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Condensation of *o*-benzoquinone with 4-hydroxy coumarins : A new synthesis of 3-aryl-4-hydroxy coumarins and coumestans

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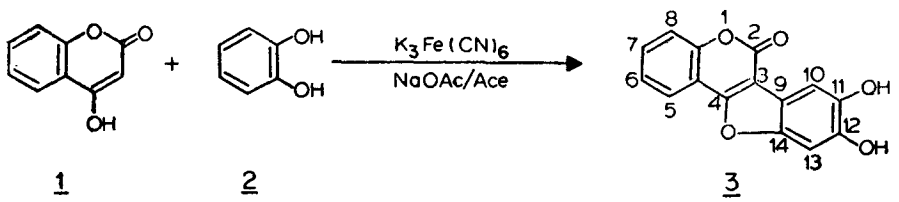
Abstract. The 4-hydroxy coumarins have been reacted with *o*-benzoquinone, in acetone in the absence of the oxidant potassium ferricyanide. The products were found to be 3-aryl-4-hydroxy coumarins which were cyclised to the corresponding 11, 12-dihydroxy coumestans. The structure of 11, 12-dihydroxy coumestan has been confirmed by an unambiguous synthesis. The structures of other compounds were confirmed on the basis of their analytical, chemical and spectral data.

Keywords. Dihydroxy phenyl; hydroxy coumarins; dihydroxy coumestans; *o*-benzoquinone condensation.

1. Introduction

4-Hydroxy coumarin (1) was reacted with catechol (2) (Wanzlick *et al* 1963) in aqueous acetone and sodium acetate using potassium ferricyanide as an oxidant and 11, 12-dihydroxy coumestan (3) was directly obtained. Wanzlick *et al* (1963) also postulated that the initial reaction proceeded through the oxidation of catechol to *o*-benzoquinone. 4-Hydroxy coumarin then adds on to the *o*-benzoquinone and the intermediate thus formed gets dehydrogenated to coumestan under the oxidative conditions.



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However there seems to be no direct evidence to show that *o*-benzoquinone is the reactive species in this reaction. In the present investigation *o*-benzoquinone was directly reacted with 4-hydroxy coumarin in the absence of oxidant. The structure of the product obtained was established on the basis of spectral and chemical evidences.

2. Results and discussion

4-Hydroxy coumarin (Boyd and Robertson 1948) and *o*-benzoquinone (4) were mixed in molar proportions in acetone and kept stirred for about 6 hr at room temperature. There was no tangible reaction and the starting material was recovered. However when the reaction was carried out at 40–45° C, the colour of the reaction mixture slowly changed and after 2 hr a grey solid separated out. This compound was filtered and recrystallised from methanol as a greyish white compound (5), m.p. 272° C. Compound (5) was soluble in aqueous sodium bicarbonate and on neutralisation was reprecipitated. It gave green colour with aqueous iron (III) chloride, characteristic of catechol system. The IR spectrum of this compound showed absorptions at 3150 cm^{-1} (broad, hydroxyls) and 1690 cm^{-1} (lactone carbonyl) indicating the presence of the 4-hydroxy coumarin system.

Compound (5) on acetylation with acetic anhydride and pyridine gave a colourless compound (6), m.p. 142° C. Compound (6) was insoluble in aqueous sodium bicarbonate and did not give the green colour with aqueous iron (III) chloride, indicating that all the hydroxyls of compound (5) have been acetylated. The IR spectrum of compound (6) showed absorptions at 1775, 1750 cm^{-1} (ester carbonyls) and 1715 cm^{-1} (lactone carbonyl). Its NMR spectrum in $CDCl_3$ showed signals at δ 1·90 (s, 3 H), δ 1·95 (s, 3 H) and δ 2·05 (s, 3 H) due to the methyl protons of acetate groups and the signals at δ 7·3 (m, 7 H) due to the aromatic protons. Although in the mass spectrum of (6) M^+ ion is not present, the subsequent fragmentation indicating the consecutive loss of three ketene units (−42) from the compound showed the presence of three acetate units and the molecular weight as 396. This is because of the labile nature of the acetate units to electron impact. The loss of ketene (m/e 42) from m/e 354 resulting in m/e 312 is confirmed by the presence of a metastable peak at m/e 275. Similarly the loss of ketene from m/e 312 resulting in m/e 270 is confirmed by the presence of a metastable peak at 233 (calculated 233·6).

