HETEROCYCLIC COMPOUNDS.

Part IX. Coumarins from Substituted Resacetophenones and Ethyl Aceto-acetate.

By R. D. Desai and M. Ekhlas.

(From the Department of Chemistry, Muslim University, Aligarh.)

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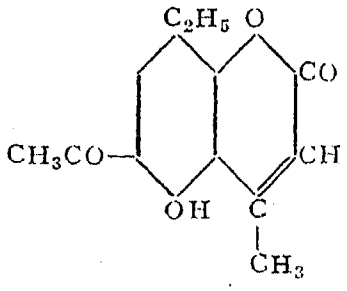
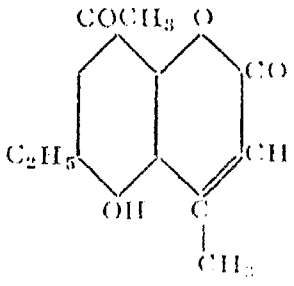
In Part IV of this series, Desai and Hamid[1] showed that resacetophenone condensed with acetoacetic ester in the presence of phosphorus oxychloride with the formation of 7-hydroxy-6-acetyl-4-methylcoumarin. The same condensation has been shown to take an entirely different course in the presence of anhydrous aluminium chloride by Sethna, Shah and Shah[2] with the formation of 5-hydroxy-6-acetyl-4-methylcoumarin, which has now been detected by us in small amounts in the $POCl_3$ method. As these types of coumarins are important intermediate products for the synthesis of furo-α-and-γ-pyrones, and coumarino-α-and-γ-pyrones, some of which occur in nature, it was thought desirable to ascertain the influence of constitutional factors on the course of this condensation. (1) 5-Ethylresacetophenone, (2) Orcacetophenone, (3) Gallacetophenone, (4) Respropiophenone, (5) Resbutyrophenone, (6) Resbenzophenone or 4-benzoylresorcinol, (7) 5-Bromoresacetophenone, (8) Methyl-β-resacetophenone carboxylate or Methyl 2 : 4-dihydroxy-5-acetyl benzoate, (9) 2 : 4-diacetylresorcinol, (10) 4 : 6-diacetylresorcinol and (11) Quinacetophenone were condensed with acetoacetic ester in the presence of phosphorus oxychloride with the results described hereunder.

Ethylresacetophenone or 2 : 4-dihydroxy-5-ethylacetophenone gave a coumarin melting at 169°. This might be either 8-ethyl-6-acetyl-5-hydroxy-4-methylcoumarin (I) or 8-acetyl-6-ethyl-5-hydroxy-4-methylcoumarin (II), but as it gave a positive colour reaction with ferric chloride, and underwent the Kostanecki Reaction with the formation of a coumarino-γ-pyrone (III), the contiguous position of OH and $-CO-CH_3$ groups was proved beyond doubt. Therefore, the coumarin has got the structure (I). On Clemmensen reduction, it gave 6 : 8-diethyl-5-hydroxy-4-methylcoumarin which was identical with the product obtained from 4 : 6-diethyl resorcinol and acetoacetic ester by Mehta and Shah.[3] We have also prepared coumarin (I) by the Fries transformation of 5-acetoxy-8-ethyl-4-methyl coumarin which was obtained from methyl 2 : 4-dihydroxy-5-ethylbenzoate and acetoacetic ester. The

Pechmann Reaction between these two substances would give either 8-ethyl 6-carbomethoxy-5-hydroxy-4-methyl-coumarin or 8-carbomethoxy 6-ethyl 5-hydroxy-4-methyl-coumarin, but the former structure was more probable owing to strong colour reaction with ferric chloride. Hydrolysis of this coumarin ester, followed by decarboxylation, gave 8-ethyl 5-hydroxy 4-methylcoumarin, which has been recently described by Sethna and Shah[2] and when its acetyl derivative was heated with aluminium chloride, the coumarin identical with (I) was obtained.



