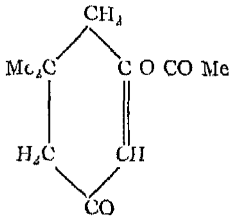
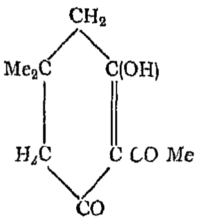
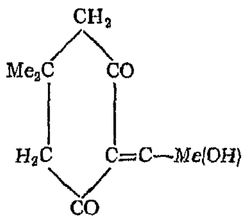
CONDENSATION OF *C*-ACETYL METHONE WITH AROMATIC ALDEHYDES*

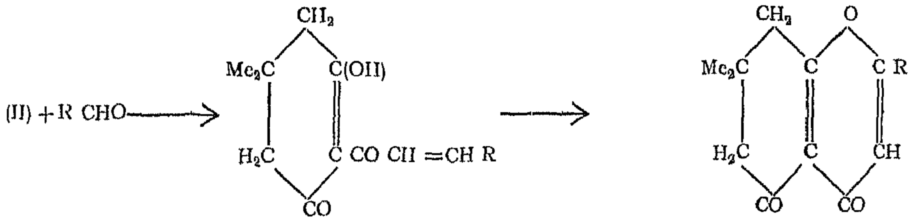
By Balkrishna H Iyer

Dieckmann and Stein (*Ber.*, 1904, **37**, 3370) prepared *O*-acetyl methone (I) by the action of acetic anhydride on methone in presence of pyridine, at ordinary temperature. It is an oil with a neutral reaction, b p 144°/18 mm. By boiling methone with acetic anhydride and sodium acetate they got *C*-acetyl methone (m p 36°, b p 127-128°/14 mm. or 250° at ordinary pressure) which they represented by the two tautomeric formulæ (II) and (III). It has a strongly acid reaction.


(I)


(II)


(III)


(IV)

(V)

If *C*-acetyl methone possessed the structure (II), its condensation with aromatic aldehydes was expected to give hydroxy chalkones of type (IV, R=aromatic aldehyde residue) from which the corresponding flavones of type (V) could be prepared by established methods. It has been known that resorcinol nucleus occurs in the vast group of natural flavone colouring matters. A good many of them have been synthesised, particularly chalkones from resacetophenone and its mono- and di-methyl ethers.

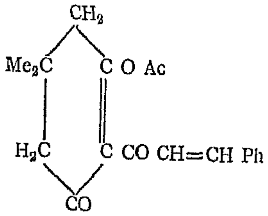
---

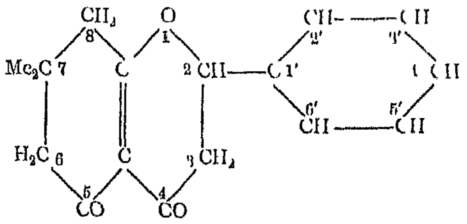
* Extracted from the author's thesis for the Ph D Degree of the University of Bombay.

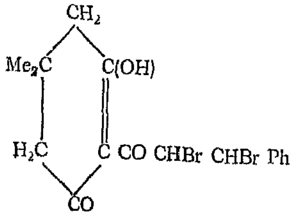
However, compounds containing a substituted hydro-aromatic ring fused with the pyrone ring in the flavone series seems to have not so far been described in literature. Hence, it was of additional interest to synthesise a few of them.

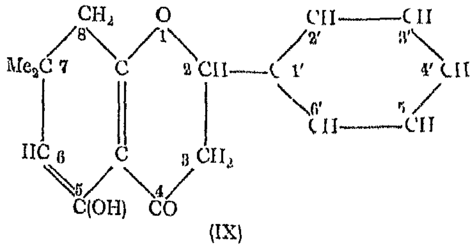
C-acetyl methone has now been successfully condensed with benzaldehyde, salicylaldehyde, salicylaldehyde-methylether, anisaldehyde and piperonal. Condensation with *o*-nitrobenzaldehyde and vanillin were not successful.

