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Conversion of 2(3*H*)-Furanones Bearing Indole Nuclei Into Novel Amide, Pyrrolone, and Imidazole Derivatives

Abdel-Sattar S. Hamad Elgazwy,[1] H. T. Zaky,[2] M. I. Mohamed,[2] H. M. Ahmed,[2] and N. G. Kandile[2]

[1]*Department of Chemistry, Faculty of Science, University of Ain Shams, Abbassia 11566, Cairo, Egypt*

[2]*Department of Chemistry, Faculty of Girls, University of Ain Shams, Heliopolis 11757, Cairo, Egypt*

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ABSTRACT: *2(3H)-Furanones* **1a–d** *having exocyclic double bond and N-acetylisatin nucleus were converted into the corresponding novel amides, pyrrolones, and imidazoles via nitrogen nucleophiles. All purposed structures were confirmed by NMR, mass spectra GC/MS, and chemical evidence.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:434–442, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10175

INTRODUCTION

Nitrogen heterocycles constitute an important class of natural and nonnatural products many of which exhibit useful biological activity [1–4]. Isatin, and a number of its derivatives, posses a reactive ketocarbonyl group that readily undergoes condensation reactions under mild conditions [5]. It was therefore speculated that isatin would be a suitable electrophilic component for the Baylis–Hillman reaction [6] and a precursor for the synthesis of other heterocycles [5,7–9]. Substituted isatins are found in plants, melosatin alkaloids can be obtained from the caribbean tumorigenic plant *Melochia tomentosa* [10–12], as well as in fungi, 6-(3′-methylbuten-2′-yl)isatin was isolated from *Streptomyces albus* [13] and 5-(3′-methylbuten-2′-yl)isatin from *Chaetomium globosum* [14]. The interest in isatin derivatives stems from their pharmacological [15–16] and industrial application [17,18].

RESULTS AND DISCUSSION

The preparation of (3*E*)-1-acetyl-3(5-aryl-2-oxofuran-3(2*H*)-ylidene)-1,3-dihydro-2*H*-indol-2-ones **1a–d** has already been described [19] as part of our previous investigation on 2-(3*H*)-furanones [20–24]. These form only as *E*-isomers. This is consistent with the result described by Long et al. who studied monosubstituted 3-methyleneoxindoles and detected for most of them only the *E*-isomer [25]. In this paper we examine the reactivity of **1a–d** toward some nitrogen nucleophiles. *N*-Acetylisatin derivatives **1a–d** were treated with anthranilic acid and *o*-phenylenediamine under different conditions (Scheme 1). With anthranilic acid in refluxing acetic acid, ring opening occurs with the formation of the *E*-isomers of amides **2a–d** in 59–78% yield (i). This

Correspondence to: Abdel-Sattar S. Hamad Elgazwy, Group de Quimica Organometalica, Departamento de Quimica Inorganica, Facultad de Quimica, Universidad de Murcia, Aptdo. 4021, E-30071 Murcia, Spain; e-mail: abhamad@um.es.

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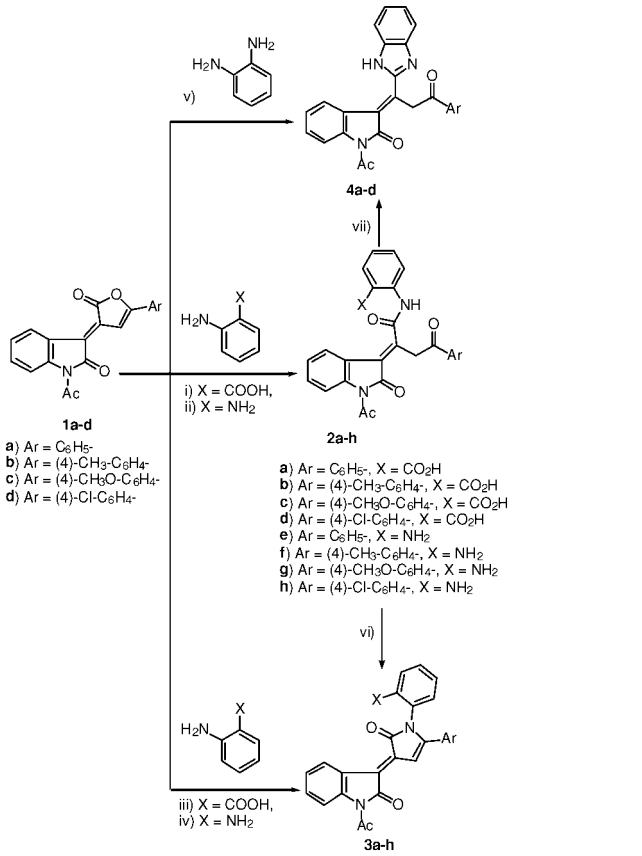


Reagents and conditions; ii) refluxed in AcOH with anthranilic acid for two days, or fusion inlet; ii) refluxed with o-phenylenediamine in ethanol for 3-5 h; iii) refluxed with anthranilic acid in AcOH in 3 mole % of NaOAc, for two days; iv) fusion with o-phenylenediamine in fused sodium acetate for 3 h; v) refluxed with o-phenylenediamine in AcOH/3 mole % of NaOAc, for 3-5h; vi) heated with fused sodium acetate at a bove melting point.; vii) refluxed in acetic acid with 3 mole% of sodium acetate.

SCHEME 1

reaction was repeated in the presence of a catalytic amount of sodium acetate (3 mol%) with ring opening and closure to give imides **3a–d** in 61–80% yield (iii). These compounds when heated neat in the presence of a catalytic amount of fused sodium acetate (3 mol%) were found (by direct comparison of analytical data) to yield products identical to those obtained by ring closure of amides **2a–d** (vi).

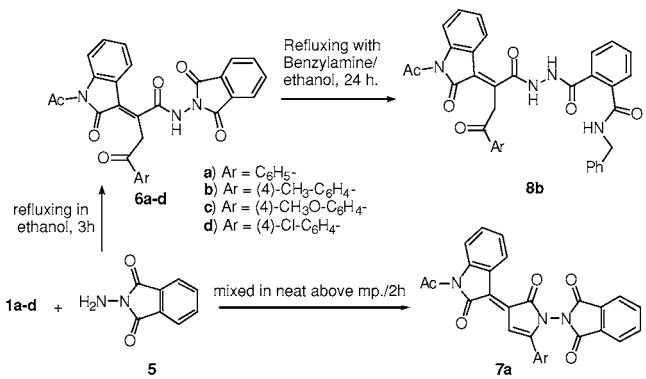
The interaction of **1a–d** with *o*-phenylenediamine was examined with or without solvent. When the reaction took place in refluxing ethanol over 3–5 h, ring opening occurred with the formation of **2e–h** in 75–85% yield (ii). But when the reaction took place by heating of pure form to above melting point in the presence of a catalytic amount of sodium acetate (3 mol%), the imides **3e–h** were formed in 56–63% yield (iv). These were found by direct comparison to be identical with the products formed from the ring closure of **2e–h** during heating of pure form with fused sodium acetate (3 mol%) (vi). This reaction was repeated with refluxing acetic acid in the presence of a catalytic amount of sodium acetate (3 mol%) over 3 h to afford benzoimidazoles **4a–d** in 49–82% yield (v). These were found by direct comparison to be identical with the products that formed from the treatment of **2e–h** with CH_3CO_2H/CH_3CO_2Na (3 mol%) at refluxing temperature (vii). These reactions revealed acid catalysis to be essential for the ring closure of **2e–h**. This reaction condition was consistent with that described by Niume et al. for the formation of *spiro*-benzimidazoles from the reaction of isatin with *o*-phenylenediamine in polar aprotic solvent [26].

