Chemoselectivity of 2-Arylmethyleneaminoisoindolin-1,3-diones toward Arenes under Friedel–Crafts Conditions: An Efficient Synthesis of Benzophenones Integrated with 2-Substituted Hydrazone Moieties

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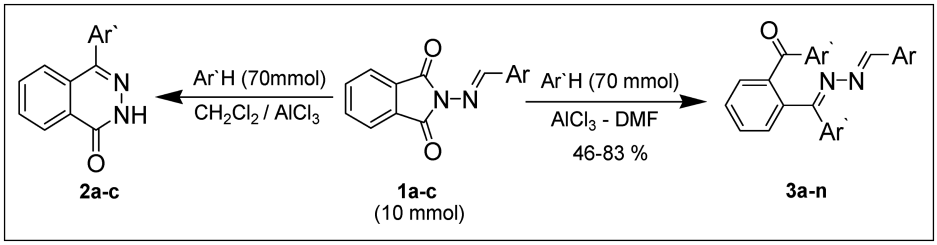

Treatment 2-arylmethyleneaminoisoindole-1,3-diones **1a–c** with arenes in the presence of $AlCl_3$-DMF complex as a catalyst afforded the novel compounds, 2-((arylidenehydrazono)(aryl)-methyl)benzophenones **3a–n** in satisfactory yields. The structure of the obtained products **3a–n** was confirmed by the use of IR, ^{1}H-NMR, ^{13}C-NMR, mass spectra, and elemental analyses.

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INTRODUCTION

Benzophenones, in particular, nitrogen-containing analogs constitute the core structure of many relevant biologically active compounds because of their diverse pharmaceutical activities, namely, antioxidant, cytotoxic, analgesic, and anti-inflammatory activities. For examples, *N*-ethylpiperidine and -morpholine moieties integrated with benzophenone framework verified their anti-inflammatory activities, while the benzophenone analog, 6-benzoylbenzothiazolone, proved its potent analgesic properties [1–3]. Further, a series of nitrogen-containing benzophenone analogs showed inhibition of TNF-alpha and IL-6 with significant antioxidant activities [4]. Recently, it has been revealed that introduction of amino groups at the C-2 or C-3 of 4-methoxybenzophenones plays an integral role for increased growth inhibition of tubulin polymerization and for maximal cytotoxicity. Morever, similar benzophenone structures with an amino group positioned at C-2 have shown antivascular effects, as well as 4-aminobenzophenones were found to be potent and selective p38 MAP kinase inhibitors [5–9]. Azines have achieved a great significance in organic synthesis, synthetic transformation, and they constitute an important class of compounds with unexpected biological activity [10–15]. Conventionally, Friedel–Crafts acylation of aromatics for the preparation of benzophenone have received more attention [16–22]. Application of this protocol on activated nitrogen heterocycles involving 2-indolinone, benzoxazolones, and benzothiazolones provided a library of unsymmetrical benzophenones [23–28]. Earlier work adopting Lewis acid-catalyzed reaction of 2-arylmethyleneaminoisoindol-1,3-diones **1** with arenes, revealed that no benzophenones were produced; however, ready transformation into 4-arylphthalazinones has occurred *via* a pathway that was believed to involve the formation of transient benzophenone structure intermediates followed by subsequent cyclization with elimination of the aldehyde moiety [29,30]. Herein, this work presents an efficient methodology for the synthesis of the novel anticipated biologically active benzophenones **3a–n**, integrated with 2-substituted hydrazone segment possessing an azomethine —N=CH proton, recently used for the development of new drugs [31], *via* the aforementioned reaction type on the heterocyclic substrates **1a–c**.

RESULTS AND DISCUSSION

The substrates, 2-arylmethyleneaminoisoindolin-1,3-diones **1a–c**, were quantitatively prepared following the reported methodologies involving that reported earlier by the author. The structure of **1** was confirmed by analogy with literature mp measurements and spectral data [29,32].

