HETEROCYCLIC COMPOUNDS.

Part VIII. Coumarins from Alkylcyclohexanone-2-carboxylates and *Trans*-β-decalone-3-carboxylate.

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In continuation of our work on the synthesis of coumarins from cyclic-β-ketonic esters,[1] we have now extended this investigation to the preparation of coumarins from 4-methyl-, 5-methyl-, and 6-methyl-cyclohexanone-2-carboxylates as well as *trans*-β-decalone-3-carboxylate by the Pechmann method. 5-Methylcyclohexanone 2-carboxylate has already been condensed with phloroglucinol, orcinol and pyrogallol in the presence of concentrated sulphuric acid, by Sen and Basu,[2] but we find that improved yields of the coumarins from these phenols are obtained by using phosphorus oxychloride, while concentrated sulphuric acid is the best condensing agent for resorcinol and α-naphthol.

Exactly identical results were obtained with 4-methyl-cyclohexanone-2-carboxylate and *trans*-β-decalone-3-carboxylate which condensed readily with the above phenols, but 6-methylcyclohexanone-2-carboxylate underwent coumarin condensation with all these phenols only in the presence of phosphorus oxychloride.

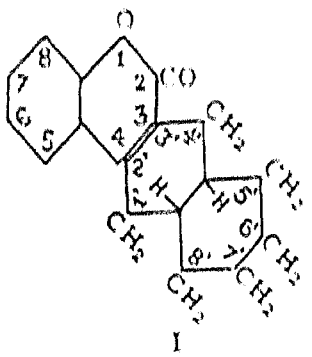
We have assumed the coumarin structure for all these products because of their unusual stability to the action of hot concentrated alkali. Sen and Basu (*loc. cit.*) have also observed the same stability in the case of their coumarins. If they had the alternative structure of substituted tetrahydroxanthones or cyclohexenochromones, they would have readily undergone fission to the alkylcyclohexanones and resorcylic acid as observed by Desai and Zafar-Uddin[3] in the case of cyclopentenochromones.

Sen and Basu (*loc. cit*) assumed that the coumarin obtained from orcinol and 5-methylcyclohexanone-2-carboxylate had the structure of 7-hydroxy-5-methyl-5′-methyl cyclohexeno-(1′ : 2′ : 4 : 3) coumarin but the absence of fluorescence and yellow colour of the alkali solution of these coumarins are against the 7-hydroxy structure. Therefore, we believe that this coumarin is 5-hydroxy-7-methyl-5′-methylcyclohexeno-(1′ : 2′ : 4 : 3)-coumarin, and the

same is the case with the other coumarins from orcinol. We have subjected the acetates of the coumarins from resorcinol and cyclic-β-ketonic esters to the Fries' Transformation in the presence of anhydrous aluminium chloride under the conditions used by Limaye[4] in the case of 7-acetoxy-4-methylcoumarin, and find that the acetyl group migrates to the ring in the 8 position. The other possible position for migration is 6, but the coumarins having this constitution have already been synthesised by the authors (in the press) from resacetophenone and respective cyclic-β-ketonic esters, and are found to be quite different.

When the cyclic-β-ketonic esters are compared with their open-chain confreres like acetoacetic esters, it is found that the former are actually more reactive than the latter, so far as the coumarin formation is concerned, although the cyclic esters can be looked upon as monosubstituted acetoacetic esters where one of the hydrogens of the methylene group, and one of the hydrogens of the methyl group are replaced by CH_2-CH_2 (in the case of cyclopentanone ester) and CH_2 CH_2-CH_2 groups (in the case of cyclohexanone esters). This is possibly due to the highly enolic character of the cyclic β-ketonic esters. The sluggishness of 6-methylcyclohexanone-2-carboxylate as compared with its 5-methyl- and 4-methyl analogues can be attributed to the steric hindrance offered by the methyl group which is in the *ortho* position to the enolic hydroxyl. Moreover, whereas the coumarins from dihydric and trihydric phenols obtained from 4-methyl and 5-methyl cyclohexanone-2-carboxylates can be methylated by dimethyl sulphate and alkali, those obtained from 6-methylcyclohexanone-2-carboxylate cannot be methylated under this condition with the exception of the coumarin from resorcinol.

