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ORIGINAL ARTICLE

A catalyst-free approach to synthesis of spiroacenaphthylene-pyranopyrazole derivatives in water media

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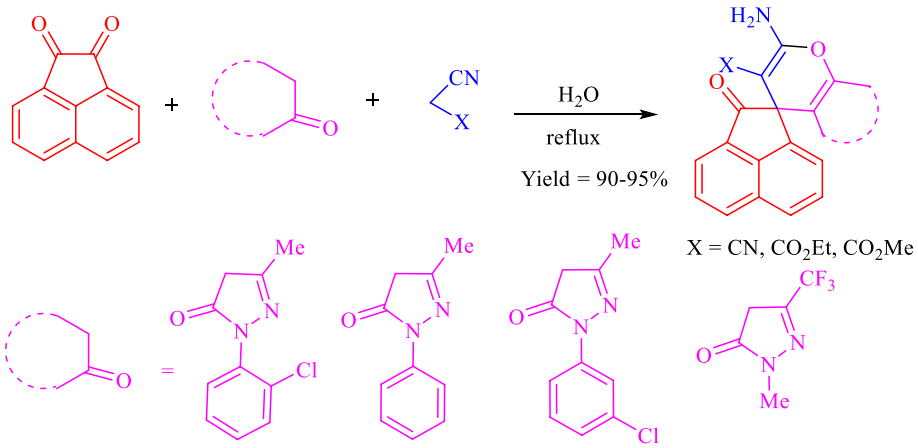
Abstract

A simple approach for the synthesis of spiroacenaphthylene-pyranopyrazole derivatives was achieved via the reaction between acenaphthoquinone, pyrazolones, and activated methylene compounds (malononitrile derivatives) in water as a green solvent without using any catalyst in order to avoid the use of transition metal. This method has the advantages of mild reaction condition, short reaction time, easy workup, excellent yields, and avoidance of environmentally hazardous solvents.

Graphic abstract



Keywords Acenaphthenequinone · Pyrazolone · One-pot reaction · Spiro systems

Introduction

Multi-component reaction (MCRs) is a chemical reactions that three or more raw materials produce a single product in one step. The target molecules have great efficiency and reagents atom economy. MCRs are used for the efficient synthesis of natural compounds for the discovery of biological activities and drugs [1–5]. The importance of multi-component compounds in organic chemistry has been proven [6, 7]. The spiro compounds are an important class of naturally occurring material characterized by highly significant biological properties. 4*H*-pyrans derivatives have been considered because their pharmacological activity [8] that include anti-anaphylactic activity [9, 10], anticancer [11], cytotoxic [12], anti-HIV [13, 14], anti-inflammatory [15], antimalarial [16, 17], antimicrobial [18], antineurodegenerative disorders like Alzheimer's, Parkinson's, and Huntington's disease and many more [19]. 4*H*-pyrans are useful intermediates for synthesis of pyranopyridine derivatives [20],

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polyazanaphthalenes [21], pyranopyrimidines, and pyridin-2-ones [22]. The 2-amino-3-cyano-4*H*-pyrans showed important photochemical activity [23]. Recently, a series of synthetic 2-amino-3-cyano-4*H*-pyrans (Fig. 1) have been appraised to possess potent anticancer, antibacterial, antifungal, and antirheumatic properties [24]. Pyrazolone structure is a well-known heterocycle in many drug materials of medicinal fields. Some pyrazolone derivatives (Fig. 2) such as antipyrine (phenazone), aminopyrine (aminophenazone), metamizol (novalgin), and 4-isopropylpyrine (propyphenazone) are all useful antipyretic and analgesic drugs [25]. Pyrazolone derivatives have applications in the development of acaricides, dyes, fungicides, herbicides, insecticides, inhibitors omnipresence, and reagents [26, 27]. Recently, several methods have been reported for the synthesis of a series of spiro-pyran derivatives [28]. However, some of the reported method such as way ammonium chloride (20 mol%) was found as catalyst for the multi-component reaction of acenaphthenequinone, 1,3-cyclohexanedione or dimedone, and malononitrile for the formation of spiroacenaphthylene-chromenes in 75–90% yields. Triethylamine (20 mol%) recently has been used to catalyst general multi-component reaction of acenaphthenequinone, containing carbonyl group CH-acids and malononitrile with the formation of spiroacenaphthylenes in 40–85% yields [29]. Our approach for the synthesis of spiroacenaphthylene without using catalyst in water under mild reaction conditions, and high yields are described.

