Indian Journal of Heterocyclic Chemistry
Vol. 28 - Number 03 (Jul-Sep 2018) 335-344

ISSN (Print) : 0971-1627
ISSN (Online) : 2456-4311

Solvent-free Synthesis of Bis-hydrazones through 1,3-dipolar cycloaddition of Sydnone and Study of their Optical, Molecular Docking, and Antioxidant Properties

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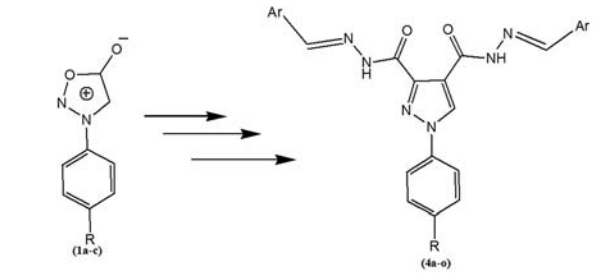
ABSTRACT A series of new 1-(aryl)-1*H*-pyrazol-3,4-bis (aryl)-3,4-dicarbohydrazones **(4)** was obtained by the condensation of 1-arylpyrazole-3,4-dicarbohydrazides **(3)** with various aryl aldehydes under solvent-free conditions. The structures of the newly synthesized hydrazones were confirmed by proton-nuclear magnetic resonance spectroscopy, infrared spectroscopy, liquid chromatography–mass spectrometry, elemental analysis, and by single crystal X-ray diffraction. All the synthesized compounds were screened for their antioxidant activity, where compound **4a** has shown percentage inhibition higher than the standard butylated hydroxyanisole. The molecular docking and photophysical property were also investigated.



R= a) H, b)CH_3, c) OCH_3

Ar= p-Phenyl, p-anisyl, 2-pyridyl, 2-thiophenyl, 2,4-dichloro-5-thiazolyl

KEYWORDS Antioxidant, Bis-hydrazones, Cycloaddition, Pyrazole derivative, Solvent-free reactions, Sydnones.

INTRODUCTION

The 1, 3-dipolar cycloaddition reactions of sydnone have gained prodigious popularity since its first discovery in 1963.[1] Many such 1,3-dipolar cycloadditions of sydnones with various dipolarophiles have been reported earlier from our laboratory.[2,3] The most studied dipolar addition involving cycloaddition of aryl sydnones with dimethyl acetylenedicarboxylate (DMAD) to give dimethyl-1-aryl-1*H*-pyrazole-3,4-dicarboxylates with the evolution of carbon dioxide.[4-7] This reaction is simple and the most convenient method for the synthesis of symmetrically substituted pyrazoles.

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Hydrazones have been well studied and have shown wide spectrum of biological activities including anticonvulsant,[8] antimicrobial,[9] antimycobacterial,[10] antitumor,[11] antibacterial,[12] and antitubercular properties.[13] Similarly, hydrazones are reported to possess excellent photochemical properties.[14,15]

Mechanochemistry has become a powerful tool in the field of synthetic organic chemistry. The green chemistry is associated with enormous advantages such as minimization or elimination of byproduct, higher yield, easy separation, faster reaction rates, economically cheap, and environment friendly. This has emerged as an efficient technique for various organic reactions such as Wittig reaction,[16] Michael addition,[17] Reformatsky reaction,[18] Grignard reaction,[19] Claisen-Schmidt condensation,[20,21] Diels–Alder cycloaddition,[22] Robinson's annelation,[23] Aldol condensation,[24] reduction reaction,[25] nitration,[26] Hunsdiecker reaction,[27] Knoevenagel condensation,[28,29] and Pechmann reaction.[30]

Prompted by these observations, we investigated the viability of utilizing the environmentally benign mechanochemical methodology for the efficient synthesis of 1-(aryl)-1*H*-pyrazol-3,4–bis(aryl)-3,4-dicarbohydrazones through 1,3-dipolar cycloaddition of sydnone by simple grinding using pestle and mortar at room temperature.

RESULTS AND DISCUSSION

The synthetic route to the target hydrazones is shown in **Scheme 1**. The starting material, namely 3-arylsydnones (**1a-c**) were synthesized as per the reported literature method.[31] Dimethyl-1-aryl-1*H*-pyrazole-3,4-dicarboxylates (**2a-c**) were prepared by the cycloaddition of 3-arylsydnones (**1a-c**) with DMAD using xylene as solvent. The esters **2a-c** were treated with hydrazine hydrate to yield 1-arylpyrazole-3,4-dicarbohydrazides (**3a-c**) according to the published literature.[32] Finally, the hydrazones (**4a-o)** were synthesized in good yield by grinding 1-arylpyrazole-3,4-dicarbohydrazides (**3a-c**) with different substituted aryl aldehydes. 2,5-dichlorothiazole-5-aldehyde was synthesized by condensation of thiazolidine-2,4-dione with N,N-dimethylformamide in phosphoryl chloride.[33] The crude product obtained was purified using steam distillation technique.