In connection to the aforementioned Lewis acid-catalyzed reactions of 2-indolinone with benzoyl chloride or its isomeric derivative, 2-arylideneaminoisoindolinones with arenes that afforded various products involving alternative utilities of both heterocycles, this work aims at reinvestigating chemoselectivity of the heterocyclic substrate **1**

toward arenes under Friedel–Crafts conditions in the hope to synthesize benzophenones **3**. Herein, compound **1** suspended in CH_2Cl_2 was treated with 7 equiv of benzene, toluene, and *m*-xylene in the presence of catalytic amounts of anhydrous $AlCl_3$, and the reaction was refluxed from 4–6 h (monitored by TLC). Examination of the yielded products by the aid of TLC, melting points, and mixed melting points revealed that no benzophenones were provided; however, 4-arylphthalazinones **2** were produced whose structure was compatible with the literature compounds formed by the use of excess arenes (coreactant and cosolvent) [29,33]. Accordingly, the reaction was repeated by performing under alternative conditions. Herein, 7 equiv of the coreactant arene–namely, benzene, toluene, m-xylene, anisole, and bromobenzene–were submitted to react at room temperature with a stirred solution mixture of the substrate **1** (10 mmol) dissolved in DMF (5.2 mL, 70 mmol) in the presence of anhydrous $AlCl_3$ (300–500 mmol). Whenever a reddish brown paste was formed, the reaction mixture was heated under reflux on an oil-bath over time, 2–6 h. (The reaction was monitored by TLC). After the reaction was completed, the obtained products have been carefully investigated by the aid of TLC, mp, mmp, and spectral data. Interestingly, it was found that a smooth reaction proceeded via two Friedel-Crafts C—C bond formations *in situ* to provide sufficient yields of the novel products which were identified as 2-((arylidenehydrazono)(aryl)methyl)benzophenones **3a–n** (Scheme 1). It was evident that under the reaction conditions the heterocycle **1** behaved efficiently as a bidentate substrate that reacted with two molecules of arenes to incorporate two aryl moieties. The reaction route was believed to involve initial acylation type, followed by a subsequent arylation type *in situ* of the electrophile, azomethine C=N group formed with progress of the reaction under the effect of the employed catalyst which finally led to the formation of the desired benzophenone derivatives **3a–n**. Obviously, this reaction route was alternative to the aforementioned reaction pathway which has been described to involve acylation of one molecule of arene followed by cyclization to give the phthalazinones **2** [29,33].

To accomplish the reaction in sufficient yields and to achieve the optimal catalytic efficiency, it was necessary to modify the molar ratio of the catalyst $AlCl_3$-DMF (Table 1). Thus, the formation of **3b**, **3c**, **3g**, and **3m** required the use of a 4:1 molar ratio that was increased up to 7:1 to yield **3e**, **3j**, and **3n**. The structure of the obtained products was inferred from a study of their spectroscopic data. Herein, the IR spectra showed the carbonyl absorption frequency of aromatic ketones at 1684–1672 cm^{-1}, in addition to the absorption bands exhibited at 1657–1621 cm^{-1} due to the azomethine C=N functionalities. Further compelling evidences for establishment of the assigned structure were received from the ^{1}H-NMR spectra. Accordingly, they revealed a singlet peak in the more downfield region at δ 10.08–8.36 ppm due to azomethine proton HC=N, as well as the signals appeared at the upfield region attributable to absorptions of aromatic CH_3 and —OCH_3 group protons. For example, the structure of **3c** was based on the three singlets revealed at δ 2.39 (6H, $2CH_3$), 2.31 (3H, CH_3), and 2.17 (3H, CH3) ppm stand to the four aromatic CH_3 protons centered at 2- and 4-positions of the incorporated aromatic rings. However, the structure of **3i** was inferred from the two singlets displayed at δ 3.78 and 3.69 ppm due to the 4-substituted —OCH_3 protons. In addition, the EI-MS showed *m/z* (%) 408 (12.46) and 303 (100) stand to (M^+-CH_2O) and the base peak (M^+-$C_6H_5CO^+$,-CH_2O), respectively. In turn, the EI-MS of **3k** showed the base peak at *m/z* (%) 285 (100) due to (M^+-C_4H_3CNS).

It was believed that the incorporation of the two aryl moieties has occurred *via* ring cleavage of *N*-acylhydrazonium ion **4** generated under the effect of Lewis acid catalyst, followed by the subsequent intermolecular Friedel–Crafts acyalkylation reaction types *in situ* (Scheme 2).

