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A Convenient and Simple Method for the Synthesis of Condensed γ-Lactams and Substituted Xanthones from Cyclic-1,3-diketones

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Dedicated to Professor K. K. Balasubramanian on the occasion of his 60th birthday

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Abstract—A systematic study of alkylation of cyclic-1,3-diones with 2-bromo-6-methoxybenzofuran-3-one was undertaken. Upon condensation in acetic acid with *p*-substituted aniline the *O*-alkylated product **3a** gave condensed γ-lactam heterocycle **4**. In contrast, the condensation of analogous *O*-alkylated derivatives **3b** and **3c** with *p*-substituted anilines furnished the substituted xanthone derivatives **6** and **7a**. The probable mechanism of formation of **4**, **6** and **7a** was discussed. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

In the literature[1–3] a considerable number of reports indicate the exclusive formation of C-alkylation products during the reaction of α-bromoketones with cyclic-1,3-diones. 1,4-dicarbonyl compounds are most reactive and versatile substrates for the general synthesis of pyrroles (Paal–Knorr Pyrrole Synthesis), which can be derived from α-bromoketones by C-alkylation of cyclic-1,3-diones. The cyclization condensation of 1,4-dicarbonyl systems with ammonia or primary amines has been well investigated and synthetically exploited in the field of pyrroles[4–6] (Scheme 1), whereas reports on analogous studies involving *O*-alkylation are lacking. The reactivity of indan-1,3-dione with phenacyl bromide has been investigated by Ramadas and Padmanabhan[7–10] with a view to synthesizing condensed heterocycles using triones as building blocks.

However, there are no reports on the use of heterocyclic α-bromoketo ethers as the alkylating agents. In this publication we wish to report a novel transformation encountered in an attempted condensation of the *O*-alkylated product **3** derived from 2-bromo-6-methoxy-benzofuran-3-one.

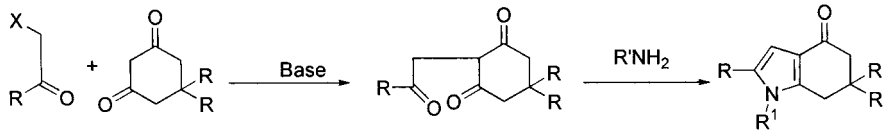
Results and Discussion

Alkylation of cyclic-1,3-diones (1)

The 2-bromo-6-methoxy-*2H*-benzo[*b*]furan-3-one (**2**), required for the study was prepared from 6-methoxybenzo[*b*]furan-3-one following the literature[11] procedure and characterized thoroughly. Alkylation of **1**with **2** in presence of K_2CO_3 in dry chloroform at room temperature gave a dark brown solid identified as the *O*-alkylated compound as the major product. The NMR spectrum of the product displayed a singlet at δ 5.75 characteristic of *O*-alkylated product **3**. This was further confirmed by the presence of a doublet in the ^{13}C NMR spectrum at δ 105. Chromatographic purification afforded **3** in 60–75% yield. Varying the solvent, the temperature, or the base[12–14] did not alter reaction course. This was found to be a genuine, unique *O*-alkylation, (Scheme 2).

Condensation of *O*-alkylated product (3a)

The condensation of *O*-alkylated product with *p*-substituted anilines gave very interesting results both from the mechanistic and synthetic point of view. The reaction was found to



Scheme 1.

Keywords: cyclic-1,3-diketones; *O*-alkylated derivatives; γ-lactams; xanthones.

