344. *Synthetical Experiments in the Chromone Group. Part X. Coumarin and Chromone Formation.*

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The action of an acid anhydride and the sodium salt of an acid on a phenolic ketone may produce the acyl derivative of the ketone, a chromone, a 3-acylated chromone, or a coumarin: the correlation of the known facts and the results of new experiments is generalised in the following table.

Anhydride.	Salt.	Product.	Ref. No.
		o-*Hydroxyaryl methyl ketones.*	
$(CH_3{\cdot}CO)_2O$	$CH_3{\cdot}CO_2Na$	3-Acetyl-2-methylchromones	1
$(Ar{\cdot}CO)_2O$	$Ar{\cdot}CO_2Na$	Usually flavones; sometimes 3-aroyl derivative also	2
$(CH_3{\cdot}CO)_2O$	$CH_2Ph{\cdot}CO_2Na$	3-Phenyl-4-methylcoumarins	3
$(CH_2Ph{\cdot}CO)_2O$	,,	,, in small yields	4
		ω-Substituted o-*hydroxyaryl methyl ketones.*	
$(CH_3{\cdot}CO)_2O$	$CH_3{\cdot}CO_2Na$	Chromones	5
$(Ar{\cdot}CO)_2O$	$Ar{\cdot}CO_2Na$	,,	6
$(CH_2Ph{\cdot}CO)_2O$	$CH_2Ph{\cdot}CO_2Na$	Coumarins	7
$(CH_3{\cdot}CO)_2O$	,,	(a) 2-Methylchromones *or* (b) 3-phenylcoumarins	8
		o-*Hydroxybenzophenones.*	
$(CH_3{\cdot}CO)_2O$	$CH_3{\cdot}CO_2Na$	(a) 4-Phenylcoumarins *or* (b) *O*-acetyl derivative of the ketone	9
$(CH_3{\cdot}CO)_2O$	$CH_2Ph{\cdot}CO_2Na$	3 : 4-Diphenylcoumarins	10

References: (1) Resacetophenone (Tahara, *Ber.*, 1892, **25**, 1302; Nagai, *ibid.*, p. 1297; Kostanecki and Rozycki, *Ber.*, 1901, **34**, 102); 2-acetyl-1-naphthol (Bhullar and Venkataraman, J., 1931, 1165; Wittig, Baugert, and Richter, *Annalen*, 1925, **446**, 155); 1-acetyl-2-naphthol (Menon and Venkataraman, J., 1931, 2376); 4 : 6-diacetylresorcinol (Gulati and Venkataraman, J., 1931, 2592); 2-hydroxy-4 : 6-dimethoxyacetophenone (Canter, Curd, and Robertson, J., 1931, 1247); phloracetophenone (Shinoda, *J. Pharm. Soc. Japan*, 1928, **48**, 214). According to Wittig, Baugert, and Richter (*loc. cit.*), however, *o*-hydroxyacetophenone gives a mixture of 4-methylcoumarin and 2-methylchromone.

(2) Robinson and Venkataraman (J., 1926, 2344; 1929, 61); Allan and Robinson (J., 1924, **125**, 2192); Bhullar and Venkataraman (*loc. cit.*); Anderson (*Canadian J. Res.*, 1932, **7**, 285).

(3) The reactivity of the methylene group of the sodium phenylacetate is the dominating factor and a 3-phenyl-4-methylcoumarin is invariably formed (Bargellini, *Atti R. Accad. Lincei*, 1925, **2**, 261); phloracetophenone (present paper).

(4) *o*-Hydroxyacetophenone (present paper), phloracetophenone, and 2-acetyl-1-naphthol.

(5) and (6) o-*Hydroxyphenyl benzyl ketone*, 1-*phenylacetyl*-2-*naphthol* (present paper); ω-methoxyresacetophenone, ω-methoxyphloracetophenone, respropiophenone, 2-propionyl-1-naphthol, 2-phenylacetyl-1-naphthol, 2-benzylacetyl-1-naphthol (J., 1929, 61; 1932, 918, 925, 1107; *J. pr. Chem.*, 1933, **137**, 47). The ω-substituent is always an aid to chromone formation and may from the point of view of increasing yield and ease of purification be arranged in the order: methoxyl, methyl, benzyl, phenyl. Chromone formation takes place as a rule more readily in the naphthalene than in the benzene series, and is often quantitative from derivatives of α-naphthol.

