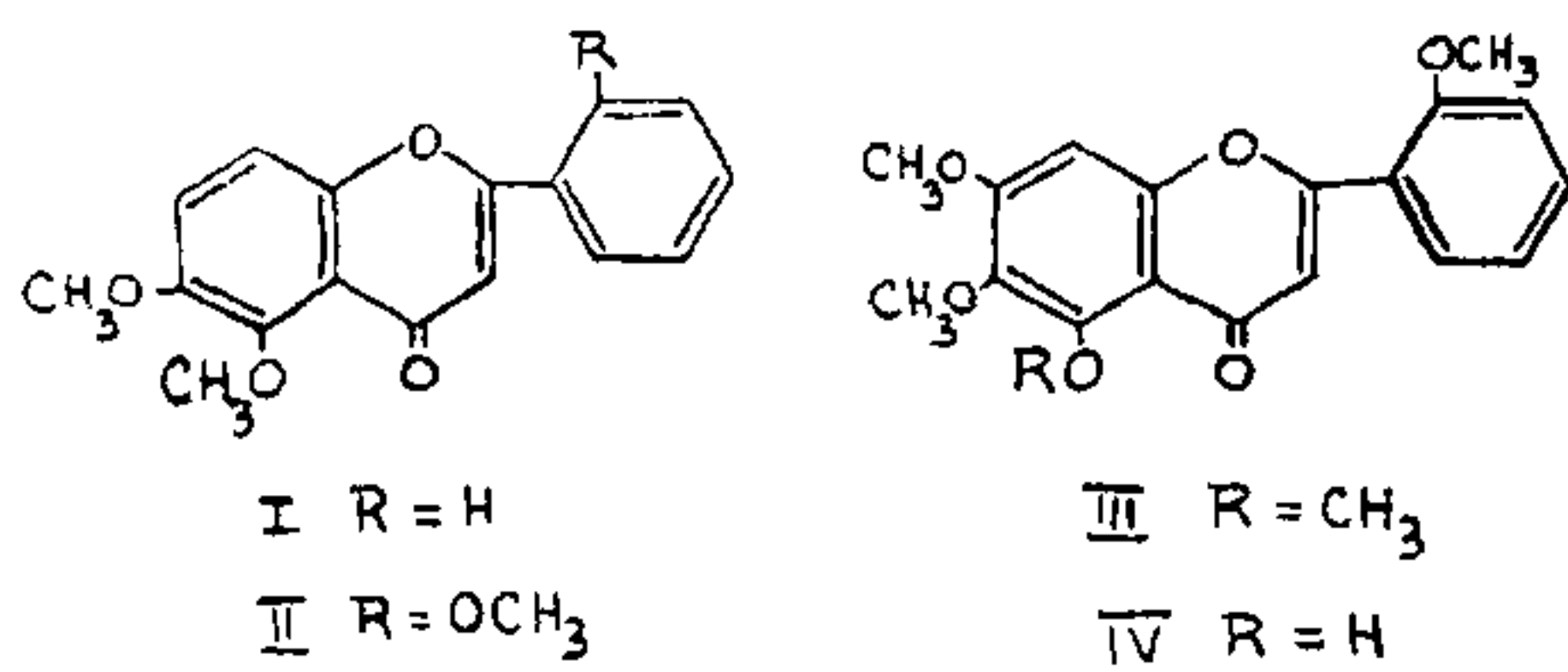


## SYNTHESIS OF SOME 2'-OXYGENATED FLAVONES\*

V. V. S. MURTI, P. V. RAMAN AND T. R. SESHADRI

Department of Chemistry, Delhi University, Delhi-7

IN addition to 5, 6-dimethoxyflavone (I) three new flavones having 2'-methoxyl substituent have been reported to occur in the Mexican tree *Casimiroa edulis*.<sup>1-3</sup> These are 5, 6, 2'-trimethoxyflavone (II), zapotin (III) and zapotinin (IV). The structures of (I) and (II) were confirmed by comparison with synthetic compounds<sup>4,5</sup> but those of (III) and (IV) were inferred from spectral data, colour reactions and degradations and no comparison with synthetic substances was made.



