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EXPERIMENTS WITH SUBSTITUTED (3,2–c)–PYRANYL–2, 10–DIONES AND BENZOPYRANYL–(3,2–c) PYRAN–2,8–DIONES

A. MUSTAFA, O. H. HSIHMAT, S. M. A. D. ZAYED and A. AHMED NAWAR
Chemistry Department, Cairo University and National Research Centre, Dokki, Cairo, U.A.R.

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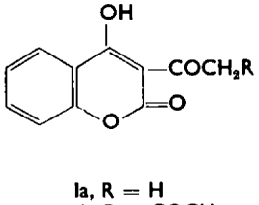
Abstract—Cyclization of the β-dicarbonyl compounds (Ib-c) gave the benzopyranyl-(3,2-c)-pyran-2, 10-diones(IIa-b). 3-Acyl-4-hydroxy-coumarins(Id-e) undergo the Kostanecki-Robinson reaction to yield (IIc-d). In the Pechmann condensation of 4-hydroxycoumarin with ethyl acetoacetate, 10-methylbenzopyranyl(3,2-c)-pyran-2,8-dione (IVa) is produced. The 10-phenyl derivative (IVb) was obtained via the Kostanecki-Robinson acetylation of 4-hydroxy-3-acetylcoumarin (Ia).

Whereas, 4-hydroxycoumarin yields 4-hydroxylaminocoumarin upon treatment with hydroxylamine hydrochloride, treatment of Ib and IIa with the same reagent result in the formation of VI.

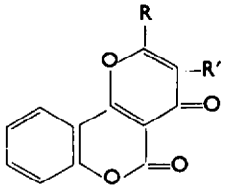
Alkaline hydrogen peroxide decomposes the substituted coumarins (cf. Table 2) to salicylic acid derivatives.

Deacylation of 3-acetoxycoumarin by the action of ethereal diazomethane solution yields 3-methoxy-coumarin.

THE β-dicarbonyl compounds (Ib-c), obtained by the Claisen condensation of 4-hydroxy-3-acetylcoumarin (Ia), have been cyclized in the presence of sulfuric acid[2a] to the corresponding substituted benzopyranyl(3,2-c)pyran-2,10-diones (IIa-b).



Ia, R = H
b, R = $COCH_3$
c, R = COC_6H_5
d, R = CH_3
e, R = C_6H_5



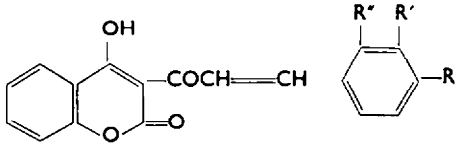
IIa, R = CH_3; R′ = H
b, R = C_6H_5; R′ = H
c, R = R′ = CH_3
d, R = CH_3; R′ = C_6H_5

The 3-acyl-4-hydroxycoumarins (Id-e) undergo the Kostanecki-Robinson reaction to the disubstituted benzopyranyl-(3,2-c)-pyran-2,10-dione derivatives (IIc-d). 8-Methylbenzopyranyl-(3,2-c)pyran-2,10-dione (IIa), identical with that described by Woods,[3] has also been obtained from 4-hydroxycoumarin and β-chlorocrotonyl-chloride in the presence of aluminium chloride.[2b]

Attempts to synthesize flavones of the type IIb from chalcones (IIIa-e) either by selenium dioxide oxidation in dry alcohol,[4] or by dehydrobromination of their dibromides with selenium dioxide in amyl alcohol were unsuccessful. In the case of the

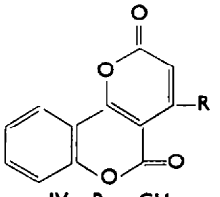
[1] V. V. Virkar and T. S. Wheeler, *J. Chem. Soc.* 1679 (1939).
[2a] M. S. Mahal and K. Venkataraman, *J. Chem. Soc.* 1767 (1934).
[2b] R. C. Elderfield *Heterocyclic Compounds*. Vol. II; p. 250. John Wiley, New York (1951).
[3] L. L. Woods, *J. Org. Chem.* **27**, 696 (1962).
[4a] S. R. Parikh and N. M. Shah, *J. Indian. Chem. Soc.* **36**, 729 (1959); [b] K. Venkataraman *et al. J. Chem. Soc.* 866 (1935); *Ibid.* 569 (1936).

dibromide of IIIa, the original chalcone IIIa was regenerated upon treatment with hydrogen peroxide in glacial acetic acid. Moreover, subjecting (IIIa-c) to the Algar-Flynn oxidation,[4a,5] using alkaline hydrogen peroxide, for the preparation of flavanols, resulting in the formation of salicylic acid (see below).