(7) Baker and Eastwood (J., 1929, 2906; "7-hydroxy-3 : 4-dibenzylcoumarin" in their paper should obviously be read as "7-hydroxy-3-phenyl-4-β-phenylethylcoumarin").

(8*a*) 2-Phenylacetyl-1-naphthol, 1-phenylacetyl-2-naphthol, 2-propionyl-1-naphthol, and ω-benzylresacetophenone (present paper). (8*b*) ω-Methoxyresacetophenone and respropiophenone (present paper).

(9) 2-Benzoyl-1-naphthol (Cheema and Venkataraman, J., 1932, 919); 1-benzoyl-2-naphthol (present paper). We were unable to confirm the observation of Dischendorfer and Danziger (*Monatsh.*, 1927, **48**, 325) that 4-phenyl-1 : 2-βα-naphthapyrone is formed by heating 1-benzoyl-2-naphthyl acetate.

(10) Bargellini (*loc. cit.*, p. 178); 1-benzoyl-2-naphthol (present paper).

EXPERIMENTAL.

Reactions involving acetic anhydride were carried out by boiling a mixture of equal weights of the ketone and the sodium salt (acetate, propionate, phenylacetate, etc.) with about ten times the weight of acetic anhydride for 24—72 hours. The whole was poured into water, and the product isolated after 12 or more hours.

2-*Acetyl*-1-*naphthyl Acetate.*—Prepared from 2-acetyl-1-naphthol, sodium methoxyacetate, and acetic anhydride and repeatedly crystallised from aqueous alcohol, this formed colourless needles, m. p. and mixed m. p. (with a specimen prepared by means of acetic anhydride–pyridine), 108°. Ullmann (*Ber.*, 1897, **30**, 1766) and Hantzsch (*Ber.*, 1906, **39**, 3096) give m. p. 96·5° and 107·5° respectively.

When sodium propionate was substituted for the methoxyacetate in the above reaction, 3-acetyl-2-methyl-1 : 4-α-naphthapyrone, m. p. 145°, was obtained (compare Bhullar and Venkataraman, *loc. cit.*).

5 : 7-*Diacetoxy*-3-*phenyl*-4-*methylcoumarin*.—Prepared from phloracetophenone, acetic anhydride, and sodium phenylacetate and twice crystallised from alcohol, this formed colourless woolly needles, m. p. 169° (Found : C, 68·0; H, 4·5. $C_{20}H_{16}O_6$ requires C, 68·2; H, 4·5%). Hydrolysis with warm 5% alcoholic potassium hydroxide and acidification gave 5 : 7-*dihydroxy*-3-*phenyl*-4-*methylcoumarin*, colourless needles (from alcohol), m. p. 282—283° (Found : C, 71·5; H, 4·4. $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%).

3-*Phenyl*-4-*methylcoumarin*.—A mixture of *o*-hydroxyacetophenone (4 g.), phenylacetyl chloride (10 g.), and sodium phenylacetate (12 g.) was heated at 180° for 6 hours. After hydrolysis with 10% alcoholic potassium hydroxide, dilution, and acidification, the dark brown oil obtained crystallised from alcohol; m. p. 153°, not depressed by admixture with authentic 3-phenyl-4-methylcoumarin (Mahal and Venkataraman, this vol., p. 617). No chromone was isolable by the general method of Wittig, Baugert, and Richter (*loc. cit.*).

2-*Benzylchromone*.—A mixture of *o*-hydroxyacetophenone (5 g.), ethyl phenylacetate (25 g.), and sodium dust (2·5 g.) was heated on the steam-bath for 4 hours, ice-cold dilute acetic acid added after 12 hours, and the oily product separated and refluxed with 10% alcoholic sulphuric acid (25 c.c.) for 1·5 hours. Addition of water gave an oil, which solidified in contact with cold 5% sodium hydroxide solution and then formed pale yellow needles (1·2 g.), m. p. 86°, from light petroleum (Found : C, 81·4; H, 5·3. $C_{16}H_{12}O_2$ requires C, 81·4; H, 5·1%).

