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Synthetic Studies of Sesamol Derivatives. X.[*1] Synthesis of Dehydroneotenone

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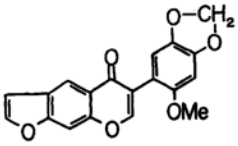
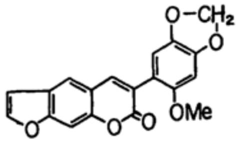
The synthesis of dehydroneotenone has been carried out using 6-hydroxy-5-(2-methoxy-4,5-methylenedioxyphenylacetyl)-2,3-dihydrobenzo[*b*]furan as an intermediate and by subjecting it to cyclization with ethyl orthoformate, followed by dehydrogenation.

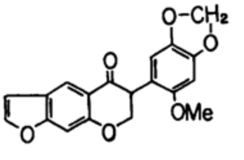
Dehydroneotenone (Erosone),[1] a colorless substance, $C_{19}H_{12}O_6$, is the first naturally-occurring furanoisoflavone (I) which has been isolated, along with pachyrrhizin (II)[2], from *Pachyrrhizus erosus* (Yam bean),[3] as well as from *Neorautanenia edulis*[4] and *N. amboensis*.[4] On the other hand, I has been derived[5] from neotenone (III), a naturally-occurring furanoisoflavanone, by dehydrogenation with manganese dioxide. The present paper will describe the total synthesis of I according to a modification of a procedure reported earlier.[6]



I



II



III

By a modified Hoesch reaction, 6-hydroxy-2,3-dihydrobenzo[*b*]furan (IV)[7] was condensed with 2-methoxy-4,5-methylenedioxyphenylacetonitrile

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[*1] This has previously been reported in a preliminary form: K. Fukui and M. Nakayama, *Experientia*, **20**, 668 (1964). Part IX: K. Fukui, M. Nakayama and T. Matsui, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **87**, 1359 (1966).

1) W. D. Ollis, "Symposium on Photochemistry," ed. by H. R. Arthur, Hong Kong Univ. Press, Hong Kong (1964), p. 145.

2) E. Simonitsch, M. Frei and H. Schmid, *Monatsh. Chem.*, **88**, 541 (1957).

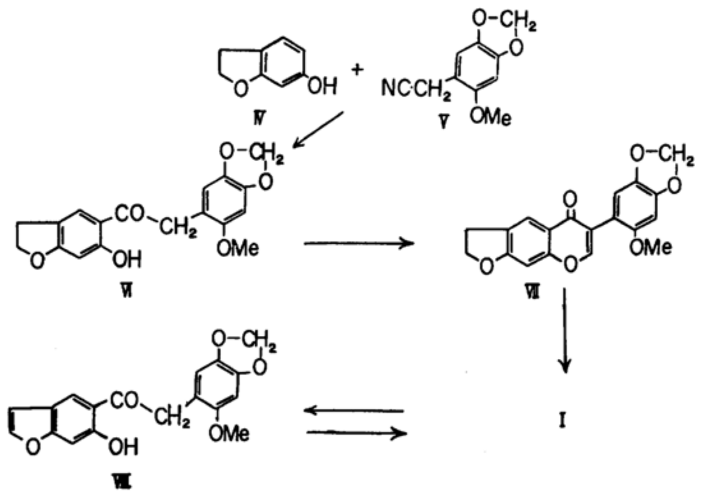
3) L. B. Norton and R. Hansberry, *J. Am. Chem. Soc.*, **67**, 1609 (1945).

4) C. v. d. M. Brink, J. J. Dekker, E. C. Hanekom, D. H. Meiring and G. J. H. Rall, *J. S. African Chem. Inst.*, **18**, 21 (1965); *Chem. Abstr.*, **63**, 14834 (1965).

5) L. Crombie and D. A. Whiting, *Tetrahedron Letters*, **1962**, 801; *J. Chem. Soc.*, **1963**, 1569.

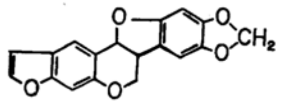
6) a) K. Fukui and M. Nakayama, *Experientia*, **19**, 621 (1963); This Bulletin, **41**, 1385 (1968); b) K. Fukui and M. Nakayama, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **85**, 444 (1964); c) K. Fukui, M. Nakayama, A. Tanaka and S. Sasatani, This Bulletin, **38**, 845 (1965).

7) J. S. H. Davies, P. A. McCrea, W. L. Norris and R. Ramage, *J. Chem. Soc.*, **1950**, 3206.



(V)[8] to give 6-hydroxy-5-(2-methoxy-4, 5-methylenedioxyphenylacetyl)-2, 3-dihydrobenzo[*b*]furan (VI). The subsequent treatment of the dihydrobenzofuran VI with ethyl orthoformate - pyridine - piperidine gave dihydrodehydroneotenone (VII). The dehydrogenation of the dihydro-compound VII with either *N*-bromosuccinimide[4,9] or 10% palladium-charcoal gave the isoflavone I. On alkaline hydrolysis, I gave 6-hydroxy-5-(2-methoxy-4,5-methylenedioxyphenylacetyl)benzo [*b*] furan (VIII).[5,9]

The partial synthesis of III had already been carried out from the isoflavone I.[5] Moreover, the racemate of (−)-neodulin (IX),[10] a naturally-occurring pterocarpan, had already been derived from the same isoflavone I *via* the corresponding isoflavanol-4.[4] Thus, the total syntheses of III and (±)-IX have been now accomplished.



