Synthesis and Biological Activity of Some New Pyrazoline and Pyrimidine Derivatives

Seham Y. Hassan

Department of Chemistry, Faculty of Science, University of Alexandria,
PO Box 426, 21321 Ibrahimia, Alexandria, Egypt

Novas séries de pirazolinas, 3-aril-4,5-dihidro-1H-pirazol-1-carbaldeídos (4-6), (aril-4,5-dihidro-1H-pirazol-1-il)etanonas (9-11) e 3-aril-4,5-dihidro-1H-pirazóis (24 e 25) foram sintetizadas pela reação de chalconas (1-3) com hidrato de hidrazina em ácido fórmico, ácido acético ou etanol, respectivamente. Novos derivados de pirimidina 6-arilpirimidina-2-amina (32-34) também foram sintetizados a partir das mesmas chalconas de partida. As estruturas dos novos compostos sintetizados foram estabelecidas através do estudo dos espectros de IV, 1H RMN, 13C RMN e análise elementar. Todos os compostos foram avaliados quanto às suas atividades antibacteriana e antifúngica. Dentre estes compostos, três mostraram atividade relevante contra C. albicans e outros também apresentaram atividade contra E. coli.

New series of pyrazoline 3-aryl-4,5-dihydro-1H-pyrazole-1-carbaldehydes (4-6), (aryl-4,5-dihydro-1H-pyrazol-1-yl)ethanones (9-11) and 3-aryl-4,5-dihydro-1H-pyrazoles (24 and 25) were synthesized by reacting chalcones (1-3) with hydrazine hydrate in either formic acid, acetic acid or ethanol, respectively. Also, new 6-arylpyrimidin-2-amine derivatives (32-34) were synthesized from the same chalcones. The structures of the newly synthesized compounds were established on the basis of IR, 1H NMR, 13C NMR, mass spectral data and elemental analyses. The compounds were evaluated for their antibacterial and antifungal activities. Three heterocycles showed relevant activity against C. albicans and some compounds also showed activity against E. coli.

Keywords: chalcones, pyrazoline, pyrimidine, antibacterial, antifungal

Introduction

Chalcones are well known intermediates for the synthesis of various heterocyclic compounds. Compounds with the chalcone backbone have been informed to possess various biological activities. They have been reported to possess antimicrobial, anti-inflammatory, antioxidant and anticancer properties. They were also found to exhibit analgesic, platelet antiaggregation, antiulcerative, antimalarial, antiviral, antileishmanial, antitubercular and antihyperglycemic properties, as well as to inhibit the enzymes tyrosinase and aldose reductase.

Much attention has been paid to the synthesis of heterocyclic compounds bearing nitrogen-containing rings, like pyrazoline and pyrimidine systems, mainly due to their potential pharmacological activity.

Pyrazolines are well known and important nitrogen-containing 5-membered heterocycles, which were found to possess a broad spectrum of biological activities such as anti-inflammatory, herbicidal, antimicrobial, antifungal, antidepressant, anticonvulsant, antitumor, antitubercular, insecticidal, antimycobacterial, molluscicidal, and antinociceptive. A classical synthesis of 2-pyrazolines involves the base catalyzed Claisen-Schmidt condensation of appropriate ketones with suitable aldehydes in the presence of potassium hydroxide in aqueous ethanolic solution at room temperature to give chalcones, which undergo a subsequent cyclization reaction with hydrazines. Several alternatives are available for this condensation, including under acidic or basic conditions. On the other hand, pyrimidines have also been reported to show a variety of biological activities.

Based on the interest in the above biological activities exhibited by the pyrazoline and pyrimidine compounds, we report here the synthesis of a new series of pyrazoline and pyrimidine compounds.
Results and Discussion

Chemistry

The sequence leading to the formation of the title compounds is outlined in Schemes 1 and 2. The desired chalcones (1-3) were prepared by the reaction of anthracene-9-carbaldehyde with different ketones (p-chloroacetophenone, p-methyl acetophenone or 2-acetylfluran) in the presence of aqueous ethanolic KOH. The IR spectra of 1-3 exhibited a band due to the unsaturated carbonyl group at 1651-1660 cm⁻¹. Their ¹H NMR spectra showed a signal at δ 7.45-7.83 ppm attributed to the =CH-2 proton adjacent to C=O with a coupling constant 16 Hz, and a doublet at the range δ 8.60-8.79 ppm due to the =CH-3 proton with the same coupling constant, which confirmed the presence of chalcones in the trans form. The ¹³C NMR of 3-(anthracen-9-yl)-1-(4-chlorophenyl)prop-2-en-1-one (1) as a prototype for the prepared chalcones showed a signal at 188.5 ppm corresponding to the C=O group.

The compounds 1-3 were converted into the corresponding 5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1H-pyrazole-1-carbaldehydes (4-6) by treatment with hydrazine hydrate in formic acid. The IR spectra of aldehydes 4-6 showed the C=O band at 1666-1674 cm⁻¹, and their proton NMR spectra showed three signals within the ranges δ 3.28-3.42, 3.85-4.09, and 6.40-6.96 ppm due to H₆, H₄, and H₃ of the pyrazoline ring, respectively, in addition to a singlet signal in the range δ 8.84-9.00 ppm due to the CHO proton.

Reaction of compounds 4 and 5 with benzoyl hydrazine gave rise to the corresponding benzoylhydrazides 7 and 8, respectively. Their IR spectra showed the NH bands at 3255, 3267, and the carbonyl absorption bands at 1659, 1662 cm⁻¹, respectively. Further, in their proton NMR spectra, they were observed the appearance of signals in the ranges δ 3.38-3.59, 3.85-4.53 and 6.71-7.86 ppm, due to H₆, H₄, and H₃ of the pyrazoline ring, respectively, a singlet at δ 8.04 and 8.41 ppm due to the N=CH=N protons, and a singlet at δ 10.48 and 10.47 ppm, corresponding to the NH protons respectively.

The 1-(5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1H-pyrazol-1-yl)ethanones 9-11 were synthesized by cyclization of chalcones 1-3 with hydrazine hydrate in acetic acid. Their structures were confirmed by IR spectra, which showed their carbonyl band in the range 1655-1667 cm⁻¹. On the other hand, their proton NMR spectra showed a new singlet in the range δ 2.15-2.37 ppm, attributable to the CH₄, protons, three doublets of doublets in the range δ 3.27-3.48, 3.85-4.03, and 6.66-6.85 ppm corresponding to H₆, H₄, and H₃ of the pyrazoline ring, respectively.

Treatment of the methyl ketones 9 and 10 with benzaldehyde in alkaline medium at room temperature afforded the corresponding α,β-unsaturated ketones 12 and 13, respectively, the IR spectra of which showed the carbonyl group at 1650 and 1652 cm⁻¹. Their proton NMR spectra showed the disappearance of the CH₄ signals and exhibited pairs of signals at δ 7.40, 8.67 and 7.28, 8.70 ppm, respectively, as doublets, due to the olefinic protons (H₂, H₃).

The desired Schiff’s bases 14-19 were prepared by heating the methyl ketones 9-11 with aryl hydrazines (phenyl hydrazine, p-nitrophenyl hydrazine) or hydrazine hydrate in ethanol. Their IR spectra showed a new absorption peak at 3285-3372 cm⁻¹ due to the NH group, while their ¹H NMR spectra displayed the CH₃ protons as singlets in the range δ 2.14-2.19 ppm. In addition, a broad singlet was observed in the range δ 9.20-10.61 ppm, corresponding to the NH moiety. In case of compound 19, the signal of the NH₂ group appeared at δ 7.22 ppm.

Heating the substituted 4,5-dihydro-1H-pyrazole derivative 14 with acetic anhydride afforded the corresponding tetrazole 20, which evidenced disappearance of NH signals in its IR and proton NMR spectra.