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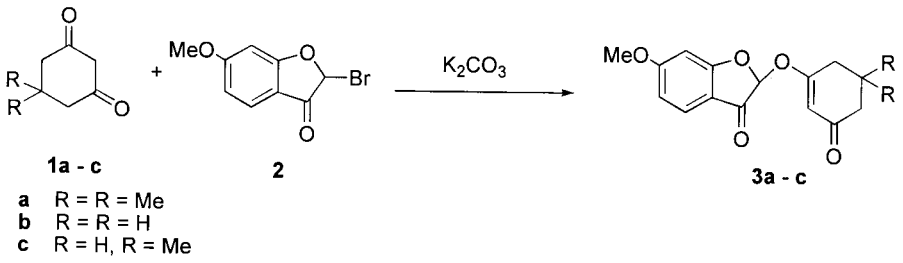
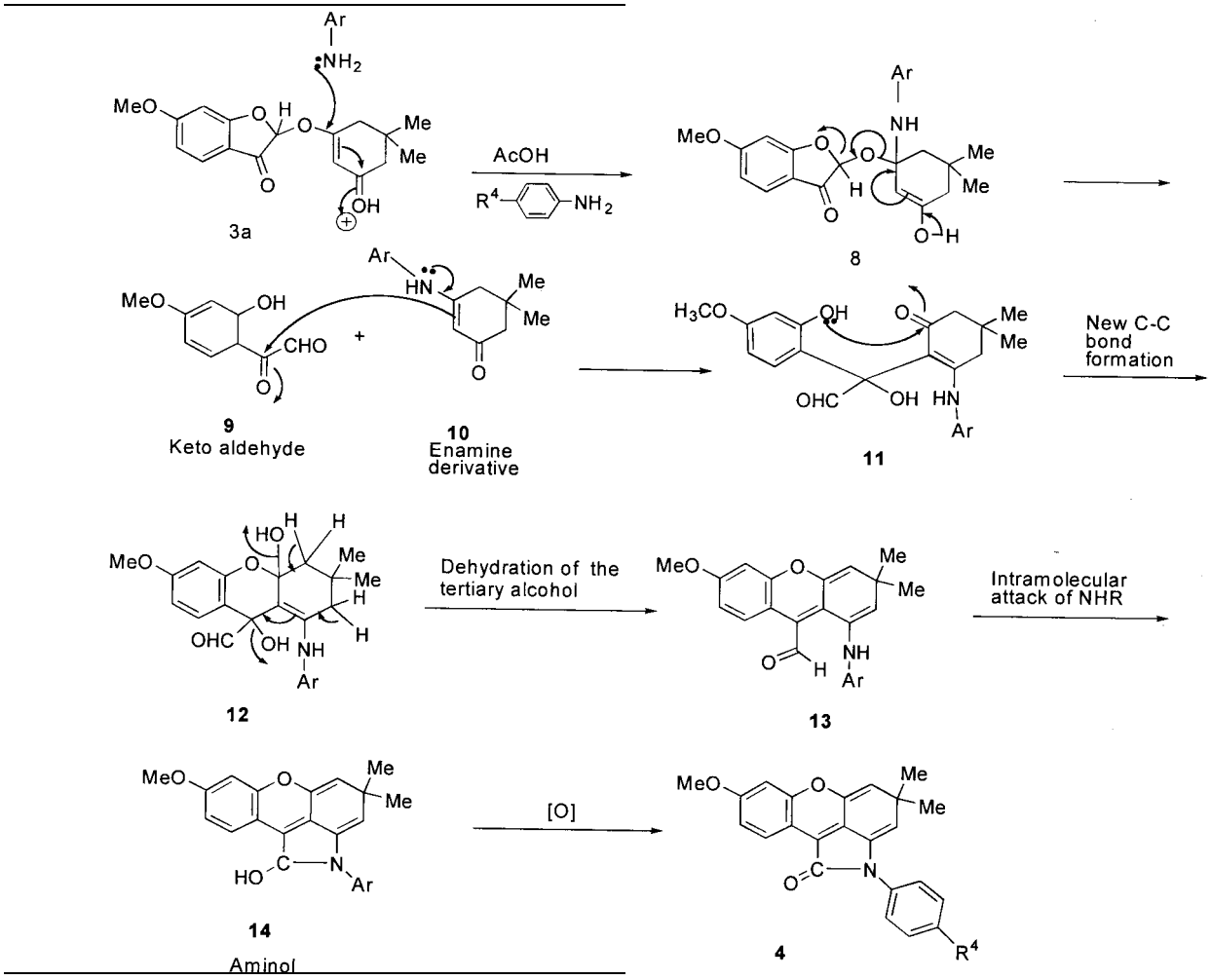


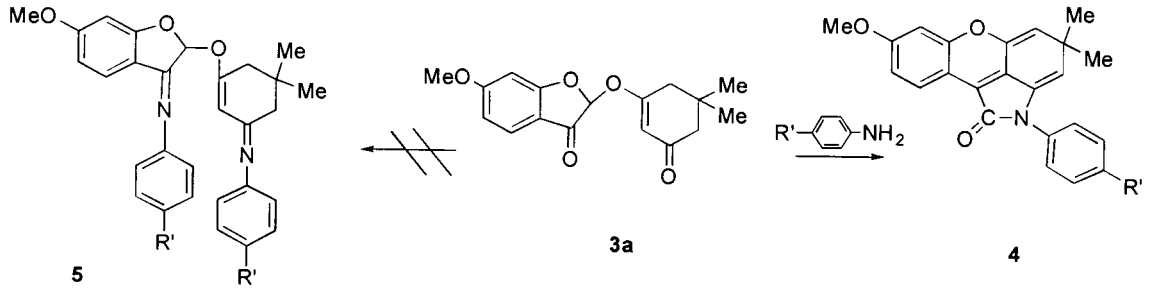
Scheme 2.