In addition, we have examined the reactions of **1a–d** with *N*-aminophthalimide **5** with or without solvent (Scheme 2). When the reaction took place in refluxing ethanol, ring opening occurs to give amides **6a–d** in 40–67% yield. But the reaction is carried out with pure form with heating above melting point over 2–3 h afforded *N*-aminopyrrolones **7a** in 46% yield.

Amide **6b** was treated with equimolar amount of benzylamine in ethanol to give hydrazide **8b** in 62% yield and not *N*,*N*′-dibenzylphthalimide as we expected [27]. Hydrazide **8b** remains under our investigations and for the coversion of this type of compounds into other heterocyclic compounds with anticipated biological activity.

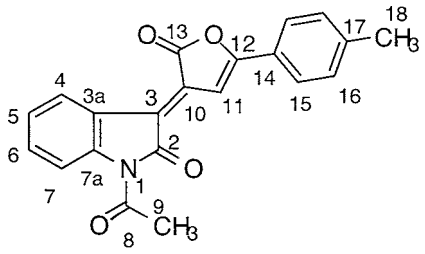
EXPERIMENTAL

Melting points were determined on a Boetius hot-stage apparatus and are uncorrected. Chromatographic separations were performed using silica gel (Merck, 70–230 mesh). Thin-layer chromatography was carried out on Macherey-Nagel precoated silica plate (0.25 mm layer thickness). ^1H and ^{13}C NMR spectra were recorded with a Gemini 200 spectrometer in $CDCl_3$ solution unless otherwise specified (internal standard TMS). Mass spectra were



SCHEME 2

TABLE 1 ^{13}C Chemical Shifts δ C[H_3]$CDCl_3$ for **1b**



C-2	163.2	C-10	134.1
C-3	134.7	C-11	106.0
C-3a	133.1	C-12	162.1
C-4	127.3	C-13	168.8
C-5	124.1	C-14	131.1
C-6	129.5	C-15	129.2
C-7	118.1	C-16	128.4
C-7a	142.8	C-17	105.9
C-8	170.3	C-18	28.8
C-9	47.8		

taken on a VG Trio-2 and GC/MS-QPL000EX (EI, 70 eV) apparatus. IR spectra were recorded with a Perkin-Elmer 1430 instrument in KBr disks. Elemental analyses were performed by M-H-W Laboratories (Phoenix, AZ) at Microanalytical Center of Cairo and Ain Shams Universities.

General Procedure for **1a–d**

2-(3*H*)-Furanones **1a–d** were prepared following the literature method [19,27], via condensation reactions of isatin (0.01 mol) with 3-aroylpropionic acid (0.01 mol) in (10 ml) acetic anhydride and fused sodium acetate (0.03 mol) under Perkin conditions, which yielded the corresponding *E*-isomers as the only product, with no detectable amount of the *Z*-isomers being identified by TLC and ^1H NMR. The reddish-green precipitate was collected by filteration and recrystallized from acetic acid to give **1a–d**.

*(3E)-1-Acetyl-3(2-oxo-5-phenylfuran-3(2H)-ylidene)-1,3-dihydro-2H-indol-2-one (***1a***).* Reddish-green crystals 2.65 g, 80% yield, mp 210–211°C (lit. [19,27] 209–211°C); IR, 3445–3155 (bv) for (NH), 1790 (C=O), 1715–1730 (C=O), 1550 (C=N), 1500 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.89–8.34 [m, 5H, Ph-H), 8.22 (s, 1H, —C<u>H</u>=), 7.83 [d, 2H, $J = 9.0$ Hz, Isatin-H (7)], 7.44 [t, 1H, $J = 9.0$ Hz, Isatin-H(6)], 7.27 [t, 1H, $J = 9.0$ Hz, Isatin-H(5)], 7.03 [d, 1H, $J = 9.0$ Hz, Isatin-H(4)], 2.75 (s, 3H, CO<u>CH</u>$_3$). Calcd. for $C_{20}H_{13}NO_4$ (331.3): C, 72.50; H, 3.95; N, 4.22. Found: C, 72.40; H, 4.20; N, 4.20.

*(3E)-1-Acetyl-3-[(5-(4-methylphenyl)-2-oxofuran-3(2H)-ylidene]-1,3-dihydro-2H-indol-2-one (***1b***).* Reddish-brown crystals 2.83 g, 82% yield, 224–226°C (lit. [19,27] 225–227°C); IR (KBr pellet): 3431–3158, (br) for (NH), 1826 (C=O), 1614–1645 (C=O), 1595 (C=N), 1538 (C=C) cm^{-1}; LRMS (EI): *m/z* 345 (M^+, 25), 303 (50), 119 (100), 85 (50); GC: $t_R = 2.81$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/5 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.97 [d, 2H, $J = 7.78$ Hz, CH_3—C_6<u>H</u>$_4$-(2)], 8.23 [d, 2H, $J = 8.06$ Hz,CH_3—C_6<u>H</u>$_4$-(3)], 7.93 (s, 1H, —C<u>H</u>=), 7.71 [d, 2H, $J = 8.14$ Hz, Isatin-H (7)], 7.40 [t, 1H, $J = 6.66$ Hz, Isatin-H(6)], 7.33 [t, 1H, $J = 6.28$ Hz, Isatin-H(5)], 7.21 [d, 1H, $J = 7.8$ Hz, Isatin-H(4)], 2.72 (s, 3H, —$COCH_3$) 2.39 (s, 3H, —CH_3); Calcd. for $C_{21}H_{15}NO_4$ (345.04): C, 73.03; H, 4.37; N, 4.05. Found: C, 73.10; H, 4.30; N, 4.00.