When *C*-acetyl methone was condensed with benzaldehyde in presence of alcoholic potassium or sodium hydroxide at ordinary temperature (*Cf* Mahal and Venkataraman, *J.C.S.*, **1933**, 617) a yellow crystalline substance, m.p. 99°, was obtained. When the same condensation was carried out at the temperature of the boiling water bath, a substance having the same melting point as before (undepressed on admixture) but having a darker colour (orange) which did not change even after repeated crystallisations using norite, was obtained. At first the resulting compound was considered to be a hydroxy chalkone of type (IV) (*Cf* Iyer, *Indian Sc Cong Proc*, 1939, **26**, 60). But attempts to prepare its acetyl derivative (VI) and convert the latter into the dibromide (VII) which on treatment with alkali would have yielded the flavone (V)—according to Kostanecki—were unsuccessful.

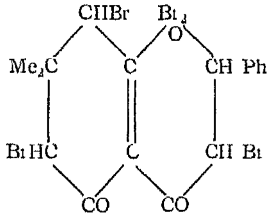

(VI)


(VIII)


(VII)


(IX)

For the reasons enumerated below, a tautomeric flavanone structure (VIII) or (IX) has now been suggested for the product The reasons are (1) Acetylation did not take place under the different conditions tried, viz, (a) with acetic anhydride and pyridine at ordinary and elevated temperatures, (b) with acetic anhydride and concentrated sulphuric acid, (c) with acetic anhydride and sodium acetate Every time the product was recovered unchanged (2) Bromine did not add up easily in the cold But on standing for long or at elevated temperature, bromination took place with vigorous evolution of HBr indicating occurrence of substitution and not of addition as should have been the case if the compound had a chalkone structure The product of bromination was a penta-bromide for which structure (X) has been tentatively assigned On treatment with alcoholic KOH, the bromo compound yielded a pasty stuff from which nothing definite could be isolated



(X)

(3) The product of condensation could not be methylated with methyl sulphate (4) On trying to prepare the corresponding flavone (V) by treating the product with hydrogen peroxide and alcoholic KOH (*Cf* Oyamada, *Bull Chem Soc*, *Japan*, 1935, **10**, 182) the original substance was recovered (5) On refluxing its solution in 2 N NaOH for 2 hours no change happened The expected flavone fission products were not formed (6) Its solution in concentrated sulphuric acid did not show any fluorescence as the flavones generally would (7) On reduction with magnesium powder and alcoholic HCl, characteristic flavanone coloration—amber in this case—was obtained Chalkone derivatives do not give coloration under these circumstances (*Cf* Shinoda, *J Pharm Soc*, *Japan*, 1928, **48**, 214, *American Chemical Abstracts*, 1928, **22**, 2947) (8) Direct formation of the flavanone is

possible as it is known that *o*-hydroxy acetophenone derivatives can be condensed with aromatic aldehydes to yeild flavanones (Kostanecki, Levi and Tambor, *Ber.*, 1899, **32**, 326). (9) From the molecular weight of the product it could be inferred that only molecular proportions of the acetyl methone and the aldehyde reacted.

The facts that the substance is soluble in 2 N. NaOH, from which solution it could be re-precipitated by carbon dioxide and that it gives coloration with ferric chloride would indicate that the CH_2–CO– grouping of the hydroaromatic ring existed in the enolic form –CH=C(OH)–. Hence the product may more properly be represented by structure (IX) than (VIII). Its nomenclature will then be 5-hydroxy-7:7-dimethyl-Δ^{6}-7:8-dihydroflavanone.

Oximation by the ordinary method and also by the method of Gulati and Ray (*Current Sci.*, 1936, **5**, 75) led to the formation of mixtures from which nothing definite could be isolated. Probably this is due to the formation of sterio-isomeric mono- and di-oximes.

The product yielded a high melting, insoluble *bis*-(2:4-dinitro-phenyl)-hydrazone. 2:4-dinitrophenylhydrazones of flavone and flavanone were previously prepared by Mozingo and Adkins (*J. Amer. Chem. Soc.*, 1938, **60**, 669).

Experiments to convert the flavanone derivative into its corresponding flavone by PCl_5 (Lowenbein, *Ber.*, 1924, **57**, 1515) and by SeO_2 (Venkataraman *et al.* *J.C.S.*, **1935**, 867) were not successful. This is explained as due to PCl_5 and SeO_2 acting on the hydro-aromatic ring also—in addition to the oxidation of the pyrone ring—thus leading to more than one product of reaction.