(I)



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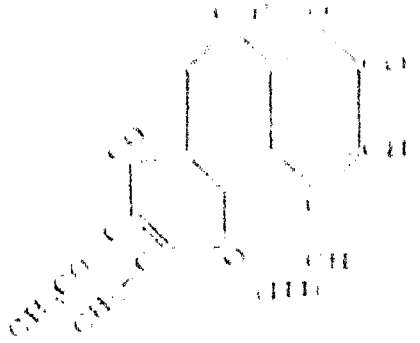


(III)

Orcacetophenone or 2 : 4-dihydroxy-6-methyl acetophenone gave 5-hydroxy-6-acetyl-4 : 7-dimethylcoumarin, the identity of which was proved by preparing it by the Fries Transformation of 5-acetoxy 4 : 7-dimethyl-coumarin. A small quantity of 5-hydroxy-4 : 7-dimethyl coumarin was always found, and this was due to the deacetylation of orcacetophenone to orcinol, and subsequent condensation with acetoacetic ester.

Gallacetophenone gave a coumarin melting at 148°, and as it gave a reddish brown coloration with ferric chloride, the acetyl group was in fact. It was, therefore, assumed to be 7 : 8-hydroxy-6-acetyl-4-methylcoumarin, but our attempts to prepare it by the Fries Transformation of 7 : 8 diacetoxy 4-methylcoumarin gave only 7 : 8-dihydroxy-4-methylcoumarin.

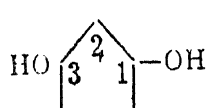
Respropiophenone gave 6-propionyl-7-hydroxy-4-methylcoumarin, which has been prepared in a very small amount by Limaye and Shenolikar[4] by the Fries Transformation of 7-propionoxy-4-methyl-coumarin. Its constitution was further proved by the preparation of the coumarino-γ-pyrone. As compared with its 6-acetyl analogue, it could be monobrominated with difficulty. Similarly resbutyrophenone gave 7-hydroxy-6-butyryl-4-methyl-coumarin as it gave a positive ferric chloride reaction and a coumarino-γ-pyrone. 4-Benzoylresorcinol gave 7-hydroxy-6-benzoyl-4-methylcoumarin which has already been prepared by Limaye[5] by the Fries Transformation of 7-benzoyloxy-4-methylcoumarin. It gave the coumarino-α-pyrone by the Kostanecki Reaction. Incidentally we have worked out the best method of preparing 4-benzoylresorcinol in quantity by the action of benzoyl chloride

on resorcinol in the presence of anhydrous aluminium chloride, and is much superior to those of Nencki[6] and Shah and Mehta.[7]

5-Bromoresacetophenone, β-methyl-resacetophenone carboxylate, 2 : 4-diacetyl-resorcinol, and 4 : 6-diacetylresorcinol did not react under any conditions, while the result with quinacetophenone was not definite. Owing to close resemblance between α-naphthol and resorcinol in the case of undergoing the Pechmann Reaction with β-ketonic esters, we condensed 4-acetyl-α-naphthol, 4-propionyl-α-naphthol and 4-butyryl-α-naphthol with acetoacetic ester, in the presence of either concentrated sulphuric acid or phosphorus oxychloride, but the acetyl, propionyl and butyryl groups were split off, and all of them gave 4-methyl-1 : 2 -α-naphthapyrone.

Thus from the above condensations, one can safely draw the conclusions that the presence of negative substituents like Br, $COOCH_3$ and $COCH_3$ hinders the coumarin-condensation of resacetophenone and acetoacetic ester in the presence of $POCl_3$, while that of the positive groups like CH_3, and C_2H_5 has got no effect at all. Moreover, as the yield of the coumarins from acetoacetic ester, and phenols goes on increasing in the order of 4-benzoyl-resorcinol, resacetophenone, respropiophenone and resbutyrophenone, the hindering effect of the acyl groups is in conformity with their acidic character, the order which is $C_6H_5CO > CH_3CO > C_2H_5CO > C_3H_7—CO$.