Results and discussion

Initially, a three-component reaction between acenaphthoquinone **1**, pyrazolone **2,** and activated methylene reagent (malononitrile) **3** was used as a model to optimize the reaction conditions. That obtained 6′-amino-1′-(2-chlorophenyl)-3′-methyl-2-oxo-1′*H*,2*H*-spiro[acenaphthylene-1,4′-pyrano[2,3-*c*]pyrazole]-5′-carbonitrile **4a**, in excellent yields (Scheme 1).

To achieve the optimal conditions for the synthesis of **4a,** we examined the condensation reaction of acenaphthenequinone **1** (1 mmol), 1-(2-chlorophenyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one **2a** (1 mmol), and malononitrile (1 mmol), in several different solvents (water, EtOH, MeOH) and also in different temperatures (Table 1). The results clearly indicate that using H_2O as a green solvent in 80 °C leads to an increase in the synthetic efficiency to 98%. Therefore, it shows superiority over the other conditions as reaction media (entry 5).

Thus, under the optimized reaction conditions, we used various substituted 1-aryl pyrazolone derivatives such as 1-(chlorophenyl)-3-methyl pyrazolone and 1-methyl-3-(trifluoromethyl)pyrazolone with malononitrile, methyl cyanoacetate, and ethyl cyanoacetate gave the desired product **4a–4l** with excellent yields (Table 2). The structures of products **4a–4l** were determined by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy as well as mass spectrometry (ESI).

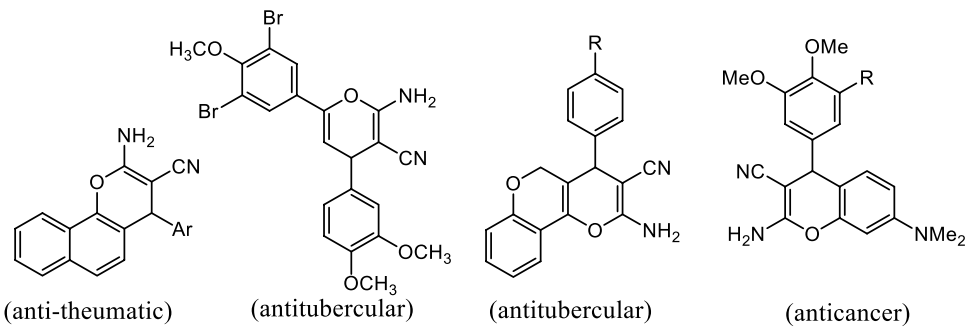


Fig. 1 Selected bioactive compounds consisted of 2-amino-4*H*-pyrans

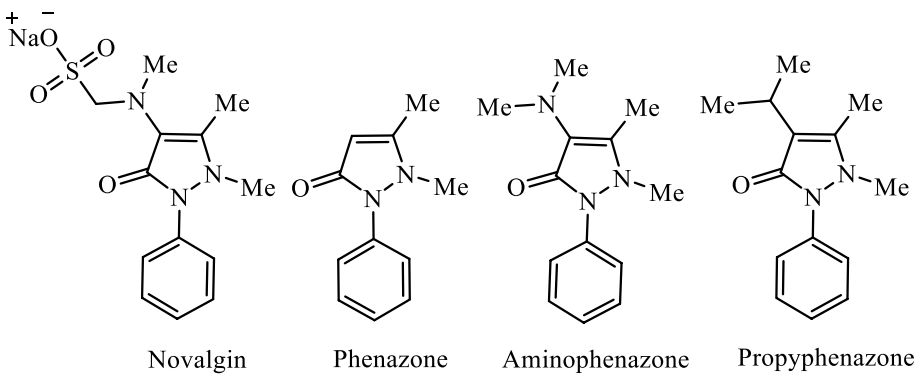


Fig. 2 Typical compounds of bioactive pyrazolones

Scheme 1 Synthesis of spiroacenaphthelyne-pyrano-pyrazole via three-component reaction