be dependent upon acetic acid and *p*-substituted anilines. Thus when **3a** was condensed with *p*-anisidine in glacial acetic acid at reflux temperature, instead of the expected diamine derivative **5** (Scheme 3), the product was found to be different, for the IR spectrum showed a carbonyl functionality at 1720 cm^{-1}. The product obtained in 50% yield after passing the crude mixture through a column of neutral alumina showed a singlet at δ 5.1 (1H) apart from the aromatic signals in its NMR spectrum. Based on spectral data and X-ray diffraction studies[15] the product was identified as γ-lactam heterocycle **4** with cross conjugation. The transformation was found to be a general one by extending the same product to other *p*-substituted anilines **4b–d** (Table 1).

The presence of a gem dimethyl group in the pyran ring alters the course of reaction as evidenced in the case of *O*-alkylated derivative **3b** wherein **6a** was isolated in 30% yield. Thus when **3b** was condensed with *p*-anisidine in glacial acetic acid at its reflux temperature, instead of the expected γ-lactam derivative, the product was found to be different, for the IR spectrum showed carbonyl functionality at 1630 cm^{-1}. The product obtained in 30% yield after passing the crude mixture through a column of neutral alumina showed a broad singlet at δ 11 apart from the aromatic signals in its NMR spectrum. Based on spectral data and X-ray diffraction studies,[16] the product was identified as xanthone derivative **6a**. Conversion of other *O*-alkylated derivatives **3b–c** to the corresponding xanthones **6b–d** and **7a** upon condensation in acetic acid revealed this transformation to be a general one (Scheme 4) (Table 1).

Probable mechanistic pathway

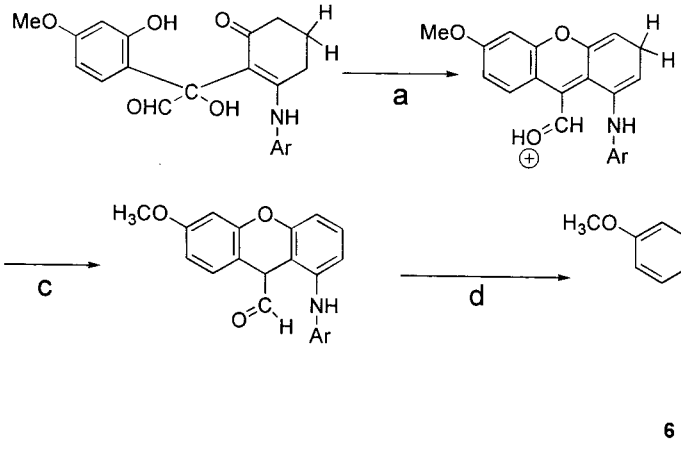




Scheme 3.

Table 1.

Entry	R^1	mp (°C)	Yield of **4** (%)	mp (°C)	Yield of **6** (%)
a	OMe	206–208	50	132–134	30
b	Me	172–174	48	116–118	28
c	H	182–184	45	140–142	25
d	Cl	202–204	40	158–160	20

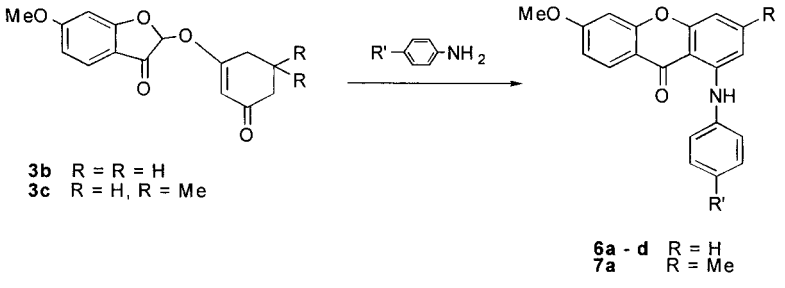


The structure assigned to **4** is supported by X-ray data.[15] The structure assigned to **6** is supported by X-ray data.[16]

Mechanistic investigations

The reaction involves initially the protonation of conjugated carbonyl followed by Michael-type of addition of the *p*-substituted aniline resulting in the formation of aminoenol **8**, which could lead to the ring opening of the five-membered furanone furnishing fission products namely ketoaldehydes **9** and enamine derivative **10**. The enamine could attack the ketoaldehyde affording **11** which by intramolecular nucleophilic attack on the carbonyl function could lead to the species **12**. This on dehydration may furnish the more stable cross-conjugated olefin **13**. The formation of γ-lactam is assumed by intramolecular nucleophilic addition of -NH_2 to the aldehydic function followed by aerial oxidation of the resulting aminol during work up. It is speculated that loss of carbon atom after the formation of benzopyran ring either by decarbonylation or decarboxylation with concomitant aerial oxidation at position **9** could lead to the xanthone skeleton. The exact mechanistic implications of the last step d are not very clear. This mechanism gains some support from observations carried out by us.

