Asian Journal of Chemistry Vol. 9, No. 1 (1997), 66–69

A Study on the Synthesis of New Phthalides Derived from 2-(3,4-Dimethylbenzoyl)benzoic acid

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2-(3,4-Dimethylbenzoyl) benzoic acid, a γ-oxoacid has been condensed with various phenols to synthesise some new phthalides.

INTRODUCTION

The chemistry of γ-oxoacids and their derivatives has received wide attention due to their interesting ring-chain tautomeric behaviour. It has been observed that generally γ-oxoacids exist as lactol or as an equilibrium mixture of ketoacid and lactol tautomeric forms[1–3]. Many chemical reactions of these acids have been explained on the basis of their cyclisation to lactols[4–9]. Recently, we have reported that a γ-oxoacid, β-(4-bromobenzoyl) acrylic acid, undergoes condensation with phenols through its lactol tautomeric form to afford butenolactones.[10] The results of this investigation motivated us to condense a structrually different γ-oxoacid, 2-(3,4-dimethylbenzoyl)benzoic acid with various phenols such as phenol, resorcinol, catechol, quinol, phloroglucinol and pyrogallol.

RESULTS AND DISCUSSION

2-(3,4-Dimethylbenzoyl) benzoic acid has been found spectroscopically to exist as a mixture of its keto-acid (1) and lactol (2) forms. It gave a cyclic acetyl derivative (3) on refluxing with acetic anhydride in the presence of fused sodium acetate. IR spectrum (in KBr, ν_{max} in cm^{-1}) of acid showed absorption bands at 1680, 1650 and 1770 (feeble) indicating the presence of carboxyl carbonyl, diaryl, ketonic carbonyl and lactonic carbonyl groups respectively. Peaks at 2620 and 3460 were assigned to carboxylic and lactol OH groups respectively. The PMR spectrum (chemical shifts in δ scale) of **1** revealed that aromatic protons appeared as a complex multiplet in the region between 7.2 and 8. Two singlets noticed at 2.1 and 2.2 are assignable to protons of two methyl groups. A singlet of low intensity at 2.5 could be ascribed to the lactol hydroxy proton. The acetyl derivative (**3**) of **1** showed in its IR spectrum has sharp peaks at 1790 and 1770 which are due to lactonic carbonyl and acetoxyl carbonyl stretching vibrations respectively. PMR spectrum of **3** did not exhibit any signal at 2.5 (present in the spectrum of **1**), instead it displayed a new signal at 2.4 which was attributed to the protons of acetoxyl group. On the basis of these spectral studies it was concluded that the acetyl derivative (**3**) possesses a cylic lactonic structure and its formation takes place through the lactol form (2) of the γ-oxoacid (1) as shows in Scheme 1.

2-(3,4-Dimethylbenzoyl)benzoic acid (**1**) reacted with phenols (**4**) in presence of conc. sulphuric acid to give a new series of substituted phthalides (**5–10**). These compounds may be regarded as unsymmetrical phthaleins because their central triphenylmethane carbon is attached to two different phenyl rings. Like butenolactones[10], the synthesis of phthalides (**5–10**) also follows a condensation reaction through the lactol form (2) of the acid **1** and with excess of phenols (**4**) the whole of the acid taken reacts as lactol (Scheme 1). The structures of the synthesised phthalides were derived on the basis of elemental analysis, bromination, acetylation, KOH degradation and IR spectral data. Bromination and acetylation of the phthalide **6** gave dibromo (**12**) and diacetyl (**11**) derivatives. KOH fusion of **6** degraded it to **1** and resorcinol.