*(3E)-1-Acetyl-3[5-(4-methoxyphenyl)-2-oxofuran-3(2H)-ylidene]-1,3-dihydro-2H-indol-2-one (***1c***).* Reddish-brown crystals 2.71 g, 75% yield, mp 228–230°C; IR (KBr pellet): 3735–3433 for (NH), 1782 (s), for (C=O), 1609–1745 (m), for (C=O), 11595–633 (s), for (C=N), 1536 (C=C) cm^{-1}; LRMS (EI): *m/z* 361 (M^+, 10), 310 (33.5), 263 (0.73), 262 (1.32), 246 (1.5), 203 (2.01), 202 (1.1), 135 (100), 101 (2), 92 (10); 77 (21), 63 (3.7), 61 (4.5); GC: $t_R = 6.919$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 9.07 [d, 2H, $J = 7.8$ Hz, CH_3O—C_6<u>H</u>$_4$-(2)], 8.34 [d, 2H, $J = 7.8$ Hz,CH_3O—C_6<u>H</u>$_4$-(3)], 8.00 (s, 1H, —C<u>H</u>=), 7.83 [d, 2H, $J = 9.02$ Hz, Isatin-H (7)], 7.44 [t, 1H, $J = 8.2$ Hz, Isatin-H(6)], 7.27 [t, 1H, $J = 5.8$ Hz, Isatin-H(5)], 7.03 [d, 1H, $J = 9.06$ Hz, Isatin-H(4)], 3.89 (s, 3H, OCH_3) 2.76 (s, 3H, $COCH_3$). Calcd. for $C_{21}H_{15}NO_5$ (361.35); C, 69.80; H, 4.18; N, 3.87. Found: C, 69.90.; H, 4.30; N, 3.80.

*(3E)-1-Acetyl-3[5-(4-chlorophenyl)-2-oxofuran-3(2H)-ylidene]-1,3-dihydro-2H-indol-2-one (***1d***).* Reddish-brown crystals 3.11 g, 85% yield, mp 216–217°C; IR (KBr pellet): 3431–3145 (br), for (—NH); 1771 (s), for (C=O), 1610–1653 (m), (C=O), 1596 (m), (C=N) 1538 (C=C) cm^{-1}; LRMS (EI): *m/z* 365 (M^+, 25), 366 (8.5), 320 (5), 325 (22), 323 (11.5), 322 (82.22), 256 (7.20), 240 (3.34), 184 (20.03), 140 (19.5), 141 (34.45), 140 (10.93), 139.95 (100), 133 (10.17), 120 (17.3), 113 (25), 112 (12.11), 111 (52.5), 100 (10.17), 60 (57), 57 (70), 56 (34); GC: $t_R = 1.89$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/5 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 9.05 [d, 2H, $J = 8.06$ Hz, Cl—C_6<u>H</u>$_4$-(2)], 8.30 [d, 2H, $J = 7.8$ Hz, Cl—C_6<u>H</u>$_4$-(3)],

8.05 (s, 1H, —C<u>H</u>=), 7.82 [d, 2H, $J = 6.8$ Hz, Isatin-H (7)], 7.60 [t, 1H, $J = 7$ Hz, Isatin-H(6)], 7.50 [t, 1H, $J = 7$ Hz, Isatin-H(4)], 7.23 [t, 1H, $J = 6.8$ Hz, Isatin-H(5)], 2.75 (s, 3H, —$COCH_3$). Calcd. for $C_{20}H_{12}ClNO_4$ (365.77): C, 65.67; H, 3.30; N, 3.82; Cl, 9.69; Found: C, 65.60; H, 3.40; N, 3.90; Cl, 9.50.

General Procedure for **2a–d**

To a suspension of **1a–d** (0.01 mol) in (25 ml) acetic acid, anthranilic acid (0.01 mol) was added and the reaction mixture was refluxed for 2 days, then cooled. The reddish soild precipitate was collected by filteration and recrystallized from acetic acid to give **2a–d**.

*2-{[(2E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-4-oxo-4-phenylbutanoyl]amino}benzoic Acid (***2a***).* Brown crystals 3.05 g, 65% yield, mp 125–127°C; IR (KBr pellet): 3423 (broad band) for (NH), 1686 (m) for (C=O), 1602 (v) for (C=O), 1550 (s), 1517 (s) for (C=N) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 13.59 (bs, 1H, CO_2<u>H</u>), 8.88 (bs, 1H, CO<u>NH</u>), 7.98–6.85 (m, 13H, Ar-H), 6.82 (s, 2H, —C<u>H_2</u>), 2.78 (s, 3H, —$COCH_3$). Calcd. for $C_{27}H_{20}N_2O_6$ (468.46); C, 69.22; H, 4.30; N, 5.97; Found: C, 69.50; H, 4.50; N, 6.00.

*2-{[(2E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-4(4-methylphenyl)-4-oxobutanoyl]amino}-benzoic Acid (***2b***).* Brown crystals 3.77 g, 78% yield, mp 175–177°C; IR (KBr pellet): 3250–3425 (broad band) for (OH and NH), 1770.3 (s) for (C=O), 1702 (m) for (C=O), 1611.5 (v) for (C=O), 1542.1 (s), and 1503 (s) for (C=N). cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 13.63 (bs, 1H, CO_2<u>H</u>), 8.9 (bs, 1H, CO<u>NH</u>) , 7.86 [d, 2H, $J = 9.06$ Hz, CH_3—C_6<u>H_4</u>-(2)], 7.75–7.11 [m, 8H, Ar-H), 7.02 [d, 2H, $J = 9.06$ Hz, CH_3—C_6<u>H_4</u>-(3)], 6.84 (s, 2H, —C<u>H_2</u>), 2.75 (s, 3H, —$COCH_3$), 2.32 (s, 3H, —CH_3). Calcd. for $C_{28}H_{22}N_2O_6$ (482.49); C, 69.70; H, 4.59; N, 5.80; Found: C, 69.80; H, 4.50; N, 6.10.

*2-{[(2E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-4(4-methoxyphenyl)-4-oxobutanoyl]-amino}benzoic Acid (***2c***).* Brown crystals 2.95 g, 59% yield, mp 270–272°C, IR (KBr pellet): 3018.4–3173.5 (bv) for (OH and NH), 1768.8 (v) for (C=O), 1694.1 (v) for (C=O), 1613.6 (v) for (C=O), 1544.6 (v), and 1502.9 (v) for (C=N) cm^{-1}; LRMS (EI): *m/z* 440 ($M^+ - 58$), 1.3), 391 (2), 320 (19.4), 319 (80.81), 291 (7), 283 (5.45), 248 (7.50), 220 (5.89), 155 (25.7), 135 (100), 120 (20), 107 (12.7), 101 (20.77), 92 (35.73), 77 (20.44), 76 (10), 75 (12.94), 64 (12.2); GC: $t_R = 7.134$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 13.62 (bs, 1H, CO_2<u>H</u>), 8.89 (bs, 1H, CO<u>NH</u>), 7.98 (s, 1H, Ar-H), 7.86 [d, 2H, $J = 9.06$ Hz, CH_3—C_6<u>H_4</u>-(2)], 7.68–7.09 [m, 7H, Ar-H), 7.02 [d, 2H, $J = 9.06$ Hz, CH_3—C_6<u>H_4</u>-(3)], 6.85 [d, 1H, $J = 6.00$ Hz, Isatin-H(4)], 6.82 (s, 2H, —C<u>H_2</u>), 3.89 (s, 3H, —OCH_3), 2.77 (s, 3H, —$COCH_3$). Calcd. for $C_{28}H_{22}N_2O_7$ (498.49); C, 67.46; H, 4.44; N, 5.61; Found: C, 67.90; H, 4.50; N, 6.00.