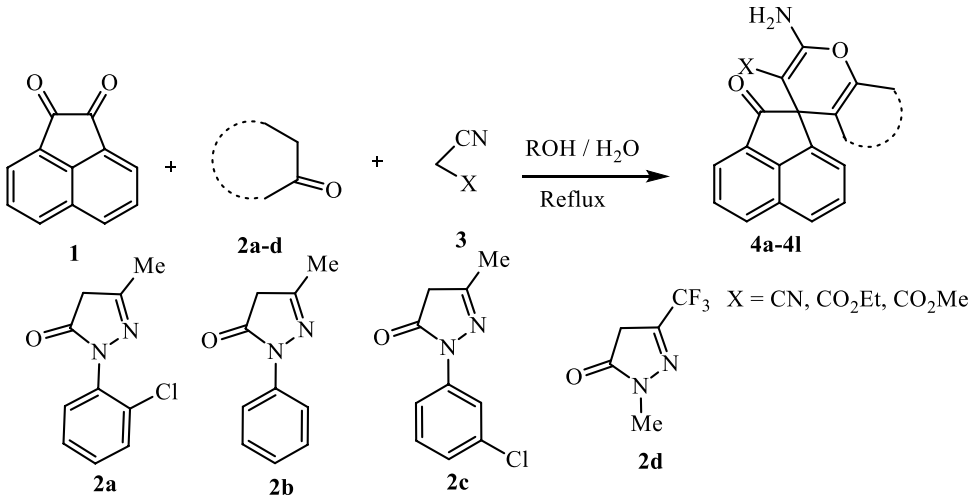


Table 1 Synthetic results of **4a** under different solvent conditions

Entry	Solvent	Temperature (°C)	Time (h)	Yield (%)[a]
1	MeOH	20	2	37
2	MeOH	65	2	65
3	EtOH	80	2	95
4	H_2O	80	1	93
5	H_2O	80	2	98

Compound acenaphthenequinone **1** (1 mmol), 1-(2-chlorophenyl)-3-methyl-1*H*-pyrazol-5(4*H*)-one **2a** (1 mmol), malononitrile (1 mmol), solvent 4 mL

[a]Yield of isolated **4a**

Synthesis of spiroacenaphthylene-pyranopyrazole derivatives without using of catalyst with acenaphthoquinone undergos a smooth reaction with special pyrazolones and activated methylene reagents (malononitrile derivatives) to reported. The yields obtained were excellent without formation of any side products, and also products are obtained in very good purity passed microanalysis (Table 2). The reaction mixture was filtered and washed with EtOH/H_2O, and the product dried without further purification. Also, the catalyst-free reactions performed in H_2O are significantly safer, nontoxic environmentally friendly, and inexpensive. The absence of catalyst for the reaction avoids the use of dampness-sensitive and heavy metal materials, such as Lewis acids. This work is applicable for the synthesis of different types of spiro-pyranopyrazole acenaphthylene derivative. The mass spectra of these products displayed molecular ion peaks at the appropriate *m/z* values. The present procedure has the advantage that not only the reaction is performed under neutral conditions but also the reactants can be mixed without any activation or modification. The simplicity of the present procedure makes it an interesting alternative to complex multi-step approaches. A presumable mechanism for the formation of product is showed in Scheme 2. Firstly, addition of acenaphthoquinone to pyrazolone leads to the formation of Knoevenagel product **5** then added activated methylene reagent (malononitrile derivatives) to intermediate **5** would give product **4**.

Conclusion

We have reported an efficient, catalyst-free, three-component method of acenaphthenequinone, pyrazolone derivatives, and malononitrile in water to give spiroacenaphthylene-pyranopyrazole derivatives in high yields under suitable conditions. The present procedure has the advantages including excellent selectivity, mild conditions, clean and simple workup and no need to isolate the products with column chromatography.

Experimental section

General remarks

All of the chemicals used in this work were purchased from Merck and Aldrich Chemical Companies. Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were recorded in KBr disks on a Shimadzu IR-460 spectrometer, and absorbencies are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were measured with a Bruker DRX-300AVANCE spectrometer at 299.87 MHz. NMR spectra were obtained in solutions of DMSO-d_6 using TMS as internal standard in ppm. Mass spectra were recorded on an Agilent Technologies 5975C VL MSD with Tripe-Axis Detector mass spectrometer operating at an ionization potential of 70 eV.