The nomenclature proposed in Part I of this series has been followed throughout, and in accordance with it, the coumarins from *trans*-β-decalone-3-carboxylate have been named *trans*-octalino-(2′ : 3′ : 4 : 3)-coumarin (I).



I

Experimental.

(A) *Coumarins from 4-methylcyclohexanone-2-carboxylate.*

7-Hydroxy-4′-methylcyclohexeno-(1′ : 2′ : 4 : 3)-*coumarin.* A cooled solution of resorcinol (2·5 g.) and 4-methylcyclohexanone-2-carboxylate

(3·5 g.) in concentrated sulphuric acid (16 c.c.) was left overni ordinary temperature. The solid obtained by pouring the mi ice, crystallised from dilute alcohol in flat needles melting at dissolved in alkali with a slight yellow colour and blue fluorescence trated sulphuric acid dissolved it to a colourless solution giv fluorescence. (Found : C, 72·8 ; H, 6·0 ; $C_{14}H_{14}O_3$ requires H, 6·1 per cent.)

The *acetyl derivative* obtained by heating the coumarin (0· acetic anhydride (5 c.c.) in presence of a few drops of pyridine fc crystallised from alcohol in long needles melting at 176° C. (Found H, 6·0 ; $C_{16}H_{16}O_4$ requires C, 70·6 ; H, 5·9 per cent.)

The *methyl ether* prepared by shaking the 5 per cent. alkalin of the coumarin (0·5 g.) with dimethyl sulphate (2 c.c.) crystal alcohol in long, fine needles melting at 123° C. (Found : C, 73·5 $C_{15}H_{16}O_3$ requires C, 73·8 ; H, 6·6 per cent.)

7-Hydroxy-8-acetyl-4′-methylcyclohexeno-(1′ : 2′ : 4 : 3)- *coum* intimate mixture of 7-acetoxy-4′-methylcyclohexeno-(1′ : 2′ : 4 : 3) (2 g.) and anhydrous aluminium chloride (5 g.) was heated in a rou flask fitted with an air condenser at the temperature of 140° C. fo The cooled mixture was decomposed with ice-cold hydrochlorice the resulting solid was purified through 5 per cent. sodium carbo tion. The solid obtained on the addition of concentrated hydroc crystallised from dilute alcohol in fine, silky needles melting at 13 alcoholic solution gave reddish-violet coloration with ferric (Found : C, 70·3 ; H, 6·1 ; $C_{16}H_{16}O_4$ requires C, 70·6 ; H, 5·9 per

Its *semicarbazone* prepared by heating its alcoholic solution w carbazide acetate for 15 minutes, crystallised from alcohol in sm melting at 236° C. (Found : C, 61·7 ; H, 5·9 ; $C_{17}H_{19}O_4N_3$ requires H, 5·8 per cent.)

7 : 8-*Dihydroxy-4′-methylcyclohexeno-*(1′ : 2′ : 4 : 3)-*coumarin,* was obtained from pyrogallol (2·5 g.) and concentrated sulphuric acid It crystallised from dilute alcohol in small, colourless cubes melting Its alcoholic solution gave a deep green colour with ferric chlor alkaline solution showed a weak blue fluorescence, while the con sulphuric acid solution was deep yellow. (Found : C, 68·1 ; $C_{14}H_{14}O_4$ requires C, 68·3 ; H, 5·7 per cent.)

The *diacetyl derivative* crystallised from dilute alcohol in fin melting at 179° C. (Found : C, 65·5 ; H, 5·6 ; $C_{18}H_{18}O_4$ requires H, 5·5 per cent.)

The *dimethyl ether* crystallised from dilute alcohol in pointed needles, melting at 154° C. (Found : C, 69·9 ; H, 6·5 ; $C_{16}H_{18}O_4$ requires C, 70·0 ; H, 6·6 per cent.)