Spectral properties

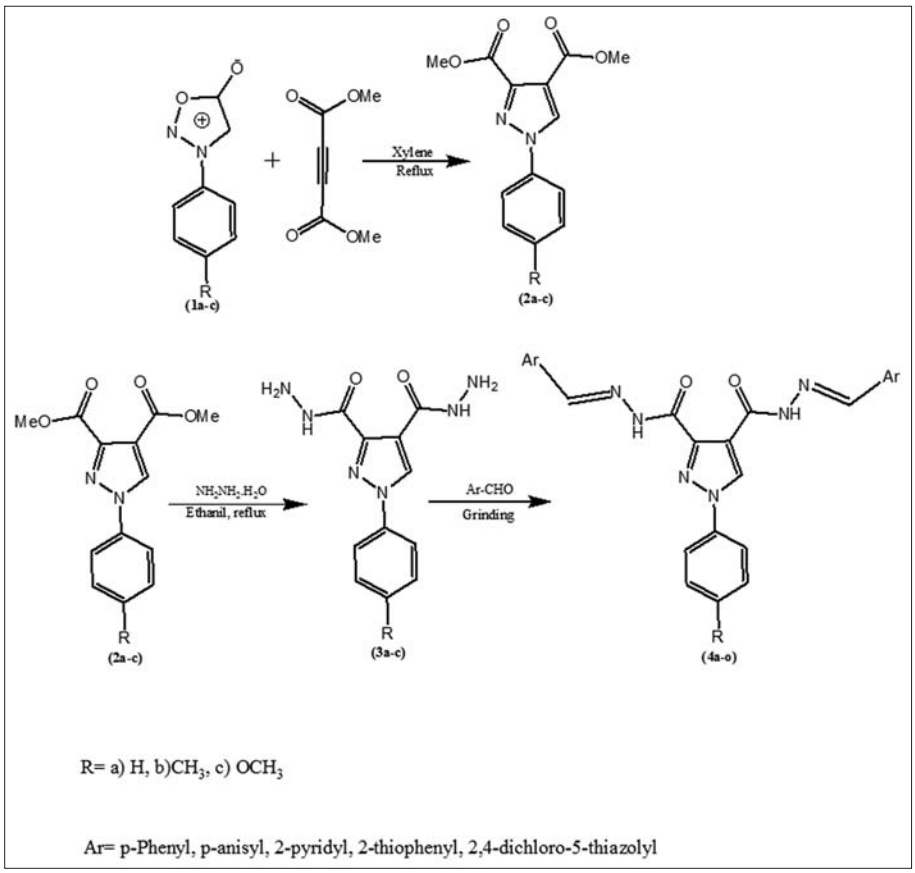
UV-visible absorption spectra

The UV-visible spectra of all the synthesized compounds **2a-c, 3a-c,** and **4a-o** were measured in dimethyl sulfoxide (DMSO) and are as shown in **Figure 1.** UV-visible absorption maxima, fluorescence emission maxima, molar absorptivity, and Stokes shift of compounds **2a-c, 3a-c,** and **4a-o** are summarized in **Table 1.**

Lambert-Beer relationship was used to calculate molar extinction coefficient ε.

$$\varepsilon = A\, l^{-1}\, c^{-1}$$

Where, A is the absorbance, l is the path length (1cm), and c is the concentration of the solution expressed in mol/L.



Scheme 1: Synthetic route of hydrazones 4a-o

Table 1: The observed UV-visible absorption maxima, fluorescence emission maxima, molar absorptivity, and Stokes shift of compounds 2a-c, 3a-c, and 4a-o

Compounds	λ_{max}^{abs} (nm)	λ_{max}^{em} (nm)	Stokes shift (nm)	ε_{max} (mol^{-1} L cm^{-1})
2a	260	338	78	46875
2b	263	349	86	13086
2c	271	340	69	34669
3a	283	407	124	47046
3b	273	344	71	20131
3c	277	340	63	42617
4a	307	367	60	258246
4b	308	423	115	341730
4c	307	383	76	210811
4d	322	382	60	168107
4e	320	382	62	157886
4f	322	388	66	274565
4g	311	376	65	316710
4h	306	373	67	94410
4i	307	381	74	185253
4j	326	418	92	525437
4k	325	389	64	213278
4l	326	385	59	241935
4m	330	-	-	103009
4n	330	393	63	185921
4o	331	395	64	187732

The UV-visible spectra of the compounds **2a-c** and **3a-c** displayed absorption maximum in the range 260–283 nm, whereas compounds **4a-o** exhibited λmax ranging from 306 to 331 and high molar extinction coefficient values (13086–525437/mol/L/cm) which are attributed to the strongly allowed π-π* transition due to the extended conjugation.