From our own work, and the investigations of Clayton,[8] Chakravarti,[9] Limaye,[10] Shah[11] and their co-workers, plausible explanation on the electronic conceptions can be given for the capacity of phenols and their substitution products to undergo coumarin condensation with open-chain as well as cyclic-β-ketonic esters. The feeble power possessed by ordinary phenol is enhanced by the presence of electron-donating groups in the *meta*-position :—*e.g.*, CH_3, OH, OCH_3, NH_2, $NHCH_3$, $N(CH_3)_2$, halogens, etc., but depressed and almost annihilated by electron-attracting groups in the same place :—*e.g.*, NO_2, SO_3H, COOH, COOME, $COCH_3$, CN, CHO, etc. Thus resorcinol derives its extraordinary power to undergo coumarin condensation at position 4 (positions 4 and 6 are identical) owing to the electron accession from the additional hydroxyl in position (1) which is in the *para*-position to the point of attack, and this activation of position 4 is so great that even the presence of electron-attracting groups at positions 2 or 6 is not sufficient to destroy this power. When position 6 is occupied



by groups which are electron-sinks, the resorcinol derivatives form coumarins with difficulty, while the presence of groups which are electron-sources does not seriously interfere with this property. Moreover, as 2-acetyl resorcin forms coumarins with acetoacetic ester in the presence of concentrated sulphuric acid, but 4-acetylresorcin does not (Limaye, *loc. cit.*) and 2-nitroresorcin condenses with methylacetoacetic ester, but 4-nitroresorcin does not (Chakravarti and co-workers, *loc. cit.*), it follows that electron-sinks exercise greater deactivating influence at position 4 than at position 2. With regard to the deactivating effects, the qualitative order is $COCH_3 > NO_2 > COOH > COOCH_3$. (Compare Desai and Hamid, *loc. cit.*; also Chakravarti and co-workers.) No data is available for CN, CHO and SO_3H groups, but they should exercise greater influence than even the $COCH_3$ group, and the order should be $CN > CHO > SO_3H$. We are trying to prepare coumarins from these resorcinol derivatives.

Before concluding, we wish to add a few remarks regarding the condensing agents as they may help the workers in this field. Despite the suggestion of a number of acidic, basic and neutral condensing agents, the best agents are concentrated or 73 per cent. sulphuric acid, phosphorus pentoxide, gaseous hydrogen chloride, phosphorus oxychloride, and anhydrous aluminium chloride. One advantage of phosphorus oxychloride is that besides being successful in cases where sulphuric acid is not, it behaves as phosphorus pentoxide in promoting the chromone formation.[12] The behaviour of anhydrous aluminium chloride is remarkable in the fact that whereas the other condensing agents promote the formation of 7-hydroxycoumarins from some resorcinol derivatives, this reagent modifies the reaction with the production of 5-hydroxycoumarins which are almost inaccessible by the hitherto known methods (Shah and co-workers, *loc. cit.*).

Experimental.

Condensation of resacetophenone with acetoacetic ester and isolation of 5-hydroxy-6-acetyl-4-methylcoumarin.—The original method of Desai and Hamid (*loc. cit.*) was slightly modified as follows: A mixture of resacetophenone (8 g.), acetoacetic ester (6 g.)., phosphorus oxychloride (2 c.c.) and dry benzene (20 c.c.) was heated on the water-bath for five hours till the evolution of hydrogen chloride ceased. After pouring off the benzene solution, the residue was extracted with two lots of benzene (20 c.c.) and the solvent was removed by distillation from the combined solution. The residue obtained from the benzene solution was recrystallised from alcohol when pure crystals of 7-hydroxy-6-acetyl-4-methylcoumarin melting at 212° were obtained. On Clemmensen reduction, it gave 7-hydroxy-6-ethyl-4-methylcoumarin which

was prepared for comparison from 4-ethylresorcinol, and acetoacetic ester by the usual method (Shah and Samant, *loc. cit.*). The alcoholic mother-liquor, on concentration, gave the same product in an impure condition. The residue left after the removal of the solvent was repeatedly extracted with petrol which, on cooling, deposited small needles melting at 160–162°. Recrystallisation from alcohol raised the m.p. to 164–165°, and the product was identified as 5-hydroxy-6-acetyl-4-methylcoumarin by comparing it with an authentic specimen prepared by the method of Shah, Sethna and Shah (*loc. cit.*).