*2-{[(2E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-4(4-chlorophenyl)-4-oxobutanoyl]amino}-benzoic Acid (***2d***).* Brown crystals 3.65 g, 72% yield, mp 245–247°C; IR (KBr pellet): 3419–3064 (broad band) for (OH and NH), 1705.4 (m) for (C=O), 1599.5 (m) for (C=O), 1545.6 (s), and 1486 (m) for (C=N) cm^{-1}; LRMS (EI): *m/z* 505 (M^+, 8), 442 (8.7), 384 (8.72), 383 (10.87), 296 (12), 256 (511.4), 234 (10), 210 (9), 191 (10), 190 (10), 156 (10), 148 (20.8), 140.95 (39.8), 139 (100), 134 (9.8), 132 (14), 129 (19.46), 128 (20), 111 (93.2), 75 (77.10); ^1H NMR ($CDCl_3$, 200 MHz): δ 13.66 (bs, 1H, CO_2<u>H</u>), 8.88 (bs, 1H, CO<u>NH</u>), 7.98 (s, 1H, Ar-H), 7.87 [d, 2H, $J = 9.06$ Hz, Cl—C_6<u>H_4</u>-(2)], 7.68–7.09 [m, 6H, Ar-H), 7.02 [d, 2H, $J = 9.06$ Hz, Cl—C_6<u>H_4</u>-(3)], 6.85 [d, 1H, $J = 6.00$ Hz, Isatin-H(4)], 6.82 (s, 2H, —C<u>H_2</u>), 3.89 (s, 3H, —OCH_3), 2.11 (s, 3H, —$COCH_3$); GC: $t_R = 8.017$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min. Calcd. for $C_{27}H_{19}ClN_2O_6$ (502.9); C, 64.48; H, 3.80; N, 5.57; Cl, 7.04; Found: C, 64.50; H, 3.70; N, 5.32; Cl, 7.70.

General Procedure for **2e–h**

To a suspension of **1a–d** (0.01 mol) in (25 ml) ethanol, *o*-phenylenediamine (0.01 mol) was added with refluxing for 3 h and then cooled. The brown precipitate was collected by filteration and recrystallized from ethanol to give **2e–h**.

*(2E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-N-(2-aminophenyl)-4-oxo-4-phenylbutanamide (***2e***).* Brown crystals 3.61 g, 82% yield, mp 263–264°C; IR (KBr pellet): 3452–3153, 3059.2 (broad band) for (—NH, —NH_2), 1745.6 (s), 1684.7 (v), for (C=O), 1606.1 (v) for (C=O), 1544.5 (s), and 1457.9 (s) for (C=N) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.77 (bs, 2H, NH_2), 8.55 (bs, 1H, CO<u>NH</u>), 8.30–6.96 (m, 13H, Ar-H), 6.94 (s, 2H, —C<u>H_2</u>), 2.69 (s, 3H, —$COCH_3$). Calcd. for $C_{26}H_{21}N_3O_4$ (439.47); C, 71.05; H, 4.81; N, 9.56; Found: C, 71.20; H, 4.60; N, 9.90.

*(2E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-N-(2-aminophenyl)-4(4-methylphenyl)-4-oxobutanamide (***2f***).* Brown crystals 3.85 g, 85% yield, mp 244–245°C; IR (KBr pellet): 3447.6, 3145.7, 3045, 3005.7 (broad band) for (—NH, —NH_2), 1745.6 (s), 1679.8 (v), for (C=O), 1608.7 (v) for (C=O), 1550.7 (s) for (C=N) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.75 (bs, 2H, NH), 8.71 (bs, 1H, CO<u>NH</u>), 8.45 (d, 2H, $J = 7.8$ Hz,CH_3—C_6<u>H_4</u>-(3)), 8.12 (d, 2H, $J = 7.8$ Hz, CH_3—C_6<u>H_4</u>-(2), 7.18-6.96 (m, 8H, Ar-H), 5.94 (s, 2H, —C<u>H_2</u>), 2.51 (s, 3H, —$COCH_3$), 1.65 (s, 3H, —CH_3). Calcd. for $C_{27}H_{23}N_3O_4$ (453.50); C, 71.51; H, 5.11; N, 9.26; Found: C, 71.20; H, 5.10; N, 9.70.

*(2E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-N-(2-aminophenyl)-4(4-methoyphenyl)-4-oxobutanamide (***2g***).* Brown crystals 3.52 g, 75% yield, mp 232–234°C; IR (KBr pellet): 3449.3, 3165.5, 3091.2 (broad band) for (—NH, —NH_2), 1688.2 (v), for (C=O), 1608.0 (v) for (C=O), 1540.2 (s) for (C=N) cm^{-1}; LRMS (EI): *m/z* 469 (M^+, 25.5), 468 ($M^+ - 1$) 27.66), 400 (21.2), 399 (21), 371 (21), 360 (21), 349 (23), 348 (27), 307 (21), 305 (21), 301 (27), 291 (30), 283 (25), 283 (23), 275 (23), 251.7 (40), 251 (100), 230 (23), 222 (31), 216 (25), 206 (27), 174 (21), 171 (21), 170 (23), 185 (27), 180 (21), 159 (23), 151 (21), 149 (23), 129 (25), 100 (25), 90 (23), 72 (23), 59 (21); GC: $t_R = 7.955$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.77 (bs, 2H, NH), 8.72 (s, 1H, CO<u>NH</u>), 8.38 (d, 2H, $J = 7.8$ Hz, CH_3O—C_6<u>H_4</u>-(3)), 8.17 (d, 2H, $J = 7.8$ Hz, CH_3O—C_6<u>H_4</u>-(2)), 8.18–6.65 (m, 8H, Ar-H), 5.98 (s, 2H, —C<u>H_2</u>), 3.89 (s, 3H, —OCH_3), 1.61 (s, 3H, —$COCH_3$). Calcd. for $C_{27}H_{23}N_3O_5$ (469.50); C, 69.07; H, 4.93; N, 8.94; Found: C, 68.80; H, 4.70; N, 9.10.