In can be concluded that the synthesis of benzophenones **2** with hydrazone moiety contained at 2-position has been efficiently achieved by the treatment of 2-arylmethyleneaminoisoindolin-1,3-diones **1** with arenes in the presence of $AlCl_3$-DMF complex as a catalyst. Interestingly, this reaction reports the first utility of the heterocycle **1** as acylating agent to produce the novel benzophenones **3a**–**n**.

Scheme 1

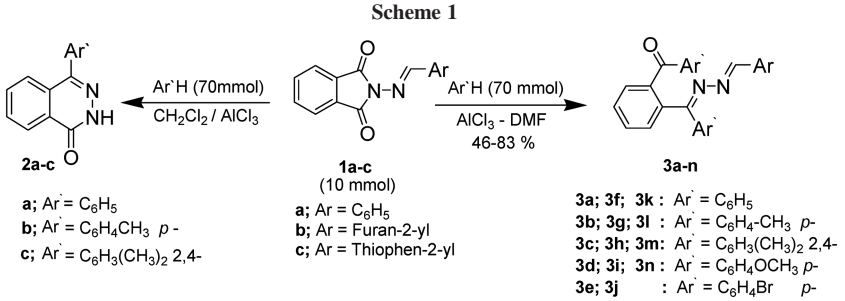
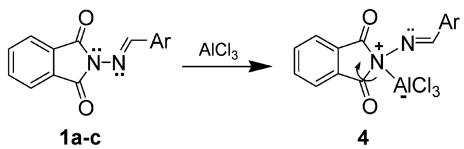


Table 1

Synthesis of 2-((arylidenehydrazono)(aryl)methyl)benzophenones **3a–n**.

Entry	Product	Yield	Time	$AlCl_3$ (g,mmol)	Ar	Ar′
1	**3a**	71	3.5	50g, 370	C_6H_5	C_6H_5
2	**3b**	83	3.5	40g, 300	C_6H_5	$C_6H_4CH_3$ *p*-
3	**3c**	64	3	40g, 300	C_6H_5	$C_6H_3(CH_3)_2$ 2,4
4	**3d**	61	6	36g, 474	C_6H_5	$C_6H_4OCH_3$ *p*-
5	**3e**	47	4.5	67g, 504	C_6H_5	C_6H_4 Br *p*-
6	**3f**	68	5	45g, 338	Furan-2-yl	C_6H_5
7	**3g**	53	3.5	42g, 316	Furan-2-yl	C_6H_4 CH_3 *p*-
8	**3h**	59	6	49g, 370	Furan-2-yl	C_6H_3 $(CH_3)_2$ 2,4-
9	**3i**	62	4	56g, 420	Furan-2-yl	$C_6H_4OCH_3$*p*-
10	**3j**	41	5	70g, 526	Furan-2-yl	C_6H_4 Br *p*-
11	**3k**	74	5	53g, 400	Thiophen-2-yl	C_6H_5
12	**3l**	66	3.5	56g, 420	Thiophen-2-yl	C_6H_4 CH_3 *p*-
13	**3m**	58	3.5	42g, 316	Thiophen-2-yl	C_6H_3 $(CH_3)_2$ 2,4-
14	**3n**	46	4	66g, 500	Thiophen-2-yl	C_6H_4 OCH_3*p*-

Scheme 2



1a-c **4**

EXPERIMENTAL

All melting points were taken on a Gallen Kamp electric melting point apparatus. IR spectra were recorded in KBr and were determined on a Perkin Elmer 2000 FTIR system. NMR spectra were determined on a Varian Gemini 300 MHz for ^{1}H-NMR and 50 MHz for ^{13}C-NMR, in $CDCl_3$ or DMSO-d_6 as a solvent and TMS as internal standard; chemical shifts are reported in δ (ppm). Mass spectra were measured on VG Autospec QMS 30 and MS 9 (AEI) spectrometers with EI 70 eV. TLC was performed using TLC aluminium sheets silica gel F_{254} (Merck). Elemental analyses were performed using a Perkin Elmer 2400 CHN Elemental Analyzer. Compounds **1a–c** were prepared following the reported methodologies [29,32].

