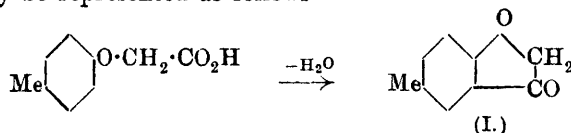


CLXIX.—*Studies in the Coumaranone Series. Part I.*
The Preparation of 4-, 5-, and 6-Methyl-
coumaran-2-ones, and some Derivatives of o-, m-,
and p-Tolyloxyacetic Acids.

By LUCY HIGGINBOTHAM and HENRY STEPHEN.

STOERMER and Bartsch (*Ber.*, 1900, **33**, 3181) were the first to prepare the above three methylcoumaranones by condensing the corresponding *p*-, *m*-, and *o*-tolylloxyacetic acids by means of phosphoric oxide. The reaction which takes place in the formation, for example, of 4-methylcoumaran-2-one (I) from *p*-tolylloxyacetic acid may be represented as follows:



Poor yields of the coumaranones were obtained by the above method, and the compounds isolated, and certain derivatives of them, were impure, as subsequent investigation has shown. The preparation of 4-methylcoumaranone (I) was carried out successfully by Auwers and Müller (*Ber.*, 1908, **41**, 4233) and Fries and Finck (*ibid.*, p. 4271) almost simultaneously, and the latter authors also describe the preparation of 5-methylcoumaranone.* The method in both cases depends on the withdrawal of the elements of hydrogen haloid from *o*-halogen-*o*-hydroxyacetophenones, but, owing to the difficulty in obtaining the required acetophenones, the method is not suitable for more general application.

The present investigation provides a method for the preparation of all three coumaranones, and is in principle analogous to the method given by Stoermer and Bartsch indicated above, but with

* Auwers (*Ber.*, 1916, **49**, 809) has recently prepared 6-methylcoumaran-2-one by a similar method.

the difference that the coumaranones are derived from the acid chlorides of the three tolyloxyacetic acids. Methods for the preparation of these acids have been known for some time, but modifications of them are described in the present paper which give improved yields and shorten the time required for reaction. The conversion of the acids into the acid chlorides was found to take place more readily using thionyl chloride rather than phosphorus pentachloride. Michael (*Amer. Chem. J.*, 1889, **9**, 216) has shown that phenoxyacetic acid, on treatment with phosphorus pentachloride, yields the acid chloride, but, at the same time, a considerable amount of a mixture of *o*- and *p*-chlorophenoxyacetyl chlorides is formed. Using thionyl chloride, almost quantitative yields of the three tolyloxyacetyl chlorides are obtained. Phenoxyacetyl chloride is also readily prepared in this way.

Stoermer and Atenstadt (*Ber.*, 1902, **35**, 3569) have shown that when phenoxyacetyl chloride is dissolved in benzene and treated with aluminium chloride, two products result from the reaction, namely, coumaran-2-one (m. p. 101°) and ω -phenoxyacetophenone (m. p. 72°). These were separated, according to the above authors, by distillation in a current of steam, coumaran-2-one being volatile and ω -phenoxyacetophenone being isolated from the residue after distillation. This procedure is not, however, in agreement with the statement of Möhlau (*Ber.*, 1882, **15**, 2497), who prepared ω -phenoxyacetophenone (m. p. 72°) from ω -bromoacetophenone and phenol in alkaline solution, and describes the ketone as being volatile in steam. It is thus difficult to understand how Stoermer and Atenstadt could have isolated the ketone in the manner described. A repetition of their experiment has been made, and, whilst no ketone was isolated, a small amount of coumaran-2-one was obtained (m. p. 101°). The latter substance was also isolated from the reaction which took place when a solution of phenoxyacetyl chloride in carbon disulphide was treated with aluminium chloride. In both cases, much residue was left after distillation with steam.

The above reaction was then applied to the three tolyloxyacetyl chlorides mentioned above, and in the first series of experiments the reaction was carried out using an excess of benzene as solvent. None of the three ω -tolylloxyacetophenones, which might have been formed in the usual way by the condensation of the tolyloxyacetyl chlorides with benzene, was obtained, the only crystalline products isolated from the reactions being the 4-, 5-, and 6-methylcoumaranones. The same compounds were formed by treating solutions of the acid chlorides in carbon disulphide with aluminium chloride. The yields of coumaranones obtained by either method of procedure are approximately the same, usually about 35 to 40 per

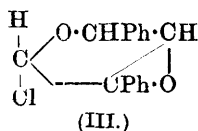
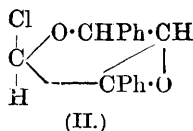
cent. of the theoretical, and although not quite so good as those obtained by Auwers and Müller and by Fries and Finck (*loc. cit.*), the method offers several advantages over that given by these investigators.

