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Note

A facile synthesis of 2(*H*)-oxo-3-substituted-1-benzopyrans†

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A simple and efficient synthesis of 2(*H*)-oxo-1-benzopyrans **3** in a single step from salicylaldehyde and malonate derivatives catalysed by anhydrous zinc chloride has been described.

2(*H*)-Oxo-1-benzopyrans have considerable importance due to their potent biological activity[1,2]. Synthesis of benzopyrans starting from salicylaldehyde or chalcone using $AlPO_4$-Al_2O_3[3], $POCl_3$[4], pyridine alkyl/aryl thiocyanates[5] and pyridine acetic acid[6] as catalyst is known. However, the reaction periods are too long and the yields range from 60-80%. We have earlier reported the anhydrous zinc chloride-catalysed condensation of aromatic aldehydes with active methylene compounds[7-9]. In the present communication, we wish to report for the first time, a simple and efficient method of one-pot synthesis of substituted benzopyrans from salicylaldehyde and suitably substituted active methylene compounds catalysed by readily available zinc chloride.

The reaction of salicylaldehyde **1** was studied by different active methylene compounds **2a-h** **(Scheme I)**. In all the cases the substituted benzopyrans were synthesised using the Knoevenagel condensation followed by cyclisation. While the Knoevenagel condensation of **1** with **2a-h** gives a single arylidene intermediate there exists two possible modes of cyclisation in the case of compounds **2d, 2e, 2g** and **2h**. In all the cases only a single product was formed showing a preferential cyclisation involving the nitrile group. The cyclisation should first result in the formation of an imino intermediate **4** which finally underwent hydrolysis to give the benzopyran system. In the case of compound **2g** the reaction was carried out in chloroform to give the corresponding arylidene derivative **5**. However, in neat phase the cyclised products **3f** and **3g** were obtained.

All the products were characterised by elemental analyses and spectral data and the melting points were comparable with those of the reported compounds (cf. **Table I**). The utility of this synthetic method is unlimited which can be extended to other active methylene compounds.

Experimental Section

General. Melting points are uncorrected. ^1H NMR spectra were recorded on a Varian Gemini-200 spectrometer using tetramethyl silane as internal standard, and mass spectra on a VG micromass 7070H instrument. Elemental analyses were carried out on a Perkin-Elmer 240B apparatus. Anhydrous zinc chloride was obtained from Loba Chemicals Limited. Benzimidazole acetonitriles **2g** and **2h**[8] and hippuric acid were prepared as reported in literature.

Preparation of 2(*H*)-oxo-3-substituted-1-benzopyrans 3: General procedure. A mixture of salicylaldehyde (5 mmoles), an active methylene compound (5 mmoles) and anhydrous zinc chloride (0.5 mmoles) was taken with or without chloroform (50 mL) and heated for a specified period (**Table I**). The solvent was stripped off and the residue treated with minimum quantity of water (5 mL). The product benzopyran was filtered, washed with hexane and dried.

Preparation of 3f: General procedure. The intermediate arylidene compound **5** was obtained from an equimolar mixture (5 mmoles) of salicylaldehyde and benzimidazole-acetonitrile **2g** and zinc chloride (0.5 mmoles) in refluxing chloroform. The solvent was stripped off and the residue treated with water (5 mL). The product was filtered, washed with hexane and dried. Thus obtained arylidene compound (5 mmoles) was mixed with zinc chloride (0.5 mmoles) and heated at