Treatment of the 3-(anthracen-9-yl)-1-arylprop-2-en-1-ones 1 or 2 with p-bromophenyl- or 2-naphthyl hydrazine hydrochloride afforded the corresponding 1,3,5-trisubstituted pyrazolines (21-23). Their ¹H NMR spectra showed three multiplets in the ranges δ 2.99-3.39, 3.78-4.09 and 6.86-6.98 ppm due to the pyrazoline protons, in addition to aromatic protons at δ 7.03-8.54 ppm.

Cyclization of the chalcones 1 and 2 with hydrazine hydrate in ethanol gave the 5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1H-pyrazoles 24 and 25, respectively. Their IR spectra exhibited a NH absorption peak in the range 3254-3284 cm⁻¹. On the other hand, their ¹H NMR spectra showed two multiplets at δ 3.42-4.11 and 6.60-6.74 ppm, due to the pyrazoline protons. The NH protons were observed at δ 8.56 and 9.63 ppm, respectively.

Furthermore, the disubstituted pyrazolines 24 and 25 were allowed to react with sodium nitrite, phenylisothiocyanate, and p-toluenesulfonfyl chloride to correspondingly furnish 5-(anthracen-9-yl)-3-aryl-1-nitroso-4,5-dihydro-1H-pyrazoles 26 and 27, 5-(anthracen-9-yl)-3-aryl-1-N-phenyl-4,5-dihydro-1H-pyrazole-1-carbothioamides 28 and 29 and 5-(anthracen-9-yl)-3-aryl-1-tosyl-4,5-dihydro-1H-pyrazoles 30 and 31, respectively, in 74-89% yield.

On the other hand, the reaction of chalcones 1-3 with an alcoholic solution of guanidine carbonate containing aqueous NaOH produced the corresponding 2-amino-4, 6-diarylpymrimidines 32-34 (Scheme 2). This transformation might proceed either by 1,4-addition or 1,2-addition of the
guanidine to the chalcones, followed by cyclization of the intermediate, which undergoes proton shift and aromatization to yield the 2-aminopyrimidines. The infrared spectra of the products showed two bands in the ranges 3054-3147 and 3323-3366 cm\(^{-1}\) corresponding to the NH\(_2\) group. Furthermore, their \(^1H\) NMR showed a D\(_2\)O exchangeable signal at \(\delta\) 5.97-6.26 ppm due to the NH\(_2\) protons. A singlet at \(\delta\) 7.35-7.91 ppm was observed due to the pyrimidine-H\(_2\).

Acetylation of the 2-aminopyrimidines 32 and 33 with Ac\(_2\)O yielded the monoacetylated compounds 35 and 36, respectively. Their infrared spectra showed peaks at 3260 and 3218 cm\(^{-1}\) corresponding to the NH group and strong sharp peaks at 1667 and 1669 cm\(^{-1}\), respectively, due to the C=O group. On the other hand, their \(^1H\) NMR showed the CH\(_3\) protons as singlets at \(\delta\) 2.25 and 2.29 ppm, in addition to the NH protons at \(\delta\) 10.77 and 10.47 ppm respectively.

Scheme 1.
Evaluation of the biological activity

Four test organisms representing different groups of microorganisms were used to evaluate the bioactivity of the designed products. The inhibition zone and minimal inhibitory concentration results are given in Table 1.

From the data, it stems that compounds 1, 3, 7, 20, 23, 31 and 34 were the most active against *E. coli*, while compounds 18, 28 and 30 were found to be active against *C. albicans*. Some chlorinated compounds exhibited activity against *C. albicans* (28 and 30) and against *E. coli* (1, 7 and 20). In addition, some sulfur-containing compounds exhibited activity against *C. albicans* (28 and 30) and against *E. coli* (31). It was noticed that furan derivatives also showed activity against *C. albicans* (18), and against *E. coli* (3 and 34). No systematic variation was observed in the antibacterial and antifungal activities for the rest of the compounds. All tested compounds showed poor biological activity against *P. aeruginosa* and *S. aureus*.

Conclusions

In summary, new series of anthracenylpyrazolines and anthracenylpyrimidines were synthesized from 3-(anthracen-9-yl)-1-aryl-prop-2-en-1-one derivatives, and spectroscopically characterized. The biological activity of the compounds was evaluated against *E. coli*, *P. aeruginosa*, *S. aureus* and *C. albicans* by the agar diffusion method. The potency of compounds 18, 28 and 30 as antifungics against *C. albicans* is about 50% of that of Clotrimazole. On the other hand, the potency of compounds 1, 3, 7, 20, 23, 31 and 34 as antibacterials against *E. coli* is about 50% of that of Ampicillin.
Table 1. *In vitro* antimicrobial activity of the test compounds and evaluation of their antimicrobial activity of the inhibition zone (IZ) and the minimal inhibitory concentration (MIC)

<table>
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<th>Compound / Microorganism</th>
<th></th>
<th>E. coli</th>
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<th>S. aureus</th>
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<th>C. albicans</th>
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<th>P. aeruginosa</th>
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<tr>
<td>Ampicillin 10 µg per disc</td>
<td>18</td>
<td>25</td>
<td>22</td>
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<td>Ciprofloxacin 5 µg per disc</td>
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<td>30</td>
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<td>-----</td>
<td>38</td>
<td>25</td>
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<tr>
<td>Clotrimazole 100 µg per disc</td>
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<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>40</td>
<td>12.5</td>
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<tr>
<td>Imipenem 10 µg per disc</td>
<td>26</td>
<td>-----</td>
<td>30</td>
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<td>30</td>
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1. 20 50 14 200 15 100 22 200
2. 20 100 14 100 13 100 22 100
3. 15 50 10 200 13 100 18 200
4. 21 100 14 100 12 100 22 200
5. 20 100 14 200 12 50 22 100
6. 15 100 12 200 12 100 16 200
7. 15 50 10 200 12 100 17 100
8. 21 100 13 200 15 100 22 200
9. 20 100 14 200 12 50 22 200
10. 20 100 14 100 12 100 22 100
11. 15 100 12 200 14 100 17 200
12. 22 100 14 100 12 100 22 100
13. 20 100 13 100 12 100 22 100
14. 20 100 13 100 12 100 22 100
15. 20 100 13 200 13 100 22 200
16. 20 100 14 100 12 100 22 200
17. 20 100 13 100 16 100 22 200
18. 16 100 13 200 13 25 17 100
19. 15 100 13 200 15 100 20 200
20. 15 50 11 100 13 100 17 200
21. 20 100 14 200 11 100 22 100
22. 22 100 14 100 12 100 22 200
23. 22 50 13 100 19 100 22 200
24. 20 100 14 200 15 100 22 100
25. 20 100 13 100 12 100 22 200
26. 16 100 12 200 13 100 17 100
27. 16 100 12 100 14 100 17 200
28. 15 100 11 200 13 25 17 100
29. 15 100 12 200 13 100 17 200
30. 16 100 12 200 14 25 19 100
31. 15 50 12 100 14 100 17 100
32. 15 100 13 200 15 100 20 100
33. 16 100 13 100 15 100 20 200
34. 16 50 14 200 15 100 20 200
35. 15 100 13 100 15 100 20 200
36. 16 100 13 200 15 50 20 200
Experimental

Chemistry

General experimental considerations

Reagent quality solvents were used without purification. Melting points were obtained in open capillary tubes by using a MEL-Temp II melting point apparatus and are uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer 1600 series Fourier transform instrument with the samples as KBr pellets. 1H NMR and 13C NMR spectra were recorded on JEOL JMS AX-500 spectrometer by using electron impact ionization at 70 eV. Elemental analyses were recorded on a JEOL JMS AX-500 spectrometer by using a MEL-Temp II melting point apparatus and are uncorrected. Melting points were obtained in open capillary tubes by using a MEL-Temp II melting point apparatus and are uncorrected.

