

Synthesis of Some Novel Pyrazole-Substituted 9-Anilinoacridine Derivatives and Evaluation for their Antioxidant and Cytotoxic Activities

R. Kalirajan,* V. Muralidharan, S. Jubie, B. Gowramma, S. Gomathy, S. Sankar, and K. Elango

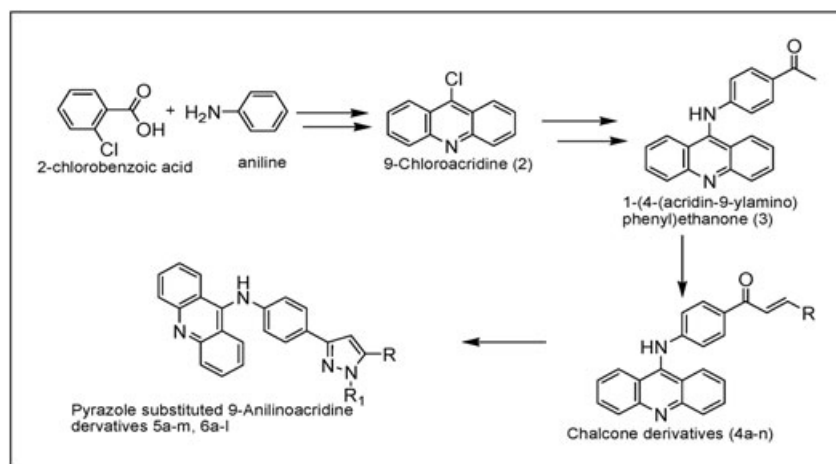
Department of Pharmaceutical Chemistry, JSS College of Pharmacy (Off Campus, JSS University, Mysore) Ootacamund, Tamilnadu 643001, India

*E-mail: rkalirajan@ymail.com or rkalirajan@jsscpcoty.org

Received September 9, 2010

DOI 10.1002/jhet.848

Published online 00 March 2012 in Wiley Online Library (wileyonlinelibrary.com).



This article focuses on the synthesis of new series of pyrazole-substituted 9-anilinoacridine derivatives **5a–m** and **6a–l**. The compounds were confirmed by physical and analytical data. The synthesized compounds when screened for *in vitro* antioxidant activity showed promising activity for many compounds. The selected compounds were screened for cytotoxic activity showed promising inhibition of HEP-2 cell line for the compounds **6c**, **6e**, and **6f**.

J. Heterocyclic Chem., **00**, 00 (2012).

INTRODUCTION

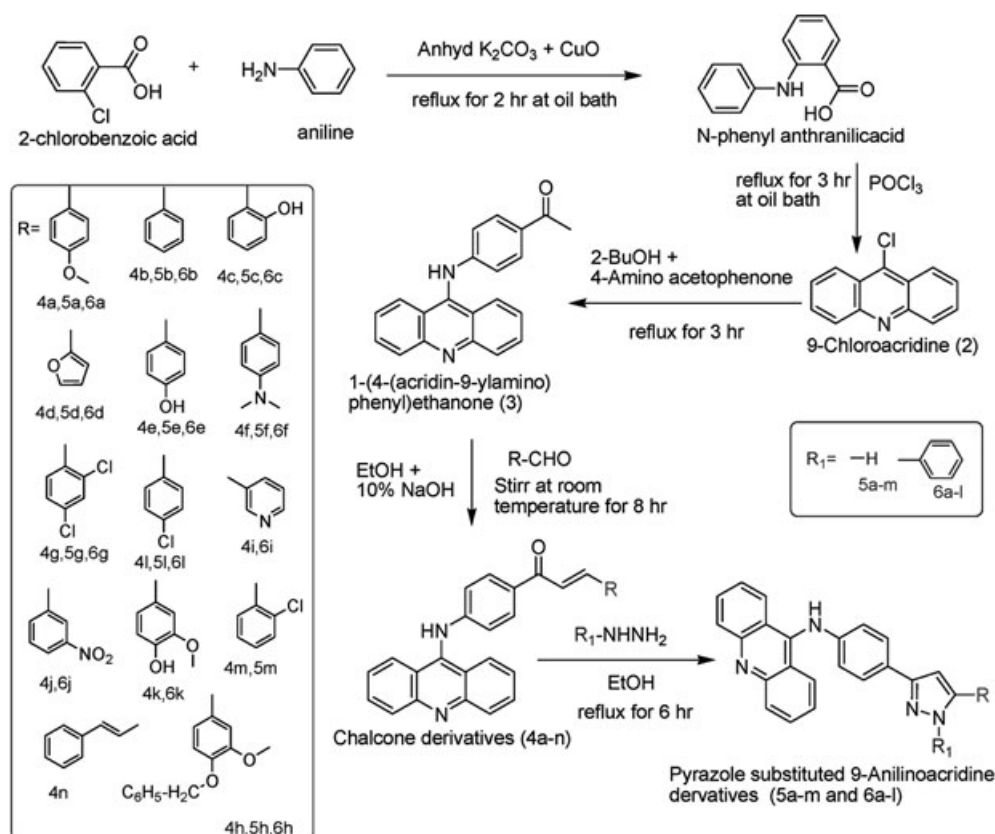
Acridine derivatives are used in medicine and have enormous potential as pharmaceutical agents due to their biological activities such as antimicrobial [1], antioxidant [2], anticancer [3], antimalarial [4], anti-inflammatory [5], analgesic [6], antileishmanial [7], and antinociceptive [8], acetyl cholinesterase inhibitors [9], and antiherpes [10]. The chemical modification of 9-anilinoacridines such as the introduction of different substitutions or heteroatoms has allowed expansion of research on the structure–activity relationship to afford new insight into molecular interactions at the receptor level [11]. In fact, it is well established that slight structural modification on 9-anilinoacridine ring may bring various pharmacological effects [12–18]. To look for some new compounds with interesting biological properties, we have synthesized some novel pyrazole-substituted 9-anilinoacridine derivatives.

RESULTS AND DISCUSSION

In this study, the title compounds **5a–m** and **6a–l** were prepared according to the procedure outlined in Scheme 1. 9-Chloroacridine (**2**) was substituted with 4-aminoacetophenone gave 1-[4-(acridin-9-ylamino)phenyl]ethanone (**3**). The compound **3** was then reacted with corresponding aromatic aldehydes (Ar-CHO) in the presence of NaOH in ethanol at room temperature gave chalcones **4a–n** (yield more than 60%). Cyclization of **4a–n** with hydrazines (R-NH-NH₂) in the presence of absolute ethanol at reflux temperature afforded pyrazole-substituted 9-anilinoacridines **5a–m** and **6a–l** in good yields.