We were interested in the structures assigned to zapotin and zapotinin for a number of reasons: (i) Work has been going on in our laboratory on the Wessely-Moser rearrangement of flavonoids, the factors which govern this change and the mechanism involved.<sup>6,7</sup> The three flavones mentioned above seemed to offer interesting possibilities for such a study.<sup>8</sup> (ii) The validity of the constitutions suggested for zapotin and zapotinin appeared to require synthetic confirmation for the following reasons: (a) Zapotin was reported to undergo only partial demethylation in the 5 position on fusion with potassium hydroxide,<sup>1</sup> a reaction known to effect fission of the pyrone ring and to bring about other drastic changes in flavonoids. (b) Salicylic acid and resorcinol were identified in the products of potash fusion of demethyl-zapotin<sup>1</sup>; while salicylic acid could be traced to the side-phenyl nucleus, the origin of resorcinol could not be definitely established.<sup>3</sup> (c) The oxygenation pattern of the A-ring of zapotin was inferred chiefly from the colour reactions of demethylzapotin, including Bargellini's test but no degradation product to substantiate this conclusion was isolated.<sup>3</sup> It is known

that this test is not specific for compounds of the 5, 6, 7-trihydroxy type and other substances also give a positive reaction.<sup>9-13</sup> It was, therefore, considered necessary to synthesise 5, 6, 7, 2'-tetramethoxyflavone and 5-hydroxy-6, 7, 2'-trimethoxyflavone by unequivocal methods and compare their properties with those of zapotin and zapotinin. This has now been done and, though direct comparison with the compounds isolated from *Casimiroa edulis* could not be carried out, the differences in the properties of the synthetic and the natural products make it clear that zapotin and zapotinin cannot have the structures attributed to them. Our work is still in progress; however, in view of the recent publication of Farkas and Nogradi<sup>14</sup> our main findings are summarised here.

The starting material for the synthesis of 5, 6, 7, 2'-tetramethoxyflavone was 2-hydroxy-4, 5, 6-trimethoxyacetophenone<sup>15</sup>; this was esterified with *o*-methoxybenzoyl chloride<sup>16</sup> and the resulting ester was isomerised to the dibenzoyl-methane using potassium hydroxide in pyridine solution.<sup>17</sup> Ring closure by boiling the diketone with sodium acetate in glacial acetic acid solution afforded the required tetramethoxyflavone. Partial demethylation of the latter with boiling 20% hydrochloric acid gave 5-hydroxy-6, 7, 2'-trimethoxyflavone and complete demethylation to 5, 6, 7, 2'-tetrahydroxyflavone was effected with hot hydriodic acid. The acetates of these compounds were prepared by the acetic anhydride-sulphuric acid method. Attempts were also made to prepare 5, 6, 7, 2'-tetramethoxy- and 5-hydroxy-6, 7, 2'-trimethoxyflavones from 5, 7, 8, 2'-tetramethoxyflavone using the Wessely-Moser rearrangement. The last substance was prepared from 2-hydroxy-3, 4, 6-trimethoxyacetophenone<sup>18</sup> following a route similar to the synthesis of 5, 6, 7, 2'-tetramethoxyflavone. Demethylation of the tetramethoxyflavone to 5-hydroxy-7, 8, 2'-trimethoxyflavone could not be effected with 20% hydrochloric acid but heating with aluminium chloride in nitrobenzene solution was successful. Complete demethylation to 5, 7, 8, 2'-tetrahydroxyflavone was carried out with aluminium chloride in boiling benzene. The acetates of these compounds were prepared by the same method as above. The m.p. and the

\* Part of the Ph.D. Thesis of P.V.R., Delhi University, August 1964.



spectral properties of some of our compounds were different from those of Farkas and Nogradi<sup>14</sup>; however, the properties of 5, 6, 7, 2'-tetramethoxy- and 5-hydroxy-6, 7, 2'-trimethoxyflavones are markedly different from those reported for zapotin and zapotinin<sup>1,3</sup> thus showing that the latter cannot have the structures ascribed to them. The properties of 5, 7, 8, 2'-tetramethoxy- and 5-hydroxy-7, 8, 2'-trimethoxyflavones also do not agree with those of zapotin and zapotinin ruling out these alternative structures also.