IIIa, R = R′ = R″ = H
b, R′ = R″ = H; R = NO_2
c, R″ = NO_2; R = R′ = H
d, R″ = H; R and R′ = :(O_2CH_2)
e, R′ = R″ = H; R = OCH_3

In the Pechmann condensation[6] of 4-hydroxycoumarin with ethyl acetoacetate yields 10-methyl-benzopyranyl-(3,2-c)pyran-2,8-dione (IVa). 3-Benzoyl-4-hydroxy-coumarin on Kostanecki-Robinson acetylation yields 10-phenylbenzopyranyl(3,2-c)pyran-2,8-dione (IVb).



IVa, R = CH_3
b, R = C_6H_5

The substituted benzopyranyl(3,2-c)pyran-2,10-dione (IIa-d) gives a yellow colouration on reduction with magnesium and hydrochloric acid,[7] a purple colour with *m*-dinitrobenzene in the presence of alkali,[8] and the potassium hydroxide test.[9]

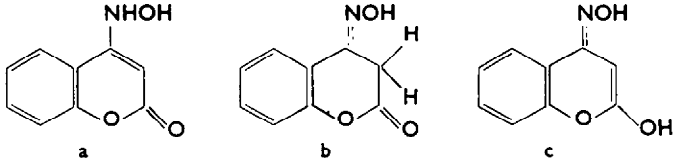
The I.R. spectra of compounds IIa-d (cf. Table 1), show a strong peak at about 5·7 μ, in agreement with the spectra of α,β-unsaturated-δ-lactone,[10] as well as a peak at about 6·0 μ, characteristic of 2-methylchromones[11] and flavones[12] attributed to $\alpha,\beta,\alpha',\beta'$-diunsaturated $\rangle C{=}O$ group.[13] The I.R. spectra of compounds (IVa-b) show a strong carbonyl peak at 5·75 μ in agreement with the spectra of α,β-unsaturated lactones.[14]

[5] J. Algar and J. P. Flynn, *Proc. Roy. Irish Academy* B. **42**, 1 (1934); *Chem. Abstr.* **29**, 161 (1935).
[6] H. V. Pechmann and C. Duisberg, *Ber. Dtsch. Chem. Ges.* **16**, 2119 (1883); H. V. Pechmann, *Ibid.*, **17**, 929 (1884); S. M. Sethna and N. M. Shah, *Chem. Revs.* **36**, 1 (1945).
[7] Y. Asahina and M. Inubuse., *Ber. Dtsch. Chem. Ges.* **61**, 1646 (1928).
[8] A. Schönberg and M. M. Sidky, *J. Org. Chem.* **21**, 476 (1956).
[9] A. Schönberg and A. Sina, *J. Chem. Soc.* 3344 (1950). A. Schönberg and A. Sina, *J. Amer. Chem. Soc.* **72**, 1611 (1950).
[10] R. N. Jones and F. Herling; *J. Org. Chem.* **19**, 1252 (1954).
[11] J. H. Looker and W. W. Hanneman, *J. Org. Chem.* **27**, 381 (1962).
[12] G. E. Inglett, *J. Org. Chem.* **23**, 93 (1958).
[13] H. W. Tompson and P. Torkington, *J. Chem. Soc.* 640 (1945).
[14] R. N. Jones and C. Sandorfy, *Technique of Organic Chemistry* (Edited by A. Weissenberger), Vol. IX, p. 455. Interscience, New York (1956); P. Yates and G. H. Stout, *J. Amer. Chem. Soc.* **76**, 5110 (1954); R. N. Jones *et al.*, *Canad. J. Chem.* **37**, 2007 (1959); H. H. Wasserman and R. C. Koch, *J. Org. Chem.* **27**, 37 (1962).