The UV absorption peak of pyrazole dicarboxylates **2b** and **2c** showed redshift (3 nm for compound **2b** and 11 nm for compound **2c**) when compared to **2a** due to the presence of electron donating groups (4-CH_3 and 4-OCH_3). However, the reverse was observed in case of pyrazole dicarbohydrazide where **3a** exhibited redshift compared with that of compounds **3b** and **3c.**

Almost in all the hydrazones **4a-o,** the absorption maxima showed a redshift (24–57 nm) and increase in absorbance, i.e., hyperchromic shift compared to starting materials **2a-c** and **3a-c** due to the increase in conjugation in the side chain on both sides which lower the energy of the excited state. Compound **4n** showed highest bathochromic shift of 57nm, whereas **4j** showed maximum hyperchromic shift at 3.9 a.u.

In case of hydrazones having tolyl pyrazole scaffold **4b, 4e, 4h, 4k, and 4n** and those having anisyl scaffold **4c, 4f, 4i, 4l, and 4o** linear increase in λmax was observed due to the introduction of pyridyl, benzyl, anisyl, thiophenyl, and 2,4-dichloro-5-thiazolyl substituent's which resulted in the increased conjugation. However, surprisingly, phenyl pyrazole scaffold bearing hydrazone **4g** has absorption maxima 311 nm slightly greater than **4a** with λmax 307 nm.

Fluorescence spectra

The fluorescence spectra were obtained in DMSO solution with a concentration of 3.3 µg/mL. The maximum absorption wavelength is used as the excitation wavelength. The fluorescence emission spectra of all the compounds are shown in **Figure 1.** The maximal emission bands ranged from 338 to 423 nm which is clearly red Stoke shift with respect to the UV absorption spectra.

The fluorescence spectra of all the compounds **4a-o** exhibited maximum emission wavelength at 338–423 nm where compound **4m** did not show photoluminescence. Compounds **4a, 4c, 4d, 4f, 4g, 4i,** and **4l** bearing H/OCH_3 at the fourth position of pyrazole phenyl ring showed hypsochromic shift, while compounds **4b, 4e, 4h, 4j, 4k,** and **4n** bearing CH_3 (except **4j** having no substitution) at the fourth position of pyrazole phenyl ring **s**howed bathochromic shift in comparison with dihydrazides.

Some of the synthesized hydrazones can be used as optical whiteners as they absorb in ultraviolet region and reemits in the visible region.

Antioxidant studies

The bis-hydrazones (**4a-o**) were evaluated for their antioxidant property. The protocol reported by Brand-Williams *et al.*[34] was used to determine free radical scavenging activity at the concentration of 100 µg/mL in DMSO using butylated hydroxyanisole (BHA) as a standard.