*(2E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-N-(2-aminophenyl)-4(4-chlorophenyl)-4-oxobutanamide (***2h***).* Brown crystals 3.8 g, 80% yield, mp 260–262°C; IR (KBr pellet): 3447.8, 3157.3, 3051.8 (broad band) for (—NH, —NH_2), 1679.6.2 (v), for (C=O), 1602.2 (v) for (C=O), 1582.2 (s), 1527.6 (s) for (C=N) cm^{-1}; LRMS (EI): *m/z* 476 ($M^+ - 2.5$), 14), 445 ($M^+ - 28.5$), 18), 443 (13), 398 (>5), 348 (>5), 299 (30), 298 (100), 270 (47), 255 (>5), 159 (47), 139 (72), 115 (44), 77 (42); GC: $t_R = 9.438$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.96 (bs, 2H, NH), 8.88 (s, 1H, CO<u>NH</u>), 8.42 (d, 2H, $J = 8.8$ Hz,Cl—C_6<u>H_4</u>-(3)), 8.15 (d, 2H, $J = 8.8$ Hz, Cl—C_6<u>H_4</u>-(2)), 8.12–6.77 (m, 8H, Ar-H), 6.34 (s, 2H, —C<u>H_2</u>), 1.77 (s, 3H, —$COCH_3$). Calcd. for $C_{26}H_{20}ClN_3O_4$ (473.91); C, 65.89; H, 4.25; N, 8.86; Cl, 7.48; Found: C, 65.50; H, 4.10; N, 8.50; Cl, 7.80.

General Procedure for **3a–d**

A mixture of **1a,b,d** (0.01 mol) and sodium acetate (0.03 mol) was fused for 3 h, above melting point, then cooled. The reddish-brown solid was collected and recrystallized from ethanol to give **3a,b,d**. Compounds **3a–d** were obtained by mixing **2a–d** with freshly prepared sodium acetate (0.03 mol) at melting point for 2–5 h, and were found by direct comparison of analytical data to be identical.

*2-[(3E)-3-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-5-phenyl-2-oxo-2,3-dihydro-1H-pyrrol-1-yl]benzoic Acid (***3a***).* Reddish-brown crystals 3.13 g, 69% yield, mp >300°C; IR (KBr pellet): 3629.9–3407.1, 3059.0 (broad band) for (—OH), 1704.4 (s) for (C=O), 1660.6 (m), 1601.4 for (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 13.59 (bs, 1H, CO_2<u>H</u>), 8.20–6.85 (m, 13H, Ar-H), 6.82 (s, 1H, —C<u>H</u>=C), 2.78 (s, 3H, —$COCH_3$). Calcd. for $C_{27}H_{18}N_2O_5$ (450.45); C, 71.99; H, 4.02; N, 6.21; Found: C, 72.30; H, 4.20; N, 6.00.

*2-[(3E)-3-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-5-(4-methylphenyl)-2-oxo-2,3-dihydro-1H-pyrrol-1-yl]benzoic Acid (***3b***).* Reddish-brown crystals 3.75 g, 80% yield, mp >300°C; IR (KBr pellet): 3425.8 (broad band) for (—OH), 1688.3 (s) for (C=O), 1593.8 (v) for (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 13.55 (bs, 1H, CO_2<u>H</u>), 7.88 [d, 2H, $J = 9.06$ Hz, CH_3—C_6<u>H_4</u>-(2)], 7.75–7.09 [m, 8H, Ar-H), 7.02 [d, 2H, $J = 9.06$ Hz, CH_3—C_6<u>H_4</u>-(3)], 6.84 (s, 1H, —C<u>H</u>=C), 2.75 (s, 3H, —$COCH_3$), 2.32 (s, 3H, —CH_3). Calcd. for $C_{28}H_{20}N_2O_5$ (464.48); C, 72.40; H, 4.34; N, 6.03; Found: C, 72.30; H, 4.20; N, 6.20.

*2-[(3E)-3-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-5-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-pyrrol-1-yl]benzoic Acid (***3c***).* To a suspension of **1d** (0.01 mol) in (25 ml) acetic acid, anthranilic acid (0.01 mol) was added with refluxing for 40 h, then cooled to solidify the product. The reddish-brown precipitate was collected by filteration and recrystallized from acetic acid to give a brown crystals 2.94 g, 61% yield, mp 263–265°C; IR (KBr pellet): 3230.3, 3118.8 (broad band) for (—OH), 1715 (s) for (C=O), 1685.3 (m), 1587.9 (s) for (C=O) cm^{-1}; LRMS (EI): *m/z* 450 ($M^+ - 30$), >5), 319 (20), 200 (8), 235 (100), 170 (40), 137 (30); GC: $t_R = 6.139$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 13.62 (bs, 1H,

$CO_2\underline{H}$), 7.98 (s, 1H, Ar-H), 7.86 [d, 2H, $J = 9.06$ Hz, $CH_3{-}C_6\underline{H}_4$-(2)], 7.82–7.12 [m, 8H, Ar-H), 7.10 [d, 2H, $J = 9.06$ Hz, $CH_3{-}C_6\underline{H}_4$-(3)], 6.82 (s, 2H, $-C\underline{H}{=}C-$), 3.89 (s, 3H, $-OCH_3$), 2.77 (s, 3H, $-COCH_3$). Calcd. for $C_{28}H_{20}N_2O_6$ (480.48); C, 69.99; H, 4.19; N, 5.83; Found: C, 69.90; H, 4.20; N, 6.10.

*2-[(3E)-3-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-5-(4-chlorophenyl)-2-oxo-2,3-dihydro-1H-pyrrol-1-yl]benzoic Acid (***3d***).* Reddish-brown crystals 3.40 g, 70% yield, mp >300°C; IR (KBr pellet): 3063.6–3402.6 (broad band) for (–OH), 1671.8.3 (s) for (C=O), 1597.1 (m) for (C=O) cm^{-1}; LRMS (EI): *m/z* 455 ($M^+ - 29.5$), 66.5), 398 (85), 348 (>5), 397 (30), 396 (100), 395 (50), 331 (29), 251 (20), 205 (15), 146 (33.47); GC: $t_R = 9.028$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 13.69 (bs, 1H, $CO_2\underline{H}$), 7.87 [d, 2H, $J = 9.06$ Hz, $Cl{-}C_6\underline{H}_4$-(2)], 7.98–7.09 [m, 7H, Ar-H), 7.02 [d, 2H, $J = 9.06$ Hz, $Cl{-}C_6\underline{H}_4$-(3)], 6.85 [d, 1H, $J = 6.00$ Hz, Isatin-H(4)], 6.84 (s, 2H, $-C\underline{H}{=}C-$), 3.89 (s, 3H, $-OCH_3$), 2.11 (s, 3H, $-COCH_3$). Calcd. for $C_{27}H_{17}ClN_2O_5$ (484.89); C, 66.88; H, 3.53; N, 5.77; Cl, 7.31; Found: C, 66.90; H, 3.70; N, 5.96; Cl, 6.90.