The *O*-alkylated product **3** is recovered unchanged, even after refluxing in glacial acetic acid without the addition of a primary amine. This suggests that ring opening of furanone occurs perhaps only in presence of *p*-substituted aniline in acid medium. The role of acetic acid (as a medium and protonating agent) appears to be unique, as this condensation failed to occur between the *O*-alkylated product and *p*-substituted aniline either in refluxing toluene or in



Scheme 4.

refluxing toluene containing catalytic amount of PTS[17] or other protonic acids.

The atmospheric oxidation of aminol **14** to the γ-lactam could be visualized during the work up, since the condensation of the *O*-alkylated product with aromatic amines gave the same fused heterocycles **4** and **6** even under a dry nitrogen atmosphere.

Our serious attempts either to isolate or synthesize the ketoaldehyde **9**, one of the reactive intermediates proposed in the above mechanism, have met with little success. Treatment of 2-bromo-6-methoxycoumaran-3-one by sodium carbonate in dioxane gave no such ketoaldehydes, on the other hand, the attempted reaction gave some decomposed products.

Thus, the condensation of *O*-alkylated product is found to be highly dependent on acetic acid and *p*-substituted aniline. The preparation of condensed γ-lactam and xanthone derivatives from cyclic-1,3-diones is novel. It constitutes entirely a new method for the synthesis of xanthones.[18–30]

Experimental

All experiments involving air or moisture sensitive reagents were performed in an atmosphere of nitrogen. The glassware was dried under vacuum and flushed with nitrogen. Chloroform was freshly distilled from calcium chloride. Cyclic 1,3 diones, *p*-substituted anilines were obtained from Aldrich Chemcal Co. Column chromatography was performed on ACME neutral aluminum oxide activated, Brockman grade II-III (70–230 mesh) and analytical TLC on silica gel 60F-254 plates. Melting points are uncorrected. Nuclear magnetic resonance spectra were recorded in $CDCl_3$, using either a Varian EM-390 or Bruker-400 spectrometer. Chemical shifts are given in parts per million downfield from tetramethylsilane. Infrared (IR) spectra were recorded on a Perkin–Elmer Spectrum 1310 FT-IR infrared spectrometer as KBr pellets. High-resolution mass spectra were recorded using Varian MATCH-7 and Finnigan MAT 8230 mass spectrometers. Elemental analyses were performed by Department of Chemistry, IIT, Chennai, India and analytical, spectroscopic division, VSSC, Trivandrum, India.

General procedure for synthesis of *O*-alkylated products (3a–c)

To a 250 ml round-bottom flask, fitted with a stir bar and Nitrogen inlet was added $CHCl_3$ (150 ml) and cyclic-1,3-dione **1a–c** (50 mmol). Freshly fused potassium carbonate (14 g, 100 mmol) was added portionwise to the flask over a period of 10 min and the reaction was stirred for 10 min at 30°C. A solution of 2-bromo-6-methoxybenzofuran-3-one (**2**, 11.25 g, 46 mmol) in dry chloroform (50 ml) was added dropwise over a period of 30 min. The reaction was stirred for 24 h at 30°C. The reaction mixture was filtered and the solid was washed thoroughly with $CHCl_3$. The $CHCl_3$ layer was dried over Na_2SO_4. The removal of chloroform in vacuo afforded a yellow orange gummy solid. Repeated crystallization from hexane-benzene (9:1) mixture gave analytically pure sample of *O*-alkylated products **3a–c**.

