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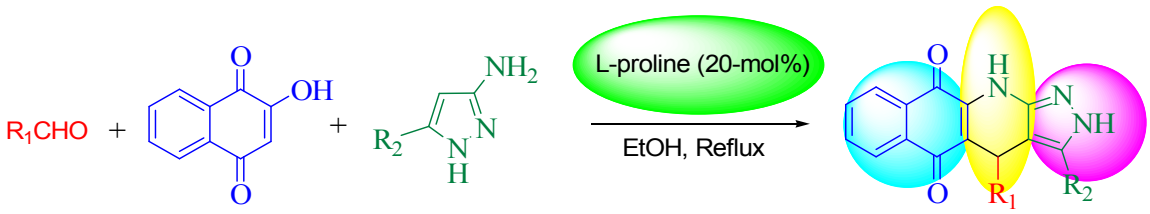
Graphical abstract

L-proline catalyzed multicomponent reactions: Facile access to 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione derivatives

Shaik Karamthulla ,[a] Suman Pal ,[a] Tasneem Parvin,[b] Lokman Hakim Choudhury[a]*



Three component reaction of 2-hydroxy 1,4-naphthoquinones, aldehydes, and aminopyrazoles in the presence of catalytic amount of L-proline has been described for the synthesis of a series of 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione derivatives.

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PAPER

L-proline catalyzed multicomponent reactions: Facile access to 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione derivatives

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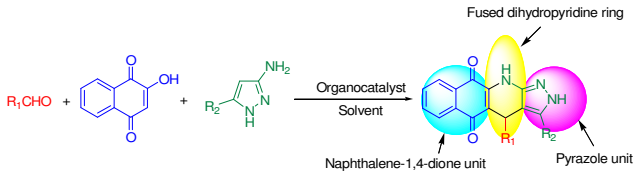
A series of 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione derivatives have been synthesized from the three component reactions of 2-hydroxy-1,4-naphthoquinone, aldehydes, and aminopyrazoles in the presence of catalytic amount of L-proline. This domino reaction proceeds smoothly in good to excellent yields and offers several advantages including no column chromatography, simple reaction procedure, metal-free reaction conditions and applicable to a broad range of aldehydes.

Introduction

Synthesis of diverse polycyclic heterocycles from the readily available starting materials in a cost and time effective manner has remained useful in organic synthesis owing to their widespread applications in pharmaceuticals, agrochemicals and in material sciences.[1] Multicomponent reactions (MCRs), where three or more reactants are mixed in a single pot to generate a product incorporating most of the atoms of the starting materials,[2] are considered as one of the best tool for the easy access of diverse heterocycles under Pot Atom and Step Economic (PASE)[3] conditions. Organocatalysis in multicomponent reactions makes the process greener as it works under the metal-free conditions and avoids the toxicity associated with metals. Considering this fact, in recent times, organo catalyzed MCRs have become very popular in organic synthesis.[4]

Recently we have, reported the virtue of imidazole as organocatalyst in MCRs for the synthesis of diverse carbo and heterocycles.[5] We also have demonstrated a three component reaction of 4-hydroxycoumarin, aldehyde and aminopyrazole for the constrtuction of a series of fused dihydroypyridines.[6] MCRs using amino pyrazoles have become very popular strategy for the construction of functionalized polycyclic heterocycles.[7] Similar to aminopyrazoles, 2-hydroxy-1,4-naphthoquinone is also a widely used starting material in MCRs.[8] Considering their usefulness and potent bioactivities we wanted to explore further these two substrates in our MCRs. In continuation of our ongoing research on MCRs,[9] we wished to develop a simple and useful three component reaction of aminopyrazole, 2-hydroxy-1,4-naphthoquinone and aldehyde using readily available organocatalyst for the synthesis of polycyclic N-heterocycles as shown in Scheme 1.



Scheme 1 Synthesis of polycyclic N-heterocycles using three component reactions.

L-proline is one of the cheap, readily available and most explored organocatalyst both in two and multicomponent reactions.[10] Due to the presence of a basic secondary amine and an acidic carboxylic group, proline can catalyze a wide range of reactions. Thus, we envisioned that L-proline will also act as an efficient organocatalyst in our proposed MCRs.

