

SYNTHETIC EXPERIMENTS IN THE BENZO-PYRONE SERIES

Part III. Syntheses of Coumarino- and Flavono- α -methyl-7 : 8-Dihydrofurans

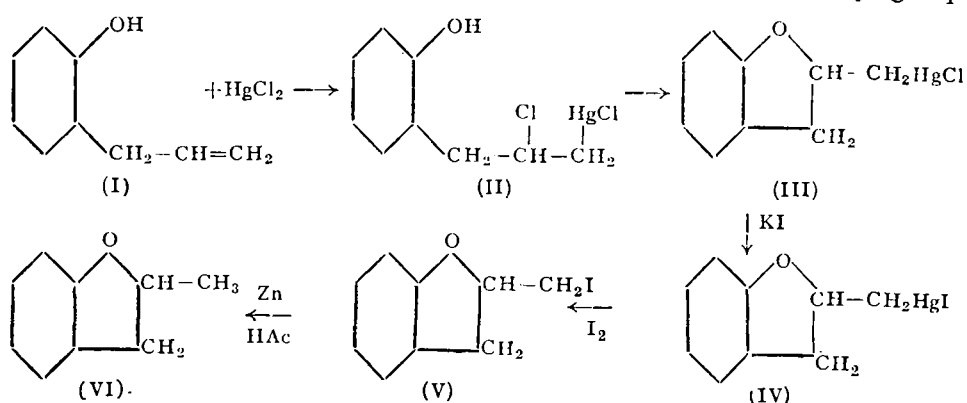
BY B. KRISHNASWAMY AND T. R. SESHADRI

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

Received October 17, 1940

In the previous papers^{1,2} of this series the methods that have been employed for building up a fresh furan ring fused to the benzene nucleus of a coumarin structure have been discussed. Besides applying the best of these for the production of flavono-furans, a new method of effecting the synthesis of unsubstituted coumarino- and flavono-furan derivatives has also been explored. Another possible procedure of easily building up α -methyl-furan rings on coumarin and flavone ring systems has now been examined and the syntheses of the angular type of compounds are described in this paper. The method is essentially the same as that adopted by Adams *et al.*,³ using *o*-allyl-phenol and mercuric chloride, though certain important modifications have been introduced with a view to simplify the procedure and improve the yields.

In their attempts to prepare acid stable organo-mercury compounds Adams *et al.*, examined the action of mercuric chloride and mercuric acetate on *o*-allyl-phenol. The products were found to be mercury derivatives of α -methyl-coumarans which were obviously transformation products of the initial addition of the mercury salts to the double bond of the allyl group.

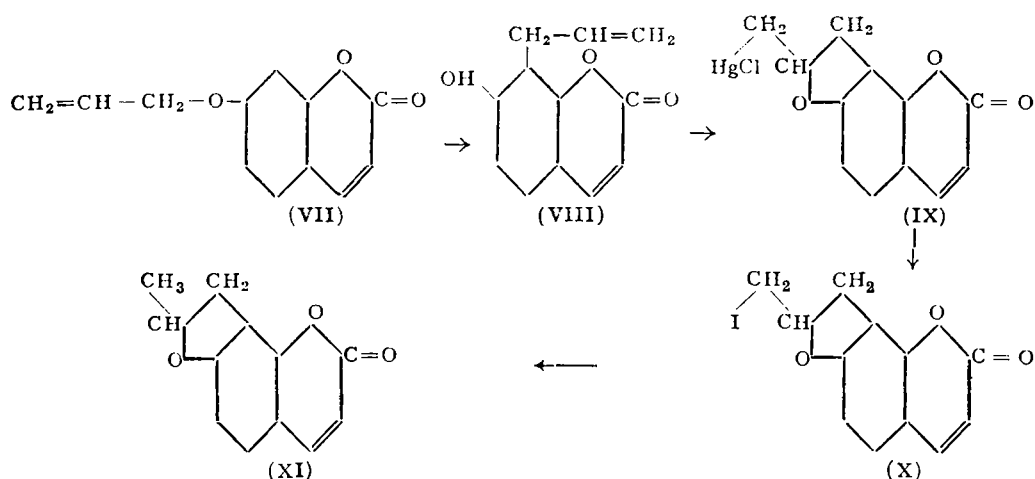


The positions of attack of the two parts of the addenda was inferred from analogy with similar additions (Markownikow's rule). The chloromercury compound (III) was found to undergo transformation readily into the iodo-mercury derivative (IV) by the action of potassium iodide and this could be converted into the corresponding iodo-compound (V). Further reduction with zinc and acetic acid gave rise to α -methyl-coumaran (VI).