For purposes of comparison, attempts have been made to prepare the three ω -tolylxyacetophenones according to the method described by Kunckell (*Ber.*, 1897, **30**, 577), who claims to have prepared ω -*m*-tolylxyacetophenone by treating ω -bromoacetophenone and *m*-cresol dissolved in alcohol with sodium hydroxide, and, in a similar way, ω -*p*-tolylxyacetophenone was prepared from ω -bromoacetophenone and *p*-cresol. Both experiments were repeated with a slight modification, using ω -chloroacetophenone instead of the corresponding bromo-compound, and from each experiment two substances were obtained, both of which contained chlorine, and melted at 118° and 148° respectively. These compounds were isolated under different conditions, the former being obtained by warming a mixture of ω -chloroacetophenone with either *m*- or *p*-cresol in the presence of alcoholic sodium hydroxide on the water-bath for an hour. After filtering off the sodium chloride formed during the reaction from the alcoholic solution, which no longer possessed the pungent odour of the chloro-ketone, although the odour of cresol was evident, fine needles were deposited which melted as above after recrystallisation from methyl alcohol. The compound of higher melting point was formed when the heating of the alcoholic solution of the mixture was continued for several hours. After similar treatment, the above-mentioned compound, melting at 148° and crystallising from methyl alcohol in small prisms, was obtained. Subsequent investigation has shown that both substances could be obtained in several ways; thus, on treating an alcoholic solution of ω -chloroacetophenone with the dry sodium compounds of phenol, *o*-, *m*-, and *p*-cresols, and β -naphthol, respectively, each experiment gave one or other of the above chloro-compounds, according to the duration of the reaction.

The action of these sodium compounds, and also that of sodium hydroxide, on ω -chloroacetophenone is the same as that of ammonia and sodium ethoxide on the same substance as was investigated by Staedel and Rügheimer (*Ber.*, 1876, **9**, 1759) and by Paal and Stern (*Ber.*, 1899, **32**, 531) respectively, and both investigations have shown that two chloro-compounds are formed, namely, the so-called α - and β -chlorodiphenacyls, melting at 117° and 154° respectively. Widman and Almström (*Annalen*, 1913, **400**, 86) have investigated the constitutions of both compounds, and shown that α -chlorodiphenacyl is *cis*-2-chloro-3:4-oxido-3:5-diphenyltetrahydrofuran (II) (m. p. 117—118°), and that the β -compound is

STUDIES IN THE COUMARANONE SERIES. PART I. 1537

the corresponding *trans*-isomeride (III) (m. p. 149°, and not 154°, as given above).



It is thus difficult to understand how various investigators in the past have succeeded in preparing ω -alkylated or ω -arylated acetophenones by the action of sodium compounds of alcohols or phenols on ω -halogenacetophenones. An investigation of this problem is being carried out by one of us.

The preparation of other derivatives of *o*-, *m*-, and *p*-tolylloxyacetic acids is described below.

EXPERIMENTAL.

o-, *m*-, and *p*-Tolylloxyacetic Acids.

The preparation of these acids by treating a mixture of chloroacetic acid and the corresponding cresol with an aqueous solution of sodium hydroxide has been known for some time, the ortho-acid having been first prepared by Ogialoro-Todaro and Cannone (*Gazzetta*, 1889, **18**, 511), and the meta- and para-acids by Ogialoro-Todaro and Forte (*Gazzetta*, 1891, **20**, 508) and Gabriel (*Ber.*, 1882, **14**, 923). Details of a modified method for the preparation of the three acids by the same reaction are given in D.R.-P. 79514 and 85490.

Numerous experiments, carried out according to the details given in the above investigations, have shown that the yields of the acids never exceed 60 per cent. of the theoretical, loss of chloroacetic acid by hydrolysis probably taking place. The present investigation has shown that the effect of hydrolysis can be minimised by adding the cresol, dissolved in alkali hydroxide, to the chloroacetic acid. In the particular case of the meta-acid, the sodium hydroxide was replaced by an equivalent amount of potassium hydroxide, which gave an increased yield of the product; in other respects, the process was the same.