General Procedure for **3e–h**

A mixture of 2(3*H*)furanones **1a–d** (0.01 mol), *o*-phenylenediamine (0.01 mol), and freshly prepared sodium acetate (0.03 mol) was fused at melting point for 2–3 h, then cooled. The soild product was collected and recrystallized from ethanol to give **3e–h**, which was formed from the reaction of **2e–h** with freshly prepared sodium acetate (0.03 mol) at melting point for 2–5 h. Compounds **3e–h** were found by direct comparison (mp and mixed mp) and GC/MS spectral data to be identical in all aspects with the authentic products.

*(3E)-1-Acetyl-3-[1-(2-aminophenyl)-5-phenyl-2-oxo-1,2-dihyro-3H-pyrrol-3-ylidene]-1,3-dihydro-2H-indol-2-one (***3e***).* Brown crystals 2.55 g, 60% yield, mp 235–237°C; IR (KBr pellet): 3429.4 (broad band) for (NH_2), 1678.6 (s) for (C=O), 1600.9 (s), 1562.2 (v) for (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.89 (bs, 2H, NH_2), 8.55–6.96 (m, 13H, Ar-H), 7.65 (s, 1H, $-C\underline{H}{=}C$), 2.70 (s, 3H, $-COCH_3$). Calcd. for $C_{26}H_{19}N_3O_3$ (421.45).; C, 74.09; H, 4.54; N, 9.97; Found: C, 74.50; H, 4.70; N, 10.00.

*(3E)-1-Acetyl-3-[1-(2-aminophenyl)-5-(4-methylphenyl)-2-oxo-1,2-dihyro-3H-pyrrol-3-ylidene]-1,3-dihydro-2H-indol-2-one (***3f***).* Brown crystals 2.75 g, 63% yield, mp 279–281°C; IR (KBr pellet): 3431.6 (broad band) for (NH_2), 1687.9 (s) for (C=O), 1639.6 (s), 1561.6 (v) for (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.75 (bs, 2H, NH), 8.55 (d, 2H, $J = 7.8$ Hz, $CH_3{-}C_6\underline{H}_4$-(3)), 8.12 (d, 2H, $J = 7.8$ Hz, $CH_3{-}C_6\underline{H}_4$-(2), 7.18–6.96 (m, 8H, Ar-H), 7.94 (s, 1H, $-C\underline{H}{=}C-$), 2.76 (s, 3H, $-COCH_3$), 1.65 (s, 3H, $-CH_3$). Calcd. for $C_{27}H_{21}N_3O_3$ (435.48); C, 74.46; H, 4.86; N, 9.64; Found: C, 74.50; H, 4.50; N, 9.50.

*(3E)-1-Acetyl-3-[1-(2-aminophenyl)-5-(4-methoxyphenyl)-2-oxo-1,2-dihyro-3H-pyrrol-3-ylidene]-1,3-dihydro-2H-indol-2-one (***3g***).* Reddish-brown crystals 2.53 g, 56% yield, mp >300°C; IR (KBr pellet): 3283.4, 3177.2, 3431.6 (broad band) for (NH_2), 1680.1 (s) for (C=O), 1601.6 (s), 1559.6 (v) for (C=O) cm^{-1}; LRMS (EI): *m/z* 330 ($M^+ - 121$), >5), 298 (2.7), 295 (17.53), 291 (100), 277 (2.3), 255 (28), 251 (20), 250 (5.5), 223 (18), 187 (15), 186 (55.45), 160 (3.27), 159 (20), 131 (50), 76 (40); GC: $t_R = 7.260$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.77 (bs, 2H, NH), 8.38 (d, 2H, $J = 7.8$ Hz, $CH_3O{-}C_6\underline{H}_4$-(3)), 8.17 (d, 2H, $J = 7.8$ Hz, $CH_3O{-}C_6\underline{H}_4$-(2)), 8.18–6.65 (m, 8H, Ar-H), 6.98 (s, 2H, $-C\underline{H}{=}C$), 3.89 (s, 3H, $-OCH_3$), 2.61 (s, 3H, $-COCH_3$). Calcd. for $C_{27}H_{21}N_3O_4$ (451.48); C, 71.82; H, 4.68; N, 9.30; Found: C, 71.70; H, 4.70; N, 9.50.

*(3E)-1-Acetyl-3-[1-(2-aminophenyl)-5-(4-chlorophenyl)-2-oxo-1,2-dihyro-3H-pyrrol-3-ylidene]-1,3-dihydro-2H-indol-2-one (***3h***).* Yellow crystals 2.65 g, 58% yield, mp 269–270°C; IR (KBr pellet): 3429.4, 3284.5, 3179.6 (broad band) for (NH_2), 1678.6 (s) for (C=O), 1601.8 (s), 1560.4 (v) for (C=O) cm^{-1}; LRMS (EI): *m/z* 463 ($M^+ - 7.5$), 2.5), 301 (1.9), 348 (>5), 298 (10), 297 (3), 271 (8.33), 159 (11.75), 139 (40), 131 (40), 114 (10.5), 113 (35.39), 112 (10), 111 (100), 105 (11), 104 (20), 80 (20.7), 77 (30), 75 (80), 52 (23); GC: $t_R = 6.476$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.98 (bs, 2H, NH), 8.72 (d, 2H, $J = 8.8$ Hz, $Cl{-}C_6\underline{H}_4$-(3)), 8.15 (d, 2H, $J = 8.8$ Hz, $Cl{-}C_6\underline{H}_4$-(2)), 8.71–6.77 (m, 8H, Ar-H), 7.84 (s, 1H, $-C\underline{H}{=}C-$), 2.77 (s, 3H, $-COCH_3$). Calcd. for $C_{26}H_{18}ClN_3O_3$ (455.90); C, 68.49; H, 3.97; N, 9.21; Cl, 7.77; Found: C, 68.60; H, 4.10; N, 9.50; Cl, 8.00.

General Procedure for **4a–d**

To a suspension of **1a–d** (0.01 mol) in (25 ml) acetic acid, *o*-phenylenediamine (0.01 mol) was added in the presence of freshly prepared fused sodium acetate (0.03 mol). The reaction mixture was refluxed

for 5 h and then cooled. The yellowish precipitate was collected by filteration, washed with water, and recrystallized from acetic acid to give **4a–d**, which was formed from the reaction of **2e–h** with acetic acid/sodium acetate (0.03 mol) for 5 h at refluxing temperature. Compounds **4a–d** were found by direct comparison (mp and mixed mp) and GC/MS spectral data to be identical with the authentic products.