General procedure for the preparation of compounds 1-3

An equimolar mixture of anthracene-9-carbaldehyde (2.06 g, 0.01 mol) and the substituted ketone (1.54 g 4-chloro acetonophenone, 1.34 g 4-methyl acetonophenone or 1.10 g 2-acetylfuran) in 2% ethanolic KOH (20 mL) was stirred at r.t. for 4 h. The solid product was cooled, collected by filtration, washed with ethanol, dried and recrystallized from chloroform/ethanol.

Yield: 90%, orange-yellow crystals, mp 124-125 ºC. IR (KBr) ν max/cm⁻¹: 1674 (C=O); 1H NMR (DMSO-d$_6$) δ 7.45-7.51 (m, 7H, =CH-2 and 6 ArH), 7.74 (d, 1H, 1H, J 7.0 Hz, ArH), 8.00 (d, 2H, J 8 Hz, ArH), 8.11 (d, 2H, J 7.0 Hz, ArH), 8.84 (s, 1H, CHO). Anal. Calc. for C$_{24}$H$_{18}$O (342.40): C, 89.41; H, 5.63. Found: C, 89.60; H, 5.70%.

3-(Anthracen-9-yl)-1-(furan-2-yl)prop-2-en-1-one (3)

Yield: 87%, yellow crystals, mp 140-141 ºC. IR (KBr) ν max/cm⁻¹: 1594 (C=O); 1H NMR (DMSO-d$_6$) δ 6.75 (t, 1H, J 8.0 Hz, ArH), 7.50-7.58 (m, 5H, =CH-2 + 4 ArH), 7.74 (d, 1H, J 3.0 Hz, ArH), 8.12 (d, 3H, J 8.0 Hz, ArH) 8.20 (d, 2H, J 8.0 Hz, ArH), 8.60 (d, 1H, J 16 Hz, =CH-3), 8.66 (s, 1H, H$_{16-10}$). Anal. Calc. for C$_{25}$H$_{16}$O$_2$ (298.33): C, 84.54; H, 4.73. Found: C, 84.65; H, 4.81%.

General procedure for the preparation of compounds 4-6

A mixture of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one (1-3, 0.001 mol) and hydrazine hydrate (3 mL) in formic acid (15 mL) was heated under reflux for 8 h. The reaction mixture was poured onto crushed ice, the precipitated product was filtered, washed with water, dried and recrystallized from chloroform/ethanol.

5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazole-1-carbaldehyde (4)

Yield: 85%, buff crystals, mp 225-226 ºC. IR (KBr) ν max/cm⁻¹: 1674 (C=O); 1H NMR (DMSO-d$_6$) δ 3.36-3.39 (m, 1H, pyrazoline-H$_2$), 3.85-4.09 (m, 1H, pyrazoline-H$_2$), 6.86-6.96 (dd, 1H, J$_{3,7}$ 13, J$_{13,18}$ 18 Hz, pyrazoline-H$_2$), 7.48 (dd, 2H, J 3, 7.0 Hz, ArH), 7.56 (d, 2H, J 7.6 Hz, ArH), 7.69 (d, 2H, J 7.0 Hz, ArH), 7.91 (d, 2H, J 7.0 Hz, ArH), 8.05 (dd, 2H, J 3.0, 7.0 Hz, ArH), 8.11 (d, 2H, J 7.6 Hz, ArH), 8.53 (s, 1H, H$_{16-10}$), 8.84 (s, 1H, CHO). Anal. Calc. for C$_{23}$H$_{18}$ClO$_2$ (384.86): C, 74.90; H, 4.45; N, 7.28. Found: C, 74.65; H, 4.23; N, 7.49%.

5-(Anthracen-9-yl)-3-p-tolyl-4,5-dihydro-1H-pyrazole-1-carbaldehyde (5)

Yield: 81%, brown crystals, mp 199-200 ºC. IR (KBr) ν max/cm⁻¹: 1666 (C=O); 1H NMR (DMSO-d$_6$) δ 2.19 (3H, s, p-CH$_3$), 3.15-3.30 (1H, m, pyrazoline-H$_2$), 4.08 (dd, 1H, J$_{1,2}$ 13, J$_{13,18}$ 18 Hz, pyrazoline-H$_2$), 6.88 (t, 1H, J 7.0, 12 Hz, pyrazoline-H$_2$), 7.37-7.58 (m, 6H, ArH), 7.67 (d, 1H, J 8.0 Hz, ArH), 7.86 (d, 2H, J 7.6 Hz, ArH), 8.00 (d, 2H, J 8.0 Hz, ArH), 8.56-8.58 (m, 2H, ArH), 9.00 (s, 1H, CHO). Anal. Calc. for C$_{25}$H$_{20}$N$_2$O (364.44): C, 82.39; H, 5.53; N, 7.69. Found: C, 82.15; H, 5.33; N, 7.90%.

5-(Anthracen-9-yl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazole-1-carbaldehyde (6)

Yield: 78%, buff crystals, mp 204-205 ºC. IR (KBr) ν max/cm⁻¹: 1670 (C=O); 1H NMR (DMSO-d$_6$) δ 3.28-3.42
General procedure for the preparation of compounds 7 and 8

To a solution of 5-(anthracen-9-yl)-3-aryl-4,5-dihydro-1H-pyrazole-1-carbaldehyde 4 (3.84 g, 0.01 mol) or 5 (3.64 g, 0.01 mol) in ethanol (30 mL) was added benzoyl hydrazine (1.63 g, 0.012 mol) and two drops of acetic acid. The reaction mixture was heated under reflux for 6 h, partially concentrated and cooled. The separated solid product was filtered, washed with ethanol, dried and crystallized from ethanol.

N'-(5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazole-1-yl)methylene] benzyllhydrazide (7)

Yield: 77%, buff crystals, mp 207-208 °C. IR (KBr) νmax/cm⁻¹: 1659 (C=O), 1325 (NH); ¹H NMR (DMSO-d₆) δ 3.38-3.59 (m, 1H, pyrazoline-H), 4.51-4.53 (m, 1H, pyrazoline-H), 6.71-6.86 (m, 1H, pyrazoline-H), 7.31-7.37 (m, 4H, ArH), 7.47-7.62 (m, 2H, ArH), 7.71-7.83 (m, 5H, ArH), 7.89-7.96 (m, 4H, ArH), 8.04 (s, 1H, N=CH=N), 8.17-8.32 (m, 2H, ArH), 8.52 (s, 1H, H-7), 10.48 (s, 1H, NH; D₂O exchangeable). Anal. Calc. for C₂₃H₂₀N₄O (502.99): C, 74.02; H, 4.61; N, 11.14. Found: C, 74.24; H, 4.85; N, 11.00%.

N'-(5-(Anthracen-9-yl)-3-p-tolyl-4,5-dihydro-1H-pyrazole-1-yl)methylene] benzyllhydrazide (8)

Yield: 74%, buff crystals, mp 181-182 °C. IR (KBr) νmax/cm⁻¹: 1662 (C=O), 3267 (NH); ¹H NMR (CDCl₃) δ 2.18 (3H, s, p-CH₃), 3.46 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 3.85 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 6.86 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 7.34-7.46 (m, 10H, ArH), 7.73-7.81 (m, 4H, ArH), 8.00-8.10 (m, 3H, ArH), 8.41 (s, 1H, N,CH=N), 8.50 (s, 1H, H-7), 10.47 (s, 1H, NH; D₂O exchangeable). Anal. Calc. for C₂₅H₂₆N₂O (482.58): C, 79.64; H, 5.43; N, 11.61. Found: C, 79.41; H, 5.60; N, 11.83%.