Ninety-six grams (1 mol.) of chloroacetic acid were heated in an oil-bath at 110–120°, and a solution of 108 grams (1 mol.) of the cresol and 100 grams (2.5 mols.) of sodium hydroxide in 400 c.c. of water was slowly added with frequent shaking. The addition of the solution was complete in two hours, when the product, after being cooled to about 40°, was acidified with approximately 2*N*-sulphuric acid. The tolyloxyacetic acid was collected, drained,

and finally washed with 20 c.c. of light petroleum to remove traces of adhering cresol. The weight of crude acid was 140 grams, and a further 10 grams were extracted with ether from the filtrate, the combined yield being 90 per cent. of the theoretical. The acid obtained in this way is pure enough for most purposes without further treatment.

The temperature stated above at which the acidification was carried out is of importance, since the meta-acid undergoes decomposition to some extent by mineral acid at higher temperatures. On the other hand, the sodium salt of the para-acid is only moderately soluble in water at 40°, and the free acid was best obtained by warming the solution to 70°, when the sodium salt dissolved, and slowly adding 2*N*-sulphuric acid at the same temperature until acid.

The acids may be purified by crystallisation from dilute alcohol, and are then obtained in thin, glistening plates, the melting points of which are 151—152°, 102°, and 135° for the ortho-, meta-, and para-acids respectively, agreeing with those given in the literature.

The acids are decomposed into the respective cresol and glycollic acid on distillation in a current of steam, or by boiling with dilute mineral acids, the meta-acid more readily than the para-, the ortho-acid being the most resistant to such treatment.

Preparation of the Ammonium Salts of the above Acids.

In connexion with the preparation of the nitriles of the tolyloxycetic acids, the ammonium salts were obtained most readily in the following way.

Twenty-five grams of the acid were dissolved in 100 c.c. of dry ether, and the solution was saturated with dry ammonia at the ordinary temperature. The anhydrous ammonium salt separated from the ethereal solution as a fine, crystalline powder.

The ammonium salts of the *o*-, *m*-, and *p*-acids decompose at 126°, 188°, and 177° respectively.

o-, *m*-, and *p*-Tolylloxycetyl Chlorides, $C_9H_9O_2Cl$.

These acid chlorides have hitherto not been described. Twenty grams (1 mol.) of the acid, previously dried by fusion, were finely powdered and placed in a small flask fitted with a reflux apparatus on a water-bath at 60°; 18 grams (1.5 mols.) of thionyl chloride were added slowly, and the reaction was moderated, if necessary, by removal of the flask from the water-bath. The reaction was complete at the end of fifteen minutes, and a pale yellow liquid remained; longer heating caused the product to darken in colour,

STUDIES IN THE COUMARANONE SERIES. PART I. 1539

resulting in a poor yield of the acid chloride. The excess of thionyl chloride was removed by distillation on the water-bath at 30° under about 15 mm. pressure, and the residue finally distilled at 10 mm. Twenty grams of each acid chloride were obtained as colourless liquids, the yields being about 90 per cent. of the theoretical, and in all three cases the products were obtained solid.

	B. p./10 mm.	M. p.
<i>o</i> -Tolyloxyacetyl chloride	120°	29—30°
<i>m</i> - " "	126	19·3
<i>p</i> - " "	124	17·9

They are all soluble in carbon disulphide, benzene, or ether, and are decomposed by water, yielding the respective acids.

o-, *m*-, and *p*-Tolyloxyacetamides, $C_9H_{11}O_2N$.

(1) Twenty grams of the ammonium salt of *o*-tolyloxyacetic acid were heated under 10 mm. pressure in a distillation flask in an oil-bath at 135°, water passed over, and the reaction was complete when the solid in the flask had liquefied, the amide formed being then at a temperature above its melting point.

In the cases of the ammonium salts of the meta- and para-acids, the temperature of the oil-bath was maintained at 190—200° in consequence of the higher decomposition points. The liquid residue solidified on cooling, and the product crystallised from alcohol.

(2) On warming the acid chlorides with an excess of ammonium carbonate on the water-bath for half an hour, and removing the ammonium chloride formed by triturating the solid mass with cold water and filtering, the amides were obtained pure after crystallisation from alcohol, and identical with those prepared by the first method.

The three compounds were purified for analysis by recrystallisation from benzene, being obtained in stout, rhombic prisms, and the purity of each substance was tested by boiling a known weight with aqueous sodium hydroxide and collecting the ammonia liberated in standard acid. The results were in close agreement with the theoretical values.

	M. p.	M. p.
<i>o</i> -Tolyloxyacetamide.....	127°	128°
<i>m</i> - " "	118	111—112
<i>p</i> - " "	119	126

The figures in the second column are those given by Forte (*Gazzetta*, 1893, **22**, ii, 526).