The chemical structure of the synthesized compounds was elucidated by IR, ¹H NMR, ¹³C NMR, and MS spectral data. According to the IR spectral data, **4a–n** showed the C=O peaks at 1600–1700 cm^{−1} region, which are disappeared for compounds **5a–m** and **6a–l**. The NH bands

Scheme 1



of **5a–m** were observed in the region 3300–3400 cm^{-1} . In the ^1H NMR spectra of **5a–m**, the -NH proton of pyrazole ring was observed as a broad singlet at about 13.00–13.85 ppm. But in **6a–l**, it was not appeared because of phenyl substitution. All other aromatic and aliphatic protons of the compounds were observed at the expected regions. ^{13}C NMR of the compounds gave prominent signals, which provide further evidence for their structures. Mass spectra of all the synthesized compounds showed $\text{M}^+/\text{M}^+ + 1$ peaks in agreement with their molecular formulae.

The *in vitro* antioxidant activity of the newly synthesized compounds **4a–n**, **5a–m**, and **6a–l** was evaluated by DPPH assay in accordance with the previously described experimental procedures [19]. The results, expressed as IC_{50} values are reported in Table 1, suggested that all compounds showed antioxidant activity but **5a, b, d, e, f, g, l, m** and **6a, b, c, d, e, f, i, j** have potent antioxidant activity. The compounds with potent antioxidant activity were screened for their *in vitro* cytotoxicity.

The *in vitro* cytotoxicity of **5e, 5f, 5g, 5l, 5m, 6a, 6c, 6e, 6f**, and **6i** was evaluated by sulforhodamine-B (SRB) assay on a human tumor cell lines, HEP-2 (laryngeal epithelial carcinoma) in accordance with the previously described

experimental procedures [20]. The results, expressed as CTC_{50} values are reported in Table 2, suggested that all compounds showed a detectable cytotoxic activity but compounds **6e** and **6f** are highly potent.

In conclusion, a series of novel pyrazole-substituted 9-anilinoacridines have been designed and synthesized. The antioxidant and cytotoxic activities of the synthesized compounds were evaluated. Among these compounds, **6e** and **6f** showed good cytotoxic activity and emerged as potential molecules for further development. With this set of analogs, we are now in a position to investigate the multiple biological activities of these compounds.

EXPERIMENTAL

Melting points were determined on a Veego VMP-1 melting point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu 8400S FTIR spectrometer. ^1H NMR spectra and ^{13}C NMR on Bruker AV III 500 MHz spectrometer (500 MHz for ^1H NMR spectra and 125 MHz for ^{13}C NMR) using TMS as an internal standard and CDCl_3 as the solvent. The chemical shifts are expressed in ppm (δ). Mass spectra were obtained on JOEL GCmate mass spectrometer. Elemental analyses were determined by using Perkin–Elmer

Table 1

Antioxidant activity of synthesized compounds by DPPH method.

Compound	IC ₅₀ values ^a (μg/mL)	Compound	IC ₅₀ values ^a (μg/mL)	Compound	IC ₅₀ values ^a (μg/mL)
4a	>1000	5a	20.50 ± 1.32	6a	10.80 ± 0.51
4b	>1000	5b	19.25 ± 0.85	6b	29.00 ± 0.83
4c	>1000	5c	97.80 ± 6.39	6c	12.00 ± 0.41
4d	>1000	5d	09.62 ± 0.55	6d	30.75 ± 1.19
4e	>1000	5e	11.80 ± 0.73	6e	12.37 ± 1.28
4f	>1000	5f	14.87 ± 0.12	6f	7.15 ± 0.31
4g	>1000	5g	14.75 ± 0.77	6g	156.00 ± 1.67
4h	>1000	5h	198.00 ± 2.07	6h	107.25 ± 2.66
4i	>1000	5l	13.92 ± 0.20	6i	21.50 ± 2.32
4j	>1000	5m	7.06 ± 0.25	6j	28.50 ± 0.95
4k	>1000	—	—	6k	46.75 ± 2.01
4l	>1000	—	—	6l	83.00 ± 2.24
4m	>1000	—	—	—	—
4n	>1000	—	—	—	—
Standard ascorbic acid	2.69 ± 0.05	—	—	—	—

^aAverage of four determinations. Values in bold represent potent antioxidant activity.

240C elemental analysis instrument. Reactions were carried out and monitored by thin layer chromatography plates (5 × 20 cm) with 0.2 mm silica gel GF and the spots were viewed in UV or iodine chamber.

Procedure for the synthesis of 9-chloroacridine (2). A mixture of 1.278 g (0.006 mol) of *N*-phenylanthranilic acid and 19.781 g (0.131 mol) of phosphorous oxy chloride was taken in a 250-mL round-bottomed flask and heated slowly in a water bath at 85–90°C for 15 min. It was observed carefully that if the reaction becomes too violent, then the flask was placed in a cold water bath for a moment (boiling subsides). Then, the flask was immersed in an oil bath, temperature was raised to 135–140°C, and maintained under reflux for 3 h. After the reaction, excess of phosphorus oxy chloride was removed by the distillation from an oil bath at 140–150°C under vacuum. After cooling to room temperature, the reaction mixture was poured into a well-stirred mixture of 5.21 mL of concentrated ammonia and 13 g of crushed ice and allowed to stand for 30 min to precipitate the solid. The precipitate was filtered by suction, washed three times with

saturated sodium carbonate solution and finally with water, dried, and crystallized from ethanol. The yield of 9-chloroacridine was 73%.

Procedure for the synthesis of 1-[4-(acridin-9-ylamino)phenyl]ethanone (3). In a 250-mL round-bottomed flask, 4.06 g (0.03 mol) of 4-aminoacetophenone was refluxed with 5.453 g (0.0256 mol) of 9-chloroacridine in 80 mL of 2-butanol for 3 h. After the reaction, the reaction mixture was allowed to cool to room temperature, then it was poured into 150 mL of ice water. The precipitate formed was filtered by suction, washed with water, dried, and recrystallized from ethanol. The yield was 68%.

General procedure for the synthesis of chalcone derivatives of 9-anilinoacridine (4a–n). Twenty-five milliliters of 10% sodium hydroxide and 25 mL of ethanol were taken in a 100 mL-flat-bottomed flask with a magnetic stirring bar and was placed on the magnetic stirrer. To this solution, 0.0115 mol of corresponding aldehyde and then 2.9952 g (0.0096 mol) of 1-[4-(acridin-9-ylamino)phenyl]ethanone (3) were added. The solution was stirred at room temperature for 8 h. After the reaction, 100 mL of water was added, the precipitate was filtered, washed three times with 50 mL of water to remove excess sodium hydroxide, dried, and recrystallized from ethanol.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (4a). Yellow crystals, yield 79%, mp 179–181°C. IR (KBr, ν, cm⁻¹): 3273 (N-H), 3100–3000 (Ar C-H), 1626 (α,β-unsaturated C=O), 1607 and 1510 (Ar C=C), 1260 (C-N), 1168 (C-O), 748 (Ar C-H). ¹H NMR (CDCl₃) δ ppm: 4.01 (s, 1H, NH), 7.56 (d, 1H, CH), 7.90 (d, 1H, CH), 8.06–6.62 (m, 14H, Ar-H), 3.73 (s, 3H, OCH₃). MS (*m/z*): 431 (M + 1). Anal. Calcd for C₂₉H₂₂N₂O₂ (430): C, 80.91; H, 5.15; N, 6.51. Found: C, 80.83; H, 5.23; N, 6.44.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-phenylprop-2-en-1-one (4b). Yellow crystals, yield 78%, mp 180–182°C. IR (KBr, ν, cm⁻¹): 3269 (N-H), 3057–3000 (Ar C-H), 1647 (α,β-unsaturated C=O), 1604 and 1516 (Ar C=C), 1226 (C-N), 759 (Ar C-H). ¹H NMR (CDCl₃) δ ppm: 4.02 (s, 1H, NH), 8.06–6.62 (m, 16H, Ar-H), 7.56 (d, 1H, CH), 7.90 (d, 1H, CH).

