SYNTHETIC EXPERIMENTS IN THE BENZOPYRONE SERIES

Part XXVII. A Note on the Synthesis of Santal

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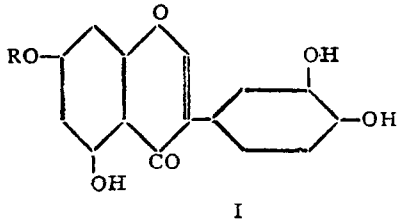
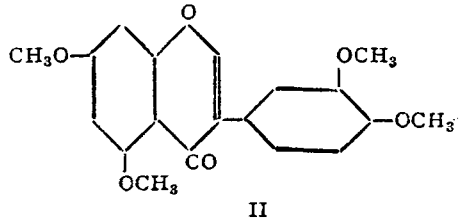
IN our earlier publication[1] was reported the synthesis of santal (I *a*) by two methods, (1) in a fair yield by the hydriodic acid demethylation of santal trimethyl ether (5:7:3':4'-tetramethoxy isoflavone) (II), and (2) in a rather poor yield by the partial methylation of norsantal (I *b*) just analogous to the earlier synthesis of prunetin.[1a] Iyer *et al.*[2] reported another synthesis from 5:7-dimethoxy-3':4'-methylenedioxy isoflavone which by demethylenation and partial demethylation using anhydrous aluminium bromide yielded santal. This seems to have been based on the assumption that demethylation of methoxyl groups in the side-phenyl nucleus of the isoflavone structure is not possible without affecting the methoxyl in the 7-position. The earlier synthesis mentioned above indicated that this assumption is not valid. In our subsequent papers[3,4] an explanation for the resistance to demethylation of the 7-methoxyl was given and conditions for the satisfactory production of the 7-methyl ethers of isoflavones in good yields by demethylating the fully methylated compounds using hydriodic acid were worked out. By this method isoformononetin (III *a*)[3] and prunetin (IV *a*)[4] were prepared in quantitative yields from daidzein dimethyl ether (III *b*) and genistein trimethyl ether (IV *b*) respectively. However this convenient method has not been used earlier for the synthetic preparation of santal. The partial demethylation of santal trimethyl ether has now been carried out using the modified conditions and the product is found to be exclusively santal obtained in

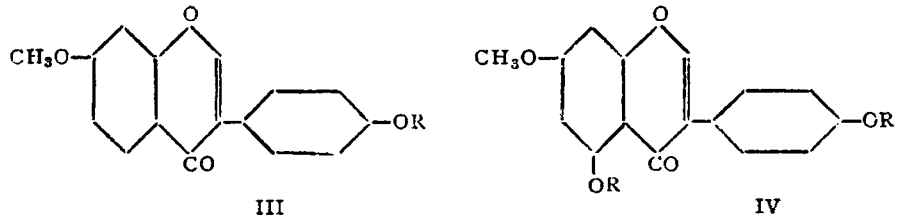


I



II

a, R=CH_3
b, R=H



III IV

a, R = H
b, R = CH_3

almost quantitative yield. Thus this method of partial demethylation is the most convenient for the preparation of this naturally occurring isoflavone.

As already mentioned[1] the alternative method of preparation involving partial methylation of nor-santal (I *b*) is of biogenetic significance. The preparation has now been repeated using larger quantities; and santal and its acetate obtained in this way have been compared with samples obtained by the method of demethylation and found to be identical.

EXPERIMENTAL

Santal

1. *By partial demethylation.*—5 : 7 : 3′ : 4′-Tetramethoxy isoflavone (1 g.) was dissolved in acetic anhydride (3 c.c.) and the solution treated with hydriodic acid (10 c.c.; sp. gr. 1·7) while cooling under the tap. The mixture was heated in an oil-bath at 115–20° for half an hour. It was then cooled and diluted with sulphurous acid. The pale yellow solid that separated was filtered, washed with water and then with aqueous sodium carbonate (1%) in which it was almost insoluble. After finally washing with water and drying in air it was crystallised from ethyl acetate from which it separated as colourless rectangular plates and prisms and melted at 220–22°.[5] It gave an intense brownish red colour with ferric chloride (Found: C, 60·8; H, 4·4; $C_{16}H_{12}O_6$, H_2O requires C, 60·4; H, 4·4%).

The triacetate crystallised from ethyl acetate as colourless clusters of needles melting at 168–70° and was identical with the product described earlier.[1, 5]

2. *Partial methylation.*—On repeating the partial methylation of nor-santal (1·5 g.) using 1 mole of dimethyl sulphate and working up the product as already described[1] santal (0·25 g.) was obtained. It gave on acetylation the triacetate which crystallised from ethyl acetate as clusters of colourless needles melting at 168–70° and was identical with the acetate described in the above experiment; a mixed melting point with that sample was undepressed (Found: C, 61·9; H, 4·4; $C_{22}H_{18}O_9$ requires C, 62·0; H. 4·2%).

SUMMARY

The partial demethylation of 5:7:3':4'-tetramethoxy isoflavone has now been effected under improved conditions and an almost quantitative yield of santal obtained. Partial methylation of nor-santal has been repeated using larger quantities and santal and its acetate prepared and studied.

REFERENCES

1. Narasimhachari and Seshadri .. *Proc. Ind. Acad. Sci.*, 1950, **32A**, 342.
1*a*. ———— .. *Ibid.*, 1950, **32A**, 256.
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3. Aghoramurty *et al.* .. *Ibid.*, 1951, **33A**, 251.
4. Narasimhachari *et al.* .. *Ibid.*, 1952, **36A**, 194.
5. Robertson *et al.* .. *J.C.S.*, 1949, 1571.