

# INSECTICIDAL PROPERTIES AND CHEMICAL CONSTITUTION

## Part. IV. Some Simple Chromones and Isoflavones

BY V. V. SREERAMA MURTI, L. RAMACHANDRA ROW  
AND T. R. SESHADRI, F.A.Sc.

*(From the Department of Chemistry, Andhra University, Waltair)*

Received August 14, 1947

IN Part II<sup>1</sup> it was pointed out that there exists a marked difference between the toxic properties of the simpler coumarins and the simpler flavones and this was attributed to the absence of the side phenyl nucleus in the former. A study of 3-phenyl- and 4-phenyl-coumarin derivatives gave ample support to this idea since they were found to be comparable in toxicity with the flavone derivatives. Another way of proving this point would be to examine simpler chromones which do not have the side phenyl nucleus. This has now been done and they are found to be feebly toxic (Nos. 1-3 in the table).

In the skeleton of rotenone and other rotenoid molecules, the side phenyl nucleus is attached to the 3-position of the pyranone ring. Consequently iso-flavones should have greater structural resemblance to them than flavones. Hence a few simple compounds of the isoflavone group have now been tested (Nos. 7-11). The hydroxy compounds appear to be more toxic than the corresponding flavones whereas the methoxy compounds are less toxic. In this respect isoflavones resemble the phenylcoumarins.<sup>1</sup>

Data presented in Part III<sup>2</sup> indicated that the presence of a free hydroxyl in the 5-position of flavones is an advantage in some cases. The chief difficulty in their study by employing the fish technique is their sparing solubility in aqueous medium. 5-Hydroxy-7-methoxy-2-methyl-isoflavone (10) is found to be more toxic than even the corresponding dimethoxy compound (11). The simple 5-hydroxy flavone (4) itself has been tested now. It could be employed only in a concentration of 10 mg. per litre and is found to be ineffective. Since in the coumarin group 5-methoxy-4-methyl-coumarin was found to be definitely more toxic than the isomeric 7-methoxy-compound, 5-methoxy-flavone (5) has been examined. It is however found to be much less toxic as compared with 7-methoxy-flavone.

A number of allyl derivatives (12-20) belonging to the chromone, flavone and isoflavone groups have also been tested. The simpler 7-allyloxy-compounds are even somewhat better than the corresponding methyl ethers. But the effect of the further presence of a nuclear allyl group in the 8-position is not uniform. In the chromone this seems to be an advantage whereas in the flavone it is a disadvantage. 8-Allylated-7-hydroxy compounds are uniformly weak, but the methylation of these compounds re-establishes the toxicity. In regard to these allyl compounds it should be remarked that besides the rapidity with which they bring about toxic effect, they seem to cause more permanent injury than the methyl ethers since the recovery of the fish after transfer to fresh-water is markedly slower and poorer. Hence some of these may prove to be useful insecticides.

The following table gives a summary of the results.

TABLE  
ge = gelatin added

Compound	Concentration in mg. per litre	Turning time
1 2-Methyl-7-hydroxy-chromone ..	100	No action in 24 hours
2 2-Methyl-3-methoxy-7-hydroxy chromone ..	50	" "
3 2-Methyl-7-methoxy-chromone ..	100	18.0 min.
	50	41.0 "
4 5-Hydroxy-flavone <sup>2</sup> ..	10	No action in 18 hours
5 5-Methoxy-flavone <sup>2</sup> ..	20 (ge)	10 min.
	10 do	34.5 "
6 5:7-Dimethoxy-flavone <sup>5</sup> ..	30 do	9.0 "
	20 do	13.5 "
7 7-Hydroxy-2-methyl-isoflavone ..	30 do	21.5 "
8 7-Methoxy-2-methyl-isoflavone ..	20 do	5.0 "
	10 do	20.0 "
9 5:7-Dihydroxy-2 methyl-isoflavone ..	50 do	6.5 "
	20 do	18.0 "
10 5-Hydroxy-7-methoxy-2-methyl-isoflavone ..	12.5 do	7.0 "
	10 do	16.0 "
11 5:7-Dimethoxy-2-methyl-isoflavone ..	30 do	9.0 "
	20 do	15.0 "
12 7-Allyloxy-2-methyl 3-methoxy-chromone <sup>4</sup> ..	20 do	No action in 18 hours
	40 do	18.5 min.
	50 do	11.0 "
13 7-Allyloxy-8-allyl-2-methyl-3-methoxy-chromone <sup>4</sup> ..	20 do	6.0 "
	10 do	12.5 "
14 7-Allyloxy-flavone <sup>4</sup> ..	10 do	4.0 "
	5 do	7.5 "
15 7-Hydroxy-8-allyl-flavone <sup>4</sup> ..	10 do	No action in 12 hours
16 7-Allyloxy-8-allyl-flavone <sup>4</sup> ..	10 do	5 hours 50 min.
17 7-Methoxy-8-allyl-flavone ..	20 do	6.5 "
	10 do	8.5 "
	5 do	17.0 "
18 7-Allyloxy-2-methyl-isoflavone ..	20 do	4.0 "
	10 do	9.0 "
19 7-Hydroxy-8-Allyl-2-methyl-isoflavone ..	10 do	No action in 2 hours
20 7-Methoxy-8-allyl-2-methyl-isoflavone ..	10 do	4.0 min.
	5 do	5.5 "

## EXPERIMENTAL

*7-Methoxy-2-methyl-isoflavone*

7-Hydroxy-2-methyl-isoflavone was prepared by the method of Baker and Robinson.<sup>6</sup> Its methylation could be conveniently effected in dry acetone medium using excess of dimethyl sulphate and anhydrous potassium carbonate and boiling for 8 hours. The solvent was then removed by evaporation and water added to the residue. The precipitated solid was filtered, washed with water and crystallised from alcohol. It was obtained as glistening needles melting at 135–36°.