Pyrazolo[3,4-*b*]quinoline derivatives (**A**) posses a wide range of medicinal properties such as antiviral,[11] antibacterial,[12] antimicrobial,[13] oncogenic Ras inhibiting,[14] and cyclooxygenase inhibiting activities.[15] In addition, these compounds exhibit luminescence[16] and fluorescence[17] properties. Considering their wide spread applications, development of new and efficient methods for the access of these classes of compounds have lot of significance. Recently Li et al.[18] have reported a microwave assisted methodology for the synthesis of benzo[*h*]pyrazolo[3,4-*b*]quinolines in acetic acid. They have successfully converted the resulting benzoquinoline products into quinoxaline-fused benzo[*h*]isoxazolo[5,4-*b*]quinolines by reacting with benzene-1,2-diamine under microwave irradiation. On the other hand, a few methods employing various catalysts such as molecular iodine[19], diammonium hydrogen phosphate[20] and $InCl_3$[21] are also known in the literature for synthesis of 4-aryl-3-methyl-1-phenyl-1*H*-benzo[*h*]pyrazolo[3,4-*b*]quinoline-5,10-diones (a 1,4-diketone derivative) by the three component condensation of 3-methyl-1-phenyl-1*H*-pyrazol-5-amine, aldehydes and 2-hydroxynaphthalene-1,4-dione. Nageswar *et al.*[22] have recently synthesized pyrazolo[3,4-*b*]quinoline derivatives by one pot three component reaction of aldehyde, aminopyrazole, and 1,3-cyclohexanedione using polyethylene glycol (PEG)-400 as reaction medium. Interestingly, all the above mentioned reported protocols describe the synthesis of Pyrazolo[3,4-*b*]quinoline

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† Electronic Supplementary Information (ESI) available:: ^{1}H NMR and ^{13}C NMR spectra for all the products are available. See DOI: 10.1039/b000000x/

derivatives with a fused pyridine ring (**A**), and our objective is to access 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione derivatives (**B**) with a fused dihydropyridine ring from the three component reaction of 2-hydroxy-1,4-naphthoquinone, aldehyde, and aminopyrazole using metal-free environmentally benign reaction conditions (Figure 1).

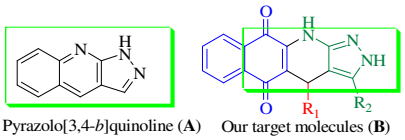
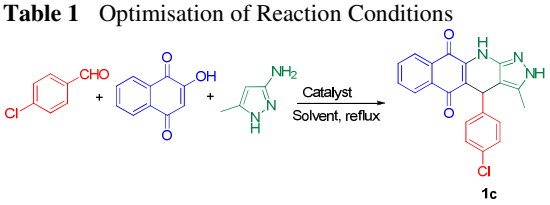


Fig. 1 Structural correlation of A and B

Result and discussion

Initially the reaction of 4-chlorobenzaldehyde (1.0 mmol), 2-hydroxy-1,4-naphthoquinone (1.0 mmol) and 3-amino-5-methylpyrazole (1.0 mmol) was studied without using any catalyst in ethanol. At room temperature, the above combination did not provide the expected three component product even after 24 hrs stirring. Interestingly, when the same set of reactants in ethanol was refluxed in absence of any catalyst for 9 hours, the desired three component product **1c** was obtained in 15% only (Table 1, entry 2). The compound **1c** was fully characterized by IR, ^{1}H, ^{13}C NMR and elemental analysis. Encouraged by this result, we shifted our attention towards optimization of the reaction conditions using various catalysts for the same model reaction in ethanol as solvent under reflux conditions. Basic organocatalysts such as DBN, Et_3N, and DABCO were screened under the similar reaction conditions to find the optimum yield and reaction time. The results are summarized in Table 1 (entries 3-5). Interestingly, L-proline (20 mol %) showed the best result among all the screened catalysts. Next, to find the best solvent for this transformation the same reaction was also screened in various solvents such as EtOH, CH_3CN, DMF, CH_2Cl_2 and THF (Table 1, entries 6 and 9-12) in the presence of 20 mol% L-proline. Among all these solvents, EtOH was found to be the best solvent for this transformation.

