# 101. *Hydroxy-carbonyl Compounds. Part XI. Phosphoryl Chloride as a Condensing Agent.*

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IN the present work it has been found that with a series of esters of acylacetic acids the Simonis reaction applied to *p*-xylenol proceeds smoothly, giving small yields of 5 : 8-dimethylchromones, but all attempts to effect similar condensations by the Pechmann method were unsuccessful. The failure to obtain products by the latter procedure, which normally produces coumarins, led us to explore the use of phosphoryl chloride, a reagent which Naik and co-workers (*J. Indian Chem. Soc.*, 1929, **6**, 801) employed to prepare coumarins from ethyl α-benzylacetoacetate and resorcinol, phloroglucinol, pyrogallol, and α-naphthol. With this reagent, ethyl acetoacetate and *p*-xylenol formed an intractable tar, but ethyl α-methyl-, ethyl α-ethyl-, and ethyl α-benzyl-acetoacetate and ethyl benzoylacetate gave rise to chromones, identical with the respective specimens obtained by the phosphoric oxide method.

On extending this procedure to the condensation of the same series of esters with *m*-4-xylenol, which has been shown to yield chromones by the Simonis method (Part X; J., **1936**, 215), it was found that, whereas ethyl acetoacetate gave rise to 4 : 6 : 8-trimethylcoumarin, ethyl α-methyl- and ethyl α-ethyl-acetoacetate yielded 2 : 3 : 6 : 8-tetramethyl- and 2 : 6 : 8-trimethyl-3-ethyl-chromone respectively; pyrones could not be isolated from the tars formed in the case of ethyl α-benzylacetoacetate and ethyl benzoylacetate.

These results, we believe, indicate that in the condensation of acylacetic esters with phenols by means of phosphoryl chloride the course of the reaction tends to follow closely that obtaining with phosphoric oxide. The exception observed in the condensation of ethyl acetoacetate with *m*-4-xylenol is not unexpected, as it has already been established that, compared with its analogues, this ester may behave abnormally in the Simonis reaction (J., **1932**, 1180, 1681). Further, the results of Naik and co-workers (*loc. cit.*) are also in keeping with this view, because the phenols employed by these authors have been shown to give rise to coumarins invariably by the Simonis reaction (J., **1931**, 1255, 1877, 2426).

## EXPERIMENTAL.

2 : 5 : 8-*Trimethylchromone*.—A mixture of *p*-xylenol (10 g.) and ethyl acetoacetate (10 g.) was heated with phosphoric oxide (15 g.) for 1¾ hours; after 1 hour, more oxide (15 g.) was added. An aqueous digest of the cooled mixture was basified with sodium hydroxide and extracted with ether. The ethereal extracts were washed several times with 2% aqueous sodium hydroxide, dried, and evaporated, leaving the *product* as an oil which gradually solidified, and then separated from light petroleum in colourless rods, m. p. 81° (Found: C, 76·5; H, 6·4. $C_{12}H_{12}O_2$ requires C, 76·6; H, 6·4%). Condensation of this substance (0·5 g.) and piperonal (0·35 g.) in boiling alcohol (10 c.c.) with sodium ethoxide (from 0·06 g. of sodium) during 1 hour gave 2-(3′ : 4′-*methylenedioxystyryl*)-5 : 8-*dimethylchromone*, forming yellow needles from alcohol, m. p. 183° (Found: C, 74·8; H, 5·1. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%).

2 : 3 : 5 : 8-*Tetramethylchromone* separated from the phosphoric oxide reaction mixture which had been digested with water and basified; it crystallised from ether or light petroleum (b. p. 40—60°) in colourless plates, m. p. 96·5—97·5° (Found: C, 77·2; H, 7·0. $C_{13}H_{14}O_2$ requires C, 77·2; H, 6·9%). Condensed with piperonal, it gave 2-(3′ : 4′-*methylenedioxystyryl*)-3 : 5 : 8-*trimethylchromone*, which separated from alcohol in yellow needles, m. p. 226° (Found: C, 75·7; H, 5·5. $C_{21}H_{18}O_4$ requires C, 75·4; H, 5·4%).

A mixture of *p*-xylenol (2 g.), ethyl α-methylacetoacetate (2 g.), and phosphoryl chloride (1 c.c.) was heated on the steam-bath for 2 hours, cooled, mixed with water, and basified with sodium hydroxide. Recrystallisation of the product from much boiling water and then light petroleum gave the chromone in plates, m. p. 98°, undepressed on admixture with an authentic specimen (Found: C, 77·3; H, 6·9%).