*7-Allyloxy-2-methyl-isoflavone*

7-Hydroxy-2-methyl-isoflavone (2.3 g.) was dissolved in anhydrous acetone (75 c.c.) and treated with allyl bromide (1.5 c.c.) and anhydrous potassium carbonate (3 g.). The mixture was refluxed for 8 hours and then the solvent removed by evaporation. Water was added to the residue and the precipitated solid filtered and washed with water. It crystallised from aqueous alcohol in the form of colourless rectangular prisms and plates melting at 107–108°. Yield 2.6 g. (Found: C, 77.8; H, 6.5;  $C_{19}H_{18}O_3$  requires C, 78.1 and H, 6.9%.)

*8-Allyl-7-hydroxy-2-methyl-isoflavone*

7-Allyloxy-2-methyl-isoflavone (0.5 g.) was heated at 220–30° for 3 hours under reduced pressure. The product was then taken up in ether and extracted thrice with 5% aqueous sodium hydroxide. When the extract was acidified with hydrochloric acid, the 8-allyl derivative was precipitated as a colourless solid. It was sparingly soluble in alcohol and crystallised from alcohol-acetic acid mixture in the form of stout rhombohedral prisms and plates melting at 256–58°. Yield 0.3 g. (Found: C, 78.4; H, 6.4;  $C_{19}H_{18}O_3$  requires C, 78.1 and H, 6.9%). Some unchanged 7-allyloxy 2-methyl isoflavone (0.1 g.) was recovered from the ether layer left after alkali extraction.

*8-Allyl-7-methoxy-2-methyl-isoflavone*

The methylation of the above compound (0.5 g.) was carried out in acetone solution with dimethyl sulphate and anhydrous potassium carbonate. The methyl ether crystallised from aqueous alcohol as long rectangular rods and prisms melting at 144–45°. Yield, 0.3 g. (Found: C, 78.8; H, 5.9;  $C_{20}H_{18}O_3$  requires C, 78.4 and H, 5.9%).

The methylation of 7-hydroxy-8-allyl-flavone was similarly carried out and *7-methoxy-8-allyl-flavone* obtained in good yield, m.p. 149–50°.

*7-Methoxy-5-hydroxy-2-methyl-isoflavone*

This was prepared earlier by Baker and Robinson<sup>6</sup> by methylating 5:7-dihydroxy-2-methyl-isoflavone with dimethyl sulphate and aqueous alkali. This partial methylation has now been effected conveniently with dimethyl sulphate and potassium carbonate in acetone medium.

A solution of the dihydroxy-isoflavone (0.5 g.) in anhydrous acetone (50 c.c.) was treated with dimethyl sulphate (0.3 g., 1.1 mol.) and anhydrous potassium carbonate (1.5 g.). The mixture was refluxed for 10 hours. The solvent was distilled off and water added. The precipitated solid was collected and crystallised from alcohol. It was obtained in the form of glistening colourless needles melting at 185–86°. Yield, 0.4 g.

*5:7-Dimethoxy-2-methyl-isoflavone*

5:7-Dihydroxy-2-methyl-isoflavone (0.5 g.) was methylated as before with excess of dimethyl sulphate and anhydrous potassium carbonate in acetone solution. It crystallised from aqueous alcohol (animal charcoal) as colourless rectangular plates and rods melting at 105–7°. Yield, 0.4 g. (Found: C, 69.1; H, 5.9;  $C_{18}H_{16}O_4$ ,  $H_2O$  requires C, 68.8; H, 5.7%).

*Chrysin-dimethyl ether (5:7-dimethoxy flavone)* has also now been prepared by the above method. It was originally obtained by synthesis<sup>5</sup> from 4:6-dimethyl ether of phloracetophenone by the Baker-Venkataraman method. Earlier attempts to methylate chrysin yielded only the monomethyl ether, tectochrysin. The dimethyl ether melted at 143° and did not dissolve in alkali nor give any colour with ferric chloride.

## SUMMARY

The simpler chromones having no side phenyl ring have poor toxic properties and resemble the simpler coumarins. Hydroxy isoflavones are more toxic than the corresponding flavones and the methoxy derivatives less toxic. In this there is resemblance to the hydroxy- and methoxy-phenyl coumarins. Among allyl-derivatives of chromones, flavones and isoflavones, ethers have high toxicity.

## REFERENCES

1. Murti and Seshadri .. *Proc. Ind. Acad. Sci.*, 1947, 25A, 333.
2. Seshadri and Viswanadham *Ibid.*, 1947, 25A, 337.
3. Rajagopalan, Rao and Seshadri *Ibid.*, 1947, 25A, 432.
4. Rangaswami and Seshadri .. *Ibid.*, 1939, 9, 1.
5. Gulati and Venkataraman .. *J. C. S.*, 1936, 268.
6. Baker and Robinson .. *Ibid.*, 1925, 1984; 1929, 160.