Table 1 Optimisation of Reaction Conditions

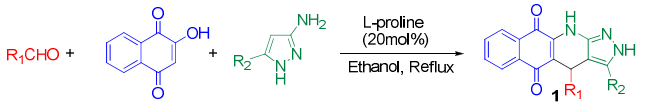


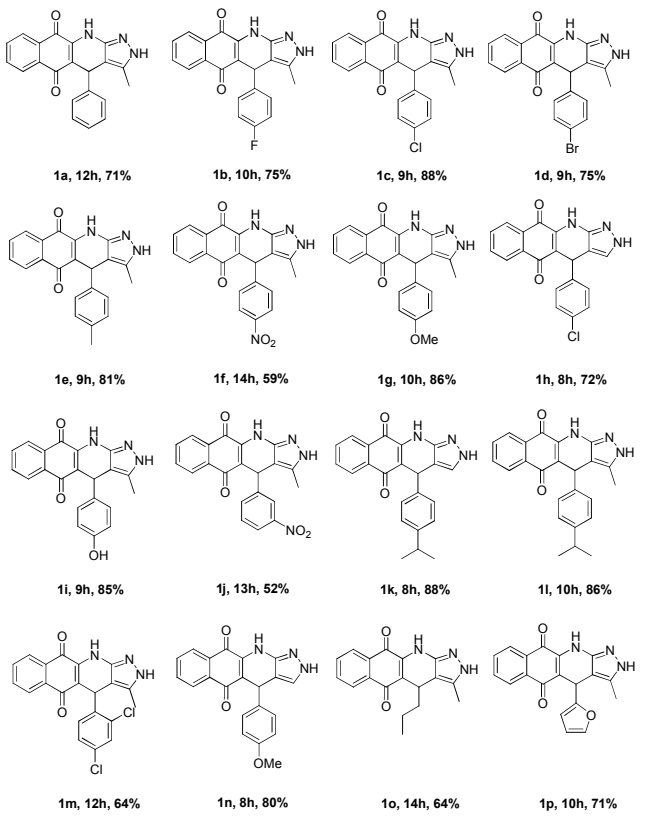
Entry	Catalyst	Mole %	Solvent	Time(h)	Yield[a]
1	-----	---	EtOH	24	NR[b]
2	-----	---	EtOH	9	15
3	DBN	20	EtOH	12	28
4	DABCO	20	EtOH	9	35
5	Et_3N	20	EtOH	9	80
6	L-Proline	20	EtOH	9	88
7	L-Proline	10	EtOH	9	75
8	L-Proline	30	EtOH	9	89
9	L-Proline	20	CH_3CN	9	68
10	L-Proline	20	DMF	9	64
11	L-Proline	20	CH_2Cl_2	9	Trace
12	L-Proline	20	THF	9	60

[a]Isolated yield [b] reaction performed at room temperature

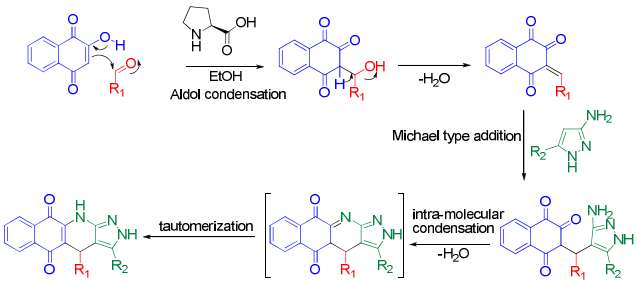
To check the generality and versatility of this method, a study on the substrate scope was carried out under the optimized reaction conditions and the results are summarized in Table 2. It can be found from the results that a wide range of aldehydes are suitable for this multicomponent reaction. Aromatic aldehydes tethered with both electron-donating and electron-withdrawing substituents like F, Cl, Br, Me, NO_2, OMe, OH, $CH(Me)_2$ afforded the desired products (**1b-1n**) in very good yields with both 3-amino-5-methylpyrazole and 3-aminopyrazole. To extend the utility of this method, aliphatic aldehyde such as butanal and heteroaromatic aldehyde i.e furfuraldehyde were also tested and the corresponding products (**1o-1p**) were obtained in good yields (Table 2).

Table 2 Synthesis of 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-diones





The plausible mechanism of this reaction is shown in Scheme 2. We believe the mechanism goes via domino Aldol reaction-Michael addition -N-cyclization-tautomerism sequence to give the final product **1** regioselectively. Interestingly, we have not isolated the ortho isomer as mentioned by Li et al. [18] It is evident from the fact that no reaction was observed when the product obtained from the above reaction was treated with o-phenylenediamine. This presumably can be an indirect evidence for the regioselectivity observed in this reaction.



Scheme 2 Proposed mechanism for the synthesis of 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-diones.

Conclusion

We have developed a facile and efficient one-pot, three component reaction for the synthesis of functionalized polycyclic N-heterocycles using readily available L-proline as organo catalyst. This domino reaction proceeded smoothly in good to excellent yields and offered several advantages including short reaction time, simple experimental procedure, no column chromatography, and no toxic by-product. Due to the presence of NH and C=O functionality in these molecules they can serve as organic ligands for the formation of metal complexes as well as further functionalization of these molecules is feasible, and work in this direction is ongoing in our laboratory and will be reported in due course.

