SYNTHETIC EXPERIMENTS IN THE BENZOPYRONE SERIES

Part XXVI. A Synthesis of 8-Methyl Isogenistein

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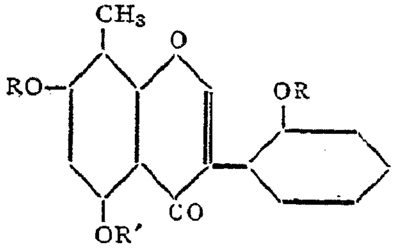
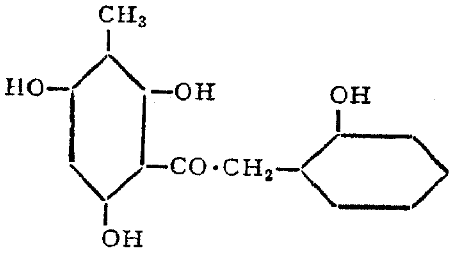
Among the crystalline products from soya beans Okano and Beppu[1] reported the isolation of the glycoside, 8-methyl isogenistin (sugar position unsettled) and its aglucone, 8-methyl isogenistein. The analytical values of the aglucone corresponded to the formula $C_{16}H_{12}O_5$. It was found to yield a dimethyl ether (I *b*), a trimethyl ether (I *c*) and a triacetate. On heating with alkali, it gave a tetrahydroxy ketone which was considered to have the structure, 2:4:6:2′-tetrahydroxy-3-methyl phenyl benzyl ketone (II) since it yielded C-methyl phloroglucinol (III *a*) and *o*-hydroxy phenyl acetic acid (IV *a*) on further degradation. The parent aglucone should therefore be 6- or 8-methyl-5:7:2′-trihydroxy isoflavone (I *a*). The location of the methyl group was determined by degradation of the trimethyl ether (I *c*) with alkali, when C-methyl phloroglucinol α-dimethyl ether (III *b*) and *o*-methoxy phenyl acetic acid (IV *b*) were obtained as the products. Hence Okano and

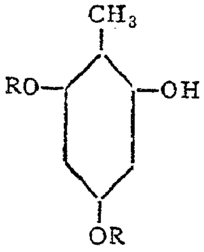


I

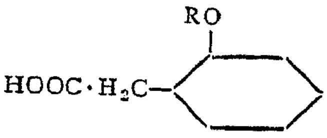
a, R = R′ = H
b, R = CH₃, R′ = H
c, R = R′ = CH₃



II



III

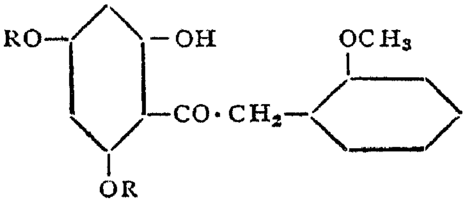


IV

a, R = H
b, R = CH₃

Beppu[1] assigned the structure of 8-methyl-5: 7: 2′-trihydroxy isoflavone (8-methyl isogenistein) (I *a*) to the natural compound.

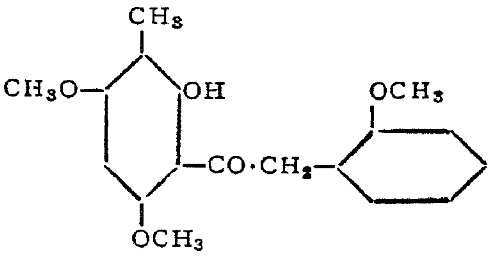
A synthesis of a compound of this structure (I *a*) has now been carried out along the lines of the synthesis of 8-methyl genistein, described in an earlier paper.[2] For this purpose, 2: 4: 6-trihydroxy-2′-methoxy phenyl benzyl ketone (V *a*) described in Part XXIV[3] is heated with excess of methyl iodide and potassium carbonate in acetone solution. The product is fractionally crystallised from alcohol. The less soluble fraction is 2-hydroxy-3-methyl-4: 6: 2′-trimethoxy phenyl benzyl ketone (VI). It does not give any blue or green colour with concentrated nitric acid[4] but gives a wine red ferric reaction. These properties are in agreement with this C-methyl formula. The more soluble fraction is identical with 2-hydroxy-4: 6: 2′-trimethoxy phenyl benzyl ketone (V *b*) described in an earlier publication.[3]



V

a, R=H

b, R=CH_3



VI

Condensation of 2-hydroxy-3-methyl-4: 6: 2′-trimethoxy phenyl benzyl ketone (VI) with ethyl formate and sodium[5] gives a good yield of 5: 7: 2′-trimethoxy-8-methyl isoflavone (I *c*).* This compound is found to melt at 178–79° and seems to be quite different from the trimethyl ether of the natural compound, whose melting point was reported as 152–53° by Okano and Beppu.[1] In this case also, as with 5: 7: 2′-trimethoxy isoflavone,[3] considerable difficulties exist in demethylation. When a mixture of acetic anhydride and hydriodic acid is employed for this purpose, a resinous product is obtained from which a small quantity of crystalline material melting at 230–32° could be isolated. The demethylation is more conveniently effected by aluminium chloride in benzene solution.[6] The product melts at 230–32° and is identical with the compound obtained by the demethylation of (I *c*) with hydriodic acid. Okano and Beppu[1] reported the melting point of the natural compound to be 300–02°. They have also mentioned that it gave a violet red colour with alcoholic ferric chloride. The deep green

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* This compound has subsequently been found to be 2-hydroxy-5: 7: 2′-trimethoxy-8-methyl isoflavanone and has been converted into 5: 7: 2′-trimethoxy-8-methyl isoflavone, m.p. 183–84°.

SUMMARY

One of the crystalline compounds occurring in soya beans has been considered by Okano and Beppu to be 8-methyl isogenistein and this structure was based on the alkali degradation of the compound and its trimethyl ether. A compound of this structure is now synthesised starting from 2:4:6-trihydroxy-2′-methoxy phenyl benzyl ketone, along the lines of synthesis of 8-methyl genistein described in Part XXII. Here also the products are found to be different from those reported by Okano and Beppu and the natural compound should therefore have a more complex structure.

REFERENCES

1. Okano and Beppu .. *J. Agri. Chem. Soc. Japan*, 1939, **15**, 645.
2. Seshadri and Varadarajan .. *Proc. Ind. Acad. Sci.*, 1953, **37A**, 145 and 508.
3. ——— ——— .. *Ibid.*, 1953, **37A**, 514.
4. Rao and Seshadri .. *Ibid.*, 1949, **30A**, 30.
5. Venkataraman *et al.* .. *J.C.S.*, 1934, 513 and 1770.
6. Seshadri *et al.* .. *Proc. Ind. Acad. Sci.*, 1947, **24A**, 213; 1947, **25A**, 432; 1949, **29A**, 72; 1952, **35A**, 34, 82 and 202.