Table 2

Cytotoxicity study of some selected compound by SRB assay.

Sl. no.	Compound	CTC ₅₀ values ^a in (μg/mL)
1	5e	90.33 ± 1.66
2	5f	60.14 ± 0.33
3	5g	125.24 ± 1.10
4	5l	115.08 ± 0.95
5	5m	50.32 ± 2.03
6	6a	>250
7	6c	40.53 ± 0.86
8	6e	34.56 ± 1.53
9	6f	35.79 ± 0.39
10	6i	62.45 ± 0.62

^aAverage of three determinations. Values in bold represent more potent.

MS (m/z): 401.1 ($M^+ + 1$). Anal. Calcd for $C_{28}H_{20}N_2O$ (400.16): C, 83.97; H, 5.04; N, 7.01. Found: C, 83.84; H, 5.12; N, 7.13.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one (4c). Yellow crystals, yield 65%, mp 209–211°C. IR (KBr, ν , cm^{-1}): 3560 (N-H), 3302 (O-H), 3100–3000 (Ar C-H), 1654 (α,β -unsaturated C=O), 1627 and 1516 (Ar C=C), 1280 (C-N), 1151 (C-O), 748 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.12 (s, 1H, NH), 5.08 (s, 1H, OH), 7.56 (d, 1H, CH), 7.90 (d, 1H, CH), 8.03–6.65 (m, 14H, Ar-H). MS (m/z): 416.2 (M^+). Anal. Calcd for $C_{28}H_{20}N_2O_2$ (416.15): C, 80.73; H, 4.85; N, 6.72. Found: C, 80.62; H, 4.91; N, 6.66.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(furan-2-yl)prop-2-en-1-one (4d). Yellow crystals, yield 66%, mp 179–181°C. IR (KBr, ν , cm^{-1}): 3300 (N-H), 3057–3034 (Ar C-H), 1651 (α,β -unsaturated C=O), 1606 and 1512 (Ar C=C), 1230 (C-N), 1176 (C-O), 759 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.04 (s, 1H, NH), 7.58 (d, 1H, CH), 7.91 (d, 1H, CH), 8.04–6.64 (m, 14H, Ar-H). MS (m/z): 391.14 ($M^+ + 1$). Anal. Calcd for $C_{26}H_{18}N_2O_2$ (390.4): C, 79.97; H, 4.64; N, 7.17. Found: C, 79.88; H, 4.53; N, 7.25.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one (4e). Yellow crystals, yield 56%, mp 208–210°C. IR (KBr, ν , cm^{-1}): 3302 (N-H), 3238 (O-H), 3059–3034 (Ar C-H), 1626 (α,β -unsaturated C=O), 1626 and 1527 (Ar C=C), 1280 (C-N), 1151 (C-O), 748 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.02 (s, 1H, NH), 5.06 (s, 1H, OH), 7.57 (d, 1H, CH), 8.02–6.62 (m, 14H, Ar-H). MS (m/z): 416.1 (M^+). Anal. Calcd for $C_{28}H_{20}N_2O_2$ (416.15): C, 80.74; H, 4.85; N, 6.75. Found: C, 80.53; H, 4.97; N, 6.64.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(4-(dimethylamino)phenyl)prop-2-en-1-one (4f). Orange crystals, yield 65%, mp 165–167°C. IR (KBr, ν , cm^{-1}): 3313 (N-H), 3099–2999 (Ar C-H), 1654 (α,β -unsaturated C=O), 1604 and 1500 (Ar C=C), 1261 (C-N), 750 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.03 (s, 1H, NH), 2.83 (s, 6H, CH_3), 7.54 (d, 1H, CH), 8.02–6.62 (m, 15H, Ar-H). MS (m/z): 444.20 ($M^+ + 1$). Anal. Calcd for $C_{30}H_{25}N_3O$ (443.5): C, 81.26; H, 5.65; N, 9.43. Found: C, 81.09; H, 5.75; N, 9.30.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(2,4-dichlorophenyl)prop-2-en-1-one (4g). Orange crystals, yield 75%, mp 228–230°C. IR (KBr, ν , cm^{-1}): 3294 (N-H), 3100–3000 (Ar C-H), 1649 (α,β -unsaturated C=O), 1606 and 1518 (Ar C=C), 1257 (C-N), 756 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.1 (s, 1H, NH), 7.34 (d, 1H, CH), 8.17 (d, 1H, CH), 8.02–6.62 (m, 14H, Ar-H). MS (m/z): 470.08 ($M^+ + 1$). Anal. Calcd for $C_{28}H_{18}Cl_2N_2O$ (469.3): C, 71.64; H, 3.89; N, 5.97. Found: C, 71.72; H, 3.77; N, 5.81.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(4-(benzyloxy)-3-methoxyphenyl)prop-2-en-1-one (4h). Orange crystals, yield 73%, mp 77–79°C. IR (KBr, ν , cm^{-1}): 3304 (N-H), 3061–3012 (Ar C-H), 1674 (α,β -unsaturated C=O), 1627 and 1506 (Ar C=C), 1265 and 1134 (C-O), 1236 (C-N), 748 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.08 (s, 1H, NH), 3.78 (s, 3H, CH_3), 5.18 (s, 2H, CH_2), 7.54 (d, 1H, CH), 7.91 (d, 1H, CH), 8.03–6.65 (m, 18H, Ar-H). MS (m/z): 537.21 ($M^+ + 1$). Anal. Calcd for $C_{36}H_{28}N_2O_3$ (536.6): C, 80.55; H, 5.25; N, 5.22. Found: C, 80.69; H, 5.35; N, 5.29.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(pyridin-3-yl)prop-2-en-1-one (4i). Orange crystals, yield 61%, mp 124–126°C.