Compound (5) on dehydrogenative cyclisation using potassium ferricyanide, acetone and sodium acetate gave a compound identical in all respects with compound (3), prepared according to the procedure of Wanzlick *et al* (1963) From the above data the structure of (5) and (6) can be 3-(3′, 4′-dihydroxy phenyl)· 4-hydroxy coumarin and 3-(3′, 4′-diacetoxy phenyl)-4-acetoxy coumarin respec-- tively. The reaction can be envisaged as shown in chart 1.

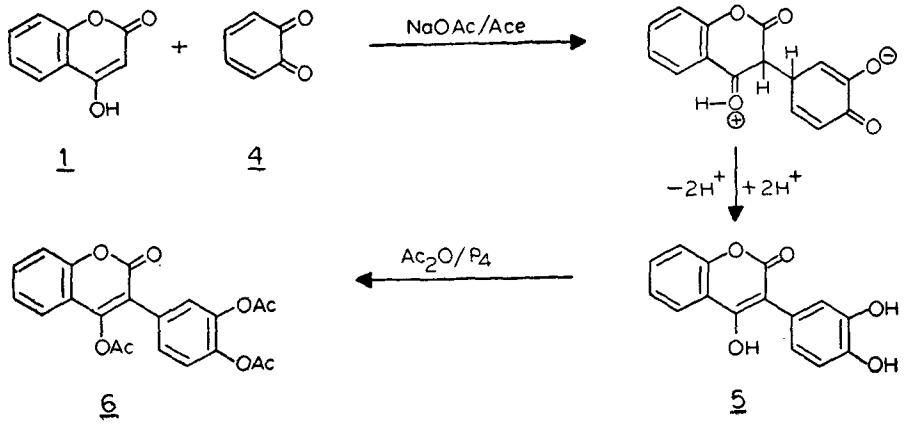
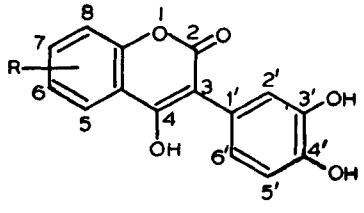


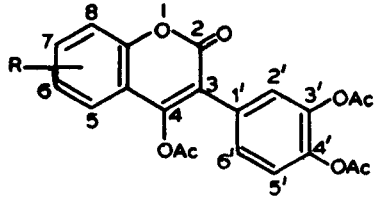
Table 1. Preparation of 3-(3′,4′-dihydroxy phenyl)-4-hydroxy coumarins by the condensation of *o*-benzoquinone with 4-hydroxy coumarins.



R	m.p. °C	% yield	IR cm^{-1} $\nu_{O=H}$	IR cm^{-1} $\nu_{C=O}$	Mol. formula	Analysis (%) Found C	Found H	Requires C	Requires H
H	272[a]	78	3150 (b),	1690	$C_{15}H_{10}O_5$	66·68	3·62	66·67	3·70
6-CH_3	280[b]	85	3250 (b),	1680	$C_{16}H_{12}O_5$	67·72	4·10	67·61	4·22
7-CH_3	265[b]	79	3250 (b),	1690	$C_{16}H_{12}O_5$	67·53	4·15	67·61	4·22
8-CH_3	278[b]	76	3200 (b),	1680	$C_{16}H_{12}O_5$	67·50	4·12	67·61	4·22
6-Cl	285[c]	79	3230 (b),	1690	$C_{15}H_9O_5Cl$	59·02	2·86	59·12	2·95
8-Cl	282[c]	73	3200 (b),	1685	$C_{15}H_9O_5Cl$	59·01	2·80	59·12	2·95
6, 8-diCl	287[c]	83	3250 (b),	1690	$C_{15}H_8O_5Cl_2$	52·93	2·20	53·10	2·36

Solvent of crystallisation : [a] methanol; [b] benzene-methanol; [c] ethyl acetate.