Experimental

General Information

All reagents and chemicals required for the reactions were procured from commercial sources and used without further purification. IR spectra were recorded in Shimadzu FTIR spectrophotometer. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on 500, 400 and 300 MHz spectrometer in DMSO-d6 using TMS as internal reference. Elemental analyses were carried out in a Perkin Elmer 2400 automatic CHN analyzer or Elementer Vario EL III. All new compounds were characterized by recording melting point without correction, ^{1}H NMR, ^{13}C NMR and elemental analysis.

Typical experimental procedure for the synthesis of 1c: To a stirred mixture of 4-chlorobenzaldehyde (1 mmol) and 2-hydroxy-1,4-naphthoquinone (1 mmol) in ethanol (5 ml), was added L-proline (0.2 mmol) and the reaction mixture was stirred under reflux conditions for 30 minutes. Then 3-amino-5-methylpyrazole (1mmol) was added to it. The resulting mixture was stirred until the reaction was completed as indicated by TLC. The resulting solid was collected by filtration and washed with ethanol to afford the product. The resulting product was pure enough for characterization.

3-methyl-4-phenyl-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1a): Yield: 71%. Brown solid. m.p. 292-294^o C. IR (KBr): 3421, 3411, 3071, 2909, 1667, 1607, 1550, 1510, 1429, 1384, 1319, 1273, 1207, 1154, 1051, 957, 742 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 12.10 (s, 1H, NH), 10.20 (s, 1H, NH), 8.05-7.70 (m, 5H, ArH), 7.50-7.30 (m, 4H, ArH), 5.40 (s, 1H, CH), 2.01 (s, 3H, CH$_3$) ppm. ^{13}C NMR (75MHz, DMSO-d$_6$): δ = 181.7, 181.3, 147.1, 146.9, 142.0, 137.0, 135.6, 133.5, 131.2, 130.3, 128.9, 126.6, 126.3, 114.7, 103.5, 80.1, 36.4, 10.3 ppm. Anal. Calcd for $C_{21}H_{15}N_3O_2$ (341.36): C, 73.89; H, 4.43; N, 12.31; Found: C, 73.93. H, 4.45; N, 12.38.

4-(4-fluorophenyl)-3-methyl-1*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1b): Yield: 75%. Dark Purple solid. m.p. 299-301°C. IR (KBr): 3435, 3419, 3024, 2950, 2867, 1670, 1611, 1551, 1344, 1224, 1156, 957, 793, 607 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d$_6$): 12.10 (s, 1H, NH), 10.20 (s, 1H, NH), 8.0 (d, *J* = 7.6 Hz, 1H, ArH), 7.84 (d, *J* = 7.6 Hz, 1H, ArH), 7.83-7.70 (m, 2H, ArH), 7.29-7.25 (m, 2H, ArH), 7.0 (t, *J* = 7.6 Hz, 2H, ArH), 5.36 (s, 1H, CH), 1.94 (s, 3H, CH$_3$) ppm. ^{13}C NMR (75MHz, DMSO-d$_6$): δ = 180.8, 180.5, 145.2, 143.5, 141.0, 135.5, 134.7, 132.6, 130.3, 129.3, 129.2, 125.7, 125.4, 114.9, 114.6, 102.9, 35.2, 9.4 ppm. Anal. Calcd for $C_{21}H_{14}FN_3O_2$ (359.35): C, 70.19; H, 3.93; N, 11.69. Found: C, 70.14; H, 3.96; N, 11.75.

4-(4-chlorophenyl)-3-methyl-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1c): Yield: 88%. Reddish Brown solid. m.p. 298-300°C. IR (KBr): 3455, 3420, 3024, 1670, 1609, 1561, 1352, 1250, 1170, 957, 785 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 12.10 (s, 1H, NH), 10.25 (s, 1H, NH), 8.0 (d, *J* = 7.6 Hz, 1H, ArH), 7.88-7.71 (m, 3H, ArH), 7.40 (d, *J* = 9.0 Hz, 2H, ArH), 7.20 (d, *J* = 7.5 Hz, 2H, ArH), 5.45 (s, 1H, CH), 1.93 (s, 3H, CH$_3$) ppm. ^{13}C NMR (125 MHz, DMSO-d$_6$): δ = 181.2, 180.9, 146.9, 145.7, 141.5, 136.0, 135.2, 133.0, 132.9, 131.4, 130.8, 130.2, 126.2, 125.9, 119.3, 114.1, 103.0, 36.1, 9.9 ppm. Anal. Calcd for $C_{21}H_{14}ClN_3O_2$ (375.81): C, 67.12; H, 3.75; N, 11.18. Found: C, 67.16; H, 3.72; N, 11.26.