2-Benzylideneaminoisoindole-1,3-dione (1a). Pale yellow crystals (EtOH), m.p. 161–163°C (lit.[32] 163–165°C). IR (KBr, ν cm^{-1}): 1783 ($CO_{5\text{-memb.}}$), 1716 ($CO_{5\text{-memb.}}$), 1623 (C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): δ 9.38 (s, 1 H, N=CH), 7.90 (m, 4H, ArH), 7.76 (m, 2 H, ArH), 7.45 (m, 3 H, ArH). Anal. Calcd. C_{15} H_{10} N_2 O_2 (250.26): C, 71.99, H 4.03, N 11.19. Found: C, 72.13, H, 3.86, N, 11.45.

2-(Furan-2-yl)methyleneamino-isoindole-1,3-dione (1b). Yellow crystals (EtOH), m.p. 160–1°C (lit.[29] 164–5°C), Yield (57%). IR (KBr, ν cm^{-1}): 1785($CO_{5\text{-memb.}}$), 1720 ($CO_{5\text{-memb.}}$), 1612 (C=N). ^{1}H-NMR ($CDCl_3$, δ ppm) 9.44 (s, 1H, HC=N), 7.81 (d, J = 1.8 Hz, 1H, H-$5_{fur.}$), 7.53 (m, 2H, ArH), 7.42 (d, J = 3.6 Hz, 1H, H-$3_{fur.}$), 7.38 (m, 2H, ArH), 6.84 (dd, J = 2.3, 1.2 Hz, 1H, H-$4_{fur.}$). EI-MS: *m/z* (%); 240 (19.7), 147 (35.6), 105 (100). Anal. Calcd. $C_{13}H_8N_2O_3$ (240.21): C,64.99; H,3.53; N,11.66. Found: C, 64.73; H, 3.40; N, 11.70.

2-(Thiophen-2-yl)methyleneamino-isoindole-1,3-dione (1c). Yellow crystals (EtOH), mp.156–70°C (lit.[32] 159–161°C), Yield (63%). IR (KBr, ν cm^{-1}): 1782($CO_{5\text{-memb.}}$), 1723 ($CO_{5\text{-memb.}}$), 1627 (C=N). ^{1}H-NMR ($CDCl_3$, δ ppm) 9.50 (s,1H, HC=N), 7.89 (dd, J = 3.8, 4.9 Hz, $2H_{thio}$), 7.76 (m, 2H, ArH) 7.51(dd, J = 8.2 Hz, 2H, ArH), 7.11 (dd, J = 4.6, 3.4 Hz, 1H, H-4_{thio}). EI-Ms: *m/z* (%); 258 (1.11, M+2), 256(23.1, M^+), 147 (9.4), 105(100), 104 (56.3). Anal. Calcd. $C_{13}H_8N_2O_2S$ (256.28): C,60.92; H,3.14; N, 10.93; S,12.51. Found: C, 60.61; H, 3.45; N, 10.61; S, 12.23.

Reaction of 2-(arylmethyleneamino)isoindole-1,3-diones (1a–c) with arenes in CH_2Cl_2 in presence of anhydrous $AlCl_3$: Synthesis of 4-arylphthalazinones 2a–c.

General procedure. Anhydrous aluminium chloride (3.33 g, 25 mmol) was added portionwise at room temperature to a stirred solution of arene (70 mmol) and CH_2Cl_2 (20 mL). 2-Arylmethylene amino-isoindole-1,3-diones (10 mmol) were added to the solution mixture with continuous stirring and heated on water bath at the refluxing temperature for 4 h. After completion of the reaction (monitored by TLC), it was cooled and then hydrolyzed by the addition of ice-concentrated HCl (30 mL). The resulting mixture was distilled, and the excess solvent was removed under reduced pressure. The solid product obtained was fitered off and crystsllized from benzene to afford the corresponding 4-arylphthalazin-1-ones **2a–c** whose structure was in accordance with the literature [29,33].