IR (KBr, ν , cm^{-1}): 3290 (N-H), 3100–3000 (Ar C-H), 1627 (α,β -unsaturated C=O), 1577 and 1498 (Ar C=C), 1280 (C-N), 748 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 3.98 (s, 1H, NH), 7.58 (d, 1H, CH), 7.89 (d, 1H, CH), 8.1–6.63 (m, 15H, Ar-H). MS (m/z): 402.15 ($M^+ + 1$). Anal. Calcd for $C_{27}H_{19}N_3O$ (401.4): C, 80.80; H, 4.77; N, 10.48. Found: C, 80.67; H, 4.60; N, 10.28.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(3-nitrophenyl)prop-2-en-1-one (4j). Orange crystals, yield 83%, mp 188–190°C. IR (KBr, ν , cm^{-1}): 3034 (N-H), 3100–3000 (Ar C-H), 1626 (α,β -unsaturated C=O), 1577 and 1498 (Ar C=C), 1529 and 1348 (NO_2), 1280 (C-N), 748 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.08 (s, 1H, NH), 7.81 (d, 1H, CH), 8.02 (d, 1H, CH), 8.2–6.64 (m, 15H, Ar-H). MS (m/z): 445.14 (M^+). Anal. Calcd for $C_{28}H_{19}N_3O_3$ (445.5): C, 75.50; H, 4.30; N, 9.42. Found: C, 75.26; H, 4.52; N, 9.51.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(3-hydroxy-4-methoxyphenyl)prop-2-en-1-one (4k). Yellow crystals, yield 58%, mp 206–208°C. IR (KBr, ν , cm^{-1}): 3560 (N-H), 3302 (O-H), 3100–3000 (Ar C-H), 1654 (α,β -unsaturated C=O), 1599 and 1496 (Ar C=C), 1278 and 1107 (C-O), 1178 (C-N), 763 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.38 (s, 1H, NH), 3.78 (s, 3H, CH_3), 4.88 (s, 1H, OH), 7.58 (d, 1H, CH), 7.88 (d, 1H, CH), 8.2–6.66 (m, 14H, Ar-H). MS (m/z): 447.05 ($M^+ + 1$). Anal. Calcd for $C_{29}H_{22}N_2O_3$ (446.5): C, 78.11; H, 4.95; N, 6.28. Found: C, 78.22; H, 4.85; N, 6.31.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(4-chlorophenyl)prop-2-en-1-one (4l). Yellow crystals, yield 64%, mp 188–190°C. IR (KBr, ν , cm^{-1}): 3302 (N-H), 3100–3000 (Ar C-H), 1651 (α,β -unsaturated C=O), 1606 and 1518 (Ar C=C), 1267 (C-N), 748 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.14 (s, 1H, NH), 7.56 (d, 1H, CH), 7.91 (d, 1H, CH), 8.2–6.60 (m, Ar-H). MS (m/z): 435.12 (M^+). Anal. Calcd for $C_{28}H_{19}ClN_2O$ (434.2): C, 77.37; H, 4.42; N, 6.44. Found: C, 77.25; H, 4.29; Cl, 8.15; N, 6.62.

(E)-1-(4-(Acridin-9-ylamino)phenyl)-3-(2-chlorophenyl)prop-2-en-1-one (4m). Cherry red crystals, yield 62%, mp 190–192°C. IR (KBr, ν , cm^{-1}): 3279 (N-H), 3109–2999 (Ar C-H), 1647 (α,β -unsaturated C=O), 1591 and 1496 (Ar C=C), 1273 (C-N), 746 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.04 (s, 1H, NH), 8.13 (d, 1H, CH), 7.35 (d, 1H, CH), 8.1–6.65 (m, 14H, Ar-H). MS (m/z): 435.16 ($M^+ + 1$). Anal. Calcd for $C_{28}H_{19}ClN_2O$ (434.1): C, 77.35; H, 4.42; 2 N, 6.44. Found: C, 77.59; H, 4.20; N, 6.25.

(2E,4E)-1-(4-(Acridin-9-ylamino)phenyl)-5-phenylpenta-2,4-dien-1-one (4n). Yellow crystals, yield 58%, mp 218–220°C. IR (KBr, ν , cm^{-1}): 3234 (N-H), 3100–3000 (Ar C-H), 1633 (α,β -unsaturated C=O), 1600 and 1514 (Ar C=C), 1254 (C-N), 761 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.10 (s, 1H, NH), 7.23 (d, 1H, CH), 7.77 (d, 1H, CH), 8.05–6.66 (m, 16H, Ar-H). MS (m/z): 427.1 ($M^+ + 1$). Anal. Calcd for $C_{30}H_{22}N_2O$ (426.2): C, 84.50; H, 5.18; N, 6.58. Found: C, 84.72; H, 5.03; N, 6.42.

Synthesis of pyrazole-substituted 9-anilinoacridines (5a–m). A solution of 0.0025 mol of the corresponding chalcones **4a–n** in 20 mL of absolute ethanol and 0.2503 g (0.005 mol) of hydrazine hydrate (99%) were taken in a 100-mL round-bottomed flask and refluxed for 6 h. After the reaction, the solvent was removed by vacuum distillation, then the residue obtained was washed with water, dried, and recrystallized from ethanol.

***N*-(4-(5-(4-Methoxyphenyl)-1H-pyrazol-3-yl)phenyl)acridin-9-amine (5a).** Orange crystals, yield 55%, mp 97–99°C. IR (KBr, ν , cm^{-1}): 3306 (N-H), 3100–2999 (Ar C-H), 1593 and 1514 (Ar C=C), 1263 and 1151 (C-O), 1246 (C-N), 750 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.01 (s, 1H, pyrazole, NH), 4.18 (s, 1H, NH), 7.80–6.65 (m, 17H, Ar-H), 3.80 (s, 3H, OCH_3). ^{13}C NMR: 126.7, 127.45, 130.89, 126.02, 127.03, 125.75, 151.74, 117.42, 134.93, 133.42, 120.35, 132.75, 123.64, 128.27, 125.16, 121.34, 123.17, 140.21, 113.71, 135.11, 129.13, 127.51, 129.13, 159.16, 121.42, 127.51, 55.32. MS EI (m/z): 441.67 (M^+ , 20%), 426.84 (24%), 397.14 (48%), 306.88 (100%), 289.93 (60%), 263.11 (64%), 217.32 (40%), 190.44 (38%), 175.51 (50%). Anal. Calcd for $\text{C}_{29}\text{H}_{22}\text{N}_4\text{O}$: C, 78.71; H, 5.01; N, 12.66; O, 3.62. Found: C, 78.57; H, 5.23; N, 12.54.

***N*-(4-(5-Phenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (5b).** Orange crystals, yield 80%, mp 110–112°C. IR (KBr, ν , cm^{-1}): 3269 (N-H), 3100–3000 (Ar C-H), 1591 and 1489 (Ar C=C), 1263 (C-N), 754 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.05 (s, 1H, pyrazole, NH), 3.96 (s, 1H, NH), 7.80–6.65 (m, 18H, Ar-H). ^{13}C NMR: 127.59, 127.73, 130.54, 127.52, 127.46, 130.51, 127.66, 151.48, 117.36, 130.88, 130.74, 120.35, 130.65, 126.14, 128.80, 126.36, 128.84, 125.79, 142.89, 114.81, 133.45, 128.83, 128.51, 128.73, 125.16, 123.85, 128.51. MS EI (m/z): 411.59 (M^+ , 100%), 391.17 (24%), 382.40 (16%), 308.90 (30%), 291.94 (22%), 266.08 (32%), 204.06 (16%), 177.54 (12%). Anal. Calcd for $\text{C}_{28}\text{H}_{20}\text{N}_4$ (412.19): C, 81.55; H, 4.89; N, 13.59. Found: C, 81.32; H, 4.91; N, 13.541.