4-(4-bromophenyl)-3-methyl-2*H*-benzo[g]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1d): Yield: 75%. Purple solid. m.p. 305-307°C. IR (KBr): 3302, 3290, 3059, 2972, 1662, 1613, 1556, 1516, 1432, 1384, 1344, 1273, 1204, 1147, 1085, 1051, 904, 760 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d$_6$): δ = 12.10 (s, 1H, NH), 10.23 (s, 1H, NH), 8.02 (d, *J* = 7.2 Hz, 1H, ArH), 7.99-7.73 (m, 3H, ArH), 7.40 (d, *J* = 8.4 Hz, 2H, ArH), 7.21 (d, *J* = 8.0 Hz, 2H, ArH), 5.34 (s, 1H, CH), 1.96 (s, 3H, CH$_3$) ppm. ^{13}C NMR (100 MHz, DMSO-d$_6$): δ = 181.7, 181.3, 147.4, 145.5, 142.0, 135.6, 133.5, 133.4, 131.9, 131.2, 130.7, 126.6, 126.3, 119.7, 114.5, 103.4, 36.5, 10.3 ppm. Anal. Calcd for $C_{21}H_{14}BrN_3O_2$ (420.26): C, 60.02; H, 3.36; N, 10.00. Found: C, 60.08; H, 3.32; N, 10.09.

3-methyl-4-p-tolyl-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1e): Yield: 81%. Purple solid. m.p. 289-291°C. IR (KBr): 3450, 3432, 3012, 1665, 1610, 1512, 1355, 1260, 1180, 958 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 12.03 (s, 1H, NH), 10.12 (s,1H, NH), 8.10-7.70 (m, 4H, ArH), 7.11 (d, *J* = 8.1 Hz, 2H, ArH), 7.00 (d, *J* = 7.8 Hz, 2H, ArH), 5.35 (s, 1H, CH), 2.25 (s, 3H, CH$_3$), 1.93 (s, 3H, CH$_3$) ppm. ^{13}C NMR (125 MHz, DMSO-d$_6$): δ = 181.2, 181.0, 144.8, 141.3, 136.0, 135.2, 135.1, 133.0, 132.9, 130.7, 129.1, 127.8, 126.1, 125.9, 114.9, 103.6, 35.9, 21.0, 9.9 ppm. Anal. Calcd for $C_{22}H_{17}N_3O_2$ (355.39): C, 74.35; H, 4.82; N, 11.82. Found: C, 74.42; H, 4.79; N, 11.90.

3-methyl-4-(4-nitrophenyl)-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1f): Yield: 59%. Dark Purple solid. m.p. 277-279°C. IR (KBr): 3215, 3210, 3025, 2965, 1678, 1611, 1592, 1518, 1345, 1249, 988 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d$_6$): δ 12.10 (s, 1H, NH), 10.30 (s, 1H, NH), 8.40 (d, *J* =

8.4 Hz, 2H, ArH), 8.11 (d, *J* = 9.0 Hz, 1H, ArH), 8.02 (d, *J* = 9.0 Hz, 1H, ArH), 7.85-7.66 (m, 2H, ArH), 7.56 (d, *J* = 9.0 Hz, 2H, ArH), 5.50 (s, 1H, CH), 1.98 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ = 180.7, 180.3, 154.4, 145.6, 141.5, 134.8, 132.4, 132.4, 130.3, 128.8, 128.3, 125.8, 125.4, 123.5, 112.9, 101.8, 36.3, 9.4 ppm. Anal. Calcd for $C_{21}H_{14}N_4O_4$ (386.36): C, 65.28; H, 3.65; N, 14.50. Found: C, 65.34; H, 3.62; N, 14.59.

4-(4-methoxyphenyl)-3-methyl-2*H*-benzo[*g*]pyrazolo[3,4-*b*] quinoline-5,10(4*H*,11*H*)-dione (1g): Yield: 86%. Purple solid. m.p. 269-271°C. IR (KBr): 3435, 3419, 3024, 2956, 1670, 1609, 1570, 1528, 1326, 1214, 957, 785 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.10 (s,1H, NH), 10.25 (s, 1H, NH), 8.0 (d, *J* = 7.2 Hz, 1H, ArH), 7.90-7.70 (m, 3H, ArH), 7.14 (d, *J* = 8.4 Hz, 2H, ArH), 6.76 (d, *J* = 8.4 Hz, 2H, ArH), 5.25 (s, 1H, CH), 3.75 (s, 3H, OCH_3), 1.95 (s, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ = 180.8, 180.5, 157.3, 145.3, 140.6, 139.4, 135.2, 134.6, 132.5, 132.4, 130.2, 128.4, 125.6, 125.3, 114.6, 113.4, 103.2, 54.8, 34.9, 9.3 ppm. Anal. Calcd for $C_{22}H_{17}N_3O_3$ (371.39): C, 71.15; H, 4.61; N, 11.31. Found: C, 71.10; H, 4.63; N, 11.40.