The carboethoxy derivative of 7-hydroxy-6-acetyl-4-methylcoumarin was obtained by cautiously adding ethyl chloroformic ester (2 c.c.) to the solution of the coumarin (0·5 g.) in 5 per cent. alkali (10 c.c.). The insoluble solid was filtered off, and crystallised from dilute alcohol in straw-coloured needles melting at 141°. (Found : C, 61·8 ; H, 4·9 ; $C_{15}H_{14}O_6$ requires C, 62·07 ; H, 4·8 per cent.)

(*A*) *Condensation of Ethylresacetophenone with acetoacetic ester and synthesis of* 5-*hydroxy*-6-*acetyl*-8-*ethyl*-4-*methylcoumarin.*—A mixture of 2 : 4-dihydroxy-5-ethylacetophenone (4 g.), acetoacetic ester (3 g.), phosphorus oxychloride (2 c.c.) and dry benzene (20 c.c.) was heated on water-bath under reflux for four hours, and worked up as described before. The benzene-soluble fraction was repeatedly extracted with hexane to remove the unreacted ketone. The hexane-insoluble portion crystallised from dilute alcohol in colourless needles melting at 169°. Its alcoholic solution gave reddish-violet coloration with ferric chloride. (Found : C, 68·1 ; H, 5·8 ; $C_{14}H_{14}O_4$ requires C, 68·3 ; H, 5·7 per cent.) Reduction with amalgamated zinc gave 5-hydroxy-6 : 8-diethyl-4-methylcoumarin, an authentic specimen of which was prepared for comparison by the method of Mehta and Shah (*loc. cit.*). *The methyl ether* of the coumarin (I) was obtained by the usual method, and crystallised from benzene-hexane mixture in needles melting at 173°. (Found : C, 69·0 ; H, 6·3 ; $C_{15}H_{16}O_4$ requires C, 69·2 ; H, 6·15 per cent.)

The acetyl derivative crystallised from dilute alcohol in prismatic needles melting at 149°. (Found : C, 66·7 ; H, 5·7 ; $C_{16}H_{16}O_5$ requires C, 66·6 ; H, 5·55 per cent.)

The semicarbazone crystallised from alcohol in colourless needles unmelted below 285°.

The Kostanecki Reaction with 4-*methyl*-5-*hydroxy*-6-*acetyl*-8-*ethylcoumarin and synthesis of* 4 : 2′-*dimethyl*-8-*ethyl*-3′-*acetyl-coumarino*-(5 : 6)-*γ-pyrone.*—A mixture of the above coumarin (1 g.), acetic anhydride (8 c.c.) and anhydrous sodium acetate (2 g.) was heated in an oil-bath at 170–180° C. for

ten hours. The solid obtained by pouring the mixture into water was collected, and treated with a cold 5 per cent. sodium hydroxide solution. The residue crystallised from acetic acid in colourless needles melting at 173°. Its alcoholic solution did not give any colour with aqueous ferric chloride. It dissolved in cold concentrated sulphuric acid and warm sodium hydroxide solution giving yellow solution. (Found : C, 68·9 ; H, 5·2 ; $C_{18}H_{16}O_5$ requires C, 69·2 ; H, 5·1 per cent.)

Synthesis of 4-methyl-5-hydroxy-6-carbomethoxy-8-ethylcoumarin.—A mixture of methyl 2 : 4-dihydroxy-5-ethyl benzoate (10 g.), acetoacetic ester (9 g.) and 73 per cent. sulphuric acid (50 c.c.) was kept in the frigidaire for 24 hours, and the solid obtained by pouring it over ice was collected. The residue left after treating it with 5 per cent. sodium bicarbonate solution, crystallised from alcohol in pale yellowish needles melting at 185–186° (5·5 g.). (Found : C, 63·8 ; H, 5·4 ; $C_{14}H_{14}O_5$ requires C, 64·1 ; H, 5·3 per cent.) The coumarin dissolved in dilute alkali with a yellow colour while its alcoholic solution gave a deep violet colour with ferric chloride. The sodium bicarbonate extract gave, on acidification, the *coumarin carboxylic acid* (0·2 g.) which crystallised from rectified spirit in needles melting at 240° (effer.).