Although coumarins do not possess any true carbonyl activity, one mole of hydroxylamine adds to the 3:4-double bond and a second causes the lactone ring to open with the formation of a hydroxamic acid.[15] Whereas coumarin is stable toward the action of hydroxylamine hydrochloride in pyridine, 4-hydroxycoumarin shows its ketonic character by the formation of V (or the possible tautomeric forms) which has also been obtained by the interaction of hydroxylamine hydrochloride with 4-chlorocoumarin.

TABLE 1. CARBONYL STRETCHING FREQUENCIES ν (C=O) OF IIa-d

Sub	Lactone carbonyl ν (C=O) in μ	γ-pyrone carbonyl in μ
IIa	5·7	6·0
IIb	5·7	6·05
IIc	5·65	6·0
IId	5·67	6·07



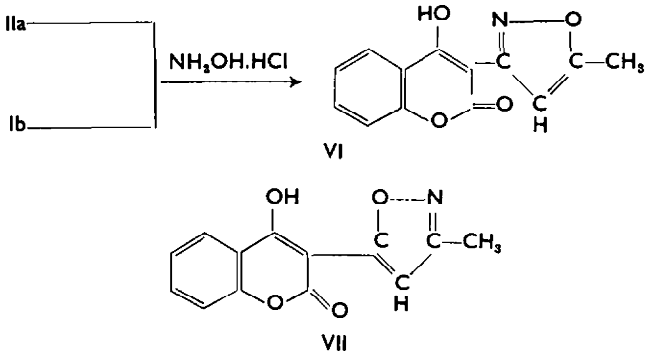
a b c

V

The stability of V towards 6N sulfuric acid at 100° for 10 hours and the fact that the I.R. spectrum shows two submaxima at 3·6 μ and 3·8 μ instead of a peak for a free OH group, indicates a strongly hydrogen bonded OH group as observed in the case of 4-hydroxycoumarin and dimeric carboxylic acids.[16] The band at 7·55 μ may be due to the OH-in plane deformation frequency as observed in the case of 4-hydroxycoumarin (ca. 1315 cm^{-1})[16] and in the case of oximes (about 1300 cm^{-1}).[17] In the region of carbonyl absorption the strong peak at 5·75 μ is in good agreement with the spectra of α,β-unsaturated-δ-lactones, and shows that the carbonyl group of the lactone is not involved in the hydrogen bonding. The tautomeric structure Vc is unlikely due to the absence of a band corresponding to conjugated C=N stretching vibration around 6·5 μ.[18]

Based on the reaction of the γ-pyrone ring in flavones[19] and in Khellin[20] with hydroxylamine hydrochloride and formation of isoxazole derivatives, the product obtained from IIa and hydroxylamine hydrochloride should have formula VI, or possibly the isomeric formula VII. The diketone Ib may be an intermediate product in this reaction, since treatment of Ib with the same reagent and similar experimental conditions, gives a product identical with VI, soluble in aqueous alkali and giving no

[15] L. Zechmeister, *Progress on the Chemistry of Organic Natural Products*. Springer-Verlag, Wien (1952). Vol. IX, p. 231.
[16] V. C. Farmer, *Spectrochim. Acta* 870 (1959).
[17] A. Palm and W. Werbin, *Canad. J. Chem.* 870 (1953).
[18] H. G. Khorana, *Chem. Revs.* **53**, 145 (1953); L. J. Bellamy, *Infra-red of Complex Molecules* (Ind. Edition) J. Wiley, London (1958).
[19] W. Baker, J. B. Harborne and W. D. Ollis, *J. Chem. Soc.* 1303 (1952).
[20] A. Schönberg and M. M. Sidky, *J. Amer. Chem. Soc.* **75**, 5128 (1953).

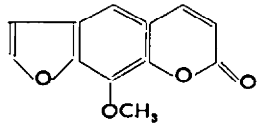


distinct colour with ferric chloride solution. Nor does it react further with hydroxylamine hydrochloride and shows high stability towards the action of 6N H_2SO_4 at 100°. The I.R. spectrum of VI shows a broad OH absorption band around 3·05 μ which is in agreement with that observed in the case of 3-substituted-4-hydroxycoumarins.[16] The shifting of ν (OH) towards lower frequencies may be indicative of the preference of the possible intramolecular hydrogen bonding in structure VI.