*(3E)-1-Acetyl-3-[1-(1H-benzimidazol-2-yl)-3-phenyl-3-oxopropylidene]-1,3-dihydro-2H-indol-2-one (**4a**).* Yellow crystals 2.07 g, 49% yield, mp 258–259°C; IR (KBr pellet): 3452.5–3142.1, 3052.2 (bm), 1686 (m), 1612.4 (v), for (C=O), 1554.4 (s), and 1507.3 (s) for (C=N) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 9.78 (bs, 1H, NH), 8.70–6.96 (m, 13H, Ar-H), 6.94 (s, 2H, $-CH_2$), 2.69 (s, 3H, $-COCH_3$). Calcd. for $C_{26}H_{19}N_3O_3$ (421.45); C, 74.09; H, 4.54; N, 9.97; Found: C, 74.30; H, 4.20; N, 9.60.

*(3E)-1-Acetyl-3-[1-(1H-benzimidazol-2-yl)-3-(methylphenyl)-3-oxopropylidene]-1,3-dihydro-2H-indol-2-one (**4b**).* Yellow crystals 3.57 g, 82% yield, mp 241–242°C; IR (KBr pellet): 3446.1–3183.9, 3149.1 (bm), 1679.4 (m), 1608.5 (v), for (C=O), 1551.8 (s) for (C=N) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 9.75 (bs, 1H, NH), 8.45 (d, 2H, $J = 7.8$ Hz, $CH_3-C_6H_4$-(3)), 8.22 (d, 2H, $J = 7.8$ Hz, $CH_3-C_6H_4$-(2), 7.98–6.96 (m, 8H, Ar-H), 5.94 (s, 2H, $-CH_2$), 2.51 (s, 3H, $-COCH_3$), 1.69 (s, 3H, $-CH_3$). Calcd. for $C_{27}H_{21}N_3O_3$ (435.48); C, 74.46; H, 4.86; N, 9.64; Found: C, 74.00; H, 5.00; N, 9.00.

*(3E)-1-Acetyl-3-[1-(1H-benzimidazol-2-yl)-3-(methoxyphenyl)-3-oxopropylidene]-1,3-dihydro-2H-indol-2-one (**4c**).* Brown crystals 3.39 g, 75% yield, mp 238–240°C; IR (KBr pellet): 3038.7–2860.3 (bm), 1682.3 (v), 1597.7 (v), for (C=O), 1541.7 (s) for (C=N) cm^{-1}; LRMS (EI): *m/z* 453 ($M^+ + 2$), 8), 340 (7.5), 321 (8.9), 311 (7), 295 (8), 294 (35), 265 (34), 235 (27), 224 (26), 221 (17), 193 (13), 187 (15), 185 (15), 158 (21), 152 (15), 151 (19), 135 (100), 130 (29.5), 121 (17), 115 (39), 114 (39), 107 (42), 105 (38), 102 (17), 92 (30), 90 (52), 97 (38), 85 (20), 76 (24), 71 (24), 85 (28), 83 (40), 82 (45), 54 (33), 51 (30); GC: $t_R = 6.973$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/5 min.; ^1H NMR ($CDCl_3$, 200 MHz): δ 9.03 (bs, 2H, NH), 8.38 (d, 2H, $J = 8.9$ Hz, $CH_3O-C_6H_4$-(2)), 8.17 [(d, 2H, $J = 8.9$ Hz, $CH_3O-C_6H_4$-(3)], 8.18–6.65 (m, 8H, Ar-H), 6.97 (s, 2H, $-CH_2$), 3.89 (s, 3H, $-OCH_3$), 2.61 (s, 3H, $-COCH_3$) ppm; Anal. Calcd. for $C_{27}H_{21}N_3O_4$ (451.48); C, 71.82; H, 4.68; N, 9.30; Found: C, 71.50; H, 4.50; N, 9.40.

*(3E)-1-Acetyl-3-[1-(1H-benzimidazol-2-yl)-3-(chlorophenyl)-3-oxopropylidene]-1,3-dihydro-2H-indol-2-one (**4d**).* Brown crystals 3.6 g, 79% yield, mp 271–273°C; IR (KBr pellet): 3164.9–3089.3 (bm), 1689.2 (v), 1608.0 (v), for (C=O), 1538.5 (s) for (C=N) cm^{-1}; LRMS (EI): *m/z* 455 (M^+), >5), 301 (10), 300 (10), 299 (14), 298 (83), 295 (11), 269 (40), 107 (27), 159 (42), 140 (32), 139 (100), 134 (10), 131 (33), 117 (27), 112 (23), 110 (75), 103 (20), 90 (23), 77 (30), 76 (24), 74 (40), 73 (15), 64 (13), 63 (15), 62 (25), 53 (11), 51 (27); GC: $t_R = 7.215$ min; column; DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/5 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 9.96 (bs, 2H, NH), 8.53 (d, 2H, $J = 8.8$ Hz, $Cl-C_6H_4$-(3)), 8.15 (d, 2H, $J = 8.8$ Hz, $Cl-C_6H_4$-(2)), 8.50–6.77 (m, 8H, Ar-H), 6.94 (s, 2H, $-CH_2$), 2.77 (s, 3H, $-COCH_3$). Calcd. for $C_{26}H_{18}ClN_3O_3$ (455.90); C, 68.49; H, 3.97; N, 9.21; Cl, 7.77; Found: C, 68.50; H, 4.00; N, 9.10; Cl, 7.80.

General Procedure for **6a–d**

To a suspension of **1a–d** (0.01 mol) in (25 ml) ethanol, *N*-aminophthalimide (0.01 mol) was added with refluxing for 3 h, then cooled. The reddish-brown precipitate was collected by filteration and recrystallized from ethanol to give **6a–d**.

*(2E)-2(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-N-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-4-phenyl-4-oxobutanamide (**6a**).* Brown crystals 2.5 g, 50% yield, mp 158–160°C; IR (KBr pellet): 3340.7 (m), 3266.2 (m), 1783.6 (s), 1722.1 (v) for (C=O) and 1607.5 (s), 1543.4 (s) for (C=N) cm^{-1}; LRMS (EI): *m/z* 493 (M^+), >5), 475 ($M^+ - 18$), >5), 488 (>5), 381 (15), 288 (30), 261 (7), 216 (5), 106 (7), 105 (100), 76 (50); GC: $t_R = 6.719$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^1H NMR ($CDCl_3$, 200 MHz): δ 10.11 (s, 1H, NH), 8.34–7.25 [m, 13H, Ar-H), 4.20 (s, 2H, $-CH_2$), 2.77 (s, 3H, $-COCH_3$). Calcd. for $C_{28}H_{19}N_3O_6$ (493.47); C, 68.15; H, 3.88; N, 8.51; Found: C, 68.10; H, 3.90; N, 8.90.