O-Alkylated products

2-[5,5-Dimethyl-3-oxo-1-cyclohexen-1-yl)oxy]-6-methoxy-3(2*H*)-benzofuranone (3a). Using the above procedure, 5,5-dimethyl-1,3-cyclohexanedione (**1a**) (7 g, 50 mmol) in chloroform (150 ml) and 2-bromo-6-methoxybenzofuran-3-one (**2**) (11.25 g, 46 mmol) in chloroform (50 ml) were reacted in presence of K_2CO_3 (14 g, 100 mmol) for 24 h. The crude mixture was purified by column chromatography (9:1 hexane/benzene) to afford **3a** (11.32 g, 75%) as a light yellow crystalline solid, mp 118–120°. IR (KBr): 1720, 1640, 1620, 1480, 1440,1360 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.6–7.6 (m, 3H), 5.82 (s, 1H), 5.75 (s, 1H), 3.8 (s, 3H), 2.45 (d, H_b, J=4 Hz), 2.35 (d, H_a, J=4 Hz), 2.28 (s, 2H), 1.2 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 199.1, 190.0, 173.9, 169.3, 126.2, 112.6, 111.7, 105.0, 96.6, 96.1, 56.1, 50.6, 41.8, 32.4, 28.4, 27.9; MS (EI): *m/z* 302 ($M^{+\cdot}$, 18), 287 (7), 243 (11), 241 (7.5), 163 (24), 135 (15); Anal.: Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 5.96. Found C, 67.72; H, 6.05.

6-Methoxy-2-[(3-oxo-1-cyclohexen-1-yl)oxy]-3(2*H*)-benzofuranone (3b). Using the above procedure 1,3-cyclohexanedione (**1b**) (5.6 g, 50 mmol) in chloroform (150 ml) and 2-bromo-6-methoxybenzofuran-3-one (**2**) (11.25 g, 46 mmol) in chloroform (50 ml) were reacted in presence of K_2CO_3 (14 g, 100 mmol) for 24 h. The crude mixture was purified by column chromatography (9:1 hexane/benzene) to afford **3b** (9.5 g, 70%) as a light yellow crystalline solid, mp 158–160°. IR (KBr): 1720, 1650, 1620, 1450, 1250 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.5–7.5 (m, 3H), 5.75 (s, 1H), 5.6 (s, 1H), 3.8 (s, 3H), 1.9–2.5 (m, 6H); MS (EI) *m/z* 274 (M^+, 8), 242 (16), 192 (2.5), 163 (66); Anal. Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.1. Found: C, 65.27; H, 4.92.

6-Methoxy-2-[(5-methyl-3-oxo-1-cyclohexen-1-yl)oxy]-3-(2*H*)-benzofuranone (3c). Using the above procedure, 5-methyl-1,3-cyclohexanedione (**1c**) (6.3 g, 50 mmol) in chloroform (150 ml) and 2-bromo-6-methoxybenzofuran-3-one (**2**) (11.25 g, 46 mmol) in chloroform (50 ml) were reacted in presence of K_2CO_3 (14 g, 100 mmol) for 24 h. The crude mixture was purified by column chromatography (9:1 hexane/benzene) to afford **3c** (8.46 g, 60%) as a light yellow crystalline solid, mp 152–154°. IR (KBr): 1720, 1650, 1620, 1400, 1250 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.5–7.6 (m, 3H), 5.8 (s, 1H), 5.7 (s, 1H), 3.9 (s, 3H), 2.1–2.7 (m, 5H), 1.2 (d, 3H); MS (EI) *m/z* 288 (M^+, 100), 273 (25), 255 (8), 219 (7), 190 (22), 163 (100); Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.58. Found: C, 66.41; H, 5.35.

Condensed γ-lactams

General procedure for synthesis of γ-lactams (4a–d) and xanthones (6a–d). To a 100 ml round bottom flask, fitted with a stirrer bar and nitrogen inlet was added glacial acetic acid (50 ml) and *O*-alkylated product **3a–c** (50 mmol). *p*-Substituted anilines (52 mmol) were added portionwise to the flask over a period of 10 min and the reaction was refluxed for 18 h with stirring. The reaction was quenched with ice cold water. The resulting solid was filtered, washed with water (2×50 ml^2) and dried under vacuum. The crude

product was chromatographed over a column of neutral alumina (100 g) (9:1 hexane/EtOAc) to obtain pure γ-lactam (**4a–d**) and xanthone (**6a–d**).