IX

The ultraviolet spectra of the isoflavone I and its dihydro-compound VII are shown in Fig. 1. There are two absorption bands, at *ca.* 230—250 mμ (band I) and at *ca.* 300—310 mμ (band II). Band I is due to furano- and dihydrofurano-benzenoid. The dehydrogenation of the dihydrofuranobenzenoid showed a marked hyperchromic effect. Many samples of this same phenomenon have been reported in previous reports.[2,6,11]

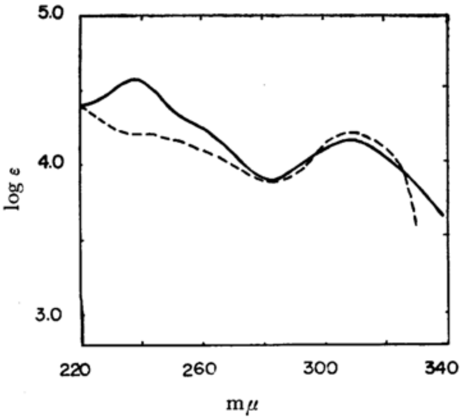


Fig. 1. UV spectra of I (——) and VII (- - -) in ethanol.

Experimental[*2]

6-Hydroxy-5-(2-methoxy-4,5-methylenedioxyphenylacetyl)-2,3-dihydrobenzo[*b*]furan (VI). To a mixture of 6-hydroxy-2,3-dihydrobenzo[*b*]furan (IV)[7] (4.0 g), 2-methoxy-4, 5-methylenedioxyphenylacetonitrile (V)[8a] (4.0 g), and fused zinc chloride (9.0 g) in dry chloroform (200 m*l*), anhydrous aluminum chloride (7.0 g) was added. Dry hydrogen chloride was passed through this mixture for 30 min at 0°C, and then dry ether (150 m*l*) was added. The resulting mixture was completely saturated with dry hydrogen chloride and then allowed to stand for 4 days in a

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[8] a) K. Fukui and M. Nakayama, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **84**, 606 (1963); b) H. Suginome, *Tetrahedron Letters*, **1960** 16; This Bulletin, **39**, 1525 (1966); c) C. A. Anirudhan and W. B. Whalley, *J. Chem. Soc.*, **1963**, 6049.

[9] K. Fukui and M. Nakayama, *Experientia*, **20**, 668 (1964).

[10] B. L. van Durren, *J. Org. Chem.*, **26**, 5014 (1961).

[11] a) K. Fukui, M. Nakayama and K. Okazaki, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **87**, 1096 (1966); b) D. K. Chatterjee, R. M. Chatterje and K. Sen, *J. Org. Chem.*, **29**, 2467 (1964).

[*2] All melting points are uncorrected; the infrared spectra were measured in Nujol, while the ultraviolet spectra were measured in an ethanol solution.

refrigerator. An ether solution was decanted from the ketimine hydrochloride, which had separated. The residue was washed with dry ether and then hydrolyzed with water (350 m*l*) on a steam bath for 1 hr. The precipitates were collected and recrystallized from ethanol to give VI as colorless needles, mp 153—154°C, which gave a brown ferric chloride reaction in ethanol; yield, 2.1 g (31%). IR: 1650 (C=O), 1038, 931 (O–CH$_2$–O) cm^{-1}. UV: λ_{max} mμ (log ε); 239 (4.21), 284 (4.14), 330 (3.70).

Found: C, 65.67; H, 4.95%. Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91%.

Dihydrodehydroneotenone(4'',5''-dihydrofurano-(3'',2'':6,7)-2'-methoxy-4',5'-methylenedioxyisoflavone) (VII). To a solution of VI (1.0 g) and ethyl orthoformate (6 m*l*) in pyridine (25 m*l*), piperidine (1 m*l*) was added. The solution was then refluxed for 24 hr. The resulting solution was cooled and acidified with dilute hydrochloric acid. The resulting precipitates were collected, washed with water, and recrystallized from ethanol to give VII as colorless needles, mp 247—248°C; yield, 1.1 g (82%) (lit.[4] mp 255°C (correct.)). IR: 1644 (γ-pyrone), 1040, 919 (O–CH$_2$–O) cm^{-1}. UV: λ_{max} mμ (log ε); 241$_i$ (4.22),[*3] 251$_i$ (4.19), 310 (4.23).

Found: C, 67.38; H, 4.47%. Calcd for $C_{19}H_{14}O_6$: C, 67.45; H, 4.17%.

Dehydroneotenone (I). A mixture of VII (500 mg), 10% palladium-charcoal (400 mg), and diphenyl ether (20 m*l*) was refluxed for 10 hr. The catalyst was then filtered off, and the solvent removed by steam distillation. The resulting precipitates were collected and recrystallized from ethanol to give I as colorless needles, mp 234—235°C; yield, 220 mg (44%) (lit. mp 242°C (correct.),[3] 239.5—240.5°C (correct.),[4] 240—241°C[5]). This was identical with an authentic sample (mp 234—235°C) obtained from VII by the *N*-bromosuccinimide method.[9] IR: 1644 (γ-pyrone), 1626, 1589, 1544, 1508 (aromatic), 1040, 942 (O–CH$_2$–O) cm^{-1} (lit.[5] 1658, 1629, 1592, 1549, 1506 cm^{-1} (chloroform solution)). UV: λ_{max} mμ (log ε); 238 (4.59), 309 (4.20) (lit.[5] 239 (4.61), 308 (4.10)).

Found: C, 68.00; H, 3.84%. Calcd for $C_{19}H_{12}O_6$: C, 67.85; H, 3.60%.

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[*3] i=Inflection point.