Phenyl Phenylacetate.—Phenylacetyl chloride (prepared from the acid and boiling thionyl chloride) (86 g., b. p. 109—110°/20 mm.) and phenol (43 g.) were heated at 150° for 8 hours, and the mixture was cooled and poured into water. The *ester* extracted by benzene distilled at 174°/3 mm. (90 g.), solidified at 0°, and crystallised from light petroleum (b. p. 50—60°) in colourless needles, m. p. 50° (Found : C, 79·1; H, 5·4. $C_{14}H_{12}O_2$ requires C, 79·2; H, 5·6%).

o-*Hydroxyphenyl Benzyl Ketone*.—A mixture of the above ester (50 g.) and aluminium chloride (50 g.) was heated on the water-bath for 1 hour and at 120° for 4 hours, and the cooled product was decomposed with ice and hydrochloric acid. The *ketone*, extracted, washed (with 0·5% sodium hydroxide solution, then with water), and dried (magnesium sulphate) in ether and recovered, was washed with cold alcohol and crystallised from light petroleum, forming large, colourless, hexagonal plates, m. p. 60° (Found : C, 79·0; H, 5·4. $C_{14}H_{12}O_2$ requires C, 79·2; H, 5·6%). It gave a deep brown colour with alcoholic ferric chloride, and formed a 2 : 4-*dinitrophenylhydrazone*, pale orange, rectangular plates, m. p. 219°, from acetic acid (Found : * N, 14·2. $C_{20}H_{16}O_5N_4$ requires N, 14·3%).

Acidification of the alkaline extract gave p-*hydroxyphenyl benzyl ketone*, which, after being washed with benzene, crystallised from dilute alcohol or water in long colourless needles, m. p. 151° (Found : C, 79·1; H, 5·5%), gave a pale brown coloration with alcoholic ferric chloride, and formed a 2 : 4-*dinitrophenylhydrazone*, deep orange, square plates, m. p. 224°, from acetic acid (Found : * N, 14·2%).

2-*Methyl*iso*flavone*.—Prepared from *o*-hydroxyphenyl benzyl ketone (1 g.), sodium acetate (2 g.), and acetic anhydride (10 g.) (170—180° for 8 hours) and crystallised from dilute alcohol, the iso*flavone* formed colourless needles (0·4 g.), m. p. 140° (Found : C, 81·1; H, 5·0. $C_{16}H_{12}O_2$ requires C, 81·4; H, 5·1%), unaffected by boiling 50% hydrochloric acid and giving in sulphuric acid a colourless solution with a weak blue fluorescence.

2 : 3-*Diphenylchromone*.—The condensation was carried out with *o*-hydroxyphenyl benzyl ketone (2 g.), sodium benzoate (4 g.), and benzoic anhydride (24 g.). After treatment with alcoholic potassium hydroxide, the mixture was poured into water; the precipitate (1·1 g.) crystallised from dilute acetic acid in colourless needles, m. p. 152° (Found : C, 84·3; H, 4·5. $C_{21}H_{14}O_2$ requires C, 84·6; H, 4·7%). The colourless solution in sulphuric acid exhibited a green fluorescence.

3-Phenyl-2-methyl-1 : 4-α-naphthapyrone, prepared from 2-phenylacetyl-1-naphthol, sodium phenylacetate, and acetic anhydride and crystallised from alcohol, had m. p. and mixed m. p. (Cheema and Venkataraman, *loc. cit.*) 203—204°.

2 : 3-Dimethyl-1 : 4-α-naphthapyrone, similarly prepared from 2-propionyl-1-naphthol,

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* Microanalyses by Mr. K. S. Narang, M.Sc., to whom we are much indebted.

crystallised from dilute alcohol in colourless needles, m. p. and mixed m. p. (Cheema, Gulati, and Venkataraman, J., 1932, 930) 142°.

7-*Hydroxy*-3-*benzyl*-2-*methylchromone*.—ω-Benzylresacetophenone was conveniently prepared as follows (compare Bargellini and Marantonio, *Gazzetta*, 1908, **38**, ii, 514; Baker, J., 1925, **127**, 2355). Fused zinc chloride (5·5 g.) was dissolved in β-phenylpropionic acid (14 g.) at 145—150°, resorcinol (3 g.) added, and the mixture kept at 145° for 1 hour. The deep red solution was poured into water and after 2 hours the precipitate was collected, powdered, and shaken with sodium bicarbonate solution. The residue crystallised from 50% acetic acid in very pale cream-coloured needles (3·5 g.), m. p. 88°.

The chromone, m. p. 284° (Found: C, 76·6; H, 5·3. Calc. for $C_{17}H_{14}O_3$: C, 76·6; H, 5·3%), was prepared by hydrolysing the product obtained from ω-benzylresacetophenone, sodium phenylacetate, and acetic anhydride with hot 50% hydrochloric acid; the acetyl derivative had m. p. 126° (Found: C, 74·0; H, 5·3. Calc.: C, 74·0; H, 5·2%) (compare Crabtree and Robinson, J., 1918, **113**, 867).