Attempts to convert 5, 7, 8, 2'-tetramethoxyflavone to 5, 6, 7, 2'-tetrahydroxyflavone by prolonged refluxing with hydriodic acid and acetic anhydride led to inconclusive results. At one stage of our investigation it was considered possible that the product could be 2', 3', 4', 6'-tetrahydroxyflavone (cf. ref. 8). The corresponding tetramethoxyflavone was synthesised from o-hydroxyacetophenone and 2, 3, 4, 6-tetramethoxybenzaldehyde<sup>19</sup> (now prepared from 1, 2, 3, 5-tetramethoxybenzene<sup>18</sup> by the dimethylformamidophosphorus oxychloride method) via the chalcone and subsequent oxidation with selenium dioxide. But this compound was different from the complete methyl ether of the hydriodic acid demethylation product of 5, 7, 8, 2'-tetramethoxyflavone. Further work on this problem and attempts to determine the correct structures of zapotin and zapotinin is in progress.

1. Kincl, F. A., Komo, J., Rosenkranz, G. and Sondheimer, F., *J.C.S.*, 1956, p. 4163.
2. Iriarte, J., Kincl, F. A., Rosenkranz, G. and Sondheimer, F., *Ibid.*, 1956, p. 4170.
3. Sondheimer, F. and Meisels, A., *Tetrahedron*, 1960, **9**, 139.
4. Baker, W., *J.C.S.*, 1939, p. 956.
5. Doporto, M. L., Gallagher, K. M., Gowan, J. E., Hughes, A. C., Philbin, E. M., Swain, T. and Wheeler, T. S., *J.C.S.*, 1955, p. 4249.
6. Mukerjee, S. K. and Seshadri, T. R., *Chem. and Ind.*, 1955, p. 271.
7. Murti, V. V. S., Seshadri, T. R., Sundaresan, V. and Venkataramani, B., *Proc. Ind. Acad. Sci.*, 1957, **46A**, 265.
8. Gallagher, K. M., Hughes, A. C., O'Donnell, M., Philbin, E. M. and Wheeler, T. S., *J.C.S.*, 1953, p. 3710.
9. Rao, P. S. and Seshadri, T. R., *Proc. Indian Acad. Sci.*, 1943, **17A**, 119.
10. — and —, *Ibid.*, 1941, **14A**, 643.
11. Rao, E. V. and Rangaswami, S., *Ibid.*, 1961, **54A**, 61.
12. Bhardwaj, D. K., Neelakantan, S. and Seshadri, T. R. (unpublished work).
13. Karmarkar, S. S., Shah, K. H. and Venkataraman, K., *Proc. Ind. Acad. Sci.*, 1955, **41A**, 192.
14. Farkas, L. and Nogradi, M., *Chem. Ber.*, 1965, **98**, 164.
15. Sastri, V. D. N. and Seshadri, T. R., *Proc. Indian Acad. Sci.*, 1966, **23A**, 262.
16. Marsh, J. T. and Stephen, H., *J.C.S.*, 1926, p. 1633.
17. Doyle, B. G., Gogan, F., Gowan, J. E., Keane, J. and Wheeler, T. S., *Sci. Proc. Roy. Dublin Soc.*, 1948, **24**, 291.
18. Baker, W., *J.C.S.*, 1941, p. 665.
19. Kuroda, C. and Nakamura, T., *Chem. Abs.*, 1932, **26**, 2442.

## CARNEGIE INSTITUTION OF WASHINGTON—YEAR-BOOK 63 \*

THE increased research activities of the various departments of the Carnegie Institution of Washington during the year 1963-64 are at once apparent from the enlarged size of the Year-Book 63. The Report of President Caryl P. Haskins occupies 20 more pages than last year's, and the Departmental Reports occupy nearly 100 more pages than last year's. Dr. Haskins's thesis on "The Process of Planning Both in and for Science" is highly thoughtful and penetratingly analytical and demands careful study.

In the Mount Wilson and Palomar Observatories programmes of work during the year on solar observations, planets and comets, radio sources and galaxies have yielded some noteworthy results. An analysis of the isotope bands  $C^{12}C^{13}$  in the spectrum of comet Ikeya (1963 a) taken with the 200-inch telescope has indicated a C(12)/C(13) ratio which is the same as in terrestrial and meteoritic material. This observation suggests that the cometary material came from the region of the terrestrial group of planets rather than from the region of the major planets, assuming, of course, that comets were formed at the same time as the solar system.

Earlier work had indicated that the chromospheric activity of a main-sequence star is

\* *Carnegie Institution of Washington—Year-Book 63*, Carnegie Institution, 1530 P Street, Northwest, Washington, D.C. 20005 Octavo, Vol. 73, Pp. xi+601. Price \$ 1.50 (cloth bound).