Table 2 Synthesis of spiroacenaphthylene-pyranopyrazole derivatives **4a–4l**

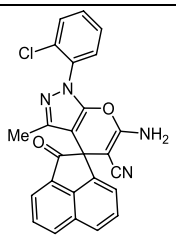
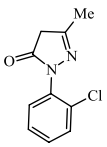
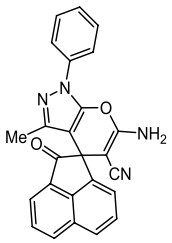
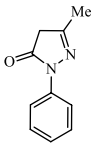
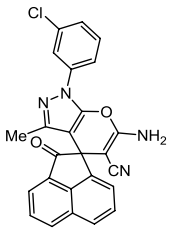
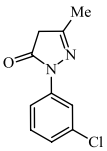
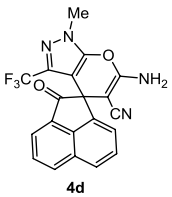
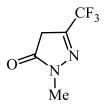
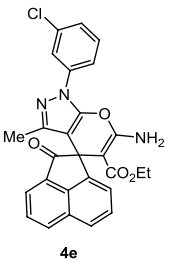
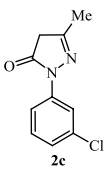
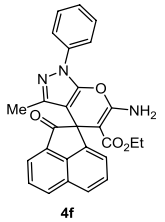
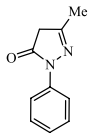
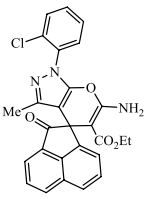
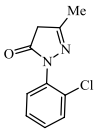
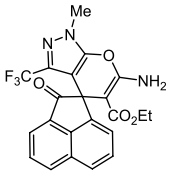
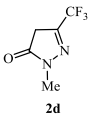
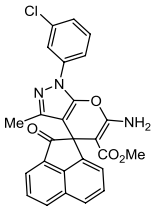
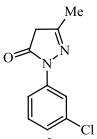
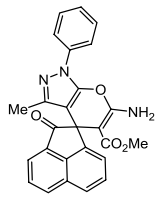
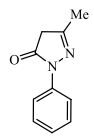
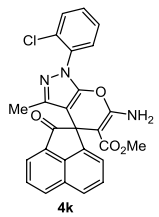
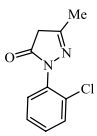
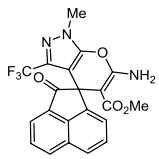
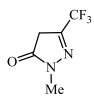
Entry	Product **4**	Pyrazolone **2**	CH-acid **3**	Time (h)	Yield (%)[a]	m.p. (°C) (dec.)
1	 **4a**	 **2a**		2	95	188–190
2	 **4b**	 **2b**		2	92	196–198 194–196 lit. [30]
3	 **4c**	 **2c**		2	90	228–230
4	 **4d**	 **2d**		2	93	264–266
5	 **4e**	 **2c**		2	94	217–218

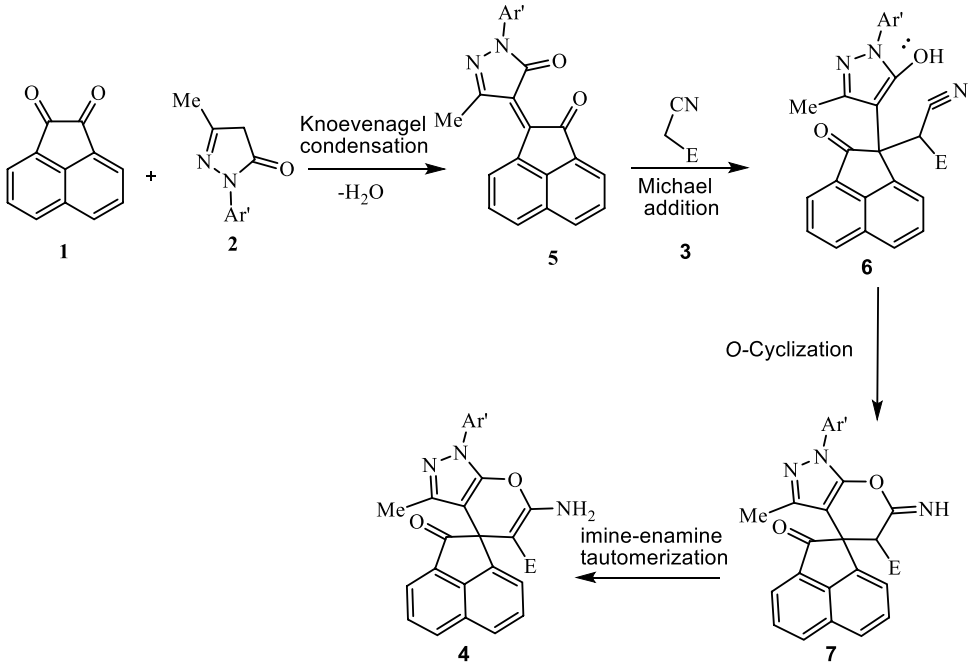
Table 2 (continued)

6	 **4f**	 **2b**		2	91	203–204
7	 **4g**	 **2a**		2	95	210–212
8	 **4h**	 **2d**		2	92	244–246
9	 **4i**	 **2c**		2	95	223–224
10	 **4j**	 **2b**		2	94	209–210
11	 **4k**	 **2a**		2	92	228–229
12	 **4l**	 **2d**		2	93	236–238