General procedure for the preparation of compounds 9-11

A mixture of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one (1-3, 0.001 mol) and hydrazine hydrate (3 mL) in acetic acid (15 mL) was heated under reflux for 8 h. The reaction mixture was poured onto crushed ice, the precipitated product was filtered, washed with water, dried and recrystallized from chloroform/ethanol.

1-(5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)ethanone (9)

Yield: 84%, buff crystals, mp 239-240 °C. IR (KBr) νmax/cm⁻¹: 1655 (C=O); ¹H NMR (CDCl₃) δ 2.35 (s, 3H, COCH₃), 3.46 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 3.85 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 6.85 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 7.33-7.48 (m, 5H, ArH), 7.55 (t, 1H, J 7.6 Hz, ArH), 7.74 (dd, 3H, J 2, 9 Hz, ArH), 8.01 (dd, 2H, J 3, 7.6 Hz, ArH), 8.41 (s, 1H, H-7), 8.49 (d, 1H, J 9 Hz, ArH), Anal. Calc. for C₂₅H₂₁ClN₂O (398.88): C, 75.28; H, 4.80; N, 7.02. Found: C, 75.08; H, 4.65; N, 7.21%.

1-(5-(Anthracen-9-yl)-3-p-tolyl-4,5-dihydro-1H-pyrazol-1-yl)ethanone (10)

Yield: 78%, buff crystals, mp 194-195 °C. IR (KBr) νmax/cm⁻¹: 1667 (C=O); ¹H NMR (CDCl₃) δ 2.37 (s, 3H, COCH₃), 2.43 (s, 3H, p-CH₃), 3.48 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 3.89 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 6.85 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 7.27 (t, 2H, J 7.6 Hz, ArH), 7.32-7.41 (m, 2H, ArH), 7.49 (t, 1H, J 7.6 Hz, ArH), 7.54-7.57 (m, 1H, ArH), 7.72 (d, 2H, J 7.6 Hz, ArH), 7.79 (d, 1H, J 8 Hz, ArH), 8.01 (d, 2H, J 8.0 Hz, ArH), 8.42 (s, 1H, H-7), 8.52 (d, 1H, J 8.0 Hz, ArH). Anal. Calc. for C₂₅H₂₁N₂O (378.47): C, 82.51; H, 5.86; N, 7.40. Found: C, 82.72; H, 5.98; N, 7.19%.

1-(5-(Anthracen-9-yl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)ethanone (11)

Yield: 80%, buff crystals, mp 200-201 °C. IR (KBr) νmax/cm⁻¹: 1657 (C=O); ¹H NMR (DMSO-d₆) δ 2.15 (3H, s, COCH₃), 3.27 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 4.03 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 6.66-6.67 (m, 1H, ArH), 6.84 (dd, 1H, J₁₂,9, J₁₂,13 18 Hz, pyrazoline-H), 6.99 (d, 1H, J 3.0 Hz, ArH), 7.42 (t, 2H, J 8.0 Hz, ArH), 7.51 (t, 1H, J 7.0 Hz, ArH), 7.56 (t, 1H, J 7.0 Hz, ArH), 7.68 (d, 1H, J 3.0 Hz, ArH), 7.90 (s, 1H, H-7), 8.07 (d, 2H, J 7.0 Hz, ArH), 8.55-8.56 (m, 2H, ArH). Anal. Calc. for C₂₅H₁₈N₂O₂ (354.40): C, 77.95; H, 5.12; N, 7.90. Found: C, 77.73; H, 5.32; N, 7.99%.

General procedure for the preparation of compounds 12 and 13

An equimolar mixture of 1-(5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1H-pyrazol-1-yl)ethanone 9 (3.98 g,
0.01 mol or 10 (3.78 g, 0.01 mol) and benzaldehyde (1.06 g, 0.01 mol) in 2% ethanolic KOH (20 mL) was stirred at r.t. for 4 h. The solid product was cooled, collected by filtration, washed with ethanol, dried, and recrystallized from chloroform/ethanol.

1-(5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenyl-prop-2-en-1-one (12)

Yield: 71%, off white needles, mp 259-260 °C. IR (KBr) ν\text{max}/cm\(^{-1}\): 1650 (C=O); \(^1\)H NMR (DMSO-\(d_6\)) δ 3.33-3.37 (m, 1H, pyrazoline-H\(_2\)), 4.07 (dd, 1H, J\(_{1,2}\) 13, J\(_{1,3}\) 18 Hz, pyrazoline-H\(_1\)), 6.88 (dd, 1H, J\(_{1,2}\) 9, J\(_{1,3}\) 13 Hz, pyrazoline-H\(_2\)), 7.40 (d, 1H, J 6.0 Hz, =CH-1), 7.35 (t, 2H, J 7.6 Hz, ArH), 7.41 (t, 2H, J 7.0 Hz, ArH), 7.50-7.58 (m, 5H, ArH), 7.66 (d, 2H, J 8.0 Hz, ArH), 7.87 (d, 2H, J 7.0 Hz, ArH), 8.56 (s, 1H, H\(_{\text{NH-ex}}\)). Anal. Calc. for C\(_{25}\)H\(_{21}\)ClN\(_2\): C, 78.92; H, 4.76; N, 5.75. Found: C, 78.92; H, 4.76; N, 5.75.

General procedure for the preparation of compounds 14-19

To a solution of 1-(5-(anthracen-9-yl)-3-aryl-4,5-dihydro-1H-pyrazol-1-yl)ethanone (9-11, 0.01 mol) in ethanol (25 mL) was added hydrazine hydrate or aryl hydrazine (0.012 mol) and two drops of acetic acid. The reaction mixture was heated under reflux for 8 h, partially concentrated and cooled. The separated solid product was filtered, washed with ethanol, dried and recrystallized from ethanol.

5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-(1-(2-phenylhydrazono)ethyl)-4,5-dihydro-1H-pyrazole (14)

Yield: 77%, buff crystals, mp 270-271 °C. IR (KBr) ν\text{max}/cm\(^{-1}\): 3295 (NH); \(^1\)H NMR (DMSO-\(d_6\)) δ 2.19 (3H, s, N=C-CH\(_3\)), 3.22-3.40 (m, 1H, pyrazoline-H\(_1\)), 4.07 (m, 1H, pyrazoline-H\(_2\)), 6.89 (dd, 1H, J\(_{1,2}\) 9, J\(_{1,3}\) 13 Hz, pyrazoline-H\(_1\)), 7.37 (t, 2H, J 8.0 Hz, ArH), 7.42 (t, 2H, J 7.0 Hz, ArH), 7.52-7.58 (m, 5H, ArH), 7.66 (d, 2H, J 8.0 Hz, ArH), 7.87 (d, 4H, J 8.0 Hz, ArH), 8.06 (d, 2H, J 7.0 Hz, ArH), 8.56 (s, 1H, H\(_{\text{NH-ex}}\)). Anal. Calc. for C\(_{37}\)H\(_{27}\)ClN\(_2\): C, 74.83; H, 5.30; N, 13.64. Found: C, 74.60; H, 5.09; N, 13.85%.
5-(Anthracen-9-yl)-3-(furan-2-yl)-1-(1-(4-nitrophenyl) hydrazono)ethyl)-4,5-dihydro-1H-pyrazole (I8)

Yield: 81%, brown crystals, mp 120-121 °C. IR (KBr) νmax/cm−1: 1323, 1502 (NO2), 3372 (NH); 1H NMR (DMSO-d6) δ 2.14 (3H, s, N=C-CH3), 3.26 (dd, 1H, J1,2 9, J2,3 18 Hz, pyrazoline-H2), 4.03 (dd, 1H, J1,2 13, J2,3 18 Hz, pyrazoline-H3), 6.84 (dd, 1H, J1,2 9, J2,3 13 Hz pyrazoline-H4), 6.98 (d, 1H, J 10 Hz, ArH), 7.42 (t, 3H, J 3.8 Hz, ArH), 7.50-7.56 (m, 4H, ArH), 7.67 (d, 1H, J 10 Hz, ArH), 7.93 (s, 1H, Hant-10), 8.07 (d, 4H, J 7.6 Hz, ArH), 8.54-8.56 (m, 2H, ArH), 9.20 (s, 1H, NH; D2O exchangeable). Anal. Calc. for C29H20N4O (489.52): C, 71.15; H, 4.74; N, 14.31. Found: C, 71.33; H, 4.51; N, 14.05%.

