

STEREOCHEMISTRY AND SYNTHESIS OF 5-CHLORO-AURONE AND 6-CHLOROFLAVONE

M. K. GURJAR

Department of Chemistry, Nagpur University, Nagpur 440 010

ABSTRACT

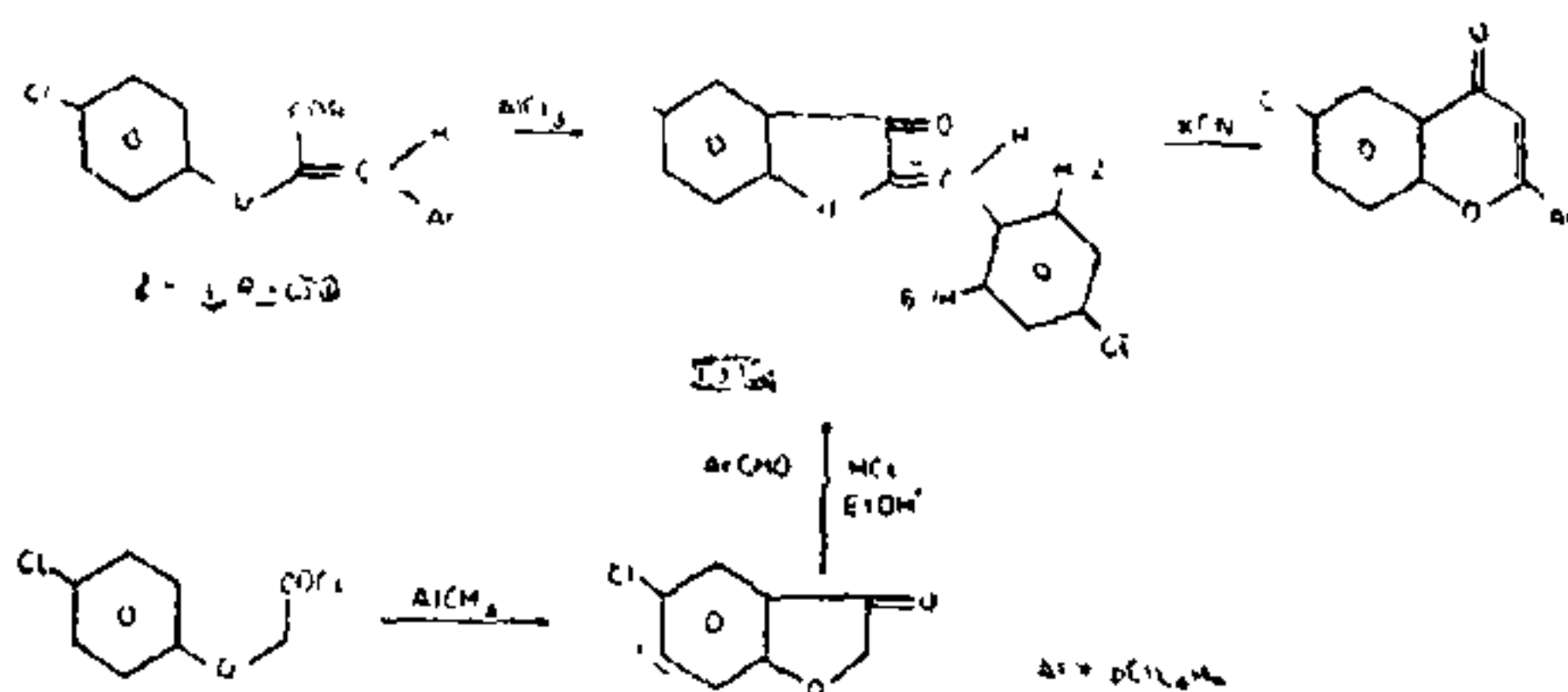
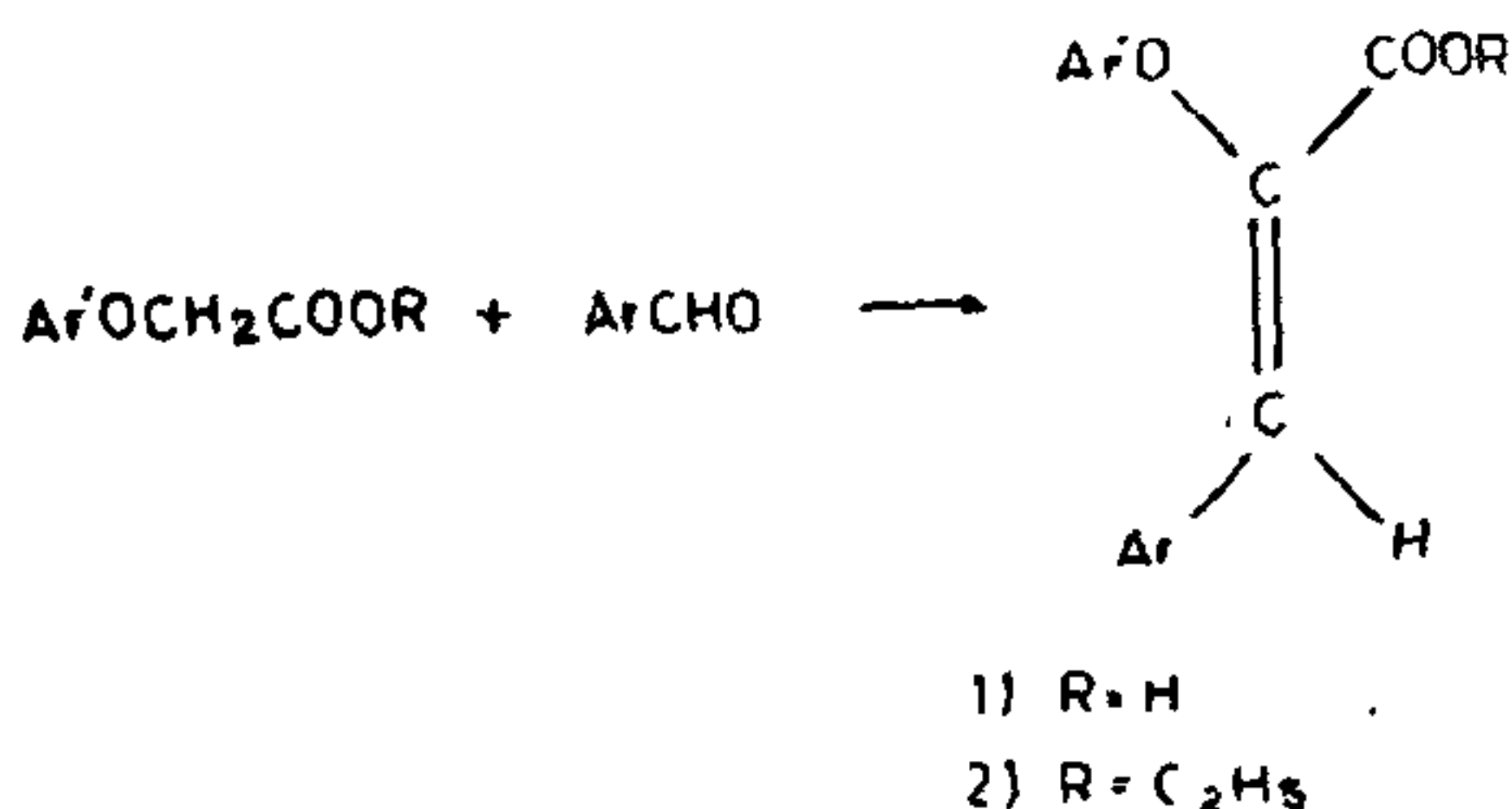
A new synthetic route to 5-chloroaurone and 6-chloroflavone has been reported. The *trans*-stereostructure of 5-chloroaurone is conclusively established, and consequently this becomes the chemical proof of the *Z*-configuration of α -(*p*-chlorophenoxy) cinnamic acids in the Perkin reaction.

MINTON and Stephen¹ have synthesised 5-chloro-2-benzylidenecoumaran-3-one by the condensation of 5-chlorocoumaran-3-one and aromatic aldehydes in ethanolic hydrochloric acid. Two geometrical isomers may result since β -aryl group in the resulting aurone may be either *cis* or *trans* to the carbonyl group.