Action of alkaline hydrogen peroxide on substituted coumarins

In contrast to the report by Molho[21] that 4-hydroxycoumarin is stable in alkaline hydrogen peroxide, it has now been shown that under similar experimental conditions, 4-hydroxycoumarin is readily converted to salicylic acid. An investigation into the action of alkaline hydrogen peroxide on substituted coumarins, has shown that whereas coumarin and alkyl substituted coumarins are stable, coumarins with electronegative groups in the α-pyrone ring behave differently. 4-Chloro-, 3-acetyl-4-hydroxy-, 4-phenylsulfonylcoumarins (X) yield salicylic acid and 3,6-dinitro-, 7-bromo-4-hydroxy 3-ω-bromoacetylcoumarin (XI) yield 4-nitro- and 4-bromosalicylic acids respectively.

Alkaline hydrogen peroxide destroys both the α-pyrone ring and the benzene ring of a furocoumarin and leaves 2,3-furan dicarboxylic acid as in the main fragment.[22] Thus the latter acid now has been readily obtained upon treatment of xanthotoxin VIII with alkaline hydrogen peroxide.

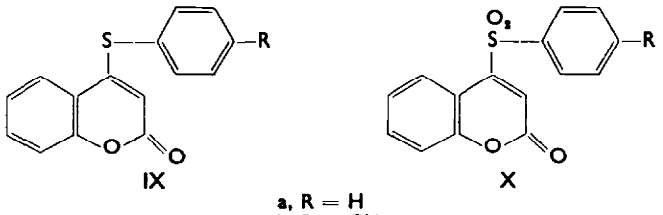


VIII

The 4-arylsulfonylcoumarins (X), required for this investigation, were obtained by the reaction of 4-chloro-coumarin with the corresponding aryl mercaptan in the presence of piperidine, followed by oxidation of the product (IX) with hydrogen peroxide in acetic acid.

[21] D. Molho, *Bull. Soc. Chim. Fr.* **39**, 46 (1946).

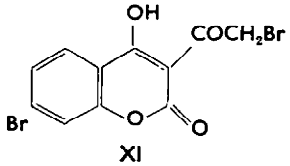
[22] L. Zechmeister, *Progress in the Chemistry of Organic Natural Products*, Springer-Verlag, Wien (1952). Vol. IX, p. 258.



IX X

a, R = H
b, R = CH_3

Bromination[23] of Ia with bromine in glacial acetic acid in absence of water[23] takes place in both the ring and the side chain, yielding 7-bromo-4-hydroxy-3-ω-bromoacetylcoumarin (XI), the structure of which is based on the fact that 4-bromosalicylic acid is formed on treatment with alkaline hydrogen peroxide.



XI

Trivedi and Sethna[24] report the formation of 3-hydroxy-4-acetylcoumarin via the Fries migration of 3-acetoxycoumarin, or in the Friedel-Crafts acetylation of 3-hydroxycoumarin. This work, however, could not be confirmed in this laboratory, 3-acetoxycoumarin undergoes deacylation, and a mixture of 3-acetoxy-, and 3-hydroxycoumarin is obtained in the Friedel-Crafts reaction. The synthesis of the isomeric chromone and coumarin derivatives of the type II and IV from 3-hydroxycoumarin will be published later.

Deacylation of 3-acetoxycoumarins. Diazomethane, in ether-methanol solution, splits esters and N-acylcompounds provided the acyl free group has no basic properties.[25] It has been found that, whereas, 4-acetoxycoumarin is stable towards diazomethane, 3-acetoxycoumarin is readily converted to 3-methoxy-coumarin. The latter compound is also obtained from 3-hydroxycoumarin either by the action of diazomethane or methyl iodide in the presence of anhydrous potassium carbonate. Deacylation of 4-acetoxy-, and 3-acetoxycoumarins is achieved by heating with piperidine at 100°.

EXPERIMENTAL

The I.R. spectra were carried out in Nujol on a Perkin-Elmer infra-cord spectrophotometer Model 137. M.p. are not corrected.

