Synthesis of Maxima Substance B

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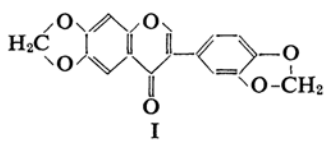
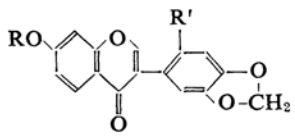
In 1954 Rangaswami and Sastry reported the isolation of three colorless substances from the roots of *Tephrosia maxima* Aers[1]. The substances were called maxima substance A, B and C[1], and later were assigned as isoflavones[2-4]. Degradative work with three crystalline, which shows that they all have the same isoflavone skeletons including the methylenedioxy group, has led to the following structures being proposed for them, maxima substance A (I)[2], B (II)[3] and C (III)[4].

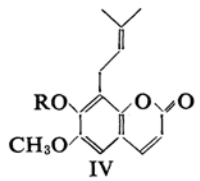
Maxima substance B was of interest as it is one of the naturally occuring γ,γ-dimethylallylethers of chromone derivatives. These ethers have been isolated and known as maxima substance C (III)[4], brayleyanin (IV)[5] and 5-hydroxy-4'-γ,γ-dimethylallyloxy-3',7-dimethoxyflavanone (V)[6]. None of these substances has so far been synthesized. We were led by our interest in the oxygen heterocyclics synthesis to attempt their synthesis and our initial aim was to prepare maxima substance B.



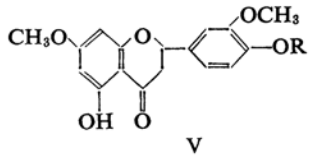
I



II; R', H
III; R', OCH_3



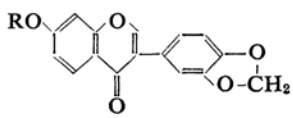
IV



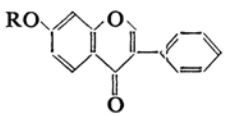
V

For II—V; R, $(CH_3)_2C{=}CH{-}CH_2$

In the present communication, we now record the synthesis of maxima substance B and related compounds. A key intermediate in our proposed synthesis was pseudobaptigenin (VI), an isoflavone which has been obtained by Späth and Schmidt[7] and synthesized by Späth[8], Venkataraman[9], Baker[10-11] and Farkas[12-13]. The reaction of pseudobaptigenin (VI), which was prepared by the Farkas' method[13], and γ,γ-dimethylallylbromide[14] with potassium carbonate gave an ether in good yield. It formed colorless needles, having an empirical formula of $C_{21}H_{18}O_5$, m. p. 134~135°C.



II; R, $(CH_3)_2C{=}CH{-}CH_2$
VI; R, H
VII; R, $(CH_3)_2CH{-}CH_2{-}CH_2$



VIII; R, $(CH_3)_2C{=}CH{-}CH_2$
X; R, H
IX; R, $(CH_3)_2CH{-}CH_2{-}CH_2$

Cleavage of an etheral linkage with sulfuric acid in acetic acid took place smoothly to give pseudobaptigenin (VI), m. p. 288~290°C, which was used as a key intermediate. Hydrogenation

1) S. Rangaswami and B. V. Rama Sastry, *Current Sci. (India)*, **23**, 397 (1954): *Chem. Abstr.*, **49**, 8568 (1955).
2) S. Rangaswami and B. V. Rama Sastry, *Proc. Indian Acad. Sci.*, **44A**, 279 (1956): *Chem. Abstr.*, **51**, 8083 (1957).
3) S. Rangaswami and B. V. Rama Sastry, *Current Sci. (India)*, **24**, 337 (1955): *Chem. Abstr.*, **50**, 13008 (1956).
4) S. Rangaswami and B. V. Rama Sastry, *Arch. Pharm.*, **292**, 170 (1959).
5) F. A. L. Anet, G. K. Hughes and E. Ritchie, *Australian J. Sci. Research*, **2A**, 608 (1949): *Chem. Abstr.*, **45**, 2938 (1951).
6) T. A. Geissman, *Australian J. Chem.*, **11**, 376 (1958): *Chem. Abstr.*, **53**, 1320 (1959).
7) E. Späth and O. Schmidt, *Monatsh. Chem.*, **53-54**, 454 (1929).
8) E. Späth and E. Lederer, *Ber.*, **63**, 743 (1930).
9) H. S. Mahal, H. S. Rai and K. Venkataraman, *J. Chem. Soc.*, **1934**, 1769.
10) W. Baker, R. Robinson and N. M. Simpson, ibid., **1937**, 805.
11) W. Baker, J. Chadderton, J. B. Harborne and W. D. Ollis, ibid., **1953**, 1852.

of the ether in the presence of platinum oxide catalyst in acetic acid afforded a dihydrocompound, m. p. 138~139°C, after one mole of hydrogen was absorbed. Pseudobaptigenin (VI) and isoamylbromide with potassium carbonate gave the 7-isoamyloxypseudobaptigenin (VII), m. p. 139~140°C, which was identical with the above dihydrocompound as shown by the infrared spectrum and the mixed melting point determination. It was shown to have structure II of the ether. The ether II was identical with the natural substance in the mixed melting point determination by Rangaswami. The structure assigned to maxima substance B has, therefore, been fully confirmed. The infrared and ultraviolet spectra of II and VII were shown in Figs. 1 and 2.

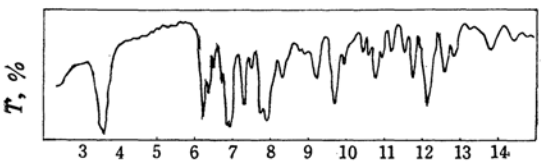


Fig. 1a. Infrared spectrum of maxima substancce B (II) (Nujol).