*(2E)-2(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-N-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-4-(4-methylphenyl)-4-oxobutanamide (**6b**).* Reddish-brown crystals 3.4 g, 67% yield, mp 120–122°C; IR (KBr pellet): 3427.5 (bv), 1722.2 (v), 1663.7 (s), for (C=O), 1615.1 (s) for (C=O) cm^{-1}; LRMS (EI): *m/z* 506 ($M^+ - 1$), (>5), 399 (>5), 391 (>5), 337 (>5), 229 (>5), 173 (>5), 119 (100), 104 (10), 79 (10); GC: $t_R = 6.950$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/5 min; ^1H NMR

($CDCl_3$, 200 MHz): δ 10.52 (s, 1H, NH), 8.75 (d, 2H, $J = 7.8$ Hz, CH_3—$C_6\underline{H}_4$-(2)), 8.12 (d, 2H, $J = 7.8$ Hz, CH_3—$C_6\underline{H}_4$-(3), 7.18–6.96 (m, 8H, Ar-H), 5.94 (s, 2H, —$C\underline{H}_2$), 2.51 (s, 3H, —$COCH_3$), 1.65 (s, 3H, —CH_3). Calcd. for $C_{29}H_{21}N_3O_6$ (507.50); C, 68.63; H, 4.17; N, 8.27; Found: C, 69.00; H, 4.30; N, 8.70.

*(2E)-2(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-N-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-4-(4-methoxyphenyl)-4-oxobutanamide (***6c***).* Brown crystals 2.1 g, 40% yield, mp 279–281°C; IR (KBr pellet): 3425.8 (bm), 3166.9 (bs), 3018.8 (bm), 2901.9 (bv), 1722.5 (s), 1661.6 (v) for (C=O), 1601.7(s), 1560.4 (s), 1494.6 (v) for (C=O) cm^{-1}; LRMS (EI): *m/z* 554 ($M^+ + 1$), >5), 371 (>5), 319 (>5), 248 (2), 220 (1), 162 (30.23), 161 (2), 135 (6), 132 (6), 118 (2), 106 (2.9), 105 (25), 104 (35), 102 (2), 101 (3), 92 (7), 91 (6), 77(89), 76 (84), 75 (53), 74 (88), 73 (22), 63 (19), 62 (19), 61 (20), 53 (40), 52 (23), 51 (100); GC: $t_R = 7.159$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 10.72 (s, 1H, NH), 8.68 (d, 2H, $J = 7.8$ Hz, CH_3O—$C_6\underline{H}_4$-(2)), 8.47 (d, 2H, $J = 7.8$ Hz, CH_3O—$C_6\underline{H}_4$-(3)), 8.68–6.65 (m, 8H, Ar-H), 5.98 (s, 2H, —$C\underline{H}_2$), 3.89 (s, 3H, —OCH_3), 1.61 (s, 3H, —$COCH_3$). Calcd. for $C_{29}H_{21}N_3O_7$ (523.50); C, 66.53; H, 4.04; N, 8.02; Found: C, 66.80; H, 4.10; N, 8.40.

*(2E)-2(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-N-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-4-(4-chlorophenyl)-4-oxobutanamide (***6d***).* Reddish-brown crystals 3.2 g, 60% yield, mp 117–119°C; IR (KBr pellet): 3482.6 (bs), 3340.5 (m), 3265.9 (s), 1783.5 (s), 1721.8 (v) for (C=O), 1607.1 (s) for (C=O) cm^{-1}; LRMS (EI): *m/z* 526 ($M^+ - 1.5$), 2.43), 514 (3), 503 (10), 502 (100), 55 (2.2), 125 (5), 96 (47), 95 (100), 79 (10), 78 (9), 65(23), 61 (47), 58 (27.77); GC: $t_R = 3.736$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/5 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 12.76 (s, 1H, N$\underline{H}$), 7.88–7.42 [m, 12H, Ar-H), 4.21 (s, 2H, —$C\underline{H}_2$), 2.76 (s, 3H, —$COCH_3$). Calcd. for $C_{28}H_{18}ClN_3O_6$ (527.92); C, 63.70; H, 3.43; N, 7.95; Cl, 6.71; Found: C, 64.10; H, 3.50; N, 8.00; Cl, 6.90.

*2-[(3E)-3-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-5-phenyl-2-oxo-2,3-dihydro-1H-pyrrol-1-yl]-1H-isoindole-1,3(2H)-dione (***7a***).* Equimolar amount of **1a** (0.01 mol) and *N*-aminophthalimide (0.01 mol) were mixed above melting point over 2 h and then cooled to solidify. The product obtained was recrystallized from ethanol to give a redish-brown crystal 2.2 g, 46% yield, mp 123–125°C; IR (KBr pellet): 3427.8–3207.9 (broad band) for (OH), 1746.0 (bv) for (C=O), 1605.2.5 (s) for (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.85–6.96 (m, 13H, Ar-H), 7.94 (s, 2H, —C$\underline{H}$=C), 2.69 (s, 3H, —$COCH_3$). Calcd. for $C_{28}H_{17}N_3O_5$ (475.46); C, 70.73; H, 3.60; N, 8.83; Found: C, 70.50; H, 3.30; N, 8.50.

*2-({2-[(3E)-2-(1-Acetyl-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-4-(4-methylphenyl)-4-oxobutanoyl]-hydrzino}-carbonyl-N-benzyl-benzamide (***8b***).* To a suspension of **6b** (0.01 mol) in (10 ml) ethanol, benzylamine (0.01 mol) was added with stirring at room temperature for 24 h. The yellowish solid precipitate was collected by filteration and recrystallized from ethanol to give yellow crystal 3.81 g, 62% yield, mp >300°C; IR (KBr pellet): 3420.6 (br.), (NH), 3173.7, 3103.9 (—NH—NH—), 1718.7 (v) for (C=O), 1668.5 (v) for (C=O) cm^{-1}; LRMS (EI): *m/z* 304 [($M^+ - 310$), 8.8], 303 (35.23), 275 (21.31), 247 (5.9), 232 (9.11), 323 (11.5), 156 (15), 127 (10), 110 (24), 101 (26.2), 92 (10), 91 (100), 90 (24), 89 (37), 65 (35.94); GC: $t_R = 8.006$ min; column: DB-5 6 m × 0.01 mm + 1 m guard column: temp. prog: 50°C/2 min/20°C/1 min/250°C/10 min): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 11.77–11.73 (bs, 2H, —NHNH—), 9.55 (s, 1H, CO$\underline{NH}$), 8.80–6.96 (m, 13H, Ar-H), 8.75 (d, 2H, $J = 7.8$ Hz, CH_3—$C_6\underline{H}_4$-(2)), 8.53 (d, 2H, $J = 7.8$ Hz, CH_3—$C_6\underline{H}_4$-(3), 5.94 (s, 2H, —$C\underline{H}_2$), 4.21 (s, 2H, —$C\underline{H}_2$), 2.51 (s, 3H, —$COCH_3$), 1.65 (s, 3H, —CH_3). Calcd. for $C_{36}H_{30}N_4O_6$ (614.66): C, 70.34; H, 4.91; N, 9.11; Found: C, 69.90; H, 4.60; N, 9.00.

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