4-Methyl-5-hydroxy-6-carboxy-8-ethylcoumarin was obtained by keeping the solution of the coumarin ester (1 g.) in 10 per cent. caustic soda (15 c.c.) for three days, and purifying the solid obtained on acidification with hydrochloric acid through sodium bicarbonate. Crystallisation from rectified spirit gave tiny needles melting at 240° (decomp.). Its alcoholic solution gave deep violet colour with aqueous ferric chloride. (Found : C, 62·7 ; H, 5·0 ; $C_{13}H_{12}O_5$ requires C, 62·9 ; H, 4·8 per cent.).

4-Methyl-5-hydroxy-8-ethylcoumarin was obtained by heating the above acid at 250° in an oil-bath for one hour. The brown solid was triturated with warm sodium bicarbonate solution, the residue dissolved in 5 per cent. caustic soda solution, and the filtered solution acidified with concentrated hydrochloric acid. The solid crystallised from dilute alcohol in colourless needles melting at 211–212°. Its solution in alkali was deep-yellow and non-fluorescent, while its alcoholic solution did not give any colour with ferric chloride. (Found : C, 70·2 ; H, 5·7 ; $C_{12}H_{12}O_3$ requires C, 70·6 ; H, 5·9 per cent.)

The acetyl derivative crystallised from dilute alcohol in small needles melting at 112–113°. (Found : C, 68·1 ; H, 5·8 ; $C_{14}H_{14}O_4$ requires C, 68·3 ; H, 5·7 per cent.)

Synthesis of 4-methyl-5-hydroxy-6-acetyl-8-ethylcoumarin.—An intimate mixture of the above acetoxy-coumarin (0·5 g.) and anhydrous aluminium

chloride (1 g.) was heated in an oil-bath at 140–145° for one hour. The cooled mass was treated with ice-cold hydrochloric acid, and the filtered solid was dissolved in alkali. The solid obtained on acidification was dried and treated with benzene which dissolved a considerable portion. The solution deposited a solid (m.p. 160–164°) which, on recrystallisation from dilute alcohol gave colourless needles melting at 169°, and was identical with the coumarin prepared from 2 : 4-dihydroxy-5-ethylacetophenone and acetoacetic ester (see before).

(*B*) *Condensation of orcacetophenone with acetoacetic ester and synthesis of 5-hydroxy-4 : 7-dimethyl-6-acetylcoumarin.*—A mixture of orcacetophenone (2 g.), acetoacetic ester (1·6 g.), phosphorus oxychloride (1 c.c.) and dry benzene (20 c.c.) was refluxed on water-bath for three hours. The benzene-soluble portion was poured out, and the residue extracted with three lots of benzene (15 c.c. each). After removing benzene, the unreacted phosphorus oxychloride was decomposed by water. After extracting orcacetophenone with water, the residue crystallised from dilute alcohol in needles melting at 178° (0·5 g.). (Found : C, 66·9 ; H, 5·0 ; $C_{13}H_{12}O_4$ requires C, 67·2 ; H, 5·2 per cent.) Its alcoholic solution gave deep violet coloration with aqueous ferric chloride. The benzene-insoluble portion (1·5 g.) crystallised from alcohol in colourless needles melting at 258–259°, and was identical with the authentic specimen of 5-hydroxy-4 : 7-dimethylcoumarin, prepared from orcinol and acetoacetic ester by the usual method. The *acetyl* derivative of 5-hydroxy-4 : 7-dimethylcoumarin crystallised from alcohol in colourless needles melting at 202°.