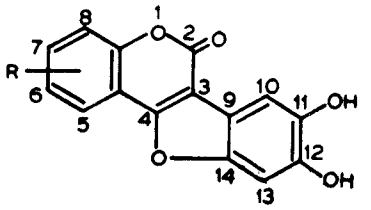
Table 2. Preparation of 3-(3′, 4′-diacetoxy phenyl)-4-acetoxy coumarins by the acetylation of 3-aryl-4-hydroxy coumarins.



R	m.p. °C	% yield	IR cm^{-1} ν_{COCH_3}	IR cm^{-1} $\nu_{C=O}$	Mol. formula	Analysis (%) Found C	Found H	Required C	Required H
H	142	84	1775 1750	1715	$C_{21}H_{16}O_8$	63·52	3·96	63·63	4·04
6-CH_3	150	87	1760 1755	1720	$C_{22}H_{18}O_8$	64·59	4·36	64·39	4·39
7-CH_3	145	82	1765 1750	1720	$C_{22}H_{18}O_8$	64·59	4·32	64·39	4·39
8-CH_3	140	77	1755 1730	1720	$C_{22}H_{18}O_8$	64·60	4·30	64·39	4·39
6-Cl	155	87	1760 1750	1715	$C_{21}H_{15}O_8Cl$	58·40	3·34	58·53	3·48
8-Cl	160	80	1765 1750	1720	$C_{21}H_{15}O_8Cl$	58·42	3·32	58·53	3·48
6, 8-diCl	152	86	1765 1755	1720	$C_{21}H_{14}O_8Cl_2$	54·10	2·90	54·19	3·01

Solvent of crystallisation = benzene.

Table 3. Preparation of 11,12-dihydroxy coumestans by the cyclisation of 3-aryl-4-hydroxy coumarins.



R	m.p. °C	% yield	IR cm^{-1} ν_{OH}	IR cm^{-1} $\nu_{C=O}$
H	>300	78	3490 3100	1720
6-CH_3	,,	76	3425 3125	1725
7-CH_3	,,	73	3350 3120	1720
8-CH_3	,,	69	3490 3050	1730
6-Cl	,,	83	3425 3125	1720
8-Cl	,,	74	3420 3150	1730
6, 8-diCl	,,	73	3350 3120	1725

Solvent of crystallisation = acetone.

3. Experimental

3.1. *Preparation of 3-aryl-4-hydroxy coumarins*

4-Hydroxy coumarins (0·01 mol) and *o*-benzoquinone (0·01 mol) were mixed in 50 ml acetone and stirred for 2 hr at 40–50° C. A greyish white solid separated not. It was filtered, dried and recrystallised as light grey needles.

3.2. *Preparation of 3-aryl-4-acetoxy coumarins*

3-Aryl-4-hydroxy coumarin (0·01 mol) was suspended in 10 ml acetic anhydride and one drop of pyridine was added. After keeping aside for 3–4 hr the mixture was poured over ice. The colourless compound that separated was filtered and recrystallised from benzene as colourless prisms.

3.3. *Preparation of 11, 12-dihydroxy coumestans*

3-Aryl-4-hydroxy coumarin (0·01 mol) was dissolved in aqueous acetone (20 ml 1 : 1) and sodium acetate (7 g). A solution of potassium ferricyanide (7 g) and

sodium acetate (7 g) in 30 ml of water was added slowly with stirring at room temperature. The green compound that separated was filtered and recrystallised from large amount of acetone as light green crystals.

4. Conclusion

This method not only establishes that *o*-benzoquinone is the reactive intermediate in the formation of coumestans under Wanzlick conditions but also constitutes a new and facile route to the synthesis of 4-hydroxy coumarins with polyoxygenated side phenyl nucleus. Adopting the above procedure the seven differently substituted 3-(3′, 4′-dihydroxy phenyl)-4-hydroxy coumarins, their acetates and corresponding coumestans prepared are given in tables 3.1, 3.2 and 3.3 respectively with their physical and analytical data.

Acknowledgement

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References

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