The Synthesis of Nootkatin, a Sesquiterpenoid Tropolone[1]

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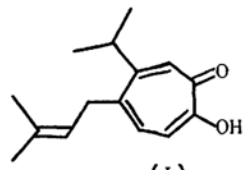
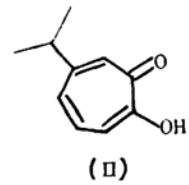
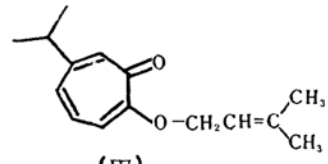
Nootkatin, the only known sesquiterpenoid tropolone, was isolated by Erdtman and his collaborators from the heart-wood of *Chamaecyparis nootkatensis* (Alaskan yellow ceder)[2]. The structure has been demonstrated as 4-isopropyl-5-(γ-methyl but-β-enyl) tropolone (I) by chemical reaction[2] and X-ray analysis[3]. As far as the authors are aware, the synthesis of nootkatin has not been attained as yet. This paper deals with the synthesis of nootkatin by a simple method.



(I)



(II)



(III)

4-Isopropyltropolone (II) has been chosen as a starting material since (II) was synthesized before[4]. The procedure initiated from 5-substituted 4-isopropyltropolones, i. e. 5-cyano and 5-formyl derivatives derived from 5-amino-4-isopropyltropolone, was fruitless.

The Claisen rearrangement reaction has been applied to the synthesis of I. Preliminary work on the rearrangements of tropolone allyl ether and 3,7-dibromotropolone allyl ether resulted in the formation of 3-allyltropolone (80% yield) and in recovery of a small amount of 3,7-dibromotropolone, respectively, and no *p*(5)-rearrangement product was observed.

1) Presented at the 11th Annual Meeting of the Chemical Society of Japan in Tokyo, April 3, 1958. This investigation was supported in part by a donation of the Sankyo Co., Tokyo.

2) B. Carlsson, H. Erdtman, A. Frank and W. E. Harvey, *Acta Chem. Scand.*, **6**, 690 (1952); H. Erdtman and W. E. Harvey, *Chem. and Ind.*, **1952**, 1267; S. R. Duff and H. Erdtman, ibid., **1954**, 432.

3) R. B. Campbell and J. M. Robertson, ibid., **1952**. 1266.

4) T. Nozoe et al., *Proc. Japan Acad.*, **26**. No. 7, 43 (1950).

However, it seemed to us that a steric effect of dimethyl group in the cyclic intermediate of rearrangement of 4-isopropyltropolone γ: γ-dimethylallyl ether (III) might bring about a possibility of *p*-rearrangement to give nootkatin.

The reaction of silver salt[5] of II with γ: γ-dimethylallyl bromide in anhydrous ether gave an oily mixture of III and its isomer. On refluxing the mixture in xylene for three hours and treating the resulting reaction mixture with aqueous sodium bicarbonate-, sodium carbonate- and then with sodium hydroxide solution, nootkatin, m. p. 95° was obtained in 7% yield from a soluble part in aqueous sodium hydroxide solution.

Anal. Found; C, 77.61; H, 8.36. Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68%.

The identity with an authentic specimen of natural nootkatin was established by mixed melting point determination, infrared and nuclear magnetic resonance spectral comparisons.

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5) H. Iinuma, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zassi*), **64**, 742 (1943).