2-(3-(4-(Acridin-9-ylamino)phenyl)-1H-pyrazol-5-yl)phenol (5c). Yellow crystals, yield 63%, mp 203–205°C. IR (KBr, ν , cm^{-1}): 3313 (N-H), 3100–2995 (Ar C-H), 1604 and 1498 (Ar C=C), 1261 (C-N), 1147 (C-O), 750 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.11 (s, 1H, pyrazole, NH), 5.04 (s, 1H, OH), 4.09 (s, 1H, NH), 7.77–6.83 (m, 17H, Ar-H). ^{13}C NMR: 125.71, 127.07, 130.02, 125.71, 125.73, 130.08, 126.76, 124.62, 151.74, 116.65, 130.90, 130.60, 120.35, 130.62, 121.46, 128.24, 124.62, 128.22, 121.34, 147.35, 115.49, 135.11, 129.13, 159.16, 129.13, 120.36, 121.35, 128.21. MS EI (m/z): 427.52 (M^+ , 20%), 356.16 (10%), 318.84 (56%), 309.87 (100%), 294.86 (68%), 266.10 (74%), 177.50 (70%). Anal. Calcd for $\text{C}_{28}\text{H}_{20}\text{N}_4\text{O}$ (428.16): C, 78.45; H, 4.73; N, 13.08. Found: C, 78.53; H, 4.47; N, 13.23.

***N*-(4-(5-(Furan-2-yl)-1H-pyrazol-3-yl)phenyl)acridin-9-amine (5d).** Brownish orange crystals, yield 78%, mp 108–110°C. IR (KBr, ν , cm^{-1}): 3100–3000 (Ar C-H), 1591 and 1485 (Ar C=C), 1263 (C-N), 1151 (C-O), 752 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.02 (s, 1H, pyrazole, NH), 4.09 (s, 1H, NH), 7.85–6.22 (m, 16H, Ar-H). ^{13}C NMR: 125.64, 127.50, 130.41, 125.10, 125.13, 130.41, 126.99, 123.65, 152.15, 105.93, 130.68, 130.41, 110.27, 130.68, 120.35, 130.68, 121.35, 128.21, 117.25, 147.42, 105.93, 142.24, 116.60, 154.89, 129.12, 127.56, 114.71. MS EI (m/z): 399.14 ($\text{M}^+ - 3$, 100%), 387.30 (20%), 308.84 (24%), 291.91 (32%), 266.04 (28%), 177.51 (24%). Anal. Calcd for $\text{C}_{26}\text{H}_{18}\text{N}_4\text{O}$ (402.15): C, 77.57; H, 4.53; N, 13.92. Found: C, 77.50; H, 4.48; N, 13.81.

4-(3-(4-(Acridin-9-ylamino)phenyl)-1H-pyrazol-5-yl)phenol (5e). Brownish orange crystals, yield 61%, mp 152–154°C. IR (KBr, ν , cm^{-1}): 3313 (N-H), 3194 (C-O), 3100–2995 (Ar C-H), 1604 and 1523 (Ar C=C), 1276 (C-N), 1261 and 1147 (C-O), 750 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.23 (s, 1H, pyrazole, NH), 3.97 (s, 1H, NH), 5.62 (s, 1H, OH),

7.86–6.79 (m, 17H, Ar-H). ^{13}C NMR: 125.71, 127.07, 130.02, 124.62, 124.63, 130.02, 126.74, 121.45, 152.27, 116.67, 133.45, 130.85, 120.37, 130.60, 120.35, 128.22, 121.34, 128.22, 127.07, 147.75, 115.49, 135.11, 129.10, 127.07, 129.10, 159.11, 121.47, 127.07. MS EI (m/z): 427.12 (M^+ , 8%), 400.15 (10%), 377.41 (12%), 309.67 (20%), 232.83 (16%), 192.44 (24%), 177.46 (44%). Anal. Calcd for $\text{C}_{28}\text{H}_{20}\text{N}_4\text{O}$ (428.16): C, 78.51; H, 4.71; N, 13.18. Found: C, 78.56; H, 4.64; N, 13.23.

***N*-(4-(5-(4-Dimethylamino)phenyl)-1H-pyrazol-3-yl)phenyl)acridin-9-amine (5f).** Brown crystals, yield 62%, mp 138–140°C. IR (KBr, ν , cm^{-1}): 3313 (N-H), 3100–3000 (Ar C-H), 1599 and 1473 (Ar C=C), 1261 (C-N), 750 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.12 (s, 1H, pyrazole, NH), 4.13 (s, 1H, NH), 3.04 (s, 6H, 2CH_3), 7.85–6.67 (m, 17H, Ar-H). ^{13}C NMR: 122.10, 127.49, 130.89, 117.35, 117.34, 130.64, 126.78, 117.28, 152.13, 112.08, 130.85, 130.64, 113.71, 130.85, 111.24, 129.55, 114.76, 147.51, 111.96, 133.42, 129.89, 128.26, 129.73, 160.81, 114.50, 128.26, 40.22, 40.31. MS EI (m/z): 454.44 (25%), 387.87 (12%), 355.46 (20%), 322.12 (56%), 308.76 (36%), 284.70 (32%), 217.80 (26%), 198.95 (32%), 176.32 (22%). Anal. Calcd for $\text{C}_{30}\text{H}_{25}\text{N}_5$ (455.21): C, 79.12; H, 5.55; N, 15.39. Found: C, 79.25; H, 5.42; N, 15.12.

***N*-(4-(5-(2,4-Dichlorophenyl)-1H-pyrazol-3-yl)phenyl)acridin-9-amine (5g).** Orange crystals, yield 64%, mp 110–112°C. IR (KBr, ν , cm^{-1}): 3282 (C-N), 3100–3000 (Ar C-H), 1606 and 1515 (Ar C=C), 1263 (C-N), 752 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.03 (s, 1H, pyrazole, NH), 4.07 (s, 1H, NH), 7.68–6.66 (m, 16H, Ar-H). ^{13}C NMR: 128.43, 129.30, 130.40, 125.15, 128.33, 131.75, 129.01, 127.58, 151.53, 117.42, 138.73, 133.67, 120.27, 133.36, 127.46, 130.60, 127.53, 130.61, 125.79, 147.44, 114.78, 138.90, 130.80, 138.90, 130.80, 138.73, 123.78, 130.40. MS EI (m/z): 480.26 (M^+ , 8%), 464.18 (32%), 455.64 (36%), 414.84 (28%), 333.68 (28%), 307.89 (100%), 290.93 (56%), 265.07 (62%), 168.47 (32%). Anal. Calcd for $\text{C}_{28}\text{H}_{18}\text{Cl}_2\text{N}_4$ (480.1): C, 69.89; H, 3.79; N, 11.67. Found: C, 69.74; H, 3.65; N, 11.82.