The other compounds prepared during the investigation were (1) 2':5-dihydroxy-7:7-dimethyl-Δ^{6}-7:8-dihydroflavanone, (2) 2'-methoxy-5-hydroxy-7:7-dimethyl-Δ^{6}-7:8-dihydroflavanone, (3) 4'-methoxy-5-hydroxy-7:7-dimethyl-Δ^{6}-7:8-dihydroflavanone, and (4) 3':4'-dioxymethylene-5-hydroxy-7:7-dimethyl-Δ^{6}-7:8-dihydroflavanone. In all these cases, the products obtained by carrying out the condensation at the temperature of the boiling water bath were of orange colour, while those prepared by conducting the experiment at ordinary temperature were yellow Their melting points and properties were similar Probably this is a case of chromo-isomerism The bis-2 4-dinitrophenylhydrazones of these products also have been prepared The bis-2 · 4-dinitrophenylhydrazone of *C*-acetyl methone was also prepared for comparison, this has not been reported in literature before

Clemmensen reduction of the benzaldehyde product yielded an oil, b p 285–290°/684 mm (decom) Its alcoholic solution did not give coloration with ferric chloride It was insoluble in alkali Owing to the meagre quantity, the oil was not further investigated Perhaps it may be the corresponding flavan derivative Mozingo and Adkins (*loc cit*) prepared flavan by the catalytic hydrogenation of flavanone

The present study seems to indicate that *C*-acetyl methone possesses a true acetyl structure (II) and not a methyl substituted hydroxymethylene-*cyclo*-hexanedione structure (III)

EXPERIMENTAL

Preparation of C-*acetyl methone* —(*Cf Dieckmann and Stein, loc cit*) —A mixture of methone (40 g), acetic anhydride (200 c c) and fused sodium acetate (8 g) was refluxed on a sand bath for 8 to 10 hours The excess of acetic anhydride was then distilled out under reduced pressure. The residue was poured into iced water and the separated oil was taken up in ether The ethereal solution was washed twice with water and then shaken with a concentrated solution of copper acetate till no more of the copper salt of *C*-acetyl methone separated out This was collected on Buchner funnel, washed successively with water, alcohol and ether On decomposing the copper salt with dilute sulphuric acid, *C*-acetyl methone was re-generated. It was taken up in ether, washed free of mineral acid, dried ($MgSO_4$) and distilled, b p *245–248°/685 mm , yield 27 g* Equally good results were obtained by heating the acetylation mixture on a boiling water bath for 42 hours

Bis-2 4-dinitrophenylhydrazone of C-acetyl methone.—To a solution of 2 4-dinitrophenylhydrazine (1 g.) in alcohol (15 c c) containing concentrated sulphuric acid (2 c c), C-acetyl methone (0.4 g.) dissolved in alcohol (5 c c) was added On mixing and shaking, a crimson precipitate separated at once It was then refluxed on a water bath for about 2 hours and the precipitate filtered out while hot It was washed with dilute acid, water, alcohol and ether, m p 315-320° decomp, yield 1 g (Found N, 20.89, $C\ H\ O_9N_8$ requires N, 20.66 per cent)

5-hydroxy-7 7-dimethyl-Δ^5-7 8-dihydroflavanone (*IX*)—To a solution of *C*-acetyl methone (1.8 g) and benzaldehyde (1 g) in a small quantity of aldehyde-free alcohol, sodium hydroxide (1.8 g) dissolved in minimum quantity of water was added More alcohol was added if necessary and the clear solution was left at ordinary temperature for about 20 hours Then it was diluted with water and either carefully acidified with dilute hydrochloric acid under ice-cooling or saturated with carbon dioxide, when a yellow precipitate resulted If the acidification was not done carefully an oil resulted which would solidify on standing or on treatment with a cold solution of sodium bicarbonate This was collected, washed with water and crystallised from dilute alcohol, yellow needles, m p. 99°, yield 1 g It is soluble in all organic solvents and also in 2 N NaOH Its alcoholic solution gives crimson coloration with ferric chloride Dissolves in concentrated sulphuric acid giving a red coloured solution When reduced with magnesium powder in alcoholic HCl, an amber colour was produced (Found C, 75.80, H, 7.56, M W by Rast's method, 259, $C_{17}H_{18}O_3$ requires C, 75.56, H, 6.67 per cent, M W 270)

When the above reaction was carried out by refluxing the mixture over a water bath for 1½ to 2 hours, the yield of the product was more or less the same, only, the colour of the product was orange

Bis-2 4-dinitrophenylhydrazone—Prepared from 0.6 g of the substance and 1 g of 2 4-dinitrophenylhydrazine in the usual manner , yield 1 g , m p 220–225° decomp Insoluble in almost all organic solvents (Found N, 17 86 , $C_{29}H_{26}O_9N_8$ requires N, 17 78 per cent)