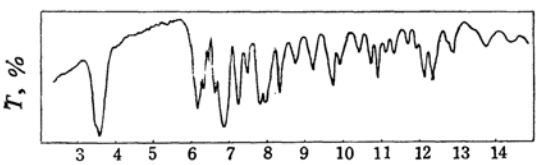


Fig. 1b. Infrared spectrum of 7-isoamyloxypseudobaptigenin (VII) (Nujol).

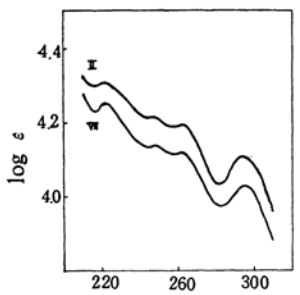


Fig. 2. Ultraviolet spectra of maxima substance B (II) and 7-isoamyloxypseudobaptigenin (VII).

By model experiment with a simple analogue, 7-γ, γ-dimethylallyloxyisoflavone (VIII) and 7-isoamyloxyisoflavone (IX), respectively m. p. 157~158°C and 149~150°C, were obtained from 7-hydroxyisoflavone (X)[15].

Experimental*

Maxima Substance B (7-γ, γ-Dimethylallyloxypseudobaptigenin) (II).—To a solution of pseudobaptigenin[13] (VI, m. p. 288~290°C, 1.0 g.) and γ, γ-dimethylallylbromide[14] (1.1 g.) in anhydrous acetone (250 ml.) was added anhydrous potassium carbonate (5.0 g.), and the mixture was refluxed for 20 hr. in a steam bath. The resulting mixture was filtered from precipitates and the solvent was distilled off. The residual product was recrystallized from ethanol to give II in the form of colorless needles, m. p. 134~135°C; yield 0.9 g. (75%). The natural substance is m. p. 126~128°C[1]. This substance showed no depression of the meltint point on admixture with the natural specimen by Rangaswami.

Found; C, 71.85; H, 5.23. Calcd. for $C_{21}H_{18}O_5$: C, 71.99; H, 5.18%.

UV λ_{max}^{EtOH} mμ (log ε): 222 (4.32), 249 (4.21), 264 (4.19), 295 (4.12).

7-Isoamyloxypseudobaptigenin (VII).—*a) From II.*—The mixture of maxima substance B (II) (300 mg.) and platinum oxide (50 mg.) in glacial acetic acid (80 ml.) was shaken in the atmosphere of hydrogen until 1.2 mol. of hydrogen was absorbed. After separation of the catalyst, the filtrate was evaporated under reduced pressure. The residual product was recystallized from ethanol to give VII in the form of colorless needles, m. p. 138~139°C; yield 150 mg. (50%).

b) From VI.—By a similar method as described for II, VII was obtained from VI (1.5 g), isoamylbromide (2.0 g.), anhydrous potassium carbonate (5.0 g.) and acetone (150 ml.); colorless needles, m. p. 139~140°C; yield 1.5 g. (76%). This substance showed no depression of the melting point on admixture with the specimen derived by the above-mentioned method a).

Found: C, 71.77; H, 5.76. Calcd. for $C_{21}H_{20}O_5$: C, 71.58; H, 5.72%.

UV λ_{max}^{EtOH} mμ (log ε): 223 (4.26), 249 (4.14), 261 (4.12), 295 (4.04).

Degradation of Maxima Substance B (II).—To maxima substance B (II) (2.0 g.) in acetic acid (100 ml.) was added concentrate sulfuric acid (1 ml.). After standing of the mixture for two days at room temperature, the solids appeared and were collected by filtration. The product was recrystallized from ethanol to give VI in the form of colorless microcrystals, m. p. 288~290°C; yield 1.4 g. (86%). Reported m. p. is 296°C[13].

Acetate of VI was prepared quantitatively by refluxing VI and acetic anhydride with anhydrous sodium acetate, m. p. 175~175.5°C. Reported m. p. is 176°C[13].

12) L. Farkas, A. Major, L. Pallos and J. Várady, *Chem. Ber.*, **91**, 2858 (1958).
13) L. Farkas and V. Szánthó, *Acta Chim. Acad. Sci. Hung.*, **19**, 217 (1959): *Chem. Abstr.*, **54**, 3398 (1960).
14) A. Bolleter, K. Eiter and H. Schmidt, *Helv. Chim. Acta*, **34**, 186 (1951).
15) V. R. Sathe and K. Venkataraman, *Current Sci. (India)*, **18**, 378 (1949): *Chem. Abstr.*, **44**, 8916 (1950).
* All melting points are uncorrected.

These substances showed no depression of the melting point on admixture with the authentic specimens.

7-γ,γ-Dimethylallyloxyisoflavone (VIII).—By a similar method as described for II, VIII was obtained from 7-hydroxyisoflavone[15] (X, m. p. 211~212°C, 1.0 g.), γ,γ-dimethylallylbromide (1.3 g.), anhydrous potassium carbonate (2.5 g.) and acetone (100 ml.); colorless plates, m. p. 157~158°C; yield 0.9 g. (70%).

Found: C, 78.61; H, 5.95. Calcd. for $C_{20}H_{18}O_3$: C, 78.41; H, 5.92%.

7-Isoamyloxyisoflavone (IX).—By a similar method as described for II, IX was obtained from X (0.5 g.), isoamylbromide (0.7 g.), anhydrous potassium carbonate (2.0 g.) and acetone (50 ml.); colorless needles, m. p. 149~150°C; yield 0.6 g. (92%).

Found: C, 77.78; H, 6.62. Calcd. for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54%.

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