5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-(1-hydrazonoethoxy)-4, 5-dihydro-1H-pyrazole (19)

Yield: 85%, pale yellow needles, mp 275-276 °C. 1H NMR (DMSO-d6) δ 2.19 (3H, s, N=C-CH3), 3.38 (m, 1H, pyrazoline-H4), 4.08 (dd, 1H, J1,2 13, J2,3 18 Hz, pyrazoline-H3), 6.91 (dd, 1H, J1,2 9, J2,3 13 Hz pyrazoline-H2), 7.22 (s, 2H, NH; D2O exchangeable), 7.37-7.43 (m, 2H, ArH), 7.51-7.57 (m, 4H, ArH), 7.67 (d, 2H, J 7.0 Hz, ArH), 7.88 (d, 2H, J 8.0 Hz, ArH), 8.09 (d, 2H, J 8.0 Hz, ArH), 8.57 (s, 1H, Hant-10). Anal. Calc. for C31H17ClN4 (491.92): C, 72.72; H, 5.13; N, 13.57. Found: C, 72.63; H, 4.95; N, 13.73%.

5-(Anthracen-9-yl)-7-(4-chlorophenyl)-3-methyl-1-phenyl-1, 5-dihydropyrazolof[1,2-ajtetrazole (20)

A mixture of 4,5-dihydro-1H-pyrazole derivative 14 (0.49 g, 0.001 mol) and acetic anhydride (10 mL) was heated on a boiling water bath for 5 h. The reaction mixture was poured onto crushed ice, the precipitated product was filtered, washed with water, dried and recrystallized from ethanol/chloroform, furnishing 20.

Yield: 65%, buff crystals, mp 169-170 °C. 1H NMR (DMSO-d6) δ 2.32 (3H, s, CH3), 4.34-4.38 (m, 1H, pyrazoline-H4), 4.50-4.53 (m, 1H, pyrazoline-H5), 7.27 (t, 2H, J 7.6 Hz, ArH), 7.37-7.51 (m, 3H, ArH), 7.68 (d, 2H, J 8.0 Hz, ArH), 7.90-7.91 (m, 2H, ArH), 7.99 (d, 2H, J 8.0 Hz, ArH), 8.04 (d, 2H, J 7.6 Hz, ArH), 8.12 (d, 2H, J 7.6 Hz, ArH), 8.17-8.19 (m, 2H, ArH), 8.68 (s, 1H, Hant-10). 13C NMR (DMSO) δ 22.16, 56.88, 122.93, 123.11, 124.36, 126.79, 127.04, 128.07, 128.30, 128.95, 129.11, 129.47, 129.69, 130.07, 130.38, 130.51, 130.58, 131.44, 131.95, 132.94, 135.62, 154.09. Anal. Calc. for C12H10ClN4 (486.99): C, 76.46; H, 4.76; N, 11.50. Found: C, 76.53; H, 4.81; N, 11.41%.

5-(Anthracen-9-yl)-1-(4-bromophenyl)-3-(4-chlorophenyl)-4, 5-dihydro-1H-pyrazole (21)

Yield: 70%, buff crystals, mp 299-300 °C. 1H NMR (DMSO-d6) δ 3.12-3.39 (1H, m, pyrazoline-H3), 3.94-4.06 (1H, m, pyrazoline-H2), 6.86-6.94 (1H, m, pyrazoline-H4), 7.03-7.15 (m, 4H, ArH), 7.30 (d, 2H, J 7.6 Hz, ArH), 7.41 (t, 2H, J 7.6 Hz, ArH), 7.48 (t, 2H, J 7 Hz, Ar-H), 7.71 (d, 2H, J 8.0 Hz, ArH), 7.91 (d, 2H, J 8.0 Hz, ArH), 8.05 (d, 2H, J 8.0 Hz, ArH), 8.53 (s, 1H, Hant-10). Anal. Calc. for C31H17BrClN4 (511.84): C, 68.05; H, 3.94; N, 5.47. Found: C, 68.27; H, 4.09; N, 5.22%.

5-(Anthracen-9-yl)-1-(4-bromophenyl)-3-p-tolyl)-4,5-dihydro-1H-pyrazole (22)

Yield: 73%, brown crystals, mp 130-131 °C. 1H NMR (DMSO-d6) δ 2.17 (s, 3H, p-CH3), 3.34 (dd, 1H, J1,2 9, J2,3 18 Hz, pyrazoline-H2), 4.09 (dd, 1H, J1,2 13, J2,3 18 Hz, pyrazoline-H3), 6.86 (dd, 1H, J1,2 9, J2,3 13 Hz pyrazoline-H4), 7.34 (t, 2H, J 7.6 Hz, ArH), 7.41 (t, 2H, J 7.6 Hz, ArH), 7.49-7.58 (m, 5H, Ar-H), 7.62 (d, 2H, J 9.0 Hz, ArH), 7.85 (d, 2H, J 8.0 Hz, ArH), 8.08 (d, 2H, J 8.0 Hz, ArH), 8.54-8.56 (m, 1H, ArH). Anal. Calc. for C20H18BrN2 (491.42): C, 73.32; H, 4.72; N, 5.70. Found: C, 73.59; H, 4.61; N, 5.51%.

5-(Anthracen-9-yl)-1-(naphthalene-2-yl)-3-p-tolyl-4, 5-dihydro-1H-pyrazole (23)

Yield: 77%, pale brown crystals, mp 160-161 °C. 1H NMR (DMSO-d6) δ 2.44 (3H, s, p-CH3), 2.99-3.39 (m, 1H, pyrazoline-H4), 3.78-4.04 (m, 1H, pyrazoline-H2), 6.92-6.98 (m, 1H, pyrazoline-H3), 7.21-7.27 (m, 4H, ArH), 7.29 (dd, 2H, J 7.6, 13 Hz, ArH), 7.39-7.43 (m, 2H, ArH), 7.57-7.79 (m, 4H, ArH), 7.81 (dd, 1H, J 3.0, 5.0 Hz, ArH), 7.97 (dd, 2H, J 7.6, 13 Hz), 8.20-8.28 (m, 2H, ArH), 8.31 (dd, 1H, J 3.0, 5.0 Hz, ArH), 8.50 (s, 1H, ArH), 8.52 (s, 1H, ArH). Anal. Calc. for C26H19N2 (462.58): C, 88.28; H, 5.57; N, 6.06. Found: C, 88.05; H, 5.43; N, 6.24%.
General procedure for the preparation of compounds 24 and 25

A mixture of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one (1, 0.34 g, 0.001 mol or 2, 0.32 g, 0.001 mol) and hydrazine hydrate (3 mL) in ethanol (20 mL) was heated under reflux for 4 h. The solid product was obtained after concentration and cooling, the precipitated product was filtered, washed with ethanol, dried and recrystallized from ethanol.