3-Acetoacetyl-4-hydroxycoumarin (Ib)

A solution of 0·005 mole (1·1 g) 3-acetyl-4-hydroxycoumarin[26] in 25 ml purified ethyl acetate was added to 1 g powdered sodium. The reaction mixture was refluxed on a water bath for 6 hr, decomposed with ice and finally extracted with ether. The aqueous layer on acidification with dil. hydrochloric acid gave a 66% yield of Ib; it forms yellow needles from ethanol, m.p. 134°; and its alcoholic

[23] K. W. Rosenmund and K. Peroepffer, *Chem. Ber.* **90,** 1922 (1957).
[24] K. N. Trivedi and S. Sethna, *J. Org. Chem.* **25,** 1817 (1960).
[25] A. Schönberg and A. Mustafa, *J. Chem. Soc.* 605 (1948), H. Bredreck, R. Sieber, L. Kamphenbel and R. Ramberger, *Chem. Ber.* **89,** 1169 (1956).
[26] Nippon Kayaku, Co., Ltd. (by Y. Sumiki, K. Yamanaka, T. Shirai and T. Narita, Japan 2619 (1960) *Chem. Abstr.* **54,** 21135 (1960).

solution gives a deep red colour with aqueous ferric chloride solution. (Found: C, 64·08; H, 4·42. $C_{18}H_{10}O_5$ requires: C, 63·41; H, 4·07%).

3-*Benzoacetyl*-4-*hydroxycoumarin* (Ic)

A mixture of 0·01 mole 3-acetyl-4-hydroxycoumarin, 25 ml ethyl benzoate and 1 g mole sodium were heated in an oil bath at 180° for 5 hr. A vigorous reaction took place, the mixture turned dark brown and after cooling was decomposed with ice, extracted with ether and the aqueous solution acidified with dil. hydrochloric acid. The product (Ic) recrystallized from ethanol in yellow crystals, m.p. 175–176° and gave a red colour with alcoholic ferric chloride solution. (Found: C, 70·56; H, 3·97. $C_{18}H_{12}O_5$ requires: C, 70·13; H, 3·90%).

Preparation of substituted benzopyranyl(3,2-c)-*pyran*-2,10-*diones* II.-8-*Methylbenzopyranyl*(3,2-c)*pyran*-2,10-*dione*(IIa)

A solution of 1 g 3-acetoacetyl-4-hydroxycoumarin (Ib) in 100 ml aqueous sulphuric acid (25%) was heated (sand bath) for 1 hr. The cooled reaction mixture was neutralized with sodium carbonate, and the product crystallized from ethanol, yellow needles m.p. 245°, yield 70%. IIa gives a yellow colour with magnesium and hydrochloric acid and a stable purple colour upon dilution with *m*-dinitrobenzene. (Found: C, 68·31; H, 3·84. $C_{13}H_8O_4$ requires: C, 68·42; H, 3·51%).

Compound IIa may also be prepared from 4-hydroxycoumarin and β-chloro-crotonylchloride as follows: To a well cooled mixture of 0·01 mole (1·26 g) 4-hydroxycoumarin and 5 g (1·85 mole) anhydrous aluminium chloride in 50 ml freshly distilled nitrobenzene, a solution of 2 g (ca. 1·5 mole) β-chlorocrotonyl chloride in 15 ml nitrobenzene was added dropwise. After addition, the reaction mixture was left overnight at room temp, and then heated on a water-bath for 4 hr. After decomposition with ice and hydrochloric acid, nitrobenzene was eliminated by steam distillation. The residue was washed with dil sodium carbonate solution, then with water and finally crystallized from alcohol, yield 60%, m.p. 246°. A mixed m.p. with IIc as well as with an authentic sample[3] gave no depression and identity with IIa was proved by I.R. spectral comparison.

8-*Phenylbenzopyranyl*-(3,2-c)*pyran*-2,10-*dione* (IIb)

This was prepared by cyclization of 1 g 3-ω-benzoylaceto-4-hydroxycoumarin (Ic) with 50 ml alcoholic sulphuric acid (50%). IIb forms colourless crystals from ethanol, m.p. 216°, yield ca. 60%. (Found: C, 74·54; H, 3·64. $C_{18}H_{10}O_4$ requires: C, 74·48; H, 3·45%).