The IR spectra of the phthalides (**5–10** and **12**) displayed a broad and strong absorption band in the region 3442 to 3405 cm^{-1} due to OH stretching vibrations. The diacetyl derivative (**11**) exhibited a band at 1772 cm^{-1} (ν(C=O) of phenolic acetate). All the phthalides (**5–12**) showed a sharp and strong band at 1772 to 1730 cm^{-1} which is characteristic of lactonic carbonyl group. Presence of this band is a significant evidence in favour of the proposed lactonic structures. Two sharp bands which appeared near 758–734 and 720–690 cm^{-1} in the IR spectra of **5** to **12** are characteristic of *o*-disubstituted phthalein ring.[11]

EXPERIMENTAL

All the melting points are uncorrected and the purity of the products was routinely checked by TLC. PMR spectra of the γ-oxoacid and its acetyl derivatives were recorded in DMSO-d_6 and $CDCl_3$ respectively on a Bruker WH-90 spectrometer and chemical shifts (δ in ppm) are reported relative to TMS as internal standard. IR spectra in KBr were taken on a Perkin-Elmer-137 spectrophotometer (ν_{max} in cm^{-1}).

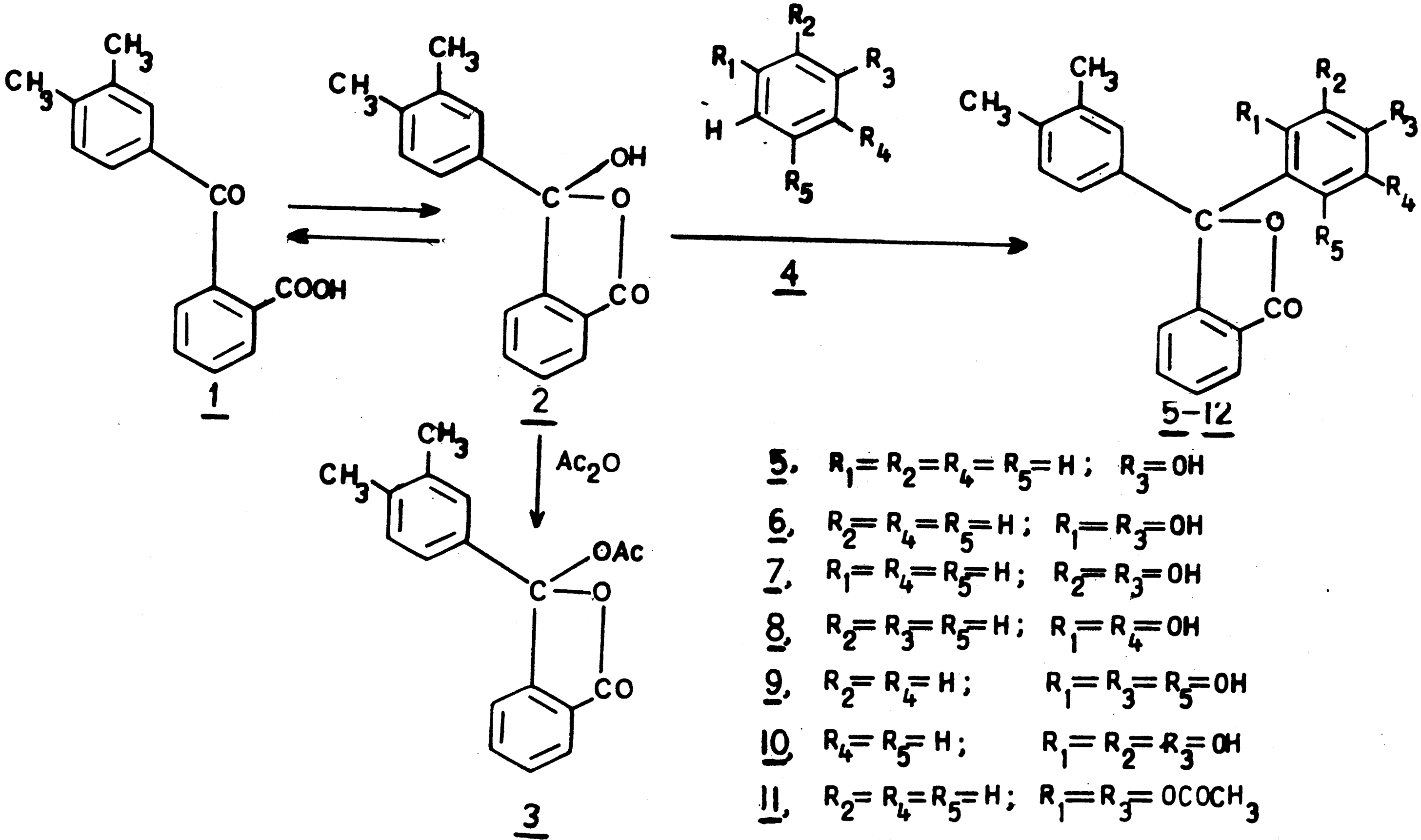
3-Acetoxy-3-(3,4-dimethylphenyl) phthalide (3)