7-*Acetoxy*-3-*phenyl*-4-*methoxymethylcoumarin*.—The oil obtained by the interaction of ω-methoxyresacetophenone, sodium phenylacetate, and acetic anhydride was dissolved in ether and the crystals which separated on slow evaporation were recrystallised twice from alcohol, giving colourless needles, m. p. 163° (Found: C, 70·2; H, 5·0. $C_{19}H_{16}O_5$ requires C, 70·4; H, 4·9%). Hydrolysis with hydrochloric acid and crystallisation from 30% alcohol gave very pale yellow needles, m. p. 213° (Found: C, 72·3; H, 5·2. $C_{17}H_{14}O_4$ requires C, 72·4; H, 5·0%). 7-Acetoxy- and 7-hydroxy-3-methoxy-2-methylchromone melt at 113° and 214° respectively (Allan and Robinson, *loc. cit.*).

7-*Acetoxy*-3-*phenyl*-4-*ethylcoumarin*, obtained from respropiophenone, sodium phenylacetate, and acetic anhydride, crystallised from alcohol in rhombic plates, m. p. 205° (Found: C, 73·8; H, 5·4. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%). The *hydroxy*-compound obtained by hydrolysis crystallised from dilute alcohol in colourless plates, m. p. 254° (Found: C, 76·3; H, 5·2. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%). The m. p.'s of 7-acetoxy- and 7-hydroxy-2 : 3-dimethylchromone are 116° and 262° respectively (Chakravarti, *J. Indian Chem. Soc.*, 1931, **8**, 133).

β-*Naphthyl Phenylacetate*.—β-Naphthol (38 g.) and phenylacetyl chloride (60 g.) were heated at 150° for 6 hours. The brown precipitate obtained when the product was poured into water was washed with sodium bicarbonate solution, dried, and crystallised twice from light petroleum (b. p. 50—60°), forming stout colourless plates, m. p. 87° (Found: C, 82·2; H, 5·4. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·3%).

1-*Phenylacetyl*-2-*naphthol*.—(1) β-Naphthyl phenylacetate (5 g.), aluminium chloride (4 g.), and carbon disulphide (10 c.c.) were heated on the water-bath for 1 hour, the solvent removed, and the residue heated at 130° for 4 hours. Ice was added, the product dissolved in hot 10% aqueous sodium hydroxide, and the filtered solution acidified. Two crystallisations from dilute acetic acid gave pale yellow needles (0·5 g.), m. p. 101° (Found: C, 82·1; H, 5·5. $C_{18}H_{14}O_2$ requires C, 82·3; H, 5·3%). An alcoholic solution gave a dark reddish-brown coloration with ferric chloride. (2) To a mixture of β-naphthol (20 g.), aluminium chloride (40 g.), and carbon disulphide (100 c.c.), cooled in ice and salt, phenylacetyl chloride (30 g.) was added during 1 hour. After 12 hours, ice and hydrochloric acid were added, the mixture was extracted with ether, and the extract shaken with 5% sodium hydroxide solution. Acidification of the alkaline solution gave a semi-solid substance, which was treated with boiling water to remove β-naphthol and crystallised from dilute acetic acid (charcoal), giving colourless needles (10 g.), m. p. 101°.

3-*Phenyl*-2-*methyl*-1 : 4-βα-*naphthapyrone*, obtained from 1-phenylacetyl-2-naphthol, acetic anhydride, and sodium acetate or phenylacetate, crystallised from dilute alcohol in long cream-coloured needles, m. p. and mixed m. p. 161° (Found: C, 83·6; H, 5·0. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%).

2 : 3-*Diphenyl*-1 : 4-βα-*naphthapyrone*, obtained from 1-phenylacetyl-2-naphthol, benzoic anhydride, and sodium benzoate, and 3 : 4-*diphenyl*-1 : 2-βα-*naphthapyrone*, from 1-benzoyl-2-naphthol, acetic anhydride, and sodium phenylacetate, formed long colourless needles, m. p. 188° (Found: C, 85·9; H, 4·3. $C_{25}H_{16}O_2$ requires C, 86·2; H, 4·6%), and colourless rhombic plates, m. p. 221—222° (Found: C, 86·0; H, 4·8%), respectively from alcohol. The yellow solution of the latter in sulphuric acid has a bright green fluorescence.

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