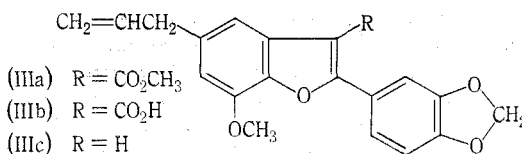
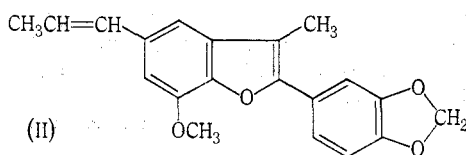
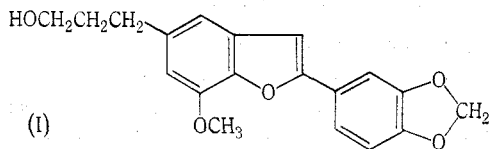
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Introduction

Egonol (I) which occurs in a number of *Styrax* species¹⁻³ belongs to a small class of natural products containing the simple benzofuran nucleus. It was first synthesized by Kawai, Nakamura, and Sugiyama⁴ who formed the benzofuran system by condensing an *o*-hydroxybenzaldehyde with an α -chlorophenylacetic ester having the correct substitution.

Following our recent use⁵ of the hydrogen peroxide oxidation of flavylum salts for the synthesis of the benzofuranoid lignan, eupomatene (II), it was of interest to utilize the same approach for a synthesis of egonol.

From the benzofuran ester (IIIa), which had already been prepared⁵ from the flavylum salt (IV), there were in fact only three steps required to obtain egonol. These were hydrolysis to the acid (IIIb), decarboxylation of this in the presence of quinoline-copper carbonate to the benzofuran (IIIc), and then anti-Markownikoff hydration of the side-chain olefinic bond, which was effected by hydroboration with oxidative work-up. Each of these reactions proceeded in good yield. A comparison with an authentic specimen of egonol was not made, but the physical constants of the product and the acetyl derivative were in agreement with the literature values. The structures were also supported by the n.m.r. spectra.



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¹ Karrer, W., "Konstitution und Vorkommen der organischen Pflanzenstoffe." p. 709. (Birkhäuser: Basel 1958.)

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³ Hopkins, C. Y., Ewing, D. F., and Chisholm, M. J., *Can. J. Chem.*, 1967, **45**, 1425.

⁴ Kawai, S., Nakamura, T., and Sugiyama, N., *Ber. dt. chem. Ges.*, 1939, **72**, 1146.

⁵ McCredie, R. S., Ritchie, E., and Taylor, W. C., *Aust. J. Chem.*, 1969, **22**, 1011.

Experimental

Melting points are uncorrected. Analyses were performed by the Australian Microanalytical Service, Melbourne. Light petroleum had b.p. 40–60°. Alumina was Peter Spence grade H. Ultraviolet spectra were measured on ethanol solutions and infrared spectra on Nujol mulls. Nuclear magnetic resonance spectra were determined by a Varian A60 instrument on approx. 10% solutions in deuterochloroform with tetramethylsilane as an internal reference; signals are reported in terms of multiplicity, intensity, chemical shift in p.p.m. from tetramethylsilane, assignment, and coupling constant in that order with the use of the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; (b), broad; signals due to OH were identified by exchange with deuterium oxide.

Hydrolysis of the Ester (IIIa)

A solution of the benzofuran ester⁵ (IIIa) (1 g) in acetone (60 ml) containing 5% KOH (15 ml) was refluxed for 24 hr. The acetone was removed by distillation and the aqueous solution washed with ether. The crude material obtained on acidification was recrystallized from acetone-methanol to give the *benzofuran acid* (IIIb) (0.7 g) as colourless needles, m.p. 215–217° (dec.) (Found: C, 68.2; H, 4.6. $C_{20}H_{16}O_6$ requires C, 68.2; H, 4.6%). ν_{\max} 2500–2700, 1680 cm^{-1} ; λ_{\max} 322 m μ (ϵ 24600); n.m.r. spectrum: s, 1, 8.8, CO_2H ; m, 5, 7.5–7.8 and 6.68–6.98, $5 \times ArH$; s, 2, 6.2, O_2CH_2 ; m, 1, 5.7–6.3, $CH=CH_2$; m, 2, 4.9–5.3, $CH=CH_2$; s, 3, 4.01, OCH_3 ; d(b), 2, 3.50, $ArCH_2CH=$, 7.

Piperonylic acid (0.1 g), m.p. and mixed m.p. 229°, was obtained from the mother liquors.

The Benzofuran (IIIc)

The acid (IIIb) (0.6 g) was refluxed for 3 min in quinoline (8 ml) in the presence of copper carbonate (0.3 g). The cooled mixture was diluted with ether and the solution washed successively with dil. H_2SO_4 and dil. NaOH. The neutral fraction (0.5 g) obtained was chromatographed on alumina (20 g). The *benzofuran* (0.42 g) was eluted by benzene-light petroleum (7:3), forming needles from benzene-light petroleum, m.p. 76° (Found: C, 74.0; H, 5.3. $C_{19}H_{16}O_4$ requires C, 74.0; H, 5.2%). ν_{\max} 1622, 1600 cm^{-1} ; λ_{\max} 220, 302, 317, 330 m μ (ϵ 38200, 29600, 35400, 27100); n.m.r. spectrum: m, 5, 6.6–7.5, $5 \times ArH$; s, 1, 6.78, benzofuran-H; s, 2, 5.98, O_2CH_2 ; m, 1, 5.7–6.4, $CH=CH_2$; m, 2, 4.9–5.3, $CH=CH_2$; s, 3, 4.01, OCH_3 ; d(b), 2, 3.45, $ArCH_2CH=$, 7.

Egonol

To a solution of (IIIc) (0.5 g) in tetrahydrofuran (5 ml) in which was suspended sodium borohydride (0.05 g) was added boron trifluoride etherate (0.2 g). After stirring for 1.5 hr at room temperature 10% NaOH (0.75 ml) and 30% hydrogen peroxide (0.35 ml) were added and stirring continued for 1 hr. The product obtained on addition of water and extraction with ether was chromatographed on alumina (10 g). Elution with benzene-ether (9:1) gave egonol (0.4 g), needles from methanol, m.p. 117° (lit.¹ 117°). N.m.r. spectrum: m, 5, 6.6–7.5, $5 \times ArH$; s, 1, 6.75, benzofuran-H; s, 2, 5.98, O_2CH_2 ; s, 3, 4.01, OCH_3 ; t, 2, 3.68; CH_2CH_2OH , 7; t, 2, 2.76, $ArCH_2CH_2$, 7; m, 2, 1.95, $CH_2CH_2CH_2$; s, 1, 1.80, OH.

The acetate formed needles from methanol, m.p. 107° (lit.³ 107°). N.m.r. spectrum: m, 5, 6.6–7.5, $5 \times ArH$; s, 1, 6.75, benzofuran-H; s, 2, 5.98, O_2CH_2 ; t, 2, 4.1, CH_2CH_2OAc , 7; s, 3, 4.03, OCH_3 ; t, 2, 2.75, $ArCH_2CH_2$, 7; s, 3, 2.06, $OCOCH_3$; m, 2, 2.0, $CH_2CH_2CH_2$.

Acknowledgment

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