***N*-(4-(5-(4-Benzoyloxy)-3-methoxyphenyl)-1H-pyrazol-3-yl)phenyl)acridin-9-amine (5h).** Brown crystals, yield 54%, mp 140–142°C. IR (KBr, ν , cm^{-1}): 3348 (N-H), 3100–3032 (Ar C-H), 1620 and 1508 (Ar C=C), 1273 (C-N), 1259 and 1139 (C-O), 748 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.63 (s, 1H, pyrazole, NH), 4.12 (s, 1H, NH), 3.78 (s, 3H, CH_3), 8.18–6.56 (m, 20H, Ar-H). ^{13}C NMR: 129.13, 129.70, 126.28, 124.55, 114.75, 149.3, 114.93, 129.18, 148.33, 116.42, 143.21, 116.48, 128.27, 148.56, 128.46, 126.60, 123.24, 148.71, 100.05, 148.64, 112.28, 150.30, 120.83, 115.90, 149.80, 56.24, 71.38, 141.25, 127.26, 129.21, 127.56. MS EI (m/z): 548.12 (M^+ , 100%). Anal. Calcd for $\text{C}_{36}\text{H}_{28}\text{N}_4\text{O}_2$ (548.23): C, 78.83; H, 5.16; N, 10.31. Found: C, 78.59; H, 5.24; N, 10.09.

***N*-(4-(5-(4-Chlorophenyl)-1H-pyrazol-3-yl)phenyl)acridin-9-amine (5i).** Yellow crystals, yield 55%, mp 198–200°C. IR (KBr, ν , cm^{-1}): 3379 (N-H), 3061–3001 (Ar C-H), 1620 and 1518 (Ar C=C), 1263 (C-N), 750 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 13.79 (s, 1H, pyrazole, NH), 4.08 (s, 1H, NH), 8.08–6.45 (m, 16H, Ar-H). ^{13}C NMR: 129.12, 129.63, 126.32, 124.63, 114.64, 149.65, 114.83, 126.62, 148.37, 116.84, 143.16, 116.48, 128.33, 148.78, 128.32, 126.53, 123.17, 148.83, 99.65, 148.76, 132.12, 148.30, 131.23, 128.86, 129.45, 134.32. MS EI (m/z):

446.15 (M^+). Anal. Calcd for $C_{28}H_{19}ClN_4$ (446.2): C, 75.27; H, 4.21; N, 12.52. Found: C, 75.13; H, 4.12; N, 12.62.

***N*-(4-(5-(2-Chlorophenyl)-1H-pyrazol-3-yl)phenyl)acridin-9-amine (5m).** Dark brown crystals, yield 84%, mp 89–91°C. IR (KBr, ν , cm^{-1}): 3057–3030 (Ar C-H), 1608 and 1518 (Ar C=C), 1263 (C-N), 752 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 13.83 (s, 1H, pyrazole, NH), 4.12 (s, 1H, NH), 8.10–6.35 (m, 16H, Ar-H). ^{13}C NMR: 129.17, 129.76, 126.37, 124.57, 114.74, 149.72, 114.79, 126.34, 148.74, 116.77, 143.12, 116.74, 128.28, 148.82, 128.36, 123.23, 126.7, 148.75, 99.81, 148.82, 130.02, 148.76, 132.31, 128.92, 129.52, 130.26. MS EI (m/z): 446.21 (M^+). Anal. Calcd for $C_{28}H_{19}ClN_4$ (446.13): C, 75.28; H, 4.18; N, 12.57. Found: C, 75.68; H, 4.04; N, 12.38.

Synthesis of pyrazole-substituted 9-anilinoacridines (6a–l). A solution of 0.0125 mol of the corresponding chalcones **4a–n** in 20 mL of absolute ethanol and 0.24 g (0.0016 mol) of phenylhydrazine hydrochloride were taken in a 100-mL round-bottomed flask and refluxed for 6 h. After the reaction, the solvent was removed by vacuum distillation, then the residue obtained was washed with water and dried.

***N*-(4-(5-(4-Methoxyphenyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6a).** Brick red crystals, yield 70%, mp 280–282°C. IR (KBr, ν , cm^{-1}): 3250 (N-H), 3091–2953 (Ar C-H), 1589 and 1496 (Ar C=C), 1273 (C-N), 1251 and 1165 (C-O), 750 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.05 (s, 1H, NH), 8.06–6.35 (m, 21H, Ar-H), 3.78 (s, 3H, OCH_3). ^{13}C NMR: 129.13, 129.75, 126.28, 128.89, 126.22, 127.03, 129.65, 125.75, 153.68, 114.72, 129.93, 130.12, 117.15, 128.25, 123.14, 128.32, 120.16, 129.4, 120.17, 114.75, 160.73, 114.71, 125.11, 144.13, 139.51, 126.33, 129.06, 127.51, 55.83. MS (m/z): 519.11 (M^+). Anal. Calcd for $C_{35}H_{26}N_4O$ (518.2): C, 81.16; H, 5.07; N, 10.83. Found: C, 81.19; H, 5.24; N, 10.65.

***N*-(4-(1,5-Diphenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6b).** Brownish black crystals, yield 64%, mp 205–207°C. IR (KBr, ν , cm^{-1}): 3100–3000 (Ar C-H), 1600 and 1496 (Ar C=C), 1273 (C-N), 750 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.11 (s, 1H, NH), 8.02–6.51 (m, 22H, Ar-H). ^{13}C NMR: 129.18, 129.64, 126.28, 124.52, 114.73, 149.25, 114.68, 148.32, 126.38, 126.33, 129.68, 129.15, 116.76, 128.43, 123.16, 128.28, 153.64, 106.08, 144.52, 127.48, 127.48, 133.16, 120.18, 129.43, 120.12, 129.73, 129.5, 126.29. MS (m/z): 489.28 (M^+ + 1). Anal. Calcd for $C_{34}H_{24}N_4$ (488.2): C, 83.68; H, 4.89; N, 11.51. Found: C, 83.39; H, 4.63; N, 11.25.

***2*-(3-(4-(Acridin-9-ylamino)phenyl)-1-phenyl-1H-pyrazol-5-yl)phenol (6c).** Brick red crystals, yield 71%, mp 290–292°C. IR (KBr, ν , cm^{-1}): 3400 (N-H), 3250 (O-H), 3088–3018 (Ar C-H), 1589 and 1506 (Ar C=C), 1273 (C-N), 1251 (C-O), 750 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.10 (s, 1H, NH), 5.08 (s, 1H, OH), 8.02–6.45 (m, 21H, Ar-H). ^{13}C NMR: 129.12, 129.74, 126.31, 124.62, 114.83, 149.65, 114.78, 148.36, 126.78, 126.73, 129.72, 129.12, 116.66, 128.33, 123.21, 128.28, 153.72, 106.02, 144.52, 120.58, 155.41, 116.36, 120.58, 129.93, 120.22, 129.38, 129.42, 126.34, 139.65. MS (m/z): 505.31 (M^+ + 1). Anal. Calcd for $C_{34}H_{24}N_4O$ (505.3): C, 80.83; H, 4.82; N, 11.15. Found: C, 80.17; H, 4.58; N, 11.02.