2,4-Dihydro-8-methoxy-2-(4-methoxyphenyl)-4,4-dimethyl-1*H*-[1]-benzopyrano[4,3,2-*cd*]-indol-1-one (4a). Using the above procedure, *O*-alkylated **3a** (1.51 g, 50 mmol) in acetic acid (50 ml) and *p*-anisidine (0.65 g, 52 mmol) were refluxed for 24 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **4a** (0.97 g, 50%) as a light yellow solid, mp 206–208°. IR (KBr): 1700, 1590, 1450, 1250 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.5–7.8 (m, 7H), 5.4 (s, 1H), 5.1 (s, 1H), 3.8 (s, 3H), 3.7 (s, 3H) 1.3 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 166.8, 160.6, 158.3, 155.3, 142.9, 132.9, 130.1, 127.5, 127.3, 124.7, 119.6, 114.4, 113.0, 111.8, 110.7, 108.3, 102.6, 55.4, 55.3, 41.6, 30.7; MS (EI) *m/z* 387 ($M^{+\cdot}$, 21), 372 (100), 359 (2), 329 (8), 301 (6), 286 (6), 258 (7), 238 (4). Anal. Calcd for $C_{24}H_{21}NO_4$: C, 74.41; H, 5.42. Found: C, 74.21; H, 5.36.

2,4-Dihydro-8-methoxy-4,4-dimethyl-2-(4-methylphenyl)-1*H*-[1]benzopyrano[4,3,2-*cd*]-indol-1-one (4b). Using the above procedure, *O*-alkylated **3a** (1.51 g, 50 mmol) in acetic acid (50 ml) and *p*-toluidine (0.55 g, 52 mmol) were refluxed for 24 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **4b** (0.89 g, 48%) as a light yellow solid, mp 172–174°. IR (KBr): 1700, 1620, 1450, 1240 cm^{-1}; ^1H NMR: δ 6.54–7.80 (m, 7H), 5.56 (s, 1H), 5.17 (s, 1H), 3.79 (s, 3H), 2.39 (s, 3H), 1.29 (s, 6H); ^{13}C NMR ($CDCl_3$): δ 166.7, 160.7, 155.3, 143.0, 136.7, 132.6, 132.3, 124.8, 119.8, 113.1, 111.8, 110.7, 108.4, 102.7, 55.4, 30.1, 21.1; MS (EI) *m/z* 371 (M^+, 24), 356 (100), 327 (4), 313 (10), 284 (4); Anal. Calcd for $C_{24}H_{21}NO_3$, C, 77.62; H, 5.66. Found: C, 77.24; H, 5.35.

2,4-Dihydro-8-methoxy-4,4-dimethyl-2-phenyl-1*H*-[1]-benzopyrano[4,3,2-*cd*]-indol-1-one (4c). Using the above procedure, *O*-alkylated **3a** (1.51 g, 50 mmol) in acetic acid (50 ml) and freshly distilled aniline (0.48 g, 52 mmol) were refluxed for 24 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **4c** (0.78 g, 45%) as a light yellow solid, mp 182–184°. IR (KBr): 1700, 1620, 1240 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.5–7.8 (m, 8H), 5.6 (s, 1H), 5.2 (s, 1H), 3.8 (s, 3H), 1.3 (s, 6H); ^{13}C NMR ($CDCl_3$): δ 166.5, 160.7, 155.2, 142.9, 135.0, 132.4, 130.3, 129.1, 126.8, 125.8, 124.7, 119.0, 113.0, 111.9, 110.6, 55.4, 41.7, 30.1; MS (EI) *m/z* 357 (M^+, 22), 342 (100), 299 (6), 270 (4); Anal. Calcd for $C_{23}H_{19}NO_3$; C, 77.31; H, 5.32. Found: C, 77.18; H, 5.08.

2-(4-Chlorophenyl)-2,4-dihydro-8-methoxy-4,4-dimethyl-1*H*-[1]benzopyrano[4,3,2-*cd*]-indol-1-one (4d). Using the above procedure, *O*-alkylated **3a** (1.51 g, 50 mmol) in acetic acid (50 ml) and *p*-chloroaniline (0.66 g, 52 mmol) were refluxed for 24 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **4d** (0.78 g, 40%) as a lemon-yellow solid, mp 202–204°. IR (KBr): 1700, 1600, 1420, 1240 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.6–7.8 (m, 7H), 5.6 (s, 1H), 5.2 (s, 1H), 3.8 (s, 3H), 1.3 (s, 6H); ^{13}C NMR ($CDCl_3$): 166.4, 160.7, 155.2, 142.9, 133.5, 132.3, 132.1, 130.5,129.3, 127.0, 124.7, 120.0, 113.0, 112.1, 110.4, 108.4, 102.7, 55.4, 41.7, 30.1; MS (EI) *m/z* 391 (M^+, 12), 376 (100), 333 (14), 270 (8), 240 (4); Anal. Calcd for $C_{23}H_{18}ClNO_3$: C, 70.58; H, 4.60. Found: C, 70.12; H, 4.35.