8,9-*Dimethylbenzopyranyl*(3,2-c)*pyran*-2,10-*dione* (IIc)

A mixture of 1 g 3-propionyl-4-hydroxycoumarin (Id), 3 g freshly fused sodium acetate, and 20 ml acetic anhydride was heated for 6 hr at 140–160° (oil bath). The cooled mixture was poured into iced–water and the product crystallized from ethanol as colourless crystals, m.p. 220°, yield ca. 73%. It gives the chromone tests. (Found: C, 69·45; H, 4·12. $C_{14}H_{10}O_4$ requires: C, 69·42; H, 4·13%).

8-*Methyl*-9-*phenylbenzopyranyl*(3,2-c)*pyran*-2,10-*dione* (IId)

Compound IId was obtained, as in the case of IIc, in 78% yield upon treatment of 1 g 3-phenylacetyl-4-hydrocoumarin (Ie) with a mixture of sodium acetate and acetic anhydride. It forms colourless crystals from ethanol, m.p. 242–243°, and gives the chromone tests. (Found: C, 74·69; H, 4·02. $C_{19}H_{12}O_4$ requires: C, 75·00; H, 3·94%).

Preparation of 10-*substituted benzopyranyl*(3,2-c)*pyran*-2,8-*dione* IV

10-*Methylbenzopyranyl*(3,2-c)*pyran*-2,8-*dione* (IVa). While stirring at 100°, 20 ml sulphuric acid (80%) was added portion-wise over a peroid of 1 hr to a mixture of 1·4 g 4-hydroxycoumarin and 2·5 ml ethyl acetoacetate. The reaction mixture was further heated for 15 min at 100°, cooled and poured onto ice. The product crystallized from ethanol as colourless crystals m.p. 243°, yield 55%. (Found: C, 68·53; H, 3·88. $C_{13}H_8O_4$ requires: C, 68·42; H, 3·5%).

10-*Phenylbenzopyranyl*(3,2-c)*pyran*-2,8-*dione* (IVb). A mixture of 0·5 g 3-benzoyl-4-hydroxycoumarin, 20 ml acetic anhydride, and 1·5 g anhydrous sodium acetate was heated for 6 hr at 150–160° (oil-bath). The cooled mixture was poured onto ice and the product washed with dil sodium bicarbonate solution, then with water, and finally crystallized from ethanol as pale yellow crystals, m.p. 204–205°, yield 60%. (Found: C, 74·55; H, 3·69. $C_{18}H_{10}O_4$ requires: C, 74·48; H, 3·47%).

Action of hydroxylamine hydrochloride

(a) *On 4-hydroxycoumarin.* To a solution of 1 g 4-hydroxycoumarin in 10 ml pyridine was added an aqueous solution of 1·5 g hydroxylamine hydrochloride in 5 ml water. The mixture was refluxed for 4 hr, cooled and acidified with 2 N HCl. 4-Hydroxylamino-coumarin (V) was obtained from benzene–pet. ether (b.p. 60–80°) as colourless crystals, m.p. 125°, yield ca. 60%. It is soluble in aqueous solution of sodium hydroxide, in dil. sodium bicarbonate solution and gives no distinct colour with alcoholic ferric chloride solution. (Found: C, 61·49; H, 4·09; N, 8·34. $C_9H_7NO_3$ requires: C, 61·01; H, 3·95; N, 7·91%).

Treatment of 4-chlorocoumarin with hydroxylamine hydrochloride under the above conditions, resulted in the formation of V in an almost quantitative yield and identified by m.p., mixed m.p. and identity of I.R. spectra. (Found: C, 61·23; H, 4·18; N, 8·14. $C_9H_7NO_3$ requires: C, 61·01; H, 3·95; N, 7·91%).

(b) *On 8-methylbenzopyranyl(3,2-c)pyran-2,10-dione* (IIa). A mixture of 1 g IIa, 1 g hydroxylamine hydrochloride, 10 ml ethanol, and 0·1 ml pyridine was heated (water-bath) for 15 min. The cooled mixture was diluted with water and the product VI crystallized from ethanol, as colourless crystals, m.p. 234°, yield ca. 80%. (Found: C, 64·42; H, 3·86; N, 5·60. $C_{13}H_9NO_4$ requires: C, 64·20; H, 3·70; N, 5·76%).

VI dissolves in aqueous sodium hydroxide (10%), and in sodium bicarbonate (10%). It is stable in 6 N sulphuric acid at 100° for 10 hr, and in excess hydroxylamine hydrochloride in pyridine at 100° for 4 hr.