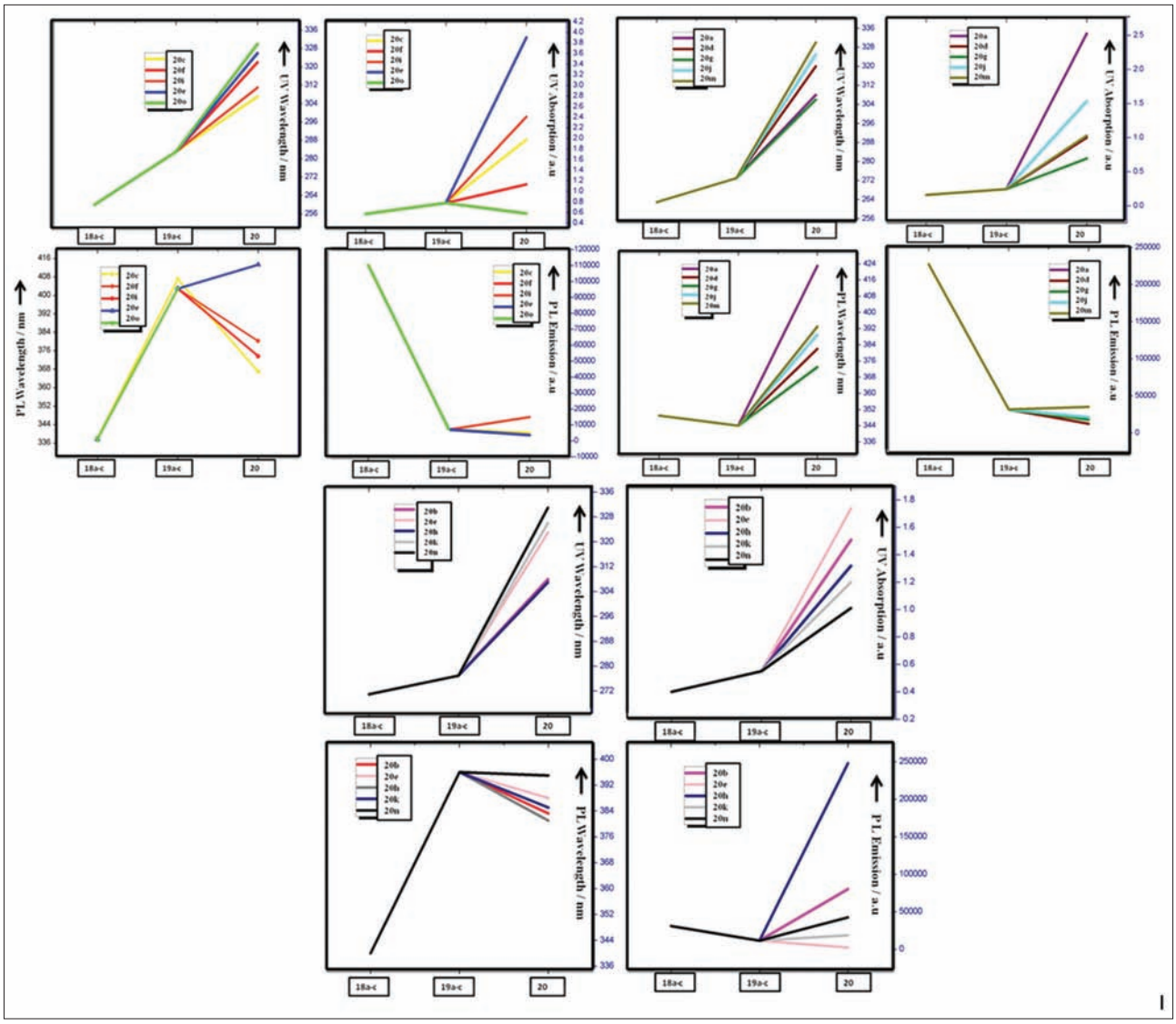


Figure 1: UV-visible absorption and fluorescence spectra of compounds 20a-o

The synthesized compounds displayed 2,2-diphenyl-1-picrylhydrazyl scavenging activity varying from 92.78% to 52.1%, whereas standard drug BHA showed 88% inhibition. Compound **4o, 4a, 4l,** and **4h** displayed highest radical scavenging activity, i.e. 92.78%, 90.28%, 83.09%, and 80.4%, respectively. The percentage radical scavenging activity of the bis-hydrazones is as described in **Figure 2.**

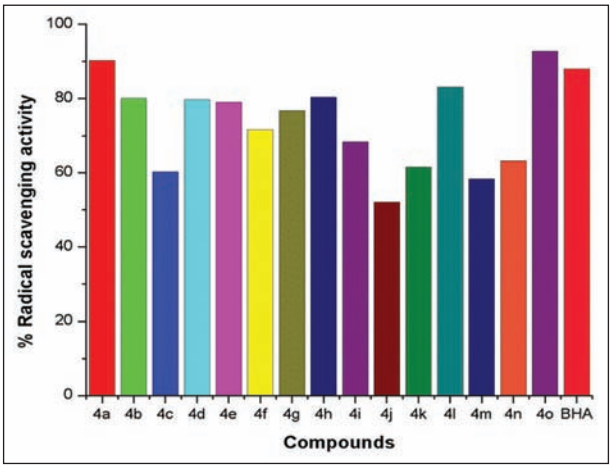


Figure 2: The 2,2-diphenyl-1-picrylhydrazyl radical scavenging activity of hydrazones 4a-o.