Philbin *et al.*² have indicated that the *trans* isomer is normally obtained in these synthetic reactions and they prepared the *cis* isomer by uv irradiation of the *trans* material. The *trans* structure was substantiated by the NMR spectral measurements. The differentiation of the two aurones was done on the basis of the chemical shifts of (2', 6') protons. The chemical shift is 8.15 δ for the *cis* isomer and 7.90 δ for the *trans*. The higher δ value of the *cis* isomer is attributed to the deshielding by the carbonyl group. They have further reported that it is not possible to differentiate the two isomers on the basis of the chemical shift of β -hydrogen because of the close values of their chemical shifts.

This note reports method for the synthesis of aurones and the corresponding flavones. It has been reported³ that the potassium *tert.* butoxide catalysed condensation of *p*-chlorophenoxy acetate and *p*-chlorobenzaldehyde leads to the formation of α -(*p*-chlorophenoxy) 4'-chlorocinnamic acid (1) and its ester (2). The acid and ester are obtained as a result of simultaneous operation of 'oxocyclic intermediate' and 'aldol pathway' reaction respectively. The acid chloride of α -(*p*-chlorophenoxy) 4'-chlorocinnamic acid (1) was cyclised in the presence of anhydrous aluminium chloride in carbon disulphide to form 5-chloro-2-(*p*-chlorobenzylidene) coumaran-3-one (3), m.p. 175° (yield 75%). Direct cyclisation of the acid with polyphosphoric acid was tried and it was observed that the same aurone was obtained but the yield was lower (37%).

Using the method of earlier workers¹, 5-chlorocoumaran-3-one was prepared by the cyclisation of *p*-chlorophenoxyacetyl chloride and dry aluminium chloride, this on treatment with *p*-chlorobenzaldehyde in ethanolic hydrochloric acid gave 5-chloro-2-(*p*-chlorobenzylidene) coumaran-3-one, m.p. 175°. The melting point and uv spectra of the aurones obtained by the two methods were identical. Further, the chemical shift of (2', 6') protons is exhibited at 7.92 δ identical with the one reported for *trans* isomer².



The formation of *trans* aurone can only arise if the starting acid has *Z*-configuration with two phenyl-groups *cis*. Flammang *et al.*⁴ have supported the *Z*-configuration for the α -(*p*-chlorophenoxy)-cinnamic acid on the basis of analogy of the Perkin-Oglioloro reaction and the uv spectral studies of the products. Since the same acid was obtained in the aldol-oxocyclic reaction, the *Z*-stereochemistry was assigned.

The data and uv relationship established above mutually prove the *trans* configuration of aurone as well as the stereochemistry of aldol/oxocyclic reaction of *p*-chlorophenoxy acetate and *p*-chlorobenzaldehyde.

The 5-chloro-2-arylidene coumaran-3-one was converted into the corresponding 6-chloroflavone (4) by the treatment of ethanolic potassium cyanide⁵.

Thus this constituted a new synthetic route to aurones and flavones by using oxocyclic intermediate reactions. This method is superior to the one reported earlier as the products are obtained in high yields.

EXPERIMENTAL

1. α -(*p*-Chlorophenoxy) 4'-chlorocinnamyl chloride
 α -(*p*-Chlorophenoxy) 4'-chlorocinnamic acid (15 g) and thionyl chloride (30 ml) were refluxed for 2 hours. Thionyl chloride was removed under suction and the last traces were removed under vacuum. The crude

acid chloride was used without further purification

2. 5-Chloro-2-(*p*-chlorobenzylidene) coumarone (3)

(a) *AlCl₃ cyclisation*: The acid chloride (from previous experiment) was dissolved in dry carbon disulphide (150 ml). Anhydrous aluminium chloride (20 g) was added to the reaction mixture in one lot. After the evolution of hydrogen chloride gas subsides, the reaction mixture was refluxed for one hour. It was cooled and aluminium complex was decomposed with ice-cold water, and 25 ml of hydrochloric acid, and carbon disulphide was distilled off. The crude residue was taken up in benzene and repeatedly washed with sodium carbonate solution and then with water.

