The Synthesis of Procerin

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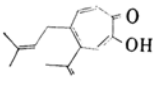
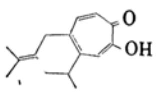
In the course of his investigation of the tropolone constituents of *Juniperus procera Hochst*, Buneberg found a propolone, $C_{15}H_{18}O_2$, of a new sesquiterpene type to which he gave the name of procerin. From the chemical and physical experimental facts, the same author proposed structure I for it.[1] However, the synthesis of procerin has not yet been published.



(I)



(II)

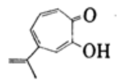
Nootkatin (II)[2,3] which has structure similar to that of procerin, has already been synthesized by Kitahara and Funamizu[4] by applying the Claisen rearrangement reaction. We have expected that procerin may be synthesized by the application of the above method to β-dolabrin (III).

The reaction of the silver complex salt of dolabrin and γ, γ-dimethyl allyl bromide in ether afforded the corresponding allyl ether (IV) of III in a 60% yield. IV was anticipated to be a mixture of two isomers, i. e., IVa and IVb, although several efforts to separate them were all unsuccessful.

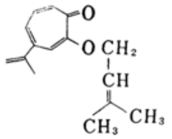
After a mixture of IVa and IVb had been heated in xylene to perform the Claisen rearrangement, the tropolone part was placed in an alkaline solution; this was extracted with ether after an acidification. From the sodium bicarbonate-soluble fraction of the ether solution, III was recovered in a 6.5% yield, while the sodium carbonate-soluble part of it gave a white crystalline compound V (m. p. 68~69°C), whose infrared spectrum is entirely the same as that of natural procerin. Furthermore, the results of the microanalysis of V and its copper complex (m. p. 199~200°C) are satisfactory for procerin and for its copper complex respectively.

We have not isolated the compound VI, which might be formed by the rearrangement which occurs at the ortho position.

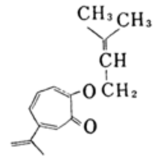
Since the synthesis of III had already been carried out, the total synthesis of procerin has now accomplished.



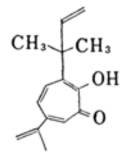
(III)



(IVa)



(IVb)



(VI)

Experimental

Silver Salt of Dolabrin (III). — Dolabrin (III) (1.62 g.) was dissolved into water (300 ml.), and the solution was neutralized with 2 N sodium hydroxide, using phenolphthalein as an indicator. To the solution was added silver nitrate (1.8 g.) in an aqueous solution (50 ml.). The separated yellow precipitate (2.5 g., 97%) were filtered off and dried at 100°C at reduced pressure for 2 hr., using phosphoric acid anhydride.

γ, γ-Dimethyl Allyl Ether IV of III.—(A) well-dried silver complex (2.5 g.) was suspended in absolute ether (30 ml.), and into this suspension γ, γ-dimethyl allyl bromide (1.5 g.) was stirred at room temperature. After being stirred for 1 hr., it was heated under reflux for 2 hr., the separated silver bromide was filtered off, and the ether was removed. Distillation of the resultant residue under reduced pressure afforded a yellow oil (IVa and IVb) (1.27 g., 60%), which has a slight color reaction to a ferric chloride solution.

The Claisen Rearrangement Reaction of γ, γ-Dimethyl Allyl Ether (IV). — A solution of IV (1.27 g.) in xylene (3 ml.) was refluxed for 3 hr. under a nitrogen atmosphere; then the solution was diluted with ether (20 ml.) and extracted with 0.1 N aqueous sodium hydroxide. The sodium hydroxide solution was acidified with sulfuric acid and extracted with ether. The combined ether

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[1] J. Buneberg, *Acta Chem. Scand.*, **15**, 645 (1961).

[2] B. Carlssin, H. Erdtman, A. Frank and W. E. Harvey, ibid., **6**, 690 (1952).

[3] W. E. Harvey, *Chem. & Ind.*, **1952**, 1267.

[4] Y. Kitahara and M. Funamizu, This Bulletin, **31**, 782 (1958).

solution was extracted three times with a saturated sodium bicarbonate aqueous solution, which was then separated from the ether solution (E_1). The combined sodium bicarbonate solution was washed with ether once, and the ether washing was combined with E_1. The sodium bicarbonate solution was acidified and extracted with ether. The ether extract gave a white crystalline compound (60 mg.) (m. p. 50~53°C), which was identified as dolabrin by mixed melting point determination. E_1 was extracted with a saturated sodium carbonate aqueous solution, which was then separated from the ether solution (E_2). The sodium carbonate solution was washed with ether once, and the ether washing was combined with E_2. The separated sodium carbonate solution was acidified and extracted with ether. The ether solution gave a white crystalline compound (70 mg., 5.5%) (m. p. 68~69°C).

Found: C, 78.72; H, 8.16. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88%.

Copper complex: m. p. 198~200°C, green needles (from ethanol).

Found: C, 69.39; H, 6.56. Calcd. for $C_{15}H_{17}O_2 \cdot Cu_{1/2}$: C, 69.01; H, 6.56%.

E_2 was washed with water and dried. The removal of the solvent gave a yellow oil.

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