***N*-(4-(5-(Furan-2-yl)-1-phenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6d).** Orange crystals, yield 56%, mp 298–300°C. IR (KBr, ν , cm^{-1}): 3323 (N-H), 3090–3022 (Ar C-H), 1599 and 1489

(Ar C=C), 1273 (C-N), 1220 and 1165 (C-O), 754 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.12 (s, 1H, NH), 8.03–6.31 (m, 20H, Ar-H). ^{13}C NMR: 129.21, 129.72, 126.33, 124.53, 114.69, 149.65, 114.65, 148.42, 126.52, 126.63, 129.66, 129.16, 116.82, 128.26, 123.18, 128.35, 152.74, 107.15, 152.57, 107.08, 127.06, 157.61, 107.32, 105.03, 142.93, 120.24, 129.35, 129.46, 126.25, 139.72. MS (m/z): 479.68 (M^+ + 1). Anal. Calcd for $C_{32}H_{22}N_4O$ (478.2): C, 80.42; H, 4.68; N, 11.73. Found: C, 80.14; H, 4.79; N, 11.58.

***4*-(3-(4-(Acridin-9-ylamino)phenyl)-1-phenyl-1H-pyrazol-5-yl)phenol (6e).** Brick red crystals, yield 63%, mp 295–297°C. IR (KBr, ν , cm^{-1}): 3250 (N-H), 3090 (O-H), 3070–3018 (Ar C-H), 1589 and 1506 (Ar C=C), 1273 (C-N), 1251 (C-O), 750 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.02 (s, 1H, NH), 5.08 (s, 1H, OH), 8.03–6.48 (m, 20H, Ar-H). ^{13}C NMR: 129.07, 129.59, 126.25, 124.38, 114.92, 149.25, 114.65, 148.73, 126.32, 126.43, 129.59, 129.06, 143.22, 116.68, 128.33, 123.21, 128.42, 153.66, 106.04, 144.48, 128.88, 116.37, 158.44, 116.41, 128.79, 120.23, 120.28, 126.38, 129.43, 139.67. MS (m/z): 505.32 (M^+ + 1). Anal. Calcd for $C_{34}H_{24}N_4O$ (504.2): C, 80.95; H, 4.73; N, 11.12. Found: C, 80.68; H, 4.91; N, 11.24.

***N*-(4-(5-(4-(Dimethylamino)phenyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6f).** Brick red crystals, yield 68%, mp 284–286°C. IR (KBr, ν , cm^{-1}): 3254 (N-H), 3086–3000 (Ar C-H), 1589 and 1506 (Ar C=C), 1273 (C-N), 1251 and 1163 (C-O), 750 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.11 (s, 1H, NH), 8.02–6.55 (m, 21H, Ar-H). ^{13}C NMR: 129.11, 129.81, 126.34, 124.53, 114.69, 148.28, 114.73, 149.75, 126.28, 126.23, 129.71, 129.21, 143.13, 116.91, 128.38, 123.14, 128.37, 153.74, 106.24, 144.47, 122.63, 128.43, 114.76, 149.49, 114.41, 128.36, 120.28, 120.21, 126.31, 129.29, 40.27, 139.67, 40.25. MS (m/z): 532.27 (M^+ + 1). Anal. Calcd for $C_{36}H_{29}N_5$ (531.25): C, 81.37; H, 5.53; N, 13.27. Found: C, 81.05; H, 5.71; N, 13.46.

***N*-(4-(5-(2,4-Dichlorophenyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6g).** Orange crystals, yield 60%, mp 230–232°C. IR (KBr, ν , cm^{-1}): 3335 (N-H), 3100–3000 (Ar C-H), 1583 and 1506 (Ar C=C), 1259 (C-N), 750 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 3.98 (s, 1H, NH), 8.06–6.47 (m, 20H, Ar-H). ^{13}C NMR: 129.22, 129.74, 126.28, 124.61, 114.78, 148.93, 114.69, 148.34, 126.39, 126.42, 129.67, 129.18, 143.33, 116.86, 128.41, 123.08, 128.28, 153.69, 106.24, 144.47, 128.13, 133.67, 130.92, 135.67, 127.56, 130.36, 120.31, 120.25, 126.36, 129.35. MS (m/z): 557.22 (M^+ + 1). Anal. Calcd for $C_{34}H_{22}Cl_2N_4$ (556.1): C, 73.35; H, 3.92; N, 10.05. Found: C, 73.43; H, 3.74; N, 10.21.

***N*-(4-(5-(4-(Benzyloxy)-3-methoxyphenyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6h).** Yellow crystals, yield 61%, mp 136–138°C. IR (KBr, ν , cm^{-1}): 3300 (N-H), 3041–2993 (Ar C-H), 1600 and 1508 (Ar C=C), 1263 (C-N), 746 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 3.67 (s, 1H, NH), 5.18 (s, 2H, CH_2), 8.12–6.50 (m, 25H, Ar-H). ^{13}C NMR: 129.12, 129.63, 126.22, 124.54, 114.65, 148.88, 114.71, 148.26, 126.25, 126.32, 129.58, 129.09, 143.13, 116.59, 128.29, 123.21, 128.21, 153.81, 106.08, 144.52, 112.18, 150.24, 130.92, 149.67, 115.56, 120.77, 120.33, 120.27, 126.31, 129.42, 56.34, 71.28, 127.35, 141.38, 129.03. MS (m/z): 625.25 (M^+ + 1). Anal. Calcd for $C_{42}H_{32}N_4O_2$ (624.15): C, 80.75; H, 5.16; N, 8.97; O, 5.12. Found: C, 80.53; H, 5.41; N, 8.72.

***N*-(4-(1-Phenyl-5-(pyridin-3-yl)-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6i).** Black crystals, yield 57%, mp 265–267°C. IR (KBr, ν , cm^{-1}): 3400 (N-H), 3030–3018 (Ar C-H), 1599 and 1494 (Ar C=C), 1273 (C-N), 748 (Ar C-H). 1H NMR ($CDCl_3$) δ ppm: 4.15 (s, 1H, NH), 8.86–6.35 (m, 21H, Ar-H). ^{13}C

NMR: 129.07, 129.64, 126.23, 124.54, 114.69, 148.63, 114.75, 148.27, 126.28, 126.34, 129.62, 129.12, 143.13, 116.69, 128.24, 123.12, 128.41, 152.49, 107.08, 127.28, 134.16, 133.21, 124.12, 148.09, 139.64, 120.28, 120.25, 126.36, 129.44. MS (*m/z*): 490.20 ($M^+ + 1$). Anal. Calcd for $C_{33}H_{23}N_5$ (489.25): C, 80.86; H, 4.74; N, 14.32. Found: C, 80.63; H, 4.92; N, 14.04.

***N*-(4-(5-(3-Nitrophenyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6j).** Black crystals, yield 59%, mp 259–261°C. IR (KBr, ν , cm^{-1}): 3080–3030 (Ar C-H), 1599 and 1506 (Ar C=C), 1558 and 1373 (NO_2), 1273 (C-N), 748 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 4.02 (s, 1H, NH), 8.06–6.46 (m, 21H, Ar-H). ^{13}C NMR: 129.14, 129.81, 126.18, 124.63, 114.78, 148.35, 114.83, 148.27, 149.69, 126.33, 126.41, 129.82, 129.20, 143.08, 116.77, 128.32, 123.07, 128.29, 153.67, 106.13, 144.43, 134.05, 133.61, 122.23, 148.78, 130.17, 121.19, 120.31, 126.40, 129.51. MS (*m/z*): 534.19 ($M^+ + 1$). Anal. Calcd for $C_{34}H_{23}N_5O_2$ (533.2): C, 76.53; H, 4.36; N, 13.11. Found: C, 76.81; H, 4.15; N, 13.46.