Compound **1** (1 mmol), **2a–2d** (1 mmol), malononitrile derivatives (1 mmol), H_2O/EtOH (3 mL), 80 °C, 2 h

[a]Yield of isolated product

Scheme 2 Proposed mechanism for the formation of **4**



General procedure for the synthesis of product 4a

Typical procedure for preparation of 6′-amino-1′-(2-chlorophenyl)-3′-methyl-2-oxo-1′*H*,2*H*-spiro[acenaphthylene-1,4′-pyrano[2,3-*c*]pyrazole]-5′-carbonitrile (**4a**) (95% yield).

A mixture of acenaphthoquinone **1** (0.182 g, 1 mmol), 1-(2-chlorophenyl)-3-methyl-2-pyrazolin-5-one **2a** (0.208 g, 1 mmol), H_2O (5 ml), was stirred at reflux condition for 1 h was then added component **3** (malomonitrile) (0.066 g, 1 mmol) in the similar condition. Upon completion, monitored by TLC on silica gel using a 1:1 mixture of ethyl acetate/*n*-hexane, the reaction mixture was allowed to cool to 4 °C 2 h (Or to room temperature). The reaction mixture was filtered to give a pure product **4a** (95% yield). Spiroacenaphthylene derivatives were analytically pure without recrystallization.

6′-Amino-1′-(2-chlorophenyl)-3′-methyl-2-oxo-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile (4a) Yellow solid, Yield, (95%). Mp: 188–190 °C, IR (KBr), ν_{max}: 3339, 3165 (NH_2), 2198 (CN), 1717 (C=O), 1653 (C=C), 1529, 1391, 1139 (C–O), 768 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 1.03 (3 H, s, CH_3), 7.51–7.60 (m, 5 H, ArH), 7.65–7.74 (m, 2 H, ArH), 7.80 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.93 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.09 (d, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 8.42 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.4, 52.7 (C_{spiro}), 57.3, 96.3, 118.6, 122.1, 123.2, 125.8, 128.9, 129.6, 130.0, 130.4, 130.5, 130.8, 131.0, 131.4, 131.9, 133.3, 134.3, 141.1, 141.6, 144.6, 146.6, 161.6, 203.9 (C=O). MS (EI) *m/z* (%): 438 (M^+, 0.8), 372 (36), 344 (19), 309 (25), 230 (100), 202 (80), 173 (59), 139 (28), 111 (42), 75 (30), 63 (17). Anal. Calcd. for $C_{25}H_{15}ClN_4O_2$ (438.87): C, 68.42; H, 3.45; N, 12.77. Found: C, 68.1; H, 3.9; N, 12.5.

6′-Amino-3′-methyl-2-oxo-1′-phenyl-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile (4b) Pale green solid, Yield, (92%). Mp: 196–198 °C, IR (KBr), ν_{max}: 3372, 3314 (NH_2), 2198 (CN), 1707 (C=O), 1651 (C=C), 1526, 1433, 1142 (C–O), 771 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 1.03 (s, 3 H, CH_3), 7.34 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.51 (t, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 7.58 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.66 (s, 2 H, ArH), 7.75–7.80 (m, 3 H, ArH), 7.92 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.06–8.10 (m, 2 H, ArH), 8.41 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.4, 52.6 (C_{spiro}), 57.3, 97.6, 118.6, 120.7, 122.3, 123.3, 125.8, 127.1, 129.6, 129.9, 130.0, 130.5, 130.9, 133.4, 137.7, 140.9, 141.6, 144.3, 145.4, 161.5, 204.0 (C=O).

6′-Amino-1′-(3-chlorophenyl)-3′-methyl-2-oxo-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile (4c) Yellow solid, Yield, (90%). Mp: 228–230 °C, IR (KBr), ν_{max}: 3314, 3192 (NH_2), 2198 (CN), 1716 (C=O), 1654 (C=C), 1591, 1518, 1433, 1135 (C–O), 993, 836, 674 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ: 1.04 (3 H, s, CH_3), 7.40 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.70–7.60 (m, 2 H, ArH), 7.75–7.82 (m, 5 H, ArH), 7.92 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.07–8.10 (m, 2 H, ArH), 8.42 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.4, 52.7 (C_{spiro}), 57.3, 96.3, 118.6, 122.1, 123.2,

125.8, 128.9, 129.6, 130.0, 130.4, 130.5, 130.8, 131.0, 131.4, 131.9, 133.3, 134.3, 141.1, 141.6, 144.6, 146.6, 161.6, 203.9 (C=O). MS (EI) *m/z* (%): 440 (M^++2, 14), 438 (M^+, 38), 412 (59, –CN), 372 (19), 343 (17), 243 (100), 208 (34), 176 (27), 139 (12), 111 (39), 75 (24). Anal. Calcd. for $C_{25}H_{15}ClN_4O_2$ (438.87): C, 68.42; H, 3.45; N, 12.77. Found: C, 68.7; H, 3.2; N, 12.5.