Molecular docking studies

The binding interaction between macromolecule and ligands was done using AutoDock 4.2. Polar hydrogen bond network was optimized, and the systematic Kollman charges were added by means of a cluster-based approach. The grid map was centered at the active site pocket of the protein by Autogrid. In all the cases, we have used grid maps with a grid box size of 60 × 60 × 60 $Å^3$ points with a grid point spacing of 0.375 Å.

All the compounds (**4a-4o**) were found to have minimum binding energy ranging from −7.66 to −9.86 kJ/mol with anti-inflammatory protein target (**PDB Code: 1KQI**). Among the molecules tested for docking study, 1-(p-tolyl)-1*H*-pyrazol-3,4-bis(phenyl)-3,4-dicarbohydrazone **(4b)** showed

minimum binding energy of −9.86 kJ/mol with ligand efficiency of −0.29. In the selected protein target, maximum numbers of residues are nearer to the drug molecule and are hydrophobic in nature.

The protein (**1KQU**) comprises 17 active site residues, which are promiscuous to the ligands. Of which five (Gly29, His47, Asp48, Lys62, and Gly31) residues are directly interacting with the ligands. All the ligands were docked deeply within the binding pocket region of 1KQU. The ligand molecules **4c**, **4k**, and **4n** revealed binding energy of -9.51, -9.61, and -9.39 kJ/mol, with ligand efficiency of −0.27, −0.3, and −0.25, respectively [**Figure 3**]. Similarly, molecules **4a**, **4h**, **4i**, and **4k** were found to show hydrogen bond interaction with active site amino acid residues Gly29, His47, Asp48, Lys62, and Gly31 at a distance of (2.198, 1.994, and 2.101), (1.931, 1.861, and 1.85), (2.046, 1.673, and 1.865), and (1.996, 1.994, and 2.072) Å, respectively [**Figure 4**]. The docking study results showed that the molecules **(4a-4o)** have good inhibition constant, vdW + Hbond + desolv energy with best RMSD value. The docking results for all ligand molecules against protein target showed minimum intermolecular energy, ligand efficiency, binding energy, inhibition constant, and vdW + Hbond + desolv energy with best RMSD value. The details of docked score results of the molecules with anti-inflammatory protein target (**PDB Code: 1KQU**) are given in **Table 2.** From this study, we have predicted that these ligands may act as potential inhibitors of anti-inflammatory protein target.

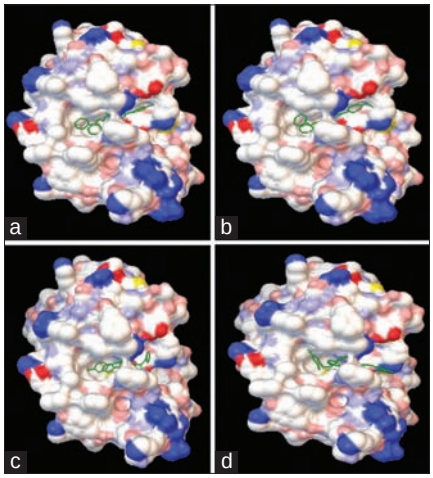


Figure 3: Enfolding of molecules (4b, 4c, 4k and 4o) in the active site (a-d) pocket of anti-inflammatory protein target (3UDI)

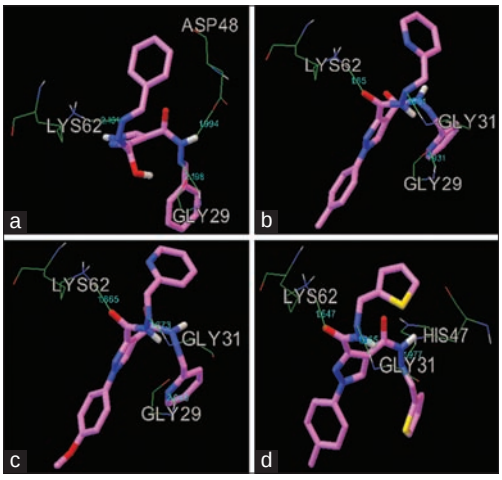


Figure 4: H-bond interaction of ligand molecules (4a-hy, 4h-hy, 4i-hy, and 4k-hy) with 3UDI

EXPERIMENTAL SECTION

Melting points were determined using Innovative DTC-967A digital melting point apparatus. IR spectra were determined in KBr pellets on a SHIMADZU FT-IR 157 spectrophotometer. ^{1}H NMR spectra were recorded on 400MHz Bruker Avance II NMR spectrometer. Mass spectra were recorded on a SHIMADZU liquid chromatography–mass spectrometry (LCMS)-8030 mass spectrometer. The X-ray diffraction measurements were determined on Rigaku Saturn 724+ diffractometer. CHN analysis was performed with Vario-EI Elementar-III model analyzer. The UV-visible spectra were obtained on a UV-1800 SHIMADZU UV spectrophotometer. Photoluminescence spectra were obtained on a Horiba FluoroMax 4 spectrophotometer.