4-(3-(4-(Acridin-9-ylamino)phenyl)-1-phenyl-1H-pyrazol-5-yl)-2-methoxyphenol (6k). Brick red crystals, yield 74%, mp 293–295°C. IR (KBr, ν , cm^{-1}): 3250 (N-H), 3090 (O-H), 3090–3000 (Ar C-H), 1589 and 1506 (Ar C=C), 1273 (C-N), 1251 and 1165 (C-O), 748 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 4.03 (s, 1H, NH), 5.05 (s, 1H, OH), 3.71 (s, 3H, CH_3), 8.02–6.42 (m, 20H, Ar-H). ^{13}C NMR: 129.07, 129.70, 126.31, 124.71, 114.83, 148.32, 114.78, 148.31, 149.80, 126.42, 126.39, 129.76, 129.17, 143.21, 116.82, 128.27, 123.13, 128.33, 153.81, 106.08, 144.37, 139.65, 126.61, 112.65, 151.83, 145.56, 117.39, 121.23, 120.27, 126.42, 129.46, 56.27. MS (*m/z*): 534.21 (M^+). Anal. Calcd for $C_{35}H_{26}N_4O_2$ (534.2): C, 78.62; H, 4.91; N, 10.48. Found: C, 78.52; H, 4.74; N, 10.27.

***N*-(4-(5-(4-Chlorophenyl)-1-phenyl-1H-pyrazol-3-yl)phenyl)acridin-9-amine (6l).** Dark brown crystals, yield 66%, mp 150–152°C. IR (KBr, ν , cm^{-1}): 3232 (N-H), 3084–3026 (Ar C-H), 1600 and 1489 (Ar C=C), 1273 (C-N), 1251 and 1165 (C-O), 750 (Ar C-H). ^1H NMR (CDCl_3) δ ppm: 4.07 (s, 1H, NH), 8.02–6.48 (m, 21H, Ar-H). ^{13}C NMR: 129.12, 129.60, 126.22, 124.63, 114.77, 148.24, 114.83, 148.24, 149.66, 126.42, 126.53, 129.66, 129.76, 143.09, 116.91, 128.31, 123.08, 128.27, 153.70, 106.12, 144.51, 139.77, 128.61, 131.17, 128.83, 129.56, 134.39, 120.18, 139.66, 120.23, 126.22, 129.33. MS (*m/z*): 523.16 ($M^+ + 1$). Anal. Calcd for $C_{34}H_{23}ClN_4$ (522.14): C, 78.12; H, 4.46; N, 10.72. Found: C, 78.27; H, 4.18; N, 10.56.

Acknowledgments. The authors thank Tamilnadu Pharmaceutical Sciences Welfare Trust, Chennai, for the financial support. We also thank our Vice Chancellor Dr. B. Suresh, JSS University, Mysore, Department of Pharmaceutical Analysis, Department of Pharmaceutical Biotechnology, JSS College of Pharmacy, Ooty, and Analytical Instrument Facility (SAIF), IIT Madras, for the technical support.

REFERENCES AND NOTES

- [1] Nadaraj, V.; Selvi, S. T.; Mohan, S. *Eur J Med Chem* 2009, 44, 976.
- [2] Dickens, B. F.; Weglicki, W. B.; Boehme, P. A.; Mak, I. T. *J Mol Cell Cardiol* 2002, 34, 129.
- [3] Rouvier, C. S.; Barret, J. M.; Farrell, C. M.; Sharples, D.; Hill, B. T.; Barbe, J. *Eur J Med Chem* 2004, 39, 1029.
- [4] Anderson, M. O.; Sherrill, J.; Madrid, P. B.; Liou, A. P.; Weisman, J. L.; DeRisi, J. L. *Bioorg Med Chem* 2006, 14, 334.
- [5] Chen, Y. L.; Chen, I. L.; Lu, C. M.; Tzeng, C. C.; Tsao, L. I.; Wang, J. P. *Bioorg Med Chem* 2003, 11, 3921.
- [6] Sondhi, S. M.; Nirupma, S.; Lahoti, A. M.; Bajaj, K.; Kumar, A.; Lozach, O. *Bioorg Med Chem* 2005, 13, 4291.
- [7] Giorgio, C. D.; Shimi, K.; Boyer, G.; Delmas, F.; Galy, J. P. *Eur J Med Chem* 2007, 42, 1277.
- [8] Llama, E. F.; Campo, C. D.; Capo, M.; Anadon, M. *Eur J Med Chem* 1989, 24, 391.
- [9] Recanatini, M.; Cavalli, A.; Belluti, F.; Piazzi, L.; Rampa, A.; Bisi, A. *J Med Chem* 2000, 43, 2007.
- [10] Goodell, J. R.; Madhok, A. A.; Hiasa, H.; Ferguson, D. M. *Bioorg Med Chem* 2006, 14, 5467.
- [11] Bacherikov, V. A.; Chang, J. Y.; Lin, Y. W.; Chen, C. H.; Pan, W. Y.; Dong, H. *Bioorg Med Chem* 2005, 13, 6513.
- [12] Denny, W. A.; Atwell, G. J.; Baguley, B. C. *J Med Chem* 1983, 26, 1625.
- [13] Su, T. L.; Lin, Y. W.; Chou, T. C.; Zhang, X.; Bacherikov, V. A.; Chen, C. H. *J Med Chem* 2006, 49, 3710.
- [14] Harrison, R. J.; Cuesta, J.; Chessari, G.; Read, M. A.; Basra, S. K.; Reszka, A. P. *J Med Chem* 2003, 46, 4463.
- [15] Gamage, S. A.; Tepsiri, N.; Wilairat, P.; Wojcik, S. J.; Figgitt, D. P.; Ralph, R. K. *J Med Chem* 1994, 37, 1486.
- [16] Chen, C. H.; Lin, Y. W.; Zhang, X.; Chou, T. C.; Tsai, T. J.; Kapuriya, N. *Eur J Med Chem* 2009, 44, 3056.
- [17] Atwell, G. J.; Cain, B. F.; Denny, W. A. *J Med Chem* 1977, 20, 520.
- [18] Kapuriya, N.; Kapuriya, K.; Zhang, X.; Chou, T. C.; Kakadiya, R.; Wu, Y. T. *Bioorg Med Chem* 2008, 16, 5413.
- [19] Hwang, B. Y.; Kim, H. S.; Lee, J. H.; Hong, Y. S.; Lee, K. S.; Lee, J. J. *J Nat Prod* 2001, 64, 82.
- [20] Philip, S.; Rista, S.; Dominic, S.; Anne, M.; James, M. *J Natl Cancer Inst* 1990, 82, 1107.