6′-Amino-1′-methyl-2-oxo-3′-(trifluoromethyl)-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carbonitrile (4d) White solid, Yield, (93%). Mp: 264–266 °C, IR (KBr), ν_{max}: 3388, 3305 (NH_2), 2193 (CN), 1722 (C=O), 1642 (C=C), 1561, 1498, 1394, 1298, 1158 (C–O), 783 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.84 (3 H, s, CH_3), 7.49 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.67–7.74 (m, 3 H, ArH), 7.87 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.03 (d, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 8.36 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 35.5, 52.0 (C_{spiro}), 58.1, 96.3, 118.1, 122.0, 123.2, 125.8, 127.2, 129.4, 129.7, 130.4, 130.7, 133.1, 133.7, 141.3, 141.6, 147.0, 160.5, 203.3 (C=O). MS (EI) *m/z* (%): 396 (M^+, 96), 370 (94, –CN), 324 (10), 297 (100), 250 (40), 188 (14), 43 (39). Anal. Calcd. for $C_{20}H_{11}F_3N_4O_2$ (396.33): C, 60.61; H, 2.80; N, 14.14. Found: C, 60.3; H, 2.4; N, 14.5.

Ethyl-6′-amino-1′-(3-chlorophenyl)-3′-methyl-2-oxo-1′H,2H-spiro[acenaphthylene-1,4′-prano[2,3-c]pyrazole]-5′-carboxylate (4e) Colorless solid, Yield, (94%). Mp: 217–218 °C, IR (KBr), ν_{max}: 3380, 3277 (NH_2), 2977, 1697 (C=O), 1645 (C=C), 1596, 1512, 1432, 1383, 1132 (C–O), 987, 771 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.9 (3 H, s, CH_3), 7.37 (t, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 7.52 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.63 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.82–7.85 (m, 3 H, ArH), 7.93 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.00 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.30 (d, $^3J_{HH}$ = 8 Hz, 3 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.6, 12.9, 52.4 (C_{spiro}), 59.1, 75.8, 100.1, 118.7, 119.8, 120.4, 121.9, 124.5, 126.7, 128.9, 129.5, 130.1, 131.6, 132.2, 133.1, 134.3, 138.9, 141.2, 144.5, 144.8, 145.3, 161.9, 168.2, 205.1 (C=O). MS (EI) *m/z* (%): 485 (M^+, 2), 412 (100, –CO_2Et), 373 (23), 277 (10), 208 (8), 176 (25), 111 (19), 75 (11). Anal. Calcd. for $C_{27}H_{20}ClN_3O_4$ (485.11): C, 66.74; H, 4.15; N, 8.65. Found: C, 66.3; H, 3.8; N, 8.3.

Ethyl-6′-amino-3′-methyl-2-oxo-1′-phenyl-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carboxylate (4f) Colorless solid, Yield, (91%). Mp: 203–204 °C, IR (KBr), ν_{max}: 3392, 3273 (NH_2), 2975, 1701 (C=O), 1646 (C=C), 1514, 1383, 1268, 1132 (C–O), 777 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.01 (3 H, s, CH_3), 7.33–7.36 (m, 2 H, ArH), 7.50 (t, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 7.63 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.81 (d, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 7.86 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.93 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.00 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.24 (s, 2 H, ArH), 8.29 (d, $^2J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.6, 12.8, 19.1, 52.5 (C_{spiro}), 59.1, 75.9, 99.7, 120.3, 120.5, 121.8, 124.4, 126.9, 128.9, 129.5, 129.9, 130.1, 132.1, 133.1, 137.8, 141.2, 144.3, 144.5, 145.0, 161.9, 162.0, 168.2, 205.1 (C=O). MS (EI) *m/z* (%): 452 (M^++1, 10), 451 (M^+, 7), 378 (100, –CO_2Et), 339 (79), 309 (41), 277 (13), 232 (11), 205 (23), 176 (31), 77 (63). Anal. Calcd. for $C_{27}H_{21}N_3O_4$ (451.48): C, 71.83; H, 4.69; N, 9.31. Found: C, 72.3; H, 4.3; N, 9.1.