Fries Transformation of 5-acetoxy-4 : 7-dimethylcoumarin.—An intimate mixture of the above acetyl derivative (1 g.) and anhydrous aluminium chloride (2 g.) was heated at 140–145° in an oil-bath for one hour. The residue obtained after decomposing the excess of aluminium chloride with ice-cold hydrochloric acid was purified through alkali, and finally crystallised from dilute alcohol when colourless needles melting at 178°, were obtained. It was identical with the coumarin, m.p. 178°, obtained from orcacetophenone and acetoacetic ester.

The acetyl derivative crystallised from dilute alcohol in needles melting at 160°. (Found : C, 65·3 ; H, 5·2 ; $C_{15}H_{14}O_5$ requires C, 65·7 ; H, 5·1 per cent.)

The semicarbazone crystallised from alcohol in colourless needles unmelted below 280°.

(*C*) *Condensation of gallacetophenone with acetoacetic ester and synthesis of 4-methyl-6-acetyl-7 : 8-dihydroxy-coumarin.*—A mixture of gallacetophenone

(2 g.), acetoacetic ester (2 g.), phosphorus oxychloride (1·5 c.c.) and dry benzene (20 c.c.) was refluxed on water-bath for three hours, and the benzene solution poured off. The residue was twice extracted with benzene and the solid recovered after the removal of the solvent was extracted with petrol (b.p. 60–80°). The petrol extract, on cooling, gave a product (m.p. 140–145°) which, on recrystallisation from dilute alcohol, gave colourless needles melting at 148° (yield = 0·5 g.). Its alcoholic solution gave a dark reddish-brown colour with aqueous ferric chloride. (Found : C, 61·2 ; H, 4·5 ; $C_{12}H_{10}O_5$ requires C, 61·5 ; H, 4·3 per cent.)

(*D*) *Condensation of respropiophenone with acetoacetic ester and synthesis of 4-methyl-6-propionyl-7-hydroxy-coumarin.*—A mixture of respropiophenone (5 g.), acetoacetic ester (4 g.), phosphorus oxychloride (2 c.c.) and dry benzene (20 c.c.) was refluxed on water-bath for three hours, and the benzene solution poured off. The residue was extracted with three lots of benzene (15 c.c. each), and the solid recovered from the benzene solution. The unchanged ketone was extracted by hot water, and the residue crystallised from methyl alcohol when white needles melting at 227–228° were obtained. (Yield 25 per cent.) It dissolved in alkali giving a red solution while its alcoholic solution gave deep red colour with aqueous ferric chloride. (Found : C, 67·0 ; H, 5·1 ; Calc. for $C_{13}H_{12}O_4$: C, 67·2 ; H, 5·2 per cent.)

The acetyl derivative crystallised from dilute alcohol in colourless needles melting at 132°.

The semicarbazone crystallised from alcohol in pale-yellow needles unmelted below 285°.

The carboethoxy derivative crystallised from dilute alcohol in colourless plates melting at 132°. (Found : C, 62·8 ; H, 5·4 ; $C_{16}H_{16}O_6$ requires C, 63·2 ; H, 5·3 per cent.)

The Kostanecki Reaction with 7-hydroxy-6-propionyl-4-methylcoumarin and synthesis of 4 : 2′ : 3′-trimethyl-coumarino-(7 : 6-)-γ-pyrone.—A mixture of the above coumarin (1 g.), acetic anhydride (10 c.c.) and anhydrous sodium acetate (2 g.) was heated at 170–180° for about ten hours. The residue obtained after decomposing the excess of acetic anhydride with water was triturated with cold alkali, and the insoluble portion crystallised from dilute acetic acid when colourless needles unmelted below 270° were obtained. Its alcoholic solution did not give any colour reaction with ferric chloride. (Found : C, 70·0 ; H, 4·8 ; $C_{15}H_{12}O_4$ requires C, 70·3 ; H, 4·7 per cent.)