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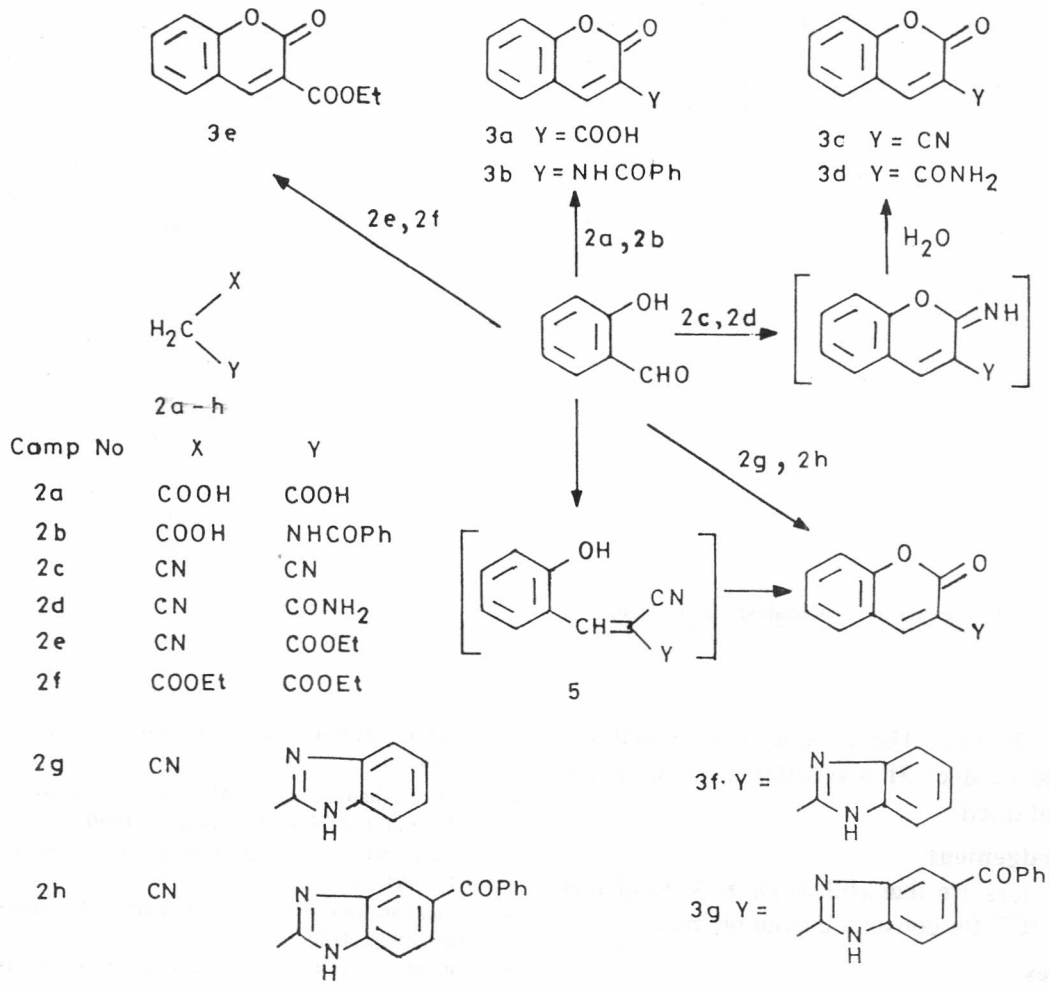

Scheme I

Table I—Characterization data of 2(*H*)-oxo-3-substituted-1-benzopyrans **3** and the arylidene derivative **5**

Compd	m.p. °C	Lit. m.p. °C	Reaction period (min)	Medium	Yield (%)	Mol. formula*	^{1}H NMR (δ, ppm)	MS (M^+)
3a	186–88	187[10]	45	$CHCl_3$	87	$C_{10}H_6O_4$	9.8 (s, 1H, –CH=) 6.8-7.5 (m, 4H, Ar-H), 10.8 (s, 1H, –OH).	190
3b	173	173[11]	45	Neat	82	$C_{16}H_{11}NO_3$	8.8 (s, 1H, –CH=), 7.3-7.9 (m, 9H, Ar-H), 8.9 (s, 1H, –NH, D_2O exchangeable).	265
3c	182–84	182[10]	30	Neat	87	$C_{10}H_5NO_2$	7.4 (s, 1H, –CH=), 7.7-8.3 (m, 4H, ArH).	171
3d	270	268–269[10]	50	Neat	83	$C_{10}H_7NO_3$	7.5 (s, 1H, –CH=), 7.6-8.3 (m, 4H, ArH), 9.3 (broad, 2H, $-NH_2$, D_2O exchangeable).	189

Contd.

Table I—Characterization data of 2(*H*)-oxo-3-substituted-1-benzopyrans **3** and the arylidene derivative **5** —*Contd.*

Compd	m.p. °C	Lit. m.p. °C	Reaction period (min)	Medium	Yield (%)	Mol. formula*	^{1}H NMR (δ, ppm)	MS (M^+)
3e	94	94[10]	45	$CHCl_3$	85	$C_{12}H_{10}O_4$	8.2 (s, 1H, –CH=), 7.2-7.8 (m, 4H, ArH), 1.4 (t, 3H, CH_3), 4.4 (q, 2H, $-CH_2$).	218
3f	243–44	—	30	Neat	92	$C_{16}H_{10}N_2O_2$	9.0 (s, 1H, –CH=), 7.1-7.8 (m, 8H, ArH), 11.2 (br, 1H, –NH).	262
3g	215–17	—	50	Neat	90	$C_{23}H_{14}N_2O_3$	8.2 (s, 1H, –CH=), 7.5-8.1 (m, 12H, ArH), 11.5 (br, 1H, –NH, D_2O exchangeable).	366
5	263–64	—	30	$CHCl_3$	84	$C_{16}H_{11}N_3O$	8.9 (s, 1H, –CH=), 7.1-7.9 (m, 9H, Ar-H), 9.7 (s, 1H, –OH).	261

*The compounds gave satisfactory analyses for C, H and N.

100°C for 30 min. The residue was treated with water. The product **3f** was filtered, washed with hexane and dried.

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