The benzene layer was distilled off and the product, 5-chloro (*p*-chlorobenzylidene) coumaran-3-one (10.2 g) was crystallised from ethanol, m.p. 175°; uv: $\lambda_{\text{max}}^{\text{EtOH}}$ 228, 258, 328 nm, log ϵ 4.14, 4.13, 4.29; ir: 1720 cm^{-1} , nmr (CDCl_3): δ 6.80 (1H, s, olefinic proton), 7.26–8.0 (7H, m, aromatic protons), Found: C, 61.74; H, 2.40; Calc. for $\text{C}_{15}\text{H}_8\text{O}_2\text{Cl}_2$: C, 61.84; H, 2.76%.

(b) *PPA cyclisation*: α -(*p*-Chlorophenoxy) 4'-chlorocinnamic acid (5 g) was added to polyphosphoric acid (from 30 g of phosphorus pentoxide and 15 ml of orthophosphoric acid, sp. gr. 1.75) and heated on oil bath at 140° for about 40 minutes, crushed ice (100 g) and water (100 ml) were introduced and extracted with ether. The ethereal phase on solvent removal gave 5-chloro-2-(*p*-chlorobenzylidene) coumaran-3-one, m.p. 175°.

3. 5-Chloro-2-(*p*-chlorobenzylidene) coumaron-3-one (authentic specimen)

p-Chlorophenoxyacetic acid (25 g) and thionyl chloride (40 ml) were refluxed for 2 hours. Thionyl chloride was removed under reduced pressure to give *p*-chlorophenoxyacetyl chloride (25 g).

This was dissolved in carbon disulphide (200 ml) and anhydrous aluminium chloride (25 g) was added in one lot. The reaction mixture was refluxed for one hour. It was cooled and the complex was decomposed with ice-cold water, 40 ml of conc. hydrochloric acid was added and carbon disulphide was distilled off.

The product, 5-chlorocoumaran-3-one, was isolated by steam distillation. The coumaranone was extracted with benzene instead of filtering it. On solvent removal it gave 5-chlorocoumaran-3-one (2 g), m.p. 113°, lit.¹ m.p. 113°.

The 5-chlorocoumaran-3-one (2 g) and *p*-chlorobenzaldehyde (1.2 g) were refluxed in the presence of ethanol (7 ml) on water bath. Hydrochloric acid (1 ml) was introduced in the reaction mixture and further refluxed for 30 minutes. The reaction mixture was cooled and 5-chloro-2-(*p*-chlorobenzylidene) coumaran-3-one (3 g) was filtered, recrystallised from ethanol, m.p. 175°. The mixed m.p. with the above product was undepressed and uv spectra was superimposable.

4. 6, 4'-Dichloroflavone (4)

5-Chloro-2-(*p*-chlorobenzylidene) coumaran-3-one (2 g) was refluxed in the presence of potassium cyanide (0.6 g) and ethanol (20 ml) for about 5 hours on water bath. The reaction mixture was cooled, diluted and acidified with hydrochloric acid. The 6, 4'-dichloroflavone (1.4 g) was crystallised from ethanol, m.p. 215°, uv $\lambda_{\text{max}}^{\text{EtOH}}$ 252, 317 nm, log ϵ 4.25, 3.83; ir: 1670 cm^{-1} .

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1. Minton, T. H. and Stephen, H., *J. Chem. Soc.*, 1922, p. 1598.
2. Brady, B. A., Healy, M. M., Kennedy, J. A., O'Sullivan, W. I. and Philbin, E. M., *Chem. Commun.*, 1970, p. 1434.
3. Patwardhan, B. H., Gurjar, M. K. and Bagavant, G., *Proc Indian Acad. Sci.*, 1975, 82A, 224.
4. Flammang, M., Wermurth, C. G. and Schreiber, J., *Bull. Soc. Chim. Fr.*, 1972, 12, 4619.
5. Wheeler, T. S., Fitzgerald, D. M., O'Sullivan, W. I. and Philbin, E. M., *J. Chem. Soc.*, 1955, p. 860.