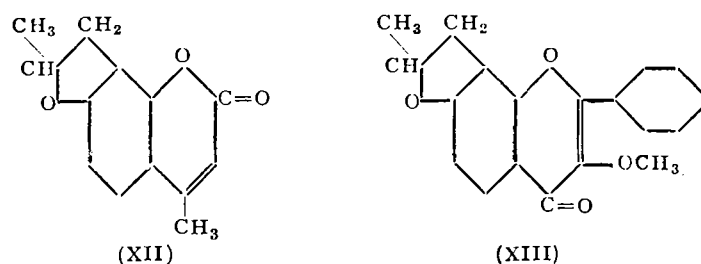
For purposes of the present investigation umbelliferone, 4-methyl-umbelliferone, and 3-methoxy-7-hydroxy-flavone have been employed as starting materials. Their allyl ethers undergo migration to form the corresponding allyl-phenols. The position taken up by the allyl group has been from close analogy assumed to be the 8-position. This point has been established by Baker and Lothian⁴ in connection with 4-methyl-umbelliferone, and by Rangaswami and Seshadri⁵ in connection with chromones and flavones. In regard to the best conditions for bringing about the Claisen migration, the work of Baker and Lothian may here be mentioned. 7-Allyloxy-4-methyl-coumarin was heated in an oil-bath. The migration was considered to be an exothermic reaction which started at 240°. After the bath had attained this temperature, the reaction was completed by cooling to 210° and maintaining this temperature for 1½ hours. But when this method was adopted in the present investigation, the product contained a good deal of resin and purification was very difficult. As a result of several experiments carried out by us under varying conditions of temperature and pressure, it was found that satisfactory yields could be obtained when the allyl ethers were heated under reduced pressure (20 mm.) at 195–200° for 1½ hours. In the preparation of 8-allyl-7-hydroxy-3-methoxy-flavones from 7-allyloxy-3-methoxy-flavone, a yield of 80% was obtained.

The action of mercuric chloride on the allyl compounds mentioned above takes place very easily in alcoholic solutions. In regard to their characterisation, estimation of mercury alone is not sufficient since in some cases no appreciable difference in the mercury content exists between simple addition products of type (II) and the further condensation product of type (III). Estimation of chlorine was found to be more useful for this purpose. That the ring closure takes place directly in all the cases examined has been established beyond doubt from analysis of carbon, halogen and mercury. Demercuration using hydrogen sulphide has been found to be useful in a large number of other compounds⁶ studied previously in these laboratories. In the present set of compounds this method has not been successful since besides demercuration opening of the dihydrofuran ring also takes place. Though the method adopted by Adams *et al.*,³ is quite good, the process could be simplified by using iodine and potassium iodide together instead of

employing them separately. By this means the preparation of iodomercuri-methyl compounds as intermediates was avoided. For the final reduction of the iodine compounds zinc and acetic acid were used in the past. This has been found to be unsatisfactory for the present purpose as complete reduction could not be effected even after long treatment. This is partly due to the insolubility of the iodo-compounds in acetic acid. On the other hand using sodium and alcohol, the reaction proceeded smoothly and satisfactory yields of the α -methyl-dihydrofurans were obtained. The course of the reactions may be represented as below using the umbelliferone series as a representative case, the final product being coumarino- α -methyl-7:8-dihydrofuran (XI).



Similarly from 4-methyl-umbelliferone, 4-methyl-coumarino- α -methyl-7:8-dihydrofuran (XII) and from 7-hydroxy-3-methoxy-flavone, 3-methoxy-flavono- α -methyl-7:8-dihydrofuran (XIII) were obtained.



The dihydrofurans that have been prepared now and described in this paper are related to the simple coumarinofuran angelicin and the flavonofuran karanjin occurring in nature. On dehydrogenation they will yield α -methylhomologues of these naturally occurring compounds and this method

seems to open up possibilities of obtaining pyrono-furans easily and in good yield. Experiments on dehydrogenation are in progress.