Reaction of 2-arylmethyleneaminoisoindole-1,3-diones (1a–c) with arenes in the presence of $AlCl_3$-DMF complex: Synthesis of 2-(((arylidene)hydrazono)(aryl)-methyl) benzophenones 3a–n.

General Procedure. Anhydrous $AlCl_3$ (40–66.6 g; 300–500 mmol) was added portionwise to the substrate **1a–c** (10 mmol; **1a**, 2.5 g; **1b**, 2.4 g; **1c**, 2.6 g) in DMF (5.2 mL, 70 mmol) with stirring at room temperature, and arene (70 mmol) was added in one portion to the solution mixture with continuous stirring and during the addition a reddish brown paste was formed. Then, the reaction mixture was heated on an oil-bath at 60°C for 2–6 h (the reaction was monitored by TLC). The reaction mixture was hydrolyzed by the addition of ice-concentrated HCl (30 mL). The organic layer was separated and neutralized with 10% aqueous $NaHCO_3$ solution and then washed with water (3 × 30 mL). The organic product was extracted with ethyl acetate, dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography using ethyl acetate and hexane (1:10) as an eluent to yield the products **3a–n** in 57–73% yields. The volumes of the used arenes (50 mmol) were as follows: benzene

(4.4 mL), toluene (5.3 mL), *m*-xylene (5.9 mL), anisole (5.4 mL), and bromobenzene (5.3 mL).

2-((Benzylidenehydrazono)(phenyl)methyl)benzophenone (3a). Bright yellow crystals, mp 194–6°C. IR (KBr, υ cm^{-1}): 1681 (C=O); 1632 (C=N), 1624 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm) 8.72(s,1H, HC=N), 7.83–7.41(m, 8H, ArHs), 7.37–6.84 (m, 9H, ArHs), 6.68 (m, 2H, ArHs). ^{13}C-NMR (DMSO-d_6, δ ppm): 195.3 (C=O); 166.1 (C=N); 153.4 (C=N); 133.6; 132.2; 130.5; 129.2; 128.4. Anal. Calcd. $C_{27}H_{20}N_2O$ (388.44): C, 83.49; H, 5.18; N, 7.21. Found: C, 83.73; H, 4.96; N, 7.43.

2-(((Benzylidenehydrazono)(p-tolyl)methyl)-4-methyl)benzophenone (3b). Bright yellow crystals, mp 212–3°C. IR (KBr, υ cm^{-1}): 1679 (C=O); 1638 (C=N), 1628 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 9.14 (s,1H, HC=N), 8.07–7.64 (m, 5H, ArHs), 7.31 (dd, *J* = 8.6, 2.1 Hz, 2H, ArH), 7.14–6.82 (m, 8 H, ArHs), 6.88 (m, 2H, ArHs), 2.41 (s,3H, CH_3), 2.27(s,3H, CH_3). Anal. Calcd. $C_{29}H_{24}N_2O$ (416.49): C, 83.63; H, 5.80; N, 6.72. Found: C, 83.47; H, 5.91; N, 6.43.

2-(((Benzylidenehydrazono)(2,4-dimethylphenyl)methyl)-4, 6-dimethyl)benzophenone (3c). Bright yellow crystals, mp 177–8°C. IR (KBr, υ cm^{-1}): 1676 (C=O); 1637 (C=N), 1621 (C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): 8.36 (s,1H, HC=N), 7.85–7.44 (m, 7H, ArHs), 7.73 (s,1H, ArHs), 7.54–7.03 (m, 6H, ArHs), 6.88 (m,1H, ArHs), 2.39 2.39 (s, 6H, $2CH_3$), 2.31 (s,3H, CH_3), 2.17 (s,3H, CH_3). Anal. Calcd. $C_{31}H_{28}N_2O$ (444.54): C, 83.76; H, 6.34; N, 6.30. Found: C, 83.55; H, 6.47; N, 6.51.