General procedure for the synthesis of 1-(aryl)-1*H*-pyrazol-3,4-dimethyl carboxylates (2a-c)

3-arylsydnones **(1a-c)** (1 mmol) and dimethyl acetylenedicarboxylate (1 mmol) in 10 mL of dry xylene were refluxed in an oil bath (120–125°C) for 1 h. The excess of solvent was removed using rotary evaporator, and the product obtained was recrystallized from ethanol.

1-(Phenyl)-1H-pyrazol-3,4-dimethyl carboxylate (2a)

Yellow crystals, m.p.: 100°C (Lit[35]. m.p.: 100–102°C).

1-(p-Tolyl)-1H-pyrazol-3,4-dimethyl carboxylate (2b)

White flakes, m.p.: 98°C (Lit[35]. m.p.: 96–97°C).

1-(p-Anisyl)-1H-pyrazol-3,4-dimethyl carboxylate (2c)

White solid, m.p.: 185°C (Lit[36]. m.p.: 185°C).

General procedure for the synthesis of 1-(aryl)-1*H*-pyrazol-3,4-dicarbohydrazides (3a-c)

Compound **2a-c** (1 mmol) and hydrazine hydrate (99 %, 10 mmol) in 10 mL of ethanol were refluxed in an oil bath (100–110°C) for 2 h. The white colored product that separated was filtered, washed with water, dried, and recrystallized from ethanol-DMF.

1-(Phenyl)-1H-pyrazol-3,4-dicarbohydrazide (3a)

White solid, m.p.: 227°C (Lit[32]. m.p.: 210–213°C).

1-(p-Tolyl)-1H-pyrazol-3,4-dicarbohydrazide (3b)

White solid, m.p.: 217–218°C (Lit[32]. m.p.: 201–204°C).

1-(p-Anisyl)-1H-pyrazol-3,4-dicarbohydrazide (3c)

White solid, m.p.: 229°C (Lit[32]. m.p.: 225–228°C).

General procedure for the synthesis of 1-(aryl)-1*H*-pyrazol-3,4-bis(aryl)-3,4-dicarbohydrazones (4)

1-Aryl-1*H*-pyrazole-3, 4-dicarbohydrazide (1 mmol) and aryl aldehyde (1 mmol) were taken in a mortar and ground

Table 2: The dock score results of the different pyrazole derivatives with anti-inflammatory protein target (PDB Code: 1KQU)

Compounds	Binding energy (kJ mol^{-1})	Ligand efficiency	Inhibition constant	vdW+H-bond+desolv energy	Number of H- bonds	Bonding residues	Bond length (Å)
4a	−7.66	−0.28	2.41	−10.06	3	1KQU: A:GLY29:HN	2.198
						1KQU: A:ASP48:OD1	1.994
						1KQU: A:LYS62:HZ3	2.101
4b	−9.86	−0.29	58.97	−11.4	2	1KQU: A:GLY29:HN	2.194
						1KQU: A:ASP48:OD1	2.17
4c	−9.51	−0.27	107.61	−11.67	2	1KQU: A:GLY29:HN	1.998
						1KQU: A:ASP48:OD1	2.045
4d	−9.3	−0.25	152.11	−11.99	2	1KQU: A:GLY29:HN	2.031
						1KQU: A:ASP48:OD1	2.014
4e	−9.11	−0.24	209.61	−10.85	1	1KQU: A:GLY31:HN	2.011
4f	−8.93	−0.23	285.35	−12.1	1	1KQU: A:GLY31:HN	2.156
4g	−7.75	−0.23	2.08	−8.97	2	1KQU: A:GLY31:HN	1.743
						1KQU: A:LYS62:HZ3	1.813
4h	−8.66	−0.25	450.13	−9.96	3	1KQU: A:GLY29:HN	1.931
						1KQU: A:GLY31:HN	1.861
						1KQU: A:LYS62:HZ3	1.85
4i	−8.55	−0.24	541.94	−10.22	3	1KQU: A:GLY29:HN	2.046
						1KQU: A:GLY31:HN	1.673
						1KQU: A:LYS62:HZ3	1.865
4j	−8.52	−0.27	568.05	−9.53	2	1KQU: A:GLY31:HN	2.144
						1KQU: A:HIS: HD1	1.804
4k	−9.61	−0.3	90.46	−11.24	3	1KQU: A:GLY31:HN	1.996
						1KQU: A:HIS47:OD1	1.994
						1KQU: A:LYS62:HZ3	2.072
4l	−8.73	−0.26	398.99	−10.99	3	1KQU: A:GLY29:HN	2.162
						1KQU: A:GLY31:HN	2.004
						1KQU: A:LYS62:HZ3	2.091
4m	−8.56	−0.24	531.0	−8.96	2	1KQU: A:GLY31:HN	2.206
						1KQU: A:LYS62:HZ3	2.014
4n	−9.1	−0.25	215.34	−9.98	1	1KQU: A:LYS62:HZ3	1.952
4o	−9.39	−0.25	130.7	−10.81	2	1KQU: A:GLY31:HN	1.894
						1KQU: A:LYS62:HZ3	1.805