Xanthone derivatives

6-Methoxy-1[(4-methoxyphenyl)amino]-9*H*-xanthene-9-one (6a). Using the above procedure, *O*-alkylated **3b** (1.37 g, 50 mmol) in acetic acid (50 ml) and *p*-anisidine (0.65 g, 52 mmol) were refluxed for 18 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **6a** (0.52 g, 30%) as a light yellow solid, mp 132–134°. IR (KBr): 3450–3300, 1630, 1600, 1450, 1260 cm^{-1}; ^1H NMR: δ 11.08 (s, 1H), 6.59–8.17 (m, 6H), 3.91 (s, 3H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$): 179.4, 164.7, 158.0, 157.2, 156.9,150.3, 135.0, 133.1, 115.8, 114.7, 112.7, 107.0, 105.5, 103.5, 99.7, 55.7, 55.4; MS (EI): *m/z* 347 (M^+, 97.5), 332 (100), 319 (2), 317 (6), 316 (5), 289 (21), 288 (22), 261 (5), 232 (2); Anal. Calcd for $C_{21}H_{17}NO_4$: C, 72.62, H, 4.89. Found: C, 72.41; H, 4.72.

6-Methoxy-1-[(4-methylphenyl)amino]-9*H*-xanthene-9-one (6b). Using the above procedure, *O*-alkylated **3b** (1.37 g, 50 mmol) in acetic acid (50 ml) and *p*-toluidine (0.55 g, 52 mmol) were refluxed for 18 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **6b** (0.46 g, 28%) as a light yellow solid, mp 116–118°. IR (KBr): 1630, 1600, 1580, 1440, 1270, 1160 cm^{-1}; ^1H NMR: δ 10.4 (s, 1H), 6.61–8.18 (m, 10H), 3.93 (s, 3H), 2.36 (s, 3H); MS (EI) *m/z* 331 (M^+, 100), 314 (3), 288 (1), 279 (5); Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.13; H, 5.13. Found: C, 75.89; H, 5.0.

6-Methoxy-1-[(phenyl)amino]-9*H*-xanthen-9-one (6c). Using the above procedure, *O*-alkylated **3b** (1.37 g, 50 mmol) in acetic acid (50 ml) and freshly distilled aniline (0.48 g, 52 mmol) were refluxed for 18 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **6c** (0.40 g, 25%) as a pale yellow solid, mp 140–142°. IR (KBr): 1640, 1600, 1400, 1270 cm^{-1}; ^1H NMR: δ 10.8 (s, 1H), 6.32–7.92 (m, 10H), 3.85 (s, 3H), MS (EI) *m/z* 317 (M^+, 100), 316 (22), 300 (22), 274 (8), 257 (12), 167 (11); Anal. Calcd for $C_{20}H_{15}NO_3$: C, 75.7; H, 4.73. Found: C, 75.52; H, 4.51.

6-Methoxy-1[(4-chlorophenyl)amino]-9*H*-xanthen-9-one (6d). Using the above procedure, *O*-alkylated **3b** (1.37 g, 50 mmol) in acetic acid (50 ml) and *p*-chloroaniline (0.66 g, 52 mmol) were refluxed for 18 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **6d** (0.35 g, 20%) as a lemon yellow solid, mp 158–160°. IR (KBr): 1640, 1600, 1400, 1270 cm^{-1}; ^1H NMR: δ 10.8 (s, 1H), 6.32–7.92 (m, 10H), 3.85 (s, 3H). MS (EI): *m/z* 351 (M^+, 100), 350 (14), 334 (18), 315 (10), 308 (4), 273 (10), 263 (22); Anal. Calcd for $C_{20}H_{14}ClNO_3$: C, 68.37; H, 3.98. Found: C, 68.15; H, 3.75.

6-Methoxy-3-methyl-1-[(4-methoxyphenyl)amino]-9*H*-xanthen-9-one (7a). Using the above procedure, *O*-alkylated **3c** (1.44 g, 50 mmol) in acetic acid (50 ml) and *p*-anisidine (0.65 g, 52 mmol) were refluxed for 18 h. The crude mixture was purified by column chromatography (9:1 hexane/EtOAc) to afford **7a** (0.36 g, 20%) as a pale yellow solid, mp 145–146°. IR (KBr): 1630, 1600, 1400,

1260 cm^{-1}; NMR: δ 11.02 (s, 1H), 6.49–8.15 (m, 9H), 3.91 (s, 3H), 3.84 (s, 3H), 2.77 (s, 3H); MS (EI): *m/z* 361 (M^+, 100), 346 (78), 303 (20), 280 (24), 252 (10); Anal. Calcd for $C_{22}H_{19}NO_4$: C, 73.13; H, 5.26. Found: C, 72.85; H, 5.01.