4-(4-chlorophenyl)-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline 5,10 (4*H*,11*H*)-dione (1h): Yield: 72%. Reddish Brown solid. m.p. 282-284°C. IR (KBr): 3246, 3202, 3078, 2909, 1672, 1609, 1553, 1510, 1432, 1384, 1326, 1238, 1207, 1172, 1113, 1038, 960, 760 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.20 (s, 1H, NH), 10.20 (s, 1H, NH), 8.05 (d, *J* = 7.2 Hz, 1H, ArH), 7.89-7.71 (m, 3H, ArH), 7.48 (s, 1H, ArH), 7.20 (d, *J* = 8.8 Hz, 2H, ArH), 7.12 (d, *J* = 8.4 Hz, 2H, ArH), 5.50 (s, 1H, CH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 181.8, 181.2, 147.8, 142.4, 135.6, 133.5, 133.4, 131.3, 131.2, 129.8, 129.0, 126.7, 126.3, 113.9, 106.2, 80.7, 36.4 ppm. Anal. Calcd for $C_{20}H_{12}ClN_3O_2$ (361.78): C, 66.40; H, 3.34; N, 11.61. Found: C, 66.34; H, 3.37; N, 11.71.

4-(4-hydroxyphenyl)-3-methyl-2*H*-benzo[*g*]pyrazolo[3,4-*b*] quinoline-5,10(4*H*,11*H*)-dione (1i): Yield: 85%. Blue solid. m.p. 276-278°C. IR (KBr): 3440, 3430, 3031, 2956, 1668, 1608, 1509, 1464, 1371, 1287, 955 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.10 (s, 1H, NH), 10.10 (s, 1H, NH), 9.12 (bs, 1H, OH), 8.0 (d, *J* = 7.5 Hz, 1H, ArH), 7.90-7.70 (m, 3H, ArH), 7.01 (d, *J* = 8.4 Hz, 2H, ArH), 6.58 (d, *J* = 8.4 Hz, 2H, ArH), 5.35 (s, 1H, CH), 1.93 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 180.6, 179.9, 157.7, 153.1, 151.7, 137.6, 135.9, 135.1, 132.9, 132.1, 129.3, 128.8, 128.4, 127.5, 126.7, 120.3, 115.2, 35.9, 14.8 ppm. Anal. Calcd for $C_{21}H_{15}N_3O_3$ (357.36): C, 70.58; H, 4.23; N, 11.76. Found: C, 70.64; H, 4.20; N, 11.85.

3-methyl-4-(3-nitrophenyl)-1*H*-benzo [*g*] pyrazolo [3,4-*b*] quinoline-5,10 (4*H*,11*H*)-dione (1j): Yield: 52%. Reddish Brown solid. m.p. 265-267°C. IR (KBr): 3436, 3420, 3100, 3031, 1663, 1609, 1510, 1467, 1345, 1272, 1149, 1101, 956, 849,790, 601 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.14 (bs, 1H, NH), 10.31 (bs, 1H, NH) 8.10 (s, 1H, ArH), 8.0 (d, *J* = 7.6 Hz, 1H, ArH), 7.97 (d, *J* = 8.0 Hz, 1H, ArH), 7.83 (d, *J* = 7.6 Hz, 1H, ArH) 7.79-7.72 (m, 3H, ArH), 7.51 (t, *J* = 7.6 Hz, 1H, ArH), 5.55 (s, 1H, CH), 1.93 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 180.7, 180.3, 149.1, 147.6, 141.4, 135.9, 134.7, 134.4, 132.5, 132.4, 130.3, 129.6, 125.7, 125.4, 121.9, 120.9, 112.9, 102.1, 35.9, 9.4 ppm. Anal. Calcd for $C_{21}H_{14}N_4O_4$ (386.36): C, 65.28; H, 3.65; N, 14.50. Found: C, 65.22; H, 3.68; N, 14.60.