2-(((Benzylidenehydrazono)(p-methoxyphenyl)methyl)-4-methoxy)benzophenone (3d). Orange crystals, mp 224–6°C. IR (KBr, υ cm^{-1}): 1681 (C=O); 1633 (C=N), 1625 (C=N).^{1}H-NMR (DMSO-d_6, δ ppm): 8.64 (s,1H, HC=N), 7.87–7.65 (m, 8H, ArHs), 7.42–6.82 (m, 4H, ArHs), 7.31 (dd, *J* = 7.8, 2.3 Hz, 1H, ArH), 6.68–6.51 (m, 4H, ArHs), 3.78 (s,3H, OCH_3), 3.70 (s,3H, OCH_3). Anal. Calcd. $C_{29}H_{24}N_2O_3$ (448.54): C, 77.65; H, 5.39; N, 6.24. Found: C, 77.81; H, 5.53; N, 6.07.

2-(((Benzylidenehydrazono)(p-bromophenyl)methyl)-4-bromo) benzophenone (3e). Pale yellow crystals, mp 189–191°C. IR (KBr, υ cm^{-1}): 1684 (C=O); 1657 (C=N), 1629 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 8.41 (s,1H, HC=N), 8.18–7.66 (m, 5H, ArHs), 7.43 (m, 2H,ArH), 7.32–7.06 (m, 8H, ArHs), 6.72–6.64 (m, 2H, ArHs). Anal. Calcd. $C_{27}H_{18}N_2OBr_2$ (546.23): C, 59.37; H, 3.32; N, 5.13; Br, 29.25. Found: C, 59.53; H, 3.42; N, 5.12; Br, 29.58.

2-((2-Furfurylidenehydrazono)(phenyl)methyl)benzophenone (3f). Bright yellow crystals, mp 194–6°C. IR (KBr, υ cm^{-1}): 1674 (C=O); 1639(C=N), 1628 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 9.63 (s, 1H, HC=N), 7.86–7.7 (m, 8H), 7.66 (d, *J* = 3.2 Hz, $2H_{fur}$, H-3, H-5), 7.31 (s, 2H, ArH), 7.14 (d, *J* = 1.8 Hz, $1H_{fur}$, H-4) ,7.06 (d, *J* = 8.6 Hz, 2H, ArH), 6.82 (t, *J* = 7.4 Hz, 2H, ArH). C-NMR (DMSO-d_6, δ ppm): 195.7 (C=O), 164.6 (C=N), 162.3 (C=N), 143.4, 142.8, 132.5, 131.1, 129.3, 127.2. EI-MS: *m/z* (%): 378 (13.25), 273 (100, M-$C_6H_5CO^+$), 181 (28.46), 105 (4.62). Anal. Calcd. $C_{25}H_{18}N_2O_2$ (378.39): C, 79.35; H, 4.79; N, 7.40. Found: C, 79.43; H, 4.86; N, 7.61.

2-(((2-Furfurylidenehydrazono)(p-tolyl)methyl)-4-methyl) benzophenone (3g). Bright yellow needles, mp143–4°C. IR (KBr, υ cm^{-1}): 1677 (C=O); 1641 (C=N), 1632 (sh, C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 9.05 (s, 1H, HC=N), 7.91 (d, *J* = 2.9 Hz, $1H_{fur}$, H-5), 7.56 (d, *J* = 3.8 Hz, $1H_{fur}$, H-3), 7.31 (m, 8H, ArH), 6.98 (m, 4H, ArH), 6.82 (dd, *J* = 2.3, 1.4 Hz, $1H_{fur}$, H-4), 2.32(s, 3H, CH3), 2.24(s, 3H, CH3). 2.32 (s, 3H, CH_3), 2.24 (s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, δ ppm): 198.1 (C=O), 165.2 (C=N), 164.7 (C=N), 150.6, 142.2, 131.3, 129.1, 114.3, 22.1, 20.7. EI-Ms: *m/z* (%): 406 (17.43), 315 (29.61), 313 (100, M-C_4H_3CNO), 295 (17.04), 105(6.08). Anal. Calcd. $C_{27}H_{22}N_2O_2$ (406.44): C, 79.79; H, 5.45; N, 6.89. Found: C, 79.66; H, 5.18; N, 7.13.