Ethyl-6′-amino-1′-(2-chlorophenyl)-3′-methyl-2-oxo-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carboxylate (4 g) Yellow solid, Yield, (95%). Mp: 210–212 °C, IR (KBr), ν_{max}: 3373, 3271 (NH_2), 2972, 1688 (C=O), 1647 (C=C), 1514, 1379, 1265, 1096 (C–O), 770 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.9 (3 H, s, CH_3), 7.31 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.49–7.57 (m, 2 H, ArH), 7.63–7.73 (m, 3 H, ArH), 7.85–8.14 (m, 5 H, ArH), 8.30 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.6, 12.8, 52.6 (C_{spiro}), 59.1, 76.0, 98.3, 120.1, 121.8, 124.4, 128.8, 128.9, 129.6, 130.1, 130.4, 130.8, 131.3, 131.7, 132.1, 133.2, 134.5, 141.1, 144.8, 145.2, 145.4, 162.1, 168.3, 205.1 (C=O). MS (EI) *m/z* (%): 486 (M^++1, 10), 485 (M^+, 3), 412 (100, –CO_2Et), 372 (71), 359 (3), 309 (65), 277 (8), 233 (14), 176 (59), 111 (47), 75 (26). Anal. Calcd. for $C_{27}H_{20}ClN_3O_4$ (485.11): C, 66.74; H, 4.15; N, 8.65. Found: C, 66.3; H, 4.5; N, 8.2.

Ethyl-6′-amino-1′-methyl-2-oxo-3′-(trifluoromethyl)-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carboxylate (4h) White solid, Yield, (92%). Mp: 244–246 °C, IR (KBr), ν_{max}: 3386, 3286 (NH_2), 2987, 1681 (C=O), 1637 (C=C), 1506, 1385, 1279, 1170, 1119 (C–O), 776 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: −0.12 (3 H, s, CH_3), 0.86 (2 H, s, CH_2), 3.82 (3 H, s, CH_3), 7.28 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.56 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.79 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.89 (t, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 8.23 (d, $^3J_{HH}$ = 8 Hz, 3 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.4, 35.3, 52.2 (C_{spiro}), 59.2, 76.4, 120.2, 121.6, 122.2, 124.6, 124.8, 128.6, 129.1, 130.2, 131.6, 133.4, 141.4, 145.1, 145.8, 161.1, 161.2, 168.0, 204.6 (C=O). MS (EI) *m/z* (%): 443 (M^+, 1), 370 (100, –CO_2Et), 342 (11), 295 (11), 250 (16), 208 (81), 43 (16). Anal. Calcd. for $C_{22}H_{16}F_3N_3O_4$ (443.11): C, 59.60; H, 3.64; N, 9.48. Found: C, 59.3; H, 3.9; N, 9.2.

Methyl-6′-amino-1′-(3-chlorophenyl)-3′-methyl-2-oxo-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carboxylate (4i) Yellow solid, Yield, (95%). Mp: 223–224 °C, IR (KBr), ν_{max}: 3380, 3281 (NH_2), 2946, 1690 (C=O), 1645 (C=C), 1594, 1508, 1429, 1377, 1269, 1132 (C–O), 770 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ:

0.8 (3 H, s, CH_3), 2.9 (3 H, s, CO_2Me), 7.37 (t, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 7.52 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.62 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.82–7.87 (m, 3 H, ArH), 7.92 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.99 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.23 (s, 2 H, ArH), 8.29 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.8, 50.75, 52.4 (C_{spiro}), 76.1, 100.2, 118.7, 119.8, 120.5, 121.8, 124.6, 126.7, 129.0, 129.5, 130.0, 131.1, 131.6, 132.1, 132.9, 134.3, 138.9, 144.6, 144.7, 145.2, 161.7, 168.3, 205.0 (C=O). MS (EI) *m/z* (%): 471 (M^+, 0.1), 412 (50, –CO_2Me), 372 (14), 343 (14), 263 (18), 208 (100), 176 (30), 151 (8), 111 (17), 70 (20). Anal. Calcd. for $C_{26}H_{18}ClN_3O_4$ (471.90): C, 66.18; H, 3.84; N, 8.90. Found: C, 66.7; H, 3.4; N, 8.7.