4-(4-isopropylphenyl)-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1k): Yield: 88%. Dark Brown solid. m.p. 266-268°C. IR (KBr): 3420, 3405, 3090, 2953, 1662, 1609, 1563, 1525, 1507, 1410, 1351, 1204, 1101, 1060, 954, 829, 760 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.20 (bs, 1H, NH), 10.20 (bs, 1H, NH), 8.0 (d, *J* = 6.8 Hz, 1H, ArH), 7.85 (d, *J* = 6.4 Hz, 1H, ArH), 7.78-7.70 (m, 1H, ArH), 7.41 (s, 1H, ArH), 7.18-7.01 (m, 5H, ArH), 5.20 (s, 1H, CH), 2.76-2.74 (m, 1H, CH), 1.10 (d, *J* = 6.8 Hz, 6H, CH_3) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 181.8, 181.3, 146.6, 146.3, 142.2, 135.6, 133.5, 133.4, 131.2, 127.8, 127.3, 127.0, 126.6, 126.4, 114.7, 106.8, 36.3, 33.9, 24.8 ppm. Anal. Calcd for $C_{23}H_{19}N_3O_2$ (369.42): C, 74.78; H, 5.18; N, 11.37. Found: C, 74.72; H, 5.20; N, 11.46.

4-(4-isopropylphenyl)-3-methyl-2*H*-benzo[*g*]pyrazolo[3,4-*b*] quinoline-5,10(4*H*,11*H*)-dione (1l): Yield: 86%.White solid. m.p. 291-293°C. IR (KBr): 3447, 3421, 3051, 2958, 1665, 1534, 1342, 1267, 1151, 959, 788, 724, 613 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.04 (bs, 1H, NH), 10.13 (bs, 1H, NH), 8.0 (d, *J* = 6.9 Hz, 1H, ArH), 7.85 (d, *J* = 7.2 Hz, 1H, ArH), 7.80-7.70 (m, 2H, ArH), 7.15 (d, *J* = 7.8 Hz, 2H, ArH), 7.07 (d, *J* = 8.1 Hz, 2H, ArH) 5.31 (s, 1H, CH), 2.70 (m, 1H, CH), 1.98 (s, 3H, CH_3), 1.12 (d, *J* = 6.9 Hz, 6H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 180.7, 180.5, 145.6, 145.3, 144.6, 140.9, 135.2, 134.6, 132.5, 130.3, 127.2, 125.9, 125.6, 125.4, 114.4, 103.2, 35.3, 32.9, 23.8, 9.4 ppm. Anal. Calcd for $C_{24}H_{21}N_3O_2$ (383.44): C, 75.18; H, 5.52; N, 10.96. Found: C, 75.12; H, 5.55; N, 10.06.

4-(2,4-dichlorophenyl)-3-methyl-1*H*-benzo[*g*]pyrazolo[3,4-*b*] quinoline-5,10(4*H*,11*H*)-dione (1m): Yield: 64%. White solid. m.p. 313-315°C. IR (KBr): 3277, 3183, 3091, 2965, 1672, 1613, 1560, 1538, 1510, 1437, 1338, 1275, 1213, 1083, 1038, 1013, 920, 848, 783 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 12.10 (bs, 1H, ArH), 10.25 (bs, 1H, ArH), 8.0 (d, *J* = 7.2 Hz, 1H, ArH), 7.80-7.72 (m, 3H, ArH), 7.48 (s, 1H, ArH), 7.26 (d, *J* = 8.4 Hz, 1H, ArH), 7.23 (d, *J* = 8.0 Hz, 1H, ArH), 5.71 (s, 1H, CH), 1.93 (s, 3H, CH_3) ppm. ^{13}C NMR (125MHz, DMSO-d_6): δ = 181.1, 180.8, 145.6, 144.1, 142.1, 136.2, 135.2, 133.0, 132.9, 132.6, 132.3, 131.4, 130.7, 128.6, 128.2, 126.2, 125.9, 113.6, 102.3, 33.7, 9.9 ppm. Anal. Calcd for $C_{21}H_{13}Cl_2N_3O_2$ (410.25): C, 61.48; H, 3.19; N, 10.24. Found: C, 61.41 H, 3.21; N, 10.35.

4-(4-methoxyphenyl)-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1n): Yield, 80%. Brown solid. m.p. 232-234 °C. IR (KBr): 3283, 3254, 2972, 1672, 1613, 1560, 1541, 1510, 1437, 1338, 1275, 1213, 1088, 1041, 923, 836, 780 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 12.30 (s, 1H, NH), 10.20 (s, 1H, NH), 8.0 (d, *J* = 9.0 Hz, 1H, ArH), 7.84 (d, *J* = 8.0 Hz, 1H, ArH), 7.70-7.60 (m, 2H, ArH), 7.41 (s, 1H, ArH), 7.12 (d, *J* = 8.5 Hz, 2H, ArH), 6.74 (d, *J* = 8.5 Hz, 2H, ArH), 5.39 (s, 1H, CH), 3.63 (s, 3H, OCH_3) ppm. ^{13}C NMR (125MHz, DMSO-d_6): δ = 181.4, 180.9, 157.8, 141.5, 140.8, 135.1, 135.1, 132.9, 130.8, 130.5, 128.5, 126.1, 125.9, 114.5, 114.0, 106.4, 55.4, 35.5 ppm. Anal. Calcd for $C_{21}H_{15}N_3O_3$ (357.36): C, 70.58; H, 4.23; N, 11.76. Found: C, 70.52; H, 4.26; N, 11.86.

