

# A NEW ROUTE TO THE SYNTHESIS OF COUMESTANS

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In earlier communications<sup>1,2</sup> from these laboratories new approaches for the synthesis of additional oxygen hetero rings in 3:4-positions of coumarin were reported. The present paper deals with the synthesis of coumestans by the condensation of 2-chlorocyclohexanone with 4-hydroxy coumarin.

2-Chlorocyclohexanone<sup>3</sup> was refluxed with 4-hydroxy coumarin in molar proportions in boiling xylene using anhydrous potassium carbonate as a basic condensing agent for four hours. At the end of the reaction, the xylene solution was decanted and concentrated to a small bulk when a white solid separated. The crude product was filtered and repeatedly digested with aqueous sodium bicarbonate solution. The bicarbonate insolubles were then washed with dilute hydrochloric acid and finally with water, free from the acid. The crude product thus obtained was recrystallised from methanol, when a colourless crystalline substance with a m.p. 173°C, different from starting material, was obtained. Elemental analysis indicated the absence of halogen and the compound accounted for C<sub>16</sub> skeleton. The I.R. spectrum of the compound did not reveal the presence of hydroxyl and showed an absorption around 1710 cm<sup>-1</sup> assignable to lactone carbonyl. This indicated that the hydroxyl in 4-hydroxy-coumarin and halogen of 2-chlorocyclohexanone were involved in the condensation, in which case the resulting product must have been an ether with the carbonyl of the cyclohexyl moiety free. The compound however did not reveal the presence of an additional carbonyl either in I.R. or by the qualitative tests. Further, in the N.M.R. of the compound, there was no indication for the presence of a free proton in 3-position of coumarin and therefore suggested that 3 and 4-positions of coumarin are involved in the condensation with 2-chlorocyclohexanone forming a fused 5-membered ring. From an analogy of the condensation of 2-chlorocyclohexanone with  $\beta$ -naphthol reported by Osdene and Russel<sup>4</sup>, it appeared probable to suppose that the reaction proceeded through an intermediate 3-(2-oxo-cyclohexyl)-4-hydroxy coumarin (I)

giving rise to a hemiketal (II) which can readily get dehydrated resulting in the formation of tetrahydrocoumestan (III) as shown below.

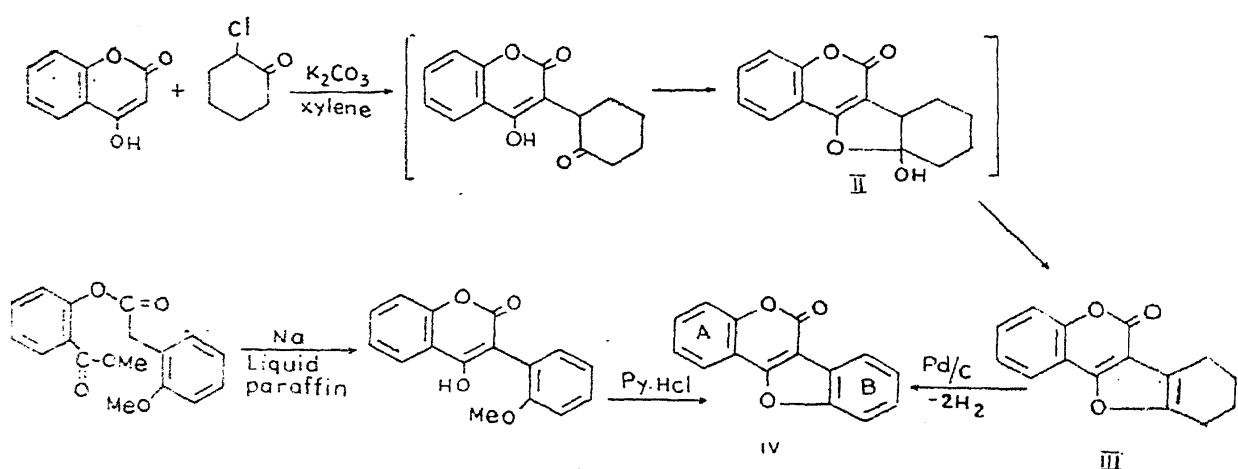


CHART 1

If the structure of the intermediate (III) shown above is correct, the dehydrogenation of this product must result in the formation of coumestan (IV). When the dehydrogenation of intermediate (III) was carried out using palladium charcoal, a compound with m.p.  $201^\circ$  was obtained. In order to confirm this structure, unsubstituted coumestan following the procedure reported in the literature by Govindachari and co-workers<sup>5</sup> was synthesised (lit. m.p.  $181^\circ$ ). The I.R. of both these compounds were superimposable and their U.V. was identical. Though they differed in their melting points, their mixed m.p. was not depressed. The compound obtained by the present procedure seems to be a dimorphic form of the one reported in literature and both of them are otherwise identical.