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References

1. Stetter, V. H.; Lawterbach, R. *Liebigs Ann.* **1972**, *52*, 40.
2. Nagarajan, K.; Shah, R. K. *Tetrahedron Lett.* **1972**, *15*, 1467.
3. Padmanabhan, P. V.; Ramadas, S. R. *Heterocycles* **1981**, *16*, 1.
4. Baltazzi, E.; Krimen, L. I. *Chem. Rev.* **1963**, *63*, 511.
5. Jones, R. A.; Bean, G. P. The Chemistry of Pyrroles, Academic: New York, 1977.
6. Patterson, J. M. *Synthesis* **1976**, 281.
7. Padmanabhan, P. V.; Ramana, D. V.; Ramadas, S. R. *Indian J. Chem. B* **1988**, *27*, 721.
8. Padmanabhan, P. V.; Ramana, D. V.; Ramadas, S. R. *Indian J. Chem. B* **1988**, *27*, 729.
9. Padmanabhan, P. V.; Ramana, D. V.; Ramadas, S. R. *Indian J. Chem. B* **1988**, *28*, 957.
10. Padmanabhan, P. V.; Ramana, D. V.; Ramadas, S. R. *Indian J. Chem. B* **1989**, *28*, 428.
11. Brady, B. A.; Geoghean, M.; McMurtey, K. D.; Sullivan, W. I. O. *J. Chem. Soc., Perkin Trans. 1* **1981**, 119.
12. Carey, F. A.; Sundberg, R. T. Advanced Organic Chemistry Part B, Reactions and Synthesis, 2nd ed; Plenum: New York, 1983 (p 19–27).
13. Lenoble, N. J. *Synthesis* **1970**, 1.
14. Zook, H. D.; Russo, T. J.; Ferrand, E. F.; Stolz, D. S. *J. Org. Chem.* **1968**, *33*, 2222.
15. Sudarsana Kumar, C.; Srinivasan, S.; Chandra Sekhar, B.; Ramadas, S. R. *Acta Cryst. C* **1990**, *46*, 1475.
16. Sudarsana Kumar, C.; Srinivasan, S.; Chandra Sekhar, B.; Ramadas, S. R. *Acta Cryst. C* **1990**, *46*, 849.
17. Olah, G. D.; Iyer, P. S.; Surya Prakash, G. K. *Synthesis* **1981**, 513.
18. Shah, G. D.; Shah, R. C.; Grover, P. K. *J. Chem. Soc. IV* **1955**, 3982.
19. Dean, N. B.; Whalley, W. B. *J. Chem. Soc., Perkin Trans. 1* **1984**, 4638.
20. Quillinan, A. J.; Schienmann, F. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1329.
21. Chairani, A.; Rampa, A.; Bisi, A.; Budriesi, R.; Valenti, P. *Arzneim-Forsch* **1992**, *42*, 797.
22. Lin, C. N.; Liou, S. S.; Ko, F. N.; Teng, C. M. *J. Pharm. Sci.* **1993**, *82*, 11.
23. Martin, N. H.; Clary, R. T.; Fudala, L. D.; Hyde, R. G.; Jackson, E. P.; Vehling, J. M.; O'Conner, F.; Pennington, G. A.; Piner, R. T. *J. Elisha Mitchell Sci. Soc.* **1992**, *108*, 102.
24. Jackson, W. T.; Boyd, R. J.; Froelich, L. L.; Gapinaki, D. M.; Mallet, B. E.; Sawyer, J. S. *J. Med. Chem.* **1993**, *36*, 1726.
25. Wilharm, P. *Ger. Offen.* DE, 4,211,420, 1993 (*Chem. Abstr.* **1994**, *120*, 134450b).
26. Mehta, G.; Shah, S. R.; Venkateswarulu, Y. *Tetrahedron* **1994**, *50*, 11729.
27. Lin, C. N.; Teng, C. M.; Chen, I. J.; Liou, S. S.; Liou, S. J.; Ko, F. N. *US Patent* 5,495,005, 1996 (*Chem. Abstr.* **1996**, *124*, 316877m).
28. Soman, S. S.; Trivedi, K. N. *Indian J. Chem. B* **1997**, *36*, 929.
29. Casillas, L. K.; Townsend, C. A. *J. Org. Chem.* **1999**, *64*, 4050.
30. Abadi, A. H.; El-Subbagh, H. I.; Al-Khamees, H. A. *Arzneim-Forsch* **1999**, *49*, 259.