2-(((2-Furfurylidenehydrazono)(2,4-dimethyphenyl)methyl)-2,4-dimthyl)benzophenone (3h). Bright yellow needles, mp 206–7°C. IR (KBr, υ cm^{-1}): 1682 (C=O); 1641 (br, 2 C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): 9.05 (s, 1H, HC=N), 7.88 (s, 2H), 7.64 (d, *J* = 3.4 Hz, $2H_{fur}$, H-3, H-5), 7.52 (m, 6H, ArH), 7.34-7.16 (m, 2H, ArH), 6.80 (dd, *J* = 2.1, 0.8 Hz, $1H_{fur}$, H-4) 2.42 (s, 6H, $2CH_3$), 2.31(s, 3H, CH_3), 2.24 (s, 3H, CH_3). EI-Ms: *m/z* (%): 434 (6.26), 404 (45.76), 328 (100, M-$C_7H_7^+$,—CH_3), 105 (31.48), 91(73.29). Anal.Cacld. $C_{29}H_{26}N_2O_2$ (434.49): C, 80.17; H, 6.02; N, 6.45. Found: C, 80.35; H, 5.87; N, 6.26.

2-(((2-Furfurylidenehydrazono)(4-methoxyphenyl)methyl)-4-methoxy)benzophenone (3i). Yellow powder, mp 238–9°C. IR (KBr, υ cm^{-1}): 1676 (C=O); 1637 (C=N), 1626 (C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): 9.26 (s, 1H, HC=N), 7.94 (s, 4H), 7.82 (m, 6H), 7.69 (d, *J* = 8.2 Hz, 2H, ArH), 7.53 (d, *J* = 3.1 Hz, $2H_{fur}$), 7.36 (t, *J* = 7.6 Hz, 1H, ArH), 3.78 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3). EI-MS: *m/z* (%): 408 (12.46, M-CH_2O), 407 (27.09, M-CH_3O), 303 (100, M-$C_6H_5CO^+$, —CH_2O), 239 (60.21), 105(27.04). Anal. Cacld. $C_{27}H_{22}N_2$-O_4 (438.42): C, 73.97; H, 5.05; N, 6.39. Found: C, 74.35; H, 4.87; N, 6.56.

2-(((2-Furfurylienehydrazono)(4-bromophenyl)methyl)-4-bromo)benzophenone (3j). Bright yellow crystals, mp 153–5°C. IR (KBr, υ cm^{-1}): 1683 (C=O); 1634 (br, 2C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): 8.66 (s, 1H, HC=N), 8.24 (d, *J* = 8.6 Hz, 1H, ArH), 7.92 (s, 3H), 7.79-7.53 (m, 6H, ArH), 7.41 (d, *J* = 2.9 Hz, $2H_{fur}$), 7.32 (s, 3H). EI-MS: *m/z* (%): 534 (14.66), 536 (29.30), 538 (14.64), 184(100), 105(37.52). Anal.Cacld.$C_{25}H_{16}N_2O_2Br_2$ (536.18): C, 56.0; H, 3.0; N, 5.22; Br, 29.80. Found: C, 55.76; H, 3.18.; N, 4.93; Br, 30.05

2-(((2-Thienylidene)hydrazono)(phenyl)methyl)benzophenone (3k). Bright yellow crystals, mp 227–9°C. IR (KBr, υ cm^{-1}): 1678 (C=O); 1638 (C=N), 1622 (sh, C=N). ^{1}H-NMR ($CDCl_3$ δ ppm): 10.08 (s, 1H, HC=N), 7.90 (d, J = 7.8 Hz, 1H, ArH), 7.56 (d, J = 3.4 Hz,1Hfur, H-5), 7.54-7.49 (m, 3H), 7.46 (d, *J* = 7.5 Hz,1H, ArH), 7.37 (d, *J* = 2.9 Hz,$1H_{fur}$, H-3), 7.26 (m, 8H, ArH), 7.05 (d, *J* = 1.4 Hz,$1H_{fur}$, H-4), 6.99 (s,1H). EI-MS: *m/z* (%): 396 (4.06), 394 (67.63), 285 (100, M^+-C_4H_3CNS), 286 (24.84), 208 (60.07), 165 (26.46), 77 (19.83). Anal. Calcd. $C_{25}H_{18}N_2OS$ (394. 47): C, 76.12; H, 4.59; N, 7.10, S, 8.13. Found: C, 76.24; H, 4.37; N, 7.26, S, 8.27.