(c) *On 3-acetoacetyl-4-hydroxycoumarin* (Ib). Treatment of a solution of 1 g Ib in 10 ml pyridine with a solution of 1·5 g hydroxylamine hydrochloride in 0·5 ml water for 4 hr at 100°, followed by acidification of the cooled mixture with dil hydrochloric acid, resulted in the formation of VI in 85% yield, identified by m.p. and mixed m.p. with a sample of VI, prepared as mentioned above, and the comparison of I.R. spectra. (Found: C, 64·44; H, 3·88; N, 5·68. $C_{13}H_9NO_4$ requires: C, 64·20; H, 3·70; N, 5·76%)

(a) *4-arylmercaptocoumarins* (IXa-b). A mixture of 0·5 g 4-chlorocoumarin, 0·4 g appropriate mercaptan, and 3 drops piperidine was heated on a boiling water-bath for 12 hr. After cooling and washing several times with pet. ether (b.p. 30–50°), the product was crystallized from absolute ethanol.

4-Phenylmercaptocoumarin (IXa) forms colourless crystals, m.p. 171–172°, yield ca. 50%. (Found: C, 70·56; H, 3·78; S, 12·30. $C_{15}H_{10}O_2S$ requires: C, 70·86; H, 3·93; S, 12·60%).

4-*p*-Tolylmercaptocoumarin (IXb) forms colourless crystals, m.p. 149–150°; yield ca. 42%. (Found: C, 71·51; H, 4·19; S, 12·22. $C_{16}H_{12}O_2S$ requires: C, 71·64; H, 4·47; S, 11·94%).

(b) *4-Arylsulfonylcoumarins* (Xa-b). A solution of 0·4 g of the appropriate 4-arylmercaptocoumarin (IX) in the least amount of hot glacial acetic acid was treated with 20 ml hydrogen peroxide (30%). The reaction mixture was heated (water-bath) for 1 hr, cooled, and diluted with water. The 4-arylsulphonylcoumarin (Xa) crystallized from ethanol in colourless crystals, m.p. 152–154°; yield ca. 70%. (Found: C, 62·90; H, 3·19; S, 11·09. $C_{15}H_{10}O_4S$ requires: C, 62·94; H, 3·49; S, 11·17%).

4-*p*-Tolylsulphonylcoumarin (Xb) forms colourless crystals, m.p. 182–183°; yield ca. 65%. (Found: C, 64·25; H, 3·69; S, 10·74. $C_{16}H_{12}O_4S$ requires: C, 64·00; H, 4·00; S, 10·67%).

(c) *7-Bromo-4-hydroxy-3-ω-bromoacetylcoumarin* XI. To a solution of 1 g 3-acetyl-4-hydroxycoumarin (Ia) in 10 ml glacial acetic acid kept at 80° was added dropwise, over a period of 1 hr, a solution of 1 ml bromide in 10 ml glacial acetic acid. The temp was then raised and kept at 100° for 4 hr. The product (ca. 0·8 g) was crystallized from acetic acid in pale yellow crystals, m.p. 157–158°. (Found: C, 36·40; H, 1·90; Br, 43·87. $C_{11}H_6Br_2O_4$ requires: C, 36·46; H, 1·66; Br, 44·19%).

Treatment of a solution of 0·5 g XI in methanol with a mixture of 15 ml aqueous sodium hydroxide (10%) and 10 ml hydrogen peroxide (30%) as described below, yielded 4-bromo-salicylic acid in 72% yield, identified by m.p. and mixed m.p.

Action of diazomethane on 3-, and on 4-acetoxycoumarins

To a cooled solution of 0·5 g 3-acetoxycoumarin in 30 ml ether was added a freshly distilled ethereal diazomethane solution (prepared from 2 g nitrosomethylurea). After keeping at 0° for 12 hr, the ether was evaporated and the residue crystallized from benzene in colourless crystals of 3-methoxycoumarin, m.p. 163°, yield 0·32 g. (Found: C, 68·05; H, 4·58. $C_{10}H_8O_3$ requires: C, 68·18; H, 4·54%).

When the above experiment was repeated in the presence of 1 ml methanol a similar result was obtained.