Methyl-6′-amino-3′-methyl-2-oxo-1′-phenyl-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carboxylate (4j) Yellow solid, Yield, (94%). Mp: 209–210 °C, IR (KBr), ν_{max}: 3376, 3279 (NH_2), 2943, 1702 (C=O), 1644 (C=C), 1510, 1436, 1377, 1269, 1130 (C–O), 763 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.8 (3 H, s, CH_3), 2.9 (3 H, s, CO_2Me), 7.33 (d, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 7.50 (t, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 7.62 (t, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.80 (d, $^3J_{HH}$ = 8 Hz, 2 H, ArH), 7.86 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.92 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.99 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 8.17 (s, 2 H, ArH), 8.29 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.8, 50.6, 52.6 (C_{spiro}), 76.2, 99.8, 120.3, 120.5 (2C), 121.7, 124.5, 126.9, 128.9, 129.5, 129.9 (2C), 130.0, 132.1, 133.0, 137.8, 140.8, 144.3, 144.4, 144.9, 161.8, 168.4, 205.0 (C=O). MS (EI) *m/z* (%): 437 (M^+, 2), 405 (13), 378 (100, –CO_2Me), 338 (63), 309 (75), 263 (11), 232 (9), 205 (15), 176 (33), 150 (13), 77 (68), 51 (17). Anal. Calcd. for $C_{26}H_{19}N_3O_4$ (437.46): C, 71.39; H, 4.38; N, 9.61. Found: C, 71.2; H, 4.6; N, 9.5.

Methyl-6′-amino-1′-(2-chlorophenyl)-3′-methyl-2-oxo-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carboxylate (4k) Yellow solid, Yield, (92%). Mp: 228–229 °C, IR (KBr), ν_{max}: 3326, 3256 (NH_2), 2986, 1726 (C=O), 1684, 1636 (C=C), 1514, 1436, 1379, 1278, 1136 (C–O), 769 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 0.8 (3 H, s, CH_3), 2.8 (3 H, s, CO_2Me), 7.29 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.54–7.72 (m, 5 H, ArH), 7.85–8.05 (m, 5 H, ArH), 8.29 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 12.7, 50.6, 52.8 (C_{spiro}), 76.3, 98.4, 120.2, 121.7, 124.5, 128.8, 128.9, 129.6, 130.0, 130.4, 130.8, 131.3, 131.7, 132.0, 133.0, 134.5, 140.7, 144.8, 145.1, 145.5, 161.9, 168.5, 204.9 (C=O). MS (EI) *m/z* (%): 472 (M^++1, 4), 412 (100, –CO_2Me), 372 (62), 344 (42), 309 (62), 263 (15), 233 (13), 205 (24), 176 (62), 139 (12), 111 (44), 75 (24). Anal. Calcd. for $C_{26}H_{18}ClN_3O_4$ (471.90): C, 66.18; H, 3.84; N, 8.90. Found: C, 66.4; H, 3.3; N, 8.6.

Methyl-6′-amino-1′-methyl-2-oxo-3′-(trifluoromethyl)-1′H,2H-spiro[acenaphthylene-1,4′-pyrano[2,3-c]pyrazole]-5′-carboxylate (4l) Yellow solid, Yield, (93%). Mp: 236–238 °C, IR (KBr), ν_{max}: 3382, 3282 (NH_2), 2955, 1688 (C=O), 1638 (C=C), 1511, 1433, 1377, 1283, 1171, 1119 (C–O), 775 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 2.83 (3 H, s, CH_3), 3.8 (3 H, s, CO_2Me), 7.27 (d, $^3J_{HH}$ = 8 Hz, 1 H, ArH), 7.52–7.59 (m, 1 H, ArH), 7.76–7.81 (m, 1 H, ArH), 7.86–7.91 (m, 3 H, ArH), 8.14–8.15 (m, 1 H, ArH), 8.22–8.24 (m, 1 H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 35.3, 50.6, 52.3 (C_{spiro}), 76.8, 97.9, 120.3, 121.9, 122.2, 124.6, 124.7, 128.6, 129.1, 130.1, 131.5, 133.3, 133.7, 141.0, 145.0, 145.9, 160.9, 168.1. MS (EI) *m/z* (%): 429 (M^+, 0.9), 370 (100, –CO_2Me), 342 (12), 295 (12), 250 (20), 201 (9), 163 (5), 43 (15). Anal. Calcd. for $C_{21}H_{14}F_3N_3O_4$ (429.36): C, 58.75; H, 3.29; N, 9.79. Found: C, 58.4; H, 3.7; N, 9.5.

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