Further structural proof was obtained by N.M.R. spectra of 7-methyl coumestan synthesized by this method which indicated the presence of a singlet at  $7.5\tau$  integrated for three protons of the C-methyl and for the other 7-aromatic protons in the region  $1.8$  to  $3.0\tau$ .

Adopting this procedure, unsubstituted, 6-methyl, 7-methyl coumestans have been prepared. In the case of 6-chloro coumestan the intermediate obtained on palladium charcoal dehydrogenation gave rise to a compound which did not contain any halogen as revealed by the elemental analysis. This was found to be identical in all respects with the unsubstituted coumestan in m.p. and I.R. It appears that in this case dehalogenation also has taken place during dehydrogenation.

## U.V. and I.R. data of tetrahydrocoumestans and coumestans

Sl. No.	Name of the substituent	Tetrahydro coumestan U.V.	Coumestan U.V.	I. R. Nujol cm <sup>-1</sup>
1.	..	290,320	233,295 310,325	1710
2.	6-Methyl	280,322	228,298 325,335	1710
3.	7-Methyl	292,324	236,293 324,332	1710
4.	6-Chloro	280,310	..	1710

TABLE I  
Coumestans and tetrahydrocoumestans m.p. and analytical data

Sl. No.	Name of the compound	m.p. °C	Solvent	Yield %	Molecular formula	Analysis	
						Found	Required
						C	H
1.	Tetrahydro- coumestan	173	Methanol	45	C <sub>15</sub> H <sub>12</sub> O <sub>3</sub>	74.8	5.1
2.	Coumestan	201	Ethanol	20	C <sub>15</sub> H <sub>8</sub> O <sub>3</sub>	76.1	3.7
3.	7-Methyl-tetra- hydrocoumestan	178	Methanol	52	C <sub>16</sub> H <sub>14</sub> O <sub>3</sub>	74.7	5.5
4.	7-Methyl-coumes- tan	197	Ethanol	25	C <sub>16</sub> H <sub>10</sub> O <sub>3</sub>	72.6	4.0
5.	6-Methyl tetra- hydrocoumestan	161	Methanol	45	C <sub>16</sub> H <sub>14</sub> O <sub>3</sub>	74.7	5.5
6.	6-Methyl coumes- tan	210	Ethanol	20	C <sub>16</sub> H <sub>10</sub> O <sub>3</sub>	72.6	4.0
7.	6-Chloro-tetra- hydrocoumestan	257	Methanol	55	C <sub>15</sub> H <sub>11</sub> O <sub>3</sub> Cl	65.5	4.0
						65.7	4.0

This method, therefore, constitutes a new route for the synthesis of coumestans with different substituents in the 'A' ring. The synthesis is facile and the yields are fairly satisfactory. Attempts to introduce substituents in the 'B' ring at the intermediate stage, in order that this method may be of general applicability, are in progress.

### EXPERIMENTAL

Melting points were taken in a sulphuric acid bath and are uncorrected

#### General Procedure

1. *Tetrahydro coumestan*.—To 4-hydroxy-coumarin (0.01 mole) dissolved in 50 ml of xylene was added anhydrous potassium carbonate (3.2 g). To the solution under reflux, 2-chloro cyclohexanone (0.01 mole) was added in small portions spread over a period of two hours. After the addition was over, the reaction mixture was refluxed for one hour. The xylene was immediately filtered and concentrated affording a solid which on recrystallisation with methanol gave colourless crystals of tetrahydro-coumestan.

2. *Coumestan*.—Tetrahydrocoumestan (0.5 g) was intimately mixed with excess of 10% palladium charcoal and heated gently at its melting point for two hours. The contents were extracted with large quantities of methanol which on evaporation gave a crude product. Recrystallisation with alcohol gave colourless needles of coumestan.

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