3-methyl-4-propyl-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10 (4*H*,11*H*)-dione (1o): Yield: 64%. White solid. m.p. 218-220°C. IR (KBr): 3210, 3188, 2961, 1683, 1653, 1573, 1453, 1340, 1262, 726, 619 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.10 (s, 1H, NH), 10.23 (s, 1H, NH), 8.0 (d, *J* = 6.9 Hz, 1H, ArH), 7.96 (d, *J* = 6.3 Hz, 1H, ArH), 7.80-7.70 (m, 2H, ArH), 5.35 (s, 1H, CH), 1.95 (s, 3H, CH_3), 1.30-0.80 (m, 7H, $2CH_2$, and CH_3) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ = 181.9, 181.2, 147.4, 142.8, 135.5, 133.5, 133.3, 131.1, 126.5, 126.4, 115.2, 102.7, 80.1, 30.0, 18.9, 15.0, 10.6 ppm. Anal. Calcd for $C_{18}H_{17}N_3O_2$ (307.35): C, 70.34; H, 5.58; N, 13.67. Found: C, 70.41; H, 5.61; N, 13.77.

3-methyl-4-(furan-2-yl)-2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione (1p): Yield: 71%. White solid. m.p. 246-248 °C. IR (KBr): 3258, 3170, 3023, 2962, 2902, 1663, 1616, 1600, 1543, 1502, 1424, 1371, 1213, 1145, 1061, 964, 842, 813, 752 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 12.15 (s, 1H, NH), 10.25 (s, 1H, NH), 8.02 (d, *J* = 7.5 Hz, 1H, ArH), 7.93 (d, *J* = 7.2 Hz, 1H, ArH), 7.86-7.74 (m, 2H, ArH), 7.74 (d, *J* = 7.2 Hz, 1H, ArH), 6.26 (dd, *J* = 3.0, 1.8 Hz, 1H, ArH), 6.04 (d, *J* = 3.0 Hz, 1H, ArH), 5.45 (s,1H, CH), 2.10 (s, 3H, CH_3) ppm. ^{13}C NMR (100MHz, DMSO-d_6): δ = 180.7, 180.4, 157.6, 141.5, 141.1, 134.8, 134.1, 132.6, 132.5, 130.3, 126.8, 125.8, 125.5, 111.4, 110.3, 104.4, 100.4, 29.4, 9.4 ppm. Anal. Calcd for $C_{19}H_{13}N_3O_3$ (331.32): C, 68.88; H, 3.95; N, 12.68. Found: C, 68.82; H, 3.98; N, 12.79.

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Graphical abstract

L-proline catalyzed multicomponent reactions: Facile access to 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione derivatives

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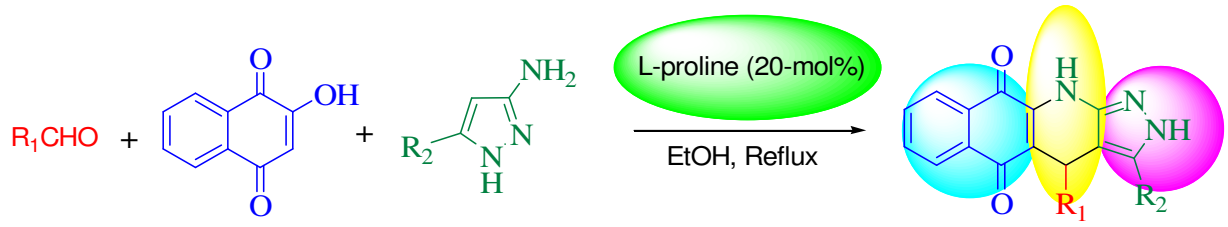

Three component reaction of 2-hydroxy 1,4-naphthoquinones, aldehydes, and aminopyrazoles in the presence of catalytic amount of L-proline has been described for the synthesis of a series of 2*H*-benzo[*g*]pyrazolo[3,4-*b*]quinoline-5,10(4*H*,11*H*)-dione derivatives.