4 -*Methylcyclohexeno*-(1′ : 2′ : 4 : 3)-1 : 2-*α-naphtha-pyrone* prepared from α-naphthol crystallised from rectified alcohol in flat needles melting at 198° C. (Found : C, 81·5 ; H, 6·0 ; $C_{18}H_{16}O_2$ requires C, 81·8 ; H, 6·1 per cent.)

5-*Hydroxy*-7-*methyl*-4′-*methylcyclohexeno*-(1′ : 2′ : 4 : 3)-*coumarin*.—A mixture of orcinol (2 g.), the ester (3 g.), phosphorus oxychloride (1 c.c.) and dry benzene (10 c.c.) was heated on a water-bath for one hour under reflux. The residue after the removal of benzene was crystallised from dilute alcohol, when tiny white plates, melting at 250° C., were obtained. Its solution in dilute alkali was yellow, and non-fluorescent. (Found : C, 73·6 ; H, 6·4 ; $C_{15}H_{16}O_3$ requires C, 73·8 ; H, 6·6 per cent.)

The *acetyl derivative* crystallised from dilute alcohol in long, fine needles melting at 185° C. (Found : C, 71·2 ; H, 6·4 ; $C_{17}H_{18}O_4$ requires C, 71·3 ; H, 6·3 per cent.)

The *methyl ether* crystallised from dilute alcohol in long, fine needles melting at 140° C. (Found : C, 74·2 ; H, 7·2 ; $C_{16}H_{18}O_3$ requires C, 74·4 ; H, 7·0 per cent.)

5 : 7-*Dihydroxy*-4′-*methylcyclohexeno* (1′ : 2′ : 4 : 3) *coumarin*, was similarly obtained from phloroglucinol (2·6 g.), the ester (3·4 g.) and $POCl_3$ (2 c.c.) and crystallised from chloroform in plates melting at 265° C. Its alkaline solution was yellow and non-fluorescent. (Found : C, 68·2 ; H, 5·8 ; $C_{14}H_{14}O_4$ requires C, 68·3 ; H, 5·7 per cent.)

The *diacetyl derivative* crystallised from dilute alcohol in long prisms melting at 128° C. (Found : C, 65·3 ; H, 5·5 ; $C_{18}H_{18}O_6$ requires C, 65·5 ; H, 5·5 per cent.)

The *dimethyl ether* crystallised from dilute alcohol in tiny plates melting at 133° C. (Found : C, 69·8 ; H, 6·4 ; $C_{16}H_{18}O_4$ requires C, 70·0 ; H, 6·6 per cent.)

(*B*) *Coumarins from 5-methylcyclohexanone-2-carboxylate.*

7-*Hydroxy*-5′-*methylcyclohexeno*-(1′ : 2′ : 4 : 3)-*coumarin*, prepared from resorcinol, crystallised from dilute alcohol in fine, colourless needles melting at 202° C. Its solution in concentrated sulphuric acid gave a violet fluorescence. The alkaline solution was faint yellow and had a blue flouresccence. (Found : C, 72·7 ; H, 6·2 ; $C_{14}H_{14}O_3$ requires C, 73·0 ; H, 6·1 per cent.)

The *acetyl derivative* crystallised from dilute a
melting at 136° C. (Found : C, 70·3 ; H
H, 5·9 per cent.)

The *methyl ether* crystallised from dilute alcohol in small needles melting at 118° C. (Found : C, 73·6 ; H, 6·8 ; $C_{15}H_{16}O_3$ requires C, 73·8 ; H, 6·6 per cent.)

7-Hydroxy-8-acetyl-5'-methylcyclohexeno-(1' : 2' : 4 : 3)-*coumarin*, obtained by the Fries' Transformation of 7-acetoxy-5'-methylcyclohexeno-(1' : 2' :4 :3)-coumarin in the usual way, crystallised from dilute alcohol in fine, silky needles melting at 142° C. Its alcoholic solution gave reddish-violet coloration with ferric chloride. (Found : C, 70·4 ; H, 6·0 ; $C_{16}H_{16}O_4$ requires C, 70·6 ; H, 5·9 per cent.)