Experimental

7-Allyloxy-coumarin.—Umbelliferone (8 g.) was dissolved in acetone (50 c.c.), allyl bromide (7 g.) and anhydrous potassium carbonate (15 g.) were added and the mixture was refluxed for 6 hours. After distilling off most of the acetone, the residue was treated with water and the resulting solid filtered and recrystallised from alcohol. It crystallised as prismatic needles melting at 79–80° C. Yield 90%. (Found: C, 71.2; H, 5.3. $C_{12}H_{10}O_3$ requires C, 71.3; H, 5.0%.)

8-Allyl-7-hydroxy-coumarin.—7-Allyloxy-coumarin (5 g.) was heated under reduced pressure (20 mm.) at 195–200° for 1½ hours. The product was then cooled and subjected to repeated crystallisations from alcohol. A pale yellow crystalline solid (tapering plates) was thus obtained melting at 162–63°. It gave a greenish blue fluorescence in dilute sodium hydroxide solution but no perceptible colour was obtained with ferric chloride. Yield 1 g. (Found: C, 71.4; H, 5.2. $C_{12}H_{10}O_3$ requires C, 71.3; H, 5.0%.)

Coumarino- α -chloromercurimethyl-7:8-dihydrofuran.—8-Allyl-umbelliferone (1 g.) dissolved in methylated spirits was mixed with a solution of mercuric chloride in the same solvent. Precipitation which commenced after 2 hours was complete within two days. The colourless substance which was obtained by filtration and washing with a little alcohol had the appearance of a micro-crystalline powder and melted at 233–35° C. Since it was sparingly soluble, it was purified by repeatedly washing with hot alcohol. Yield 2 g. (Found: C, 32.8; Hg, 45.8; Cl, 7.8. $C_{12}H_9O_3$ HgCl requires C, 32.9; Hg, 45.9; Cl, 8.1. $C_{12}H_{10}O_3$ HgCl₂ requires C, 30.4; Hg, 42.4; Cl, 15.0 %.)

Coumarino- α -iodomethyl-7:8-dihydrofuran.—The above chloromercuri-compound (1 g.) was shaken with a fairly concentrated solution of iodine in potassium iodide (5 c.c.) with warming on a water-bath. Soon a distinct change in the nature of the solid was observed and about 15 minutes of this treatment was found to be enough for complete demercuration. The product was filtered and recrystallised from alcohol, when it was obtained as broad rectangular plates, melting at 168–69° C. The yield was almost quantitative. (Found: I, 38.4. $C_{12}H_9O_3I$ requires I, 38.7%.)

Coumarino- α -methyl-7:8-dihydrofuran (α -methyl-dihydroangelicin).—The above iodomethyl compound (0.4 g.) was dissolved in alcohol (10 c.c.) and small pieces of sodium (2 g.) were added one by one and kept pressed

to the bottom of the container by means of a glass rod in order to prevent the metal from floating to the top. After the reaction was over, the alcoholic solution was diluted with water, acidified and the resulting precipitate filtered. On recrystallisation from alcohol it was obtained as thin needles melting at 148–49° C. Yield 0.1 g. (Found: C, 71.2; H, 5.1. $C_{12}H_{10}O_3$ requires C, 71.3; H, 5.0%.) The molecular weight of the compound was determined by Rast's method and found to be 197 ($C_{12}H_{10}O_3 = 202$).

8-Allyl-4-methyl-umbelliferone.—It was prepared by subjecting 7-allyloxy-4-methyl-coumarin to Claisen migration under the modified conditions. The product was crystallised from alcohol when it melted at 193–94° C. (Baker and Lothian, m.p. 193–94°). Yield 25%.

4-Methyl-coumarino- α -chloromercurimethyl-7 : 8-dihydrofuran was readily obtained by means of the method already described. It crystallised from boiling alcohol as colourless short needles melting at 225–27° C. Yield 90%. (Found: Cl, 8.0. $C_{13}H_{11}O_3$ HgCl requires Cl, 7.9%. $C_{13}H_{12}O_3$ HgCl₂ requires Cl, 14.6%.)