Bromination of 4-methyl-6-propionyl-7-hydroxy-coumarin to 3-bromo-4-methyl-6-propionyl-7-hydroxy-coumarin.—To a solution of the coumarin (2 g.) in glacial acetic acid (30 c.c.), bromine (1 c.c.) dissolved in glacial acetic acid

(5 c.c.) was gradually added. After the addition of a trace of iodine the mixture was exposed to sunlight for six hours, and heated on water-bath for one hour. The solid obtained by pouring the mixture into water crystallised from acetic acid in colourless needles melting at 140°. (Found: Br, 25·2; $C_{13}H_{11}O_4Br$ requires Br, 25·7 per cent.)

(*E*) *Condensation of resbutyrophenone with acetoacetic ester and synthesis of 4-methyl-6-butyryl-7-hydroxy-coumarin.*—A mixture of resbutyrophenone (3 g.), acetoacetic ester (2·5 g.), phosphorus oxychloride (2 c.c.) and dry benzene (20 c.c.) was refluxed on water-bath for three hours. After the removal of benzene, water was added, and the unreacted ketone was removed by repeated extraction with water. The residue crystallised from methyl alcohol in colourless needles melting at 151°. (Yield 30 per cent.) The coumarin dissolved in alkali with yellow colour, and its alcoholic solution gave reddish violet coloration with ferric chloride. (Found: C, 68·1; H, 5·9; $C_{14}H_{14}O_4$ requires C, 68·1; H, 5·7 per cent.)

The acetyl derivative crystallised from methyl alcohol in colourless needles melting at 156°. (Found: C, 66·3; H, 5·7; $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6 per cent.)

Synthesis of 4 : 2′-dimethyl-3′-ethyl-coumarino-(7 : 6)-γ-pyrone.—A mixture of the coumarin (1 g.), acetic anhydride (10 c.c.) and anhydrous sodium acetate (2 g.) was heated at 170–175° for ten hours. After decomposing the excess of acetic anhydride, the solid was triturated with alkali, and the residue crystallised from acetic acid when colourless needles melting at 244°-245° were obtained. (Found: C, 70·9; H, 5·1; $C_{16}H_{14}O_4$ requires C, 71·1, H; 5·2 per cent.)

(*F*) *Condensation of 4-benzoylresorcinol with acetoacetic ester and synthesis of 4-methyl-6-benzoyl-7-hydroxy-coumarin.*—4-Benzoylresorcinol was best prepared as follows:—Resorcinol (10 g.) and benzoyl chloride (15 g.) were alternately added to the solution of anhydrous aluminium chloride (12·5 g.) in nitrobenzene (80 c.c.) and the mixture allowed to remain at the ordinary temperature for 48 hours. Nitrobenzene was steam-distilled off after the decomposition of aluminium chloride with ice-cold hydrochloric acid, and the recovered solid was dissolved in 5 per cent. caustic soda, acidified, filtered, and again treated with sodium bicarbonate solution to get rid of benzoic acid. The residue crystallised from hexane in colourless needles melting at 145°. (Yield 70 per cent.)

Synthesis of 4-methyl-6-benzoyl-7-hydroxy-coumarin.—A mixture of 4-benzoylresorcinol (5 g.), acetoacetic ester (3 g.), phosphorus oxychloride (2 c.c.) and dry benzene (20 c.c.) was refluxed on water-bath for three hours.

After pouring off the benzene solution, the residue was extracted twice with benzene, and the solid was recovered from the combined extracts. The residue crystallised from methyl alcohol in greenish needles melting at 168–170°, but on recrystallisation from the same solvent, colourless needles melting at 180° were obtained. (Yield 10 per cent.) Its alcoholic solution gave a deep red colour with ferric chloride. It could neither be methylated nor acetylated by the usual methods. (Found : C, 72·5 ; H, 4·2 ; Calc. for $C_{17}H_{12}O_4$: C, 72·9 ; H, 4·3 per cent.)

The semicarbazone crystallised from methyl alcohol in needles melting at 240°.