vigorously using pestle until gray/yellow solid appears (1–5 min). The solid was scratched and transferred into a beaker containing crushed ice. The coarse product was filtered and washed with water and dried. Recrystallization was done from ethanol-DMF mixture. Characterization data of 1-(aryl)-1*H*-pyrazol-3,4–bis (aryl)-3,4-dicarbohydrazones **(4a-o)** are given in **Table 3**.

1-(Phenyl)-1H-pyrazol-3,4-bis(phenyl)-3,4-dicarbohydrazone (4a)

IR (KBr cm^{-1}) 3100-3115 (NH), 2856 (C–H, aromatic), 1650 (C=O), 1537(C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.07–8.10 (m, 15H, Ar–H), 8.61 (s, 1H, -N=C-H), 8.99 (s, 1H, -N=C-H), 12.18 (s, 1H, NH), 13.59 (s, 1H, NH), 9.13 (s, 1H, H of pyrazole ring); MS: m/z: 437.20 [M+1].

1-(p-Tolyl)-1H-pyrazol-3,4-bis(phenyl)-3,4-dicarbohydrazone (4b)

IR (KBr cm^{-1}) 3135 (NH), 2810 (C–H, aromatic), 1644 (C=O), 1550 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) **δ** 2.34 (s, 3H, CH3), 7.05–8.05 (m, 14H, Ar–H), 8.41 (s, 1H, -N=C-H), 9.01 (s, 1H, -N=C-H), 12.20(s, 1H, NH), 13.6 (s, 1H, NH), 9.06 (s, 1H, H of pyrazole ring); MS: m/z: 451.23 [M+1].

1-(p-Anisyl)-1H-pyrazol-3,4-bis(phenyl)-3,4-dicarbohydrazone (4c)

IR (KBr cm^{-1}) 3103 (NH), 2818 (C–H, aromatic), 1647 (C=O), 1544 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 3.82 (s, 3H, OCH_3), 7.04 (d, 2H, J = 9.04 Hz, o-protons of p-anisyl ring), 7.98 (d, 2H, m-protons of p-anisyl ring),

7.39–7.79 (m, 10H, Ar–H), 8.35 (s, 1H, -N=C-H), 9.07 (s, 1H, -N=C-H), 12.21 (s, 1H, NH), 13.63 (s, 1H, NH), 9.07 (s, 1H, H of pyrazole ring); MS: m/z: 467.20 [M+1].

1-(Phenyl)-1H-pyrazol-3,4-bis(p-anisyl)-3,4-dicarbohydrazone (4d)

IR (KBr cm^{-1}) 3118–3280 (NH), 3043 (C–H, aromatic), 1674 (C=O), 1571 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 3.83 (s, 6H, 2 X OCH_3), 7.03 (d, 2H, J = 8.84 Hz, Ar–H), 7.06 (d, 2H, J = 8.8 Hz, Ar-H), 7.72 (d, 2H, J = 8.76 Hz, Ar–H), 7.76 (d, 2H, J = 8.84 Hz, Ar-H),8.16 (d, 2H, J = 7.76 Hz, o-protons of phenyl ring), 7.48–7.63 (m, 4H, m and p-protons of phenyl ring), 8.32 (s, 1H, -N=C-H), 8.60 (s, 1H, -N=C-H), 12.18 (s, 1H, NH), 13.38(s, 1H, NH), 9.27 (s, 1H, H of pyrazole ring); MS: m/z: 497.20 [M+1].