4-Methyl-coumarino- α -iodomethyl-7 : 8-dihydrofuran which was prepared by the action of iodine in potassium iodide on the above chloromercuri-compound crystallised from alcohol as broad rectangular plates melting at 158–59° C. The yield was almost quantitative. (Found: I, 36.8. $C_{13}H_{11}O_3$ I requires I, 37.1%.)

4-Methyl-coumarino- α -methyl-7 : 8-dihydrofuran (α : 4-dimethyl-dihydro-angelicin).—The removal of iodine was effected by means of sodium and alcohol as already described. The product crystallised out of alcohol as thin rectangular plates melting at 182–83° C. Yield 25% on the weight of the iodine compound. (Found: C, 72.4; H, 5.4. $C_{13}H_{12}O_3$ requires C, 72.2; H, 5.6%.) The molecular weight by Rast's method was found to be 212 ($C_{13}H_{12}O_3 = 216$).

7-Allyloxy-3-methoxy-flavone.—7-Hydroxy-3-methoxy-flavone prepared by Allan and Robinson's method, was allylated as in the previous cases. The allyl ether when recrystallised from alcohol yielded colourless rhombic plates melting at 107–08° C. Yield was almost quantitative. (Found: C, 73.9; H, 5.0. $C_{19}H_{16}O_4$ requires C, 74.0; H, 5.2%.)

8-Allyl-7-hydroxy-3-methoxy-flavone was obtained by subjecting the above allyl ether to Claisen migration under reduced pressure (20 mm.). It was recrystallised from alcohol when it was obtained in the form of short needles melting at 243–44° C. Yield was 80% of the theoretical. On treatment with alkali the substance first dissolved giving an yellow solution but soon the

sodium salt precipitated out. It did not give any perceptible colour with ferric chloride but exhibited a greenish yellow fluorescence in sulphuric acid solution. (Found: C, 74.2; H, 5.3. $C_{19}H_{16}O_4$ requires C, 74.0; H, 5.2%.)

3-Methoxy-flavono- α -iodomethyl-7:8-dihydrofuran.—On treatment with mercuric chloride the above allyl-hydroxy-flavone gave the chloromercuri-compound which was yellow in colour. It did not give a definite melting point but decomposed on heating just above 200° . On treatment with iodine and potassium iodide it smoothly underwent conversion into the α -iodomethyl compound which was recrystallised from alcohol. It was obtained in the form of colourless long rectangular plates melting at $205-06^\circ$. (Found: I, 28.9. $C_{19}H_{15}O_4I$ requires I, 29.3%.)

3-Methoxy-flavono- α -methyl-7:8-dihydrofuran (α -methyl-dihydrokaranjin) was prepared by reduction of the iodine compound with sodium and alcohol in an yield of 40%. On recrystallisation from alcohol it was obtained as colourless thin rectangular plates melting at $133-34^\circ$. It was insoluble in cold as well as hot dilute sodium hydroxide and gave no colour with ferric chloride. (Found: C, 74.2; H, 5.3. $C_{19}H_{16}O_4$ requires C, 74.0; H, 5.2%.)

Summary

A fresh method for building up furan rings on to coumarin and flavone compounds has been studied. Starting with umbelliferone, 4-methyl-umbelliferone and 3-methoxy-7-hydroxy-flavone the corresponding angular α -methyl-dihydrofuran derivatives have been obtained. The 8-allyl compounds are first prepared and these are subjected successively to treatment with mercuric chloride, iodine in potassium iodide solution and sodium in alcohol.

REFERENCES

1. Row and Seshadri .. *Proc. Ind. Acad. Sci. (A)*, 1940, **11**, 206.
2. Rangaswami and Seshadri .. *Ibid.*, 1939, **9**, 259.
3. Adams *et al.* .. *J. A. C. S.*, 1922, 1781.
4. Baker and Lothian .. *J. C. S.*, 1935, 631.
5. Rangaswami and Seshadri .. *Proc. Ind. Acad. Sci., (A)*, 1939, **11**, 1.
6. Rao and Seshadri .. *Ibid.*, 1936, **4**, 162 and 630.
Rangaswami, Rao and Seshadri .. *Ibid.*, 1938, **7**, 296 and 312.
- Rao, Sastri and Seshadri .. *Ibid.*, 1939, **9**, 22.