Kostanecki Reaction with 4-methyl-6-benzoyl-7-hydroxy-coumarin and synthesis of 4-methyl-4'-phenyl-coumarino- (7 : 6)-*α-pyrone.*—A mixture of the coumarin (1 g.), acetic anhydride (10 c.c.) and anhydrous sodium acetate (2 g.) was heated at 170–175° for ten hours. The residue obtained after decomposing the acetic anhydride was triturated with alkali, and the insoluble portion crystallised from alcohol when the *coumarino-α-pyrone* was obtained in colourless needles melting at 255°. Its alcoholic solution did not give any coloration with ferric chloride. (Found : C, 74·7 ; H, 4·1 ; $C_{19}H_{12}O_4$ requires C, 75·0 ; H, 3·9 per cent.)

(*G*) *Attempted condensations of 4-acetyl-α-naphthol and 5-bromo-resacetophenone with acetoacetic ester.*—A mixture of 4-acetyl-α-naphthol (2 g.), acetoacetic ester (1·5 g.), phosphorus oxychloride (1 c.c.) and dry benzene (10 c.c.) was refluxed for two hours. After the removal of benzene, the residue crystallised from dilute alcohol in colourless needles melting at 173°. The same coumarin was obtained by using concentrated sulphuric acid. 4-Propionyl-α-naphthol, as well as 4-butyryl-α-naphthol gave the same coumarin melting at 173°. This was identified as 4-methyl-α-naphthapyrone. During the course of unsuccessful experiments of condensing 5-bromo-resacetophenone, the following compounds which are new were prepared.

3 *or* 5-*Bromoresacetophenone* was prepared by gradually adding bromine (2 c.c.) dissolved in glacial acetic acid (10 c.c.) to a solution of resacetophenone (5 g.) in glacial acetic acid (25 c.c.), and pouring the mixture into water after keeping it at ordinary temperature for 24 hours. The solid melted at 155°, but recrystallisation from dilute alcohol gave needles melting at 167°. A small quantity of the dibromo-derivative melting at 173–74° was obtained. (Found : Br, 34·8 ; $C_8H_7O_3Br$ requires Br, 34·6 per cent.) It was recovered unchanged on boiling with alkali.

The dimethyl ether was prepared by repeatedly shaking the alkaline solution (0·5 g. in 5 c.c. of 10 per cent. NaOH) with dimethylsulphate

(1·5 c.c.), and crystallised from dilute alcohol in fine, colourless needles melting at 146°. Its alcoholic solution did not give any colour with ferric chloride. (Found : Br, 30·6 ; $C_{10}H_{11}O_3Br$ requires Br, 30·9 per cent.)

The diacetyl derivative was obtained by heating a mixture of the bromoketone (0·5 g.), acetic anhydride (5 c.c.) and anhydrous sodium acetate (1 g.) for three hours. The residue obtained after decomposing the excess of acetic anhydride with water was triturated with alkali and the insoluble solid crystallised from methyl alcohol when straw-coloured needles melting at 161–162° were obtained. (Found : Br, 25·7 ; $C_{12}H_{11}O_5Br$ requires Br, 25·4 per cent.

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Summary.

The condensation of acetoacetic ester with substituted resacetophenones in the presence of phosphorus oxychloride has been studied. Ethylresacetophenone, orcacetophenone, respropiophenone, resbutyrophenone, 4-benzoylresorcinol, and gallacetophenone underwent the desired condensations giving the derivatives of 7-hydroxy-4-methylcoumarins. Negative results were obtained with bromoresacetophenone, methyl, β-resacetophenone carboxylate, 2 : 4-diacetylresorcinol, 4 : 6-diacetylresorcinol, 4-acetyl-α-naphthol, 4-propionyl-α-naphthol, and 4-butyryl-α-naphthol. We have also studied the condensation of methyl 2 : 4-dihydroxy-5-ethylbenzoate with acetic ester for the synthesis of 5-hydroxy-8-ethyl-4-methylcoumarin. An explanation on the electronic conception has been offered regarding the capacity of phenols and their substitution products to undergo the Pechmann Reaction.

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