2 : 5 : 8-*Trimethyl*-3-*ethylchromone* was obtained with the aid of phosphoric oxide and on crystallisation from ether formed colourless elongated prisms, m. p. 86·5° (Found: C, 78·0; H, 7·6. $C_{14}H_{16}O_2$ requires C, 77·8; H, 7·4%). With piperonal it gave 2-(3′ : 4′-*methylenedioxystyryl*)-5 : 8-*dimethyl*-3-*ethylchromone*, which formed yellow needles from methyl alcohol, m. p. 153° (Found: C, 75·7; H, 5·7. $C_{22}H_{20}O_4$ requires C, 75·8; H, 5·8%).

The same chromone was obtained when phosphoryl chloride was used as condensing agent, m. p. and mixed m. p. 87° (Found: C, 78·0; H, 7·5%).

5 : 8-*Dimethylflavone*.—Condensation of *p*-xylenol (4 g.) with ethyl benzoylacetate (4·7 g.) by means of phosphoric oxide (15 g.) for periods varying from 15 minutes to 1½ hours gave rise to viscous, dark brown products. Slow evaporation of alcoholic solutions of this material deposited the *flavone*, which then separated readily from warm alcohol in pale yellow, elongated, flat prisms, m. p. 171°, identical with a specimen obtained from the cleaner reaction product formed by the phosphoryl chloride method (Found: C, 81·5; H, 5·6. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%).

3-*Benzyl*-2 : 5 : 8-*trimethylchromone*.—(A) Condensation of *p*-xylenol and ethyl α-benzylacetoacetate with phosphoric oxide in the usual manner, followed by treatment of the reaction mixture with excess water and then sodium hydroxide, gave rise to a semi-solid, which was isolated with ether. On cooling, a solution of this material in a small volume of warm alcohol deposited a compound (X) in colourless prismatic needles, m. p. 93° after repeated crystallisation from alcohol (Found : C, 76·9; H, 6·7%). This compound, which failed to give a styryl derivative with piperonal under the usual conditions, does not appear to be a coumarin and, although it is insoluble in water and 8% aqueous sodium hydroxide, is not precipitated from an alcoholic solution by the latter reagent.

Evaporation of the alcoholic residues from the crude compound (X) left oily material, which was shown to contain the chromone, since on warming with alcoholic sodium ethoxide and piperonal it gave 2-(3′ : 4′-*methylenedioxystyryl*)-3-*benzyl*-5 : 8-*dimethylchromone*, forming sparingly soluble, yellow needles, m. p. 222°, from acetic acid or acetic acid–alcohol (Found : C, 79·3; H, 5·6. $C_{27}H_{22}O_4$ requires C, 79·0; H, 5·4%).

(B) Condensation of *p*-xylenol (10 g.) with ethyl α-benzylacetoacetate (10 g.) in the presence of phosphoryl chloride (5 g.) on the water-bath for 4 hours gave rise to a cleaner reaction product than is produced by method (A). From this material the substance (X), m. p. 93°, was isolated as before. The alcoholic mother-liquors left on removal of (X) were mixed with excess of 8% aqueous sodium hydroxide and the resulting precipitate was collected, dissolved in a little alcohol and reprecipitated in the same manner. The product thus obtained consisted mainly of 3-*benzyl*-2 : 5 : 8-*trimethylchromone*, which was purified by repeated crystallisation from a small volume of methyl alcohol, forming colourless prismatic needles, m. p. 101° (Found : C, 82·0; H, 6·5. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5%). On condensation with piperonal this compound gave an almost theoretical yield of the styryl derivative, m. p. and mixed m. p. 222°, after crystallisation from alcohol–acetic acid.

4 : 6 : 8-*Trimethylcoumarin*.—The dark blue mixture produced by heating *m*-4-xylenol (2 g.), ethyl acetoacetate (2 g.) and phosphoryl chloride (1 g.) for 3 hours was mixed with excess of water, and the solution basified. Crystallisation of the resulting solid from light petroleum (b. p. 40—60°) gave material, m. p. 108—109°, from which 4 : 6 : 8-trimethylcoumarin was obtained by repeated crystallisation from dilute alcohol, m. p. 113—114°, undepressed by admixture with an authentic specimen, m. p. 114° (Part X, *loc. cit.*) (Found : C, 76·4; H, 6·4%). It is not unlikely that this coumarin was accompanied by traces of the isomeric chromone.

When ethyl acetoacetate was replaced by ethyl α-methylacetoacetate in the above reaction, 2 : 3 : 6 : 8-tetramethylchromone was obtained, m. p. 135—136° (Found : C, 76·9; H, 7·1%). Similarly, ethyl α-ethylacetoacetate gave 2 : 6 : 8-trimethyl-3-ethylchromone, m. p. 112° (Found : C, 77·7; H, 7·5%). Both chromones were identified by comparison with authentic specimens (Part X, *loc. cit.*).

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