5-(Anthracen-9-yl)-3-(4-chlorophenyl)-4, 5-dihydro-1H-pyrazole (24)

Yield: 74%, pale brown crystals, mp 230-231 °C. IR (KBr) ν_max/cm⁻¹: 3254 (NH); ¹H NMR (DMSO-d₆) δ 3.60-4.11 (m, 2H, pyrazoline-H₁-H₂), 6.71-6.74 (m, 1H, pyrazoline-H₃), 7.01-7.11 (m, 2H, ArH), 7.25-7.40 (m, 2H, ArH), 7.50-7.71 (m, 4H, ArH), 7.83-7.91 (m, 4H, ArH), 8.18 (s, 1H, H_am(10)), 8.56 (s, 1H, NH; D₂O exchangeable), MS m/z: 356, 358 (M). Anal. Calc. for C₁₅H₁₂ClN₂ (356.43): C, 77.41; H, 4.80; N, 7.85. Found: C, 77.60; H, 4.60; N, 7.63%.

5-(Anthracen-9-yl)-3-p-tolyl-4, 5-dihydro-1H-pyrazole (25)

Yield: 71%, reddish brown crystals, mp 145-146 °C. IR (KBr) ν_max/cm⁻¹: 3284 (NH); ¹H NMR (DMSO-d₆) δ 2.44 (s, 3H, p-CH₃), 3.42-4.08 (m, 2H, pyrazoline-H₁-H₂), 6.60-6.73 (m, 1H, pyrazoline-H₃), 7.17 (d, 2H, J 8.0 Hz, ArH), 7.64 (d, 2H, J 7.6 Hz, ArH), 7.70 (d, 2H, J 7.6 Hz, ArH), 7.90 (dd, 2H, J 3.0, 5.0 Hz, ArH), 8.12 (d, 2H, J 8.0 Hz, ArH), 8.18 (dd, 2H, J 3.0, 5.0 Hz, ArH), 8.47 (s, 1H, H_am(10)), 9.63 (s, 1H, NH; D₂O exchangeable). Anal. Calc. for C₁₇H₁₄N₂O (363.43): C, 85.68; H, 5.99; N, 8.33. Found: C, 85.60; H, 5.79; N, 8.52%.

General procedure for the preparation of compounds 26 and 27

To an ice cold solution of 5-(anthracen-9-yl)-3-aryl-4,5-dihydro-1H-pyrazole 24 (0.35 g, 0.001 mol) or 25 (0.33 g, 0.001 mol) in hydrochloric acid (50%, 15 mL) was added NaN₃ (0.07 g, 0.001 mol) and the reaction mixture was stirred for 3 h. The separated solid product was filtered, washed with ethanol, dried and recrystallized from ethanol.

5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-nitroso-4, 5-dihydro-1H-pyrazole (26)

Yield: 89%, pale brown crystals, mp 150-151 °C. ¹H NMR (DMSO-d₆) δ 3.28 (dd, 1H, J₁,₂, 13.8, J₁,₃, 16.8 Hz, pyrazoline-H₁), 3.67 (dd, 1H, J₁,₁, 13.8, J₁,₃, 16.8 Hz, pyrazoline-H₁), 6.39 (t, 1H, J₁, 13.8 Hz, pyrazoline-H₁), 7.43-7.52 (m, 6H, ArH), 7.69 (d, 2H, J 8.0 Hz, ArH), 8.06 (d, 2H, J 7.6 Hz, ArH), 8.41 (d, 2H, J 8.0 Hz, ArH), 8.55 (s, 1H, H_am(10)). Anal. Calc. for C₂₃H₁₅ClN₃O (385.85): C, 71.59; H, 4.18; N, 10.89. Found: C, 71.70; H, 4.32; N, 10.70%.

5-(Anthracen-9-yl)-1-nitroso-p-tolyl-4, 5-dihydro-1H-pyrazole (27)

Yield: 84%, buff crystals, mp 129-130 °C. ¹H NMR (DMSO-d₆) δ 2.43 (3H, s, p-CH₃), 3.25-3.44 (m, 1H, pyrazoline-H₁), 3.69-4.09 (m, 1H, pyrazoline-H₁), 7.00-7.24 (m, 1H, pyrazoline-H₁), 7.18 (d, 2H, J 9 Hz, ArH), 7.39 (d, 2H, J 9.0 Hz, ArH), 7.59 (t, 2H, J 8.0 Hz, ArH), 7.69 (d, 2H, J 8.0 Hz, ArH), 7.82 (t, 2H, J 8 Hz, ArH), 7.88 (d, 2H, J 8.0 Hz, ArH), 8.17 (s, 1H, H_am(10)). Anal. Calc. for C₁₇H₁₅N₂O (365.43): C, 78.88; H, 5.24; N, 11.50. Found: C, 78.75; H, 4.98; N, 11.74%.

General procedure for the preparation of compounds 28 and 29

To a solution of 5-(anthracen-9-yl)-3-aryl-4,5-dihydro-1H-pyrazole (24, 0.35 g, 0.001 mol or 25, 0.33 g, 0.001 mol) in dry ether (20 mL) was added an equal amount of phenylisothiocyanate (0.14 g) and the reaction mixture was stirred for 6 h. The solid product obtained was filtered, washed with ethanol, dried and recrystallized from ethanol.

5-(Anthracen-9-yl)-3-(4-chlorophenyl)-N-phenyl-4, 5-dihydro-1H-pyrazole-1-carbothioamide (28)

Yield: 82%, pale grey crystals, mp 250-251 °C. IR (KBr) ν_max/cm⁻¹: 949, 1143, 1346, 1552 (NCS amide I, II, III, IV respectively), 3260 (NH); ¹H NMR (DMSO-d₆) δ 3.29-3.31 (m, 1H, pyrazoline-H₁), 3.82-3.95 (m, 1H, pyrazoline-H₁), 7.10-7.25 (m, 1H, pyrazoline-H₁), 7.30-7.35 (m, 2H, ArH), 7.39-7.45 (m, 3H, ArH), 7.48-7.54 (m, 2H, ArH), 7.58-7.64 (m, 2H, ArH), 7.69-7.73 (d, 2H, J 8.0 Hz, ArH), 7.78-7.86 (d, 2H, J 7.0 Hz, ArH), 7.90-7.97 (m, 2H, ArH), 8.08-8.17 (m, 2H, ArH), 8.17 (s, 1H, H_am(10)), 11.10 (s, 1H, NH; D₂O exchangeable). Anal. Calc. for C₂₀H₁₃ClN₂S (492.03): C, 73.23; H, 4.51; N, 8.54. Found: C, 73.40; H, 4.62; N, 8.30%.

5-(Anthracen-9-yl)-N-phenyl-3-p-tolyl-4, 5-dihydro-1H-pyrazole-1-carbothioamide (29)

Yield: 85%, buff crystals, mp 215-216 °C. IR (KBr) ν_max/cm⁻¹: 938, 1168, 1327, 1588 (NCS amide I, II, III, IV respectively), 3243 (NH); ¹H NMR (DMSO-d₆) δ 2.44 (s, 3H, p-CH₃), 3.34-3.69 (m, 1H, pyrazoline-H₁), 3.80-4.03 (m, 1H, pyrazoline-H₁), 7.28-7.33 (m, 2H, ArH), 7.36-7.41 (m, 2H, ArH), 7.44-7.49 (m, 3H, ArH), 7.51-7.58 (m, 1H,
pyrazoline-\(H_2\)), 7.62-7.68 (d, 2H, J 9 Hz, ArH) 7.70-7.75 (m, 2H, ArH), 7.79-7.83 (d, 2H, J 8.0 Hz, ArH), 7.86-7.90 (m, 2H, ArH), 8.04-8.10 (m, 2H, ArH), 8.39 (s, 1H, \(H_{\text{anth-10}}\)), 11.15 (s, 1H, NH; D\(2\)O exchangeable). Anal. Calc. for \(C_{31}H_{27}N_2S\) (511.62): C, 78.95; H, 5.34; N, 8.91. Found: C, 78.76; H, 5.12; N, 9.00%.