The amides are sparingly soluble in cold methyl and ethyl alcohols or benzene, but dissolve readily on warming, and are slowly hydrolysed by boiling with water.

These anilides may be readily prepared by the following method. Ten grams (1 mol.) of the acid chloride were dissolved in 100 c.c. of dry benzene in a flask fitted with a reflux apparatus, and 10 grams (2 mols.) of freshly distilled aniline slowly added with vigorous shaking. After cooling, the solid which had separated was filtered, and the benzene solution containing some aniline was evaporated, and the residue added to the main bulk. The whole was then triturated with dilute hydrochloric acid to remove aniline hydrochloride, and finally treated with cold dilute sodium carbonate solution to remove traces of acid. The substance was then crystallised from ethyl alcohol, in which the ortho-compound was the most and the para-compound the least soluble, the meta-compound being moderately soluble. They are readily hydrolysed on boiling with dilute hydrochloric acid.

STUDIES IN THE COUMARANONE SERIES. PART I. 1541

	M. p.
<i>o</i> -Tolyloxyacetanilide (cubes)	108.5°
<i>m</i> - " (needles).....	95
<i>p</i> - " (").....	109

These values are in close agreement with those given by Forte (*ibid.*).

4-Methylcoumaran-2-one (I).

Ten grams (1 mol.) of *p*-tolyloxyacetyl chloride were dissolved in 15 grams (3 mols.) of dry benzene, and 8 grams of finely powdered aluminium chloride slowly added with vigorous shaking, the mixture being cooled in ice. The reaction proceeded slowly, and the solution became dark red, but if the temperature was allowed to rise, the mixture rapidly turned into a dark-coloured, tarry mass, and the yield of coumaranone was considerably diminished, in consequence of decomposition. The red solution, after remaining in the cold for two hours, was poured on powdered ice mixed with hydrochloric acid, and the oil suspended in the water submitted to distillation in a current of steam for several hours until the distillate no longer showed a reducing action with Fehling's solution, and the characteristic odour of the coumaranone was imperceptible. The upper layer of benzene, containing some coumaranone in solution, was separated from the aqueous layer, and the latter was extracted with ether several times to remove coumaranone dissolved in the water. The combined benzene and ethereal extracts were dried over anhydrous sodium sulphate, the solvents removed on the water-bath, and, on cooling, the residue solidified to a mass of fine needles. The substance crystallised from ethyl alcohol in white needles melting at 51°. The yield was 3 grams.

The semicarbazone (yellow needles from alcohol) melted at 228° (heated slowly), and the oxime at 143—144° (Stoermer and Bartsch, *loc. cit.*, give 181° and 144° respectively).

The *p*-nitrophenylhydrazone was obtained by adding a solution of *p*-nitrophenylhydrazine in dilute acetic acid to an aqueous solution of the coumaranone. The hydrazone soon separated as a red, crystalline powder, and, after crystallisation from dilute acetic acid, it melted and decomposed at 230—232° (Found: N=14.4. $C_{15}H_{13}O_3N_3$ requires N=14.85 per cent.).

5-Methylcoumaran-2-one was prepared in a manner similar to that described above from *m*-tolyloxyacetyl chloride, and was obtained in needles melting at 85°. The semicarbazone and oxime melted at 208° and 156° respectively. For the latter, Fries and Finck (*loc. cit.*) give 165°, probably a misprint. The *p*-nitro-

1542 COPISAROW : CARBAZOLE-BLUE AND CARBAZOLE-VIOLET.

phenylhydrazone crystallises from dilute acetic acid in red needles melting and decomposing at 214—216°.

6-*Methylcoumaran-2-one*, prepared from *o*-tolylloxyacetyl chloride, crystallised in needles melting at 88°. The semicarbazone and oxime melted at 227° and 148° respectively, and the *p*-nitrophenylhydrazone (red needles) at 195° with decomposition.

The above coumaranones give purple colorations with ferric chloride, they reduce Fehling's solution on warming, and give an immediate precipitate of silver with Tollens' reagent. On treatment with concentrated sulphuric acid, they dissolve, with the production of an intense red colour, and subsequent formation of tarry matter. On remaining in the air for some time, the crystals of the coumaranones become coated with a bright red-coloured substance, probably an oxidation product. They have a characteristic odour resembling that of hyacinth.

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CHEMICAL DEPARTMENT,
THE UNIVERSITY,
MANCHESTER.

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