The *semicarbazone* was a microcrystalline solid melting at 232° C.

5'-Methylcyclohexeno-(1' : 2' : 4 : 3)-1 : 2-*α-naphtha-pyrone*, prepared from α-naphthol, crystallised from dilute alcohol in needles melting at 173° C. (Found : C, 81·7 ; H, 6·3 ; $C_{18}H_{16}O_2$ requires C, 81·8 ; H, 6·1 per cent.)

7 : 8-*Dihydroxy-5'-methylcyclohexeno-*(1': 2' : 4 : 3)-*coumarin*, obtained from pyrogallol, crystallised from dilute alcohol in tiny plates melting at 231° C. Its solution in dilute alkali was yellow and fluorescent (blue). The alcoholic solution gave deep green colour with ferric chloride. (Found : C, 68·0 ; H, 5·8. Calc. for $C_{14}H_{14}O_4$: C, 68·3 ; H, 5·7 per cent.)

The *diacetyl derivative* crystallised from dilute alcohol in small needles melting at 214° C. (Found : C, 65·2 ; H, 5·7 ; $C_{18}H_{18}O_6$ requires C, 65·5 ; H, 5·5 per cent.)

The *dimethyl ether* crystallised from hexane in needles melting at 123° C. (Found : C, 69·8 ; H, 6·6 ; $C_{16}H_{18}O_4$ requires C, 70·0 ; H, 6·6 per cent.)

5-Hydroxy-7-methyl-5'-methylcyclohexeno-(1' : 2' : 4 : 3)-*coumarin, prepared* from orcinol, crystallised from dilute alcohol in colourless needles melting at 260° C. [Sen and Basu (*loc. cit*) give 249° C]. Its alkaline solution was yellow and non-fluorescent. (Found : C, 73·5 ; H, 6·8. Calc. for $C_{15}H_{16}O_3$: C, 73·8 ; H, 6·6 per cent.)

The *acetyl derivative* crystallised from dilute alcohol in fine needles melting at 134° C. (Found : C, 71·0 ; H, 6·2 ; $C_{17}H_{18}O_4$ requires C, 71·3 ; H, 6·3 per cent.)

The *methyl ether* crystallised from hexane in flat needles melting at 98° C. (Found : C, 74·1 ; H, 7·1 ; $C_{16}H_{18}O_3$ requires C, 74·4 ; H, 7·0 per cent.)

5 : 7-*Dihydroxy-5'-methylcyclohexeno-*(1': 2': 4 : 3)-*coumarin*, prepared from phloroglucinol crystallised from chloroform in tiny plates melting at 262° C. It dissolved in alkali with a yellow colour and no fluorescence. (Found : C, 68·0 ; H, 5·9. Calc. for $C_{14}H_{14}O_4$: C, 68·3 ; H, 5·7 per cent.)

The *diacetyl derivative* crystallised from dilute alcohol in small needles melting at 117° C. (Found : C, 65·4 ; H, 5·4 ; $C_{18}H_{18}O_6$ requires C, 65·5 ; H, 5·5 per cent.)

(*C*) *Coumarins from 6-methylcyclohexanone-2-carboxylate.*

This ester condenses with phenols in the presence of $POCl_3$ only.

7-Hydroxy-6'-methylcyclohexeno-(1' : 2' : 4 : 3)-coumarin.—A mixture of resorcinol (2·4 g.), the ester (4·5 g.), $POCl_3$ (2 c.c.), and dry benzene (10 c.c.) was heated under reflux on water-bath for two hours. Benzene was decanted off, and the residue was extracted with three lots of benzene (15 c.c. each time). The solvent was removed from the combined extracts, and the residue crystallised from alcohol in thick, lustrous plates melting at 205° C. The yellow alkaline solution showed a blue fluorescence while its solution in concentrated sulphuric acid was colourless but gave violet fluorescence. (Found : C, 72·7 ; H, 5·9 ; $C_{14}H_{14}O_3$ requires C, 73·0 ; H, 6·1 per cent.)