3-Methoxycoumarin is readily obtained in 75% yield by treatment of 3-hydroxycoumarin with ethereal diazomethane solution as described above; and in 82% yield upon refluxing for 9 hr an acetone solution of 3-hydroxycoumarin with excess of methyl iodide in the presence of anhydrous potassium carbonate.

When 4-acetoxycoumarin was treated with ethereal diazomethane, under similar conditions to that adopted in the case of 3-acetoxycoumarin, the only product isolated was unchanged 4-acetoxycoumarin.

Action of alkaline hydrogen peroxide on substituted coumarin

To 0·5 g of the appropriate coumarin in methyl alcohol (or without solvent), was added while cooling, and with occasional shaking, 15 ml 10% sodium hydroxide and 10 ml 30% hydrogen peroxide. The mixture was kept overnight at room temp. and then acidified with cold 2N HCl.

Methanol was removed under red. press. and the aqueous solution extracted with ether. After evaporation of ether, the residue was purified and identified by mixed m.p. with an authentic sample. The results are listed in Table 2; use of pyridine for sodium hydroxide gave similar results.

TABLE 2. EFFECT OF ALKALINE HYDROGEN PEROXIDE ON COUMARINS

Coumarin used	Reaction time (hr)	Product
Coumarin	12 h	Unchanged
4-Hydroxy 1-thiocoumarin	12 h	Unchanged
4,6-Dimethylcoumarin	24 h	Unchanged
4-Hydroxycoumarin	12 h	Salicylic acid
4-Chlorocoumarin	36 h	Salicylic acid
IIIa-c	12 h	Salicylic acid
Xa-b	48 h	Salicylic acid
3,6-Dinitrocoumarin	24 h	5-Nitrosalicylic acid
XI	24 h	4-Bromosalicylic acid
VIII	24 h	Furan dicarboxylic acid

Behaviour of (a) *3-cinnamoyl-4-hydroxycoumarin* (IIIa) *toward selenium dioxide.* Treatment of a solution of 1 g IIIa in 25 ml amyl alcohol with 1·1 g selenium dioxide at the b.p. of the solvent for 20 hr, resulted in unchanged IIIa.

(b) *3-(α′,β′-Dibromocinnamoyl)-4-hydroxycoumarin*[27] *toward selenium dioxide.* Similar treatment of the dibromo compound under the above mentioned conditions resulted in the recovery of the starting material.

(c) *3-(α′-β′-Dibromocinnamoyl)-4-hydroxycoumarin toward hydrogen peroxide.* To 0·5 g of the dibromide in 40 ml glacial acetic acid was added 5 ml 30% hydrogen peroxide and after 12 hr at room temp the original 3-cinnamoyl-4-hydroxycoumarin separated out.

Preparation of the chalcones IIIa-e

To a mixture of 1 mole 3-acetyl 4-hydroxycoumarin in 4 ml 10% sodium hydroxide solution was added 1·5 mole aldehyde. The mixture was shaken and left for 3 days at room temp. It was then acidified with dil. hydrochloric acid, filtered and crystallized from the proper solvent.

IIIb was obtained in 40% yield as yellow crystals, m.p. 262–263°. It was crystallized from acetic acid and gave an orange colour with ferric chloride solution. (Found: C, 64·85; H, 3·5. $C_{18}H_{11}O_6N$ requires: C, 64·09; H, 3·26%).

IIIc was crystallized from alcohol m.p. 174–175, yield 37%. (Found: C, 64·31; H, 3·42. $C_{18}H_{11}O_6N$ requires: C, 64·09; H, 3·26%).

IIIe gave 45% yellow crystals m.p. 184°. It gave a reddish brown colour with ferric chloride (crystallization from alcohol or acetic). (Found: C, 70·66; H, 4·82. $C_{15}H_{14}O_5$ requires: C, 70·80; H, 4·35%).

IIIa, melts at 212–213° after crystallization from alcohol.[27]

IIId, melts at 252 after crystallization from acetic acid.[28]

[27] E. Ziegler, G. Wildtgrube and H. Junek, *Monatsh.* **87**, 439 (1956).

[28] G. G. Badcock, F. M. Dean, A. Robertson and W. B. Whalley, *J. Chem. Soc.* 903 (1950).