2-(((2-Thienylidenehydrazono)(p-tolyl)methyl)-4-methyl) benzophenone (3l). Brownish yellow crystals, mp 209–10°C. IR (KBr, υ cm^{-1}): 1679 (C=O); 1655 (br, 2C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): 9.27 (s, 1H, HC=N), 7.83 (d, *J* = 5.3 Hz, $1H_{thio}$), 7.54 (m, 5H, ArH), 7.38 (d, *J* = 7.8 Hz, 2H, ArH), 7.30 (m, 4H, ArH), 6.93 (d, *J* = 4.4 Hz, $2H_{thio}$), 6.57 (t, *J* = 7.8 Hz, 1H, ArH), 2.39(s, 3H, CH_3), 2.32(s, 3H, CH_3). ^{13}C-NMR ($CDCl_3$, δ ppm): 197.6 (C=O), 163.8 (C=N), 137.9 (C=N, 131.4, 128.7, 22.4 (CH_3), 21.8 (CH_3). EI-MS: *m/z* (%): 331(100, M-$C_7H_7^+$), 313 (13.65, M-C_4H_3CNS), 297 (44.71), 119 (32.09), 91(74.31). Anal. Cacld. $C_{27}H_{22}N_2OS$ (422.52): C, 76.75; H, 5.24; N, 6.63; S, 7.59. Found: C, 77.03; H, 4.87; N, 6.74; S, 7.38.

2-(((2-Thienylidenehydrazono)(2,4-dimethyphenyl)methyl)-2,4-dimethyl)benzophenone (3m). Brownish yellow powder, mp 174–5°C. IR (KBr, υ cm^{-1}): 1682 (C=O); 1657 (C=N) ,1633 (sh, C=N). ^{1}H-NMR ($CDCl_3$, δ ppm): 9.40 (s, 1H, HC=N), 7.61 (d, *J* = 5.2 Hz,$1H_{thio}$), 7.54 (d, *J* = 8.2 Hz, 1H,

ArH), 7.58 (d, J = 4.8 Hz, $2H_{thio}$), 7.30−7.06 (m, 8H, ArH), 6.92 (t, J = 7.4 Hz, 1H), 2.41 (s, 3H, CH_3), 2.33 (s, 6H, $2CH_3$), 2.27 (s, 3H, CH_3). ^{13}C-NMR (DMSO-d_6, δ ppm): 196.5 (C=O), 162.8 (C=N), 139.1 (C=N), 131.3, 22.3 (CH_3), 21.8 (CH_3). EI-MS: *m/z* (%): 452 (2.82), 450 (56.34), 345 (100, M-$C_7H_7^+$,—CH_3), 341(28.02), 317 (36.70), 91(37.82). Anal. Cacld. $C_{29}H_{26}N_2OS$ (450.57): C, 77.31; H, 5.81; N, 6.22; S, 7.12. Found: C, 77.23.; H, 6.07; N, 6.34; S, 6.89.

2-(((2-Thienylidenehydrazono)(4-methoxyphenyl)methyl)-4-methoxy)benzophenone (3n). Yellow powder, mp 226–8°C. IR (KBr, υ cm^{-1}): 1682 (C=O); 1637 (C=N), 1631 (C=N). ^{1}H-NMR (DMSO-d_6, δ ppm): 9.08 (s, 1H, HC=N), 8.24 (d, J = 8.2 Hz, 1H), 7.63 (m, 3H), 7.53 (m, 6H), 7.41 (d, J = 4.8 Hz, $2H_{thio}$), 7.32 (t, 2H), 6.85 (d, J = 5.5 Hz, $1H_{thio}$), 3.78 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3). EI-MS: *m/z* (%): 424 (24.83, M-CH_2O), 423 (54.16, M-OCH_3), 345 (100, M-C_4H_3CNS), 319(12.70), 299(22.69), 105(35.68). Anal.Cacld. $C_{27}H_{22}N_2O_3S$ (454.50): C, 71.35; H, 4.87; N, 6.16; S, 7.05. Found: C, 71.18; H, 4.94; N, 6.33; S, 7.28.

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