The *acetyl derivative* crystallised from dilute alcohol in needles, melting at 174° C. (Found : C, 70·5 ; H, 6·1 ; $C_{16}H_{16}O_4$ requires C, 70·6 ; H, 5·9 per cent.)

The *methyl ether* crystallised from alcohol in colourless needles, melting at 112° C. (Found : C, 73·6 ; H, 6·5 ; $C_{15}H_{16}O_3$ requires C, 73·8 ; H, 6·6 per cent.)

7 : 8-Dihydroxy-6'-methylcyclohexeno-(1' : 2' : 4 : 3)-coumarin, obtained from pyrogallol, crystallised from alcohol in tiny plates melting at 227° C. (Found : C, 68·0 ; H, 5·8 ; $C_{14}H_{14}O_4$ requires C, 68·3 ; H, 5·7 per cent.)

The *diacetyl derivative* crystallised from dilute alcohol in prisms melting at 140° C. (Found : C, 65·2 ; H, 5·5 ; $C_{18}H_{18}O_6$ requires C, 65·5 ; H, 5·5 per cent.)

5 : 7-Dihydroxy-6'-methylcyclohexeno-(1' : 2' : 4 : 3)-coumarin, obtained from phloroglucinol, crystallised from alcohol in small plates melting, at 275°C. (Found : C, 68·4 ; H, 5·7 ; $C_{14}H_{14}O_4$ requires C, 68·3 ; H, 5·7 per cent.)

The *diacetyl derivative* crystallised from dilute alcohol in needles melting at 127° C. (Found : C, 65·4 ; H, 5·7 ; $C_{18}H_{18}O_6$ requires C, 65·5 ; H, 5·5 per cent.)

7-Hydroxy-6-ethyl-6'-methylcyclohexeno-(1' : 2' : 4 : 3)-coumarin, obtained from 4-ethylresorcinol, crystallised from alcohol in rhombic needles, melting at 232° C. Its colourless solution in concentrated sulphuric acid gave violet fluorescence, while the yellow, alkaline solution gave blue fluorescence. (Found : C, 74·3 ; H, 7·2 ; $C_{16}H_{18}O_3$ requires C, 74·4 ; H, 7·0 per cent.)

The *acetyl derivative* crystallised from alcohol in lustrous p at 118° C. (Found : C, 71·8 ; H, 6·9 ; $C_{18}H_{20}O_4$ requires C, 7 per cent.)

The *methyl ether* crystallised from dilute alcohol in long li melting at 109° C. (Found : C, 74·7 ; H, 7·7 ; $C_{17}H_{20}O_3$ requ H, 7·6 per cent.)

5-*Hydroxy*-7-*methyl*-6′-*methylcyclohexeno*-(1′ : 2′ : 4 : 3)-*couma* from orcinol, crystallised from alcohol in tiny plates melting a alkaline solution was yellow and devoid of fluorescence. (Fou H, 6·7 ; $C_{15}H_{16}O_3$ requires C, 73·8 ; H, 6·6 per cent.)

The *acetyl derivative* crystallised from alcohol in tiny needle 124° C. (Found : C, 71·0 ; H, 6·5 ; $C_{17}H_{18}O_4$ requires C, 71·3 cent.)

6′-*Methylcyclohexeno*-(1′ : 2′ : 4 : 3)-1 : 2-*α-naphthapyrone*, p α-naphthol, crystallised from dilute alcohol in long needles melti (Found : C, 81·6 ; H, 6·2 ; $C_{18}H_{16}O_2$ requires C, 81·8 ; H, 6·1 1

(*D*) *Coumarins from trans-β-decalone-3-carboxylate.*

7-*Hydroxy-trans-octalino*-(2′ : 3′ : 4 : 3)-*coumarin*, prepared fr and the ester, crystallised from rectified spirit in pale-brown p at 245° C. Its yellow, alkaline solution gave blue fluorescence. less solution in concentrated sulphuric acid gave violet fluoresc chloride gave green colouration to its alcoholic solution. (Fou H, 6·8 ; $C_{17}H_{18}O_3$ requires C, 75·4 ; H, 6·7 per cent.)