General procedure for the preparation of compounds 30 and 31

To a solution of 5-(anthracen-9-yl)-3-aryl-4, 5-dihydro-1H-pyrazole 24 (0.35 g, 0.001 mol) or 25 (0.33 g, 0.001 mol) in dry pyridine (10 mL) was added an equivalent amount of \(p\)-tosyl chloride (0.19 g). The reaction mixture was heated on a boiling water bath for 3 h, cooled and then poured onto crushed ice. The solid product separated was filtered, washed with water, dried and recrystallized from ethanol.

5-(Anthracen-9-yl)-3-(4-chlorophenyl)-1-tosyl-4,5-dihydro-1H-pyrazole (30)

Yield: 76%, buff crystals, mp 135-136 °C. \(^1\)H NMR (DMSO-\(d_6\)): 2.44 (3H, s, CH\(_3\)), 3.42-4.02 (m, 2H, pyrazoline-\(H_2\)), 6.60-6.67 (m, 1H, pyrazoline-\(H_2\)), 7.35 (d, 2H, J 7.6 Hz, ArH), 7.43 (d, 2H, J 8 Hz, ArH), 7.56 (t, 2H, J 8.0 Hz, ArH), 7.76 (d, 2H, J 8.0 Hz, ArH), 7.91 (t, 2H, J 8.0 Hz, ArH), 8.01 (m, 2H, ArH), 8.13 (d, 2H, J 7.6 Hz, ArH), 8.51 (m, 2H, ArH), 8.57 (s, 1H, \(H_{\text{anth-10}}\)). Anal. Calc. for \(C_{31}H_{27}N_2ClO\) (511.63): C, 70.51; H, 4.54; N, 5.48. Found: C, 70.32; H, 4.45; N, 5.69%.

5-(Anthracen-9-yl)-3-p-tolyl-1-tosyl-4,5-dihydro-1H-pyrazole (31)

Yield: 74%, buff crystals, mp 200-201 °C. \(^1\)H NMR (DMSO-\(d_6\)): 2.44 (3H, s, CH\(_3\)), 2.44 (3H, CH\(_3\)), 3.40-4.00 (m, 2H, pyrazoline-\(H_2\)), 6.60-6.64 (m, 1H, pyrazoline-\(H_2\)), 7.05 (d, 2H, J 3 Hz, ArH), 7.22 (d, 2H, J 8 Hz, ArH), 7.29 (t, 2H, J 8 Hz, ArH), 7.33 (d, 2H, J 7.0 Hz, ArH), 7.38 (d, 2H, J 15.0 Hz, ArH), 7.67 (d, 2H, J 7.0 Hz, ArH), 7.89 (d, 2H, J 15.0 Hz, ArH), 7.90 (t, 2H, J 3.0 Hz ArH), 8.47 (s, 1H, \(H_{\text{anth-10}}\)). Anal. Calc. for \(C_{21}H_{23}N_2O\) (490.62): C, 75.89; H, 5.34; N, 5.71. Found: C, 75.70; H, 5.22; N, 5.89%.

General procedure for the preparation of compounds 32-34

A mixture of 3-(anthracen-9-yl)-1-(aryl)prop-2-en-1-one 1-3 (0.01 mol) and guanidine carbonate (1.21 g, 0.01 mol) in ethanol (50 mL) was heated under reflux, while a 5 mol L\(^{-1}\) solution of sodium hydroxide (10 mL) was added portion-wise during one hour. Refluxing was continued for a further 10 h, when the reaction mixture was concentrated, diluted with water and extracted with benzene. The solid product was obtained after concentration and cooling; the precipitated product was filtered, dried and recrystallized from chloroform.

4-(Anthracen-9-yl)-6-(4-chlorophenyl)pyrimidin-2-amine (32)

Yield: 83%, buff crystals, mp 310-311 °C. IR (KBr) \(\nu_{\text{max}}\) cm\(^{-1}\): 3054, 3358 (NH\(_2\)); \(^1\)H NMR (DMSO-\(d_6\)): 7.76 (s, 2H, NH\(_2\); D\(2\)O exchangeable), 7.17 (d, 2H, J 8.0 Hz, ArH), 7.35 (s, 1H, pyrimidine-H\(_2\)), 7.44 (t, 2H, J 8.0 Hz, ArH), 7.59 (t, 2H, J 7.8 Hz, ArH), 7.98 (d, 2H, J 8.0 Hz, ArH), 8.05 (d, 2H, J 9.0 Hz, ArH), 8.18 (d, 2H, J 9.0 Hz, ArH), 8.68 (s, 1H, \(H_{\text{anth-10}}\)). Anal. Calc. for \(C_{21}H_{23}N_2\) (381.86): C, 75.49; H, 4.22; N, 11.00. Found: C, 75.21; H, 4.00; N, 11.26%.

4-(Anthracen-9-yl)-6-p-tolylypyrimidin-2-amine (33)

Yield: 81%, buff crystals, mp 210-211 °C. IR (KBr) \(\nu_{\text{max}}\) cm\(^{-1}\): 3142, 3366 (NH\(_2\)); \(^1\)H NMR (DMSO-\(d_6\)): 7.25 (s, 3H, \(p\)-CH\(_3\)), 6.07 (s, 2H, NH\(_2\); D\(2\)O exchangeable), 7.46-7.52 (m, 4H, ArH), 7.57-7.59 (m, 4H, ArH), 7.63-7.65 (d, 2H, J 9.0 Hz, ArH), 7.71-7.86 (d, 2H, J 8.0 Hz, ArH), 7.91 (s, 1H, pyrimidine-H\(_2\)), 8.18 (s, 1H, \(H_{\text{anth-10}}\)). Anal. Calc. for \(C_{21}H_{23}N_2\) (361.44): C, 83.08; H, 5.30; N, 11.63. Found: C, 83.29; H, 5.56; N, 11.42%.

4-(Anthracen-9-yl)-6-(furan-2-yl)pyrimidin-2-amine (34)

Yield: 78%, buff crystals, mp 263-264 °C. IR (KBr) \(\nu_{\text{max}}\) cm\(^{-1}\): 3147, 3323 (NH\(_2\)); \(^1\)H NMR (DMSO-\(d_6\)): 6.26 (s, 2H, NH\(_2\); D\(2\)O exchangeable), 7.53 (s, 1H, pyrimidine-H\(_2\)), 7.60-7.64 (m, 1H, ArH), 7.73-7.80 (m, 1H, ArH), 7.85-7.89 (m, 1H, ArH), 7.98 (dd, 2H, J 3.0, 6.0 Hz, ArH), 8.06-8.08 (m, 4H, ArH), 8.17 (dd, 2H, J 3.0, 6.0 Hz, ArH), 8.33 (s, 1H, \(H_{\text{anth-10}}\)). Anal. Calc. for \(C_{21}H_{23}N_2\) (337.37): C, 78.32; H, 4.48; N, 12.46. Found: C, 78.56; H, 4.27; N, 12.25%.

General procedure for the preparation of compounds 35 and 36

A mixture of 4-(anthracen-9-yl)-6-arylpyrimidin-2-amine (32, 0.38 g, 0.001 mol or 33, 0.36 g, 0.001 mol) and acetic anhydride (10 mL) was heated on boiling water bath for 2 h. The reaction mixture was poured onto cold water and the precipitated product was filtered, washed with water, dried and recrystallized from ethanol/chloroform.