The acid **1** (1 g) was refluxed with acetic anhydride (15 mL) and fused sodium acetate (1 g) for about 4 h. The contents were poured into ice-cold water, stirred well and the residue was filtered. It was washed with water and recrystallised from acetone into a white crystlline compound (0.5 g), m.p. 108–109°C (Found: C, 72.94; H, 5.45. $C_{18}H_{16}O_4$ requires: C, 72.9; H, 5.4%).

Phthalides (5–10)

The preparation, purification of the phthalides (**5–10**), acetylation of phthalide (**6**) and bromination of phthalide (**6**) were carried out by the procedure reported for butenolactones in our earlier communication[10]. Physical data of the synthesised products are presented in Table 1.

SCHEME-1



5, $R_1 = R_2 = R_4 = R_5 = H$; $R_3 = OH$

6, $R_2 = R_4 = R_5 = H$; $R_1 = R_3 = OH$

7, $R_1 = R_4 = R_5 = H$; $R_2 = R_3 = OH$

8, $R_2 = R_3 = R_5 = H$; $R_1 = R_4 = OH$

9, $R_2 = R_4 = H$; $R_1 = R_3 = R_5 = OH$

10, $R_4 = R_5 = H$; $R_1 = R_2 = R_3 = OH$

11, $R_2 = R_4 = R_5 = H$; $R_1 = R_3 = OCOCH_3$

12, $R_5 = H$; $R_2 = R_4 = Br$; $R_1 = R_3 = OH$

TABLE–1
1 PHYSICAL DATA OF PHTHALIDES (**5–10**)

Phthalide	Colour	Yield %	m.p. (°C)	Mol. formula*	ν_{max} (cm^{-1})
5	Pinkish white	53	99–100	$C_{22}H_{18}O_4$	3416, 1730, 755, 720
6	White	78	137–38	$C_{22}H_{18}O_4$	3423, 1741, 757, 719
7	Brown	61	158–60	$C_{22}H_{18}O_4$	3431, 1740, 755, 719
8	Greyish white	61	136–38	$C_{22}H_{18}O_4$	3405, 1741, 754, 694
9	Light brownish red	60	150–52	$C_{22}H_{18}O_5$	3415, 1733, 745, 715
10	Light brown	56	158–60	$C_{22}H_{18}O_5$	3442, 1748, 734, 690
11	Light yellow	70	109–10	$C_{26}H_{22}O_6$	—, 1772, 758, 694
12	Brownish red	32	164–65	$C_{22}H_{16}O_4Br_2$	3424, 1771, 748, 718

*All the compounds gave satisfactory elemental analysis.

Caustic potash fusion of 6

The phthalide **6** (1 g) was mixed with a paste of KOH pellets (10 g) and the mixture was strongly heated at 250°C for about 3 h. The contents were cooled, dissolved in water and filtered. The filtrate was just neutralised with dil. HCl, when a white residue (A) settled out, which was filtered and washed with water. The filtrate was acidified by adding an excess of HCl and allowed to stand for few hours to deposit a white residue (B); this was also filtered and washed thoroughly with water. The filtrate was shaken with ether; and on evaporation of the ether a brownish-red residue (C) was left behind. Residues A, B and C were identified as unreacted phthalide **6**, the acid **1** and resorcinol respectively by direct comparison (m.m.p., co-TLC and co-IR) with their authentic samples.

ACKNOWLEDGEMENTS

The authors extend their respectful thanks to Prof. P.C. Gupta for helpful suggestions and interest in the work; the director, CDRI, Lucknow and the Head, RSIC, IIT Madras for providing analytical and spectral data.

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(*Received*: 9 May 1996; *Accepted*: 29 August 1996) AJC-1155