Bromination of (IX) Formation of the penta-bromide (X) —To a solution of the flavanone derivative (2 g) in dry carbon disulphide (50 c c), dry bromine (2 c c) was very gradually added The reaction mixture was kept boiling by heating on an electrically heated water bath There was copious evolution of HBr When the reaction was over, carbon disulphide was distilled out and ether added to the residue The resulting white solid was collected on filter paper, washed with ether and dried (2 6 g) It was crystallised from toluene (80 c c), fine white silky needles, 1 6 g , m p 178° It is insoluble in methyl and ethyl alcohols and carbon tetrachloride , soluble in chloroform, toluene and xylene (Found Br, 58 89 and 59 2 , $C_{17}H_{15}O_3Br_5$ requires Br, 59 97 per cent)

2′ 5- Dihydroxy- 7 7-dimethyl- Δ^5*- 7 8-dihydroflavanone-* (*Cf IX*) —This was prepared as in the former case from *C*-acetyl methone (3 6 g), salicylaldehyde (2 5 g) and sodium hydroxide (3 6 g), crystallised from methyl alcohol or aqueous ethyl alcohol , yellow needles, m p 150–151°, yield 1 3 g (Found C, 70 94, H, 6 43, $C_{17}H_{18}O_4$ requires C, 71 33 , H, 6 29 per cent)

Bis-2 4-dinitrophenylhydrazone —This was prepared from 0 7 g of the flavanone and 1 g of 2 4-dinitrophenylhydrazine , yield 0 5 g , m p 215–218° decomp (Found N, 17 81 , $C_{29}H_{26}O_{10}N_8$ requires N, 17 34 per cent)

2′-Methoxy-5-hydroxy-7 7-dimethyl- Δ^6*-7 8-dihydroflavanone* (*Cf IX*) —Prepared from salicylaldehyde methyl ether (2 8 g), *C*-acetyl methone (3 6 g) and NaOH (3 6 g) , yellow crystals from alcohol, yield 4 g , m p 105–107° (Found C, 72 07 , H, 6 59 , $C_{18}H_{20}O_4$ requires C, 72 00 , H, 6 67 per cent)

Bis-2 4-dinitrophenylhydrazone —0 75 g of the flavanone gave 1 2 g of this derivative , m p. 237–240° decomp (Found. N, 17 07 , $C_{30}H_{28}O_{10}N_8$ requires N, 16 97 per cent)

4′-Methoxy-5-hydroxy-7 7-dimethyl-Δ^5-7 8-dihydroflavanone (Cf IX)—Prepared from anisaldehyde (1.36 g), C-acetyl methone (1 8 g) and NaOH (1 8 g), yellow crystals from alcohol, 1 7 g, m p 132–133° (Found C, 71 85, H, 7 09, $C_{18}H_{20}O_4$ requires C, 72 00, H, 6 67 per cent)

Bis-2 4-dinitrophenylhydrazone—0 75 g of the flavanone yielded 0 8 g of the hydrazone, m p 195-200° decomp (Found N, 17 28, $C_{30}H_{28}O_{10}N_8$ requires N, 16 97 per cent)

3′ 4′-Dioxymethylene-5-hydroxy-7 7-dimethyl-Δ^5-7 8-dihydroflavanone (Cf IX)—Prepared from piperonal (1 5 g), C-acetyl methone (1 8 g) and NaOH (1 8 g), silky needles from alcohol, 1 35 g, m p 115° (Found C, 68 62, H, 5.59, $C_{18}H_{18}O_5$ requires C, 68 79, H, 5 73 per cent).

Bis-2 4-dinitrophenylhydrazone—Prepared from 0 7 g. of flavanone, yield 1 1 g, m p 215–216° decomp (Found N, 17 09, $C_{30}H_{28}O_{11}N_8$ requires N, 16.62 per cent)

SUMMARY

C-acetyl methone has been condensed with benzaldehyde, salicylaldehyde, salicylaldehyde methyl ether, anisaldehyde and piperonal in presence of alcoholic alkali The resulting products have been characterised as hydroxy flavanones

The author's grateful thanks are due to Prof P C. Guha, D SC, F N.I, for his kind interest in this investigation

Department of Pure and Applied Chemistry,
Indian Institute of Science,
Bangalore.

[25–2–1941]

Printed at the Hosali Press, Ulsoor, Bangalore, by D N Hosali, Proprietor