N-(4-(Anthracen-9-yl)-6-(4-chlorophenyl)pyrimidin-2-yl)acetamide (35)

Yield: 83%, buff crystals, mp 130-131 °C. IR (KBr) \(\nu_{\text{max}}\) cm\(^{-1}\): 1667 (C=O), 3260 (NH); \(^1\)H NMR (DMSO-\(d_6\))
Δ 2.25 (s, 3H, NCOCH₃), 7.28 (t, 2H, J 8.0 Hz, ArH), 7.47 (t, 2H, J 6.0 Hz, ArH), 7.61 (d, 2H, J 7.6 Hz, ArH), 7.89 (d, 2H, J 6.0 Hz, ArH), 8.00 (s, 1H, pyrimidine-H₃), 8.06 (d, 2H, J 8.0 Hz, ArH), 8.17 (d, 2H, J 7.6 Hz, ArH), 8.70 (s, 1H, H₃amph), 10.77 (s, 1H, NH; D₂O exchangeable). Anal. Calc. for C₂₇H₁₉N₉O₄ (423.89): C, 73.89; H, 4.01; N, 9.75%.

N-(4-(Anthracen-9-yl)-6-p-tolylpyrimidin-2-yl)acetamide (36)

Yield: 78%, buff crystals, mp 119-120 °C. IR (KBr) vmax/cm⁻¹: 1669 (C=O), 3218 (NH); ¹H NMR (DMSO-d₆) δ 2.29 (s, 3H, NCOCH₃), 2.36 (s, 3H, p-CH₃), 7.30-7.63 (m, 4H, ArH), 7.90-7.92 (m, 4H, ArH), 8.17-8.19 (m, 4H, ArH), 8.37 (s, 1H, pyrimidine-H₃), 8.74 (s, 1H, H₃amph), 10.47 (s, 1H, NH; D₂O exchangeable). Anal. Calc. for C₂₇H₁₉N₉O₄ (403.48): C, 80.37; H, 5.25; N, 10.41. Found: C, 80.56; H, 5.01; N, 10.23%.

Biological activity assay

Measurement of the inhibition zone (IZ)

Compounds 1-36 were evaluated in vitro for antimicrobial activity against *Escherichia coli* ATCC8739 and *Pseudomonas aeruginosa* ATCC 9027 as gram-negative bacteria, *Staphylococcus aureus* ATCC 6538P as an example of gram-positive bacteria and *Candida albicans* ATCC 2091 as yeast-like fungus. The agar-diffusion method was used for the determination of antibacterial and antifungal activity. From 1 mg mL⁻¹ solutions of each of the test compounds in N,N-dimethylformamide (DMF), 75 µL was placed in a 6 mm diameter well in an agar plate seeded with the appropriate test organism in triplicates. Amoxicillin trihydrate (10 µg per disc), Ciprofloxacin (5 µg per disc), Imipenem (10 µg per disc) and Clotrimazole (100 µg per disc) were used as standard antibacterial and antifungal agents, respectively. The plates were incubated at 37 °C for 24 h. The results were recorded for each tested compound as the average diameter of inhibition zone of bacterial growth in mm (Table 1). DMF alone (control) showed no inhibition zone.

Minimal inhibitory concentration (MIC)

The microdilution susceptibility test in Muller-Hinton broth (oxygen) and Sabouraud liquid medium (oxygen) were used for the determination of antibacterial and antifungal activity with the same test organisms. The MIC measurements were carried out for compounds that showed significant inhibition zones using the two-fold serial dilution technique with solutions in the concentration range 500-15.63 µg mL⁻¹. Suspensions of the microorganisms at 10⁶ CFU mL⁻¹ (Colony Forming Units mL⁻¹) were used to inoculate the prepared test compounds in the above mentioned serial dilution broth. The culture tubes were incubated at 37 °C for 24-48 h. At the end of the incubation period the growth of bacteria was observed in the form of turbidity. The MIC is defined as the lowest concentration that showed no bacterial growth (Table 1).

**Supplementary Information**

Supplementary data are available free of charge at http://jbcs.sbq.org.br as PDF file.

**References**

Synthesis and Biological Activity of Some New Pyrazoline and Pyrimidine Derivatives

Seham Y. Hassan

Department of Chemistry, Faculty of Science, University of Alexandria, PO Box 426, 21321 Ibrahimia, Alexandria, Egypt

Figure S1. $^1$H NMR spectrum of compound 1.

*e-mail: sehanyassen@yahoo.com
Figure S2. $^1$H NMR spectrum of compound 1.

Figure S3. $^{13}$C NMR spectrum of compound 1.
Figure S4. $^{13}$C NMR spectrum of compound I.

Figure S5. $^{13}$C NMR spectrum of compound I.
Figure S6. $^1$H NMR spectrum of compound 3.

Figure S7. $^1$H NMR spectrum of compound 3.
Figure S8. $^1$H NMR spectrum of compound 3.

Figure S9. $^1$H NMR spectrum of compound 5.
Figure S10. $^1$H NMR spectrum of compound 5.

Figure S11. $^1$H NMR spectrum of compound 5.
Figure S12. $^1$H NMR spectrum of compound 8.

Figure S13. $^1$H NMR spectrum of compound 8.
Figure S14. $^1$H NMR spectrum of compound 8.

Figure S15. $^1$H NMR spectrum of compound 9.
Figure S16. $^1$H NMR spectrum of compound 9.

Figure S17. $^1$H NMR spectrum of compound 9.
Figure S18. $^1$H NMR spectrum of compound 9.

Figure S19. 2D NMR spectrum of compound 9.
Figure S20. 2D NMR spectrum of compound 9.

Figure S21. 2D NMR spectrum of compound 9.
Figure S22. 2D NMR spectrum of compound 9.

Figure S23. $^1$H NMR spectrum of compound 10.
Figure S24. $^1$H NMR spectrum of compound 10.

Figure S25. $^1$H NMR spectrum of compound 10.
Figure S26. $^1$H NMR spectrum of compound 10.

Figure S27. $^1$H NMR spectrum of compound 11.
Figure S28. $^1$H NMR spectrum of compound 11.

Figure S29. $^1$H NMR spectrum of compound 11.
Figure S30. $^1$H NMR spectrum of compound 11.

Figure S31. $^1$H NMR spectrum of compound 11.
Figure S32. $^1$H NMR spectrum of compound 14.

Figure S33. $^1$H NMR spectrum of compound 14.
Figure S34. $^1$H NMR spectrum of compound 15.

Figure S35. $^1$H NMR spectrum of compound 15.
Figure S36. $^1$H NMR spectrum of compound 17.

Figure S37. $^1$H NMR spectrum of compound 17.
Figure S38. ^1^H NMR spectrum of compound 17.

Figure S39. ^1^H NMR spectrum of compound 18.
Figure S40. $^1$H NMR spectrum of compound 18.

Figure S41. $^1$H NMR spectrum of compound 18.
Figure S42. $^1$H NMR spectrum of compound 18.

Figure S43. $^1$H NMR spectrum of compound 19.
Figure S44. $^1$H NMR spectrum of compound 19.

Figure S45. $^1$H NMR spectrum of compound 19.
Figure S46. $^1$H NMR spectrum of compound 20.

Figure S47. $^1$H NMR spectrum of compound 20.
Figure S48. $^1$H NMR spectrum of compound 20.

Figure S49. $^1$H NMR spectrum of compound 22.
Figure S50. $^1$H NMR spectrum of compound 22.

Figure S51. $^1$H NMR spectrum of compound 22.
Figure S52. $^1$H NMR spectrum of compound 26.

Figure S53. $^1$H NMR spectrum of compound 26.
**Figure S54.** $^1$H NMR spectrum of compound 26.

**Figure S55.** $^1$H NMR spectrum of compound 26.
Figure S56. $^1$H NMR spectrum of compound 33.

Figure S57. $^1$H NMR spectrum of compound 33.
Figure S58. $^1$H NMR spectrum of compound 36.

Figure S59. $^1$H NMR spectrum of compound 36.
Figure S60. $^1$H NMR spectrum of compound 36.

Figure S61. IR spectrum of compound 20.
Figure S62. $^{13}$C NMR spectrum of compound 20.

Figure S63. $^{13}$C NMR spectrum of compound 20.