The *acetyl derivative* crystallised from alcohol in fine colou melting at 192° C. (Found : C, 72·8 ; H, 6·6 ; $C_{19}H_{20}O_4$ requ H, 6·4 per cent.)

The *methyl ether* crystallised from alcohol in colourless plat 178° C. (Found : C, 75·9 ; H, 7·1 ; $C_{18}H_{20}O_3$ requires C, 76·1 cent.)

7-*Hydroxy*-8-*acetyl-trans-octalino*-(2′ : 3′ : 4 : 3)-*coumarin*, was the Fries' Transformation of 7-acetoxy-*trans*-octalino-(2′ : 3′ : 4 : and crystallised from alcohol in silky needles melting at 167° C. solution gave reddish-violet colour with ferric chloride. (Four H, 65 ; $C_{19}H_{20}O_4$ requires C, 73·1 ; H, 6·4 per cent.)

The *semicarbazone* crystallised from alcohol in small plate 258° C.

Trans-octalino-(2′ : 3′ : 4 : 3)-1 : 2-*α-naphthapyrone*, obtained naphthol, crystallised from acetic acid in pointed needles meltir (Found : C, 82·6 ; H, 67 ; $C_{21}H_{20}O_2$ requires C, 82·9 ; H, 6·6 :

7 : 8 *Dihydroxy-trans-octalino-*(2′ : 3′ : 4 : 3)-*coumarin*, obtained from pyrogallol, crystallised from alcohol in prismatic needles melting at 267° C. The coumarin forms a very sparingly soluble sodium salt, and cannot be methylated by dimethyl sulphate. Its alcoholic solution gives deep bluish green coloration with ferric chloride, while concentrated sulphuric acid dissolves it with a yellow colour. (Found : C, 71·0 ; H, 6·5 ; $C_{17}H_{18}O_4$ requires C, 71·3 ; H, 6·3 per cent.)

The *di-acetyl derivative* crystallised from alcohol in fine needles melting at 200° C. (Found : C, 68·0 ; H, 5·9 ; $C_{21}H_{22}O_6$ requires C, 68·1 ; H, 6·0 per cent.)

5-*Hydroxy-7-methyl-trans-octalino-*(2′ : 3′ : 4 : 3)-*coumarin*, prepared from orcinol, was a microcrystalline powder melting at 315° C. It could not be satisfactorily crystallised from any solvent. Its alkaline solution was yellow and non fluorescent. It could not be methylated by dimethyl sulphate and alkali. (Found : C, 75·8 ; H, 7·2 ; $C_{18}H_{20}O_3$ requires C, 76·1 ; H, 7·0 per cent.)

The *acetyl derivative* crystallised from alcohol in tiny needles melting at 184° C. (Found : C, 73·4 ; H, 6·5 ; $C_{20}H_{24}O_3$ requires C, 73·6 ; H, 6·7 per cent.)

5 : 7 *Dihydroxy trans-octalino-*(2′ : 3′ : 4 : 3)-*coumarin*, obtained from phloroglucinol, crystallised from alcohol in small plates melting at 265° C. Its alcoholic solution gave green coloration with ferric chloride. The yellow, alkaline solution was devoid of fluorescence. It could not be methylated by sulphate and alkali. (Found : C, 71·1 ; H, 6·4 ; $C_{17}H_{18}O_4$ requires C, 71·3 ; H, 6·3 per cent.)

The *diacetyl derivative* crystallised from alcohol in needles melting at 173° C. (Found : C, 67·9 ; H, 6·2 ; $C_{21}H_{22}O_6$ requires C, 68·1 ; H, 6·0 per cent.)

Summary.

Coumarins have been prepared from alkylcyclo-hexanone-2-carboxylates and *trans-β*-decalone-3-carboxylate by condensing various dihydric and trihydric phenols either in the presence of concentrated sulphuric acid or phosphorus oxychlorid. The Fries' Transformation of the 7-acetoxy-derivatives of the various coumarins has been studied with the purpose of comparing the 7-hydroxy-8-acetyl derivatives with their 7-hydroxy-6-acetyl isomers.

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