1-(p-Tolyl)-1H-pyrazol-3,4-bis(p-anisyl)-3,4-dicarbohydrazone (4e)

IR (KBr cm^{-1}) 3200 (NH), 3037 (C–H, aromatic), 1671 (C=O), 1550 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*)

δ 2.39 (s, 3H, CH_3), 3.87 (s, 6H, 2 X OCH_3), 7.03 (d, 2H, J = 8.84 Hz, Ar–H), 7.06 (d, 2H, J = 8.8Hz, Ar-H), 7.72 (d, 2H, J = 8.76 Hz, Ar–H), 7.75 (d, 2H, J = 8.84 Hz, Ar-H), 7.15–8.0 (m, 4H, Ar-H), 8.31 (s, 1H, -N=C-H), 8.49 (s, 1H, -N=C-H), 12.14 (s, 1H, NH), 13.36 (s, 1H, NH), 9.19 (s, 1H, H of pyrazole ring); MS: m/z: 511.20 [M+1].

1-(p-Anisyl)-1H-pyrazol-3,4-bis(p-anisyl)-3,4-dicarbohydrazone (4f)

IR (KBr cm^{-1}) 3292 (NH), 3024 (C–H, aromatic), 1674 (C=O), 1508 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 3.82 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 7.03(d, 2H, J = 8.84 Hz, Ar–H), 7.06 (d, 2H, J = 8.8 Hz, Ar-H), 7.72(d, 2H, J = 8.76 Hz, Ar–H), 7.76 (d, 2H, J = 8.8 Hz, Ar-H), 8.06 (d, 2H, J = 9.04 Hz, Ar-H), 7.13 (d, 2H, J = 9.08 Hz, Ar-H), 8.31 (s, 1H, -N=C-H), 8.5 (s, 1H, -N=C-H), 12.16 (s, 1H, NH), 13.41 (s, 1H, NH), 9.16 (s, 1H, H of pyrazole ring); MS: m/z: 527.15 [M+1].

1-(Phenyl)-1H-pyrazol-3,4-bis(2-pyridyl)-3,4-dicarbohydrazone (4g)

IR (KBr cm^{-1}) 3320 (NH), 2930(C–H, aromatic), 1676 (C=O), 1585 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.16–8.4 (m, 13H, Ar–H), 8.56 (s, 1H, -N=C-H), 8.78 (s, 1H, -N=C-H), 13.63 (s, 1H, NH), 16.05 (s, 1H, NH), 9.13 (s, 1H, H of pyrazole ring); MS: m/z: 439.20 [M+1].

1-(p-Tolyl)-1H-pyrazol-3,4-bis(2-pyridyl)-3,4-dicarbohydrazone (4h)

IR (KBr cm^{-1}) 3325 (NH), 2922 (C–H, aromatic), 1675 (C=O), 1589 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 2.4 (s, 3H, CH_3), 7.18–8.30 (m, 12H, Ar–H), 8.62 (s, 1H, -N=C-H), 8.83 (s, 1H, -N=C-H), 13.78 (s, 1H, NH), 16.08 (s, 1H, NH), 9.21 (s, 1H, H of pyrazole ring); MS: m/z: 453.43 [M+1].

1-(p-Anisyl)-1H-pyrazol-3,4-bis(2-pyridyl)-3,4-dicarbohydrazone (4i)

IR (KBr cm^{-1}) 3323 (NH), 2904 (C–H, aromatic), 1675 (C=O), 1587 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*)

δ 3.89 (s, 3H, OCH_3), 7.18–8.34 (m, 12H, Ar–H), 8.64 (s, 1H, -N=C-H), 8.86 (s, 1H, -N=C-H), 13.87 (s, 1H, NH), 16.11 (s, 1H, NH), 9.23 (s, 1H, H of pyrazole ring); MS: m/z: 469.23 [M+1].

1-(Phenyl)-1H-pyrazol-3,4-bis(2-thiophenyl)-3,4-dicarbohydrazone (4j)

IR (KBr cm^{-1}) 3460–3527 (NH), 3059 (C–H, aromatic), 1665 (C=O), 1591 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.07–8.11 (m, 11H, Ar–H), 8.60 (s, 1H, -N=C-H), 8.85 (s, 1H, -N=C-H), 12.19(s, 1H, NH), 13.56 (s, 1H, NH), 9.15 (s, 1H, H of pyrazole ring); MS: m/z: 449.05 [M+1].

1-(p-Tolyl)-1H-pyrazol-3,4- bis(2-thiophenyl)-3,4-dicarbohydrazone (4k)

IR (KBr cm^{-1}) 3387–3429 (NH), 2920 (C–H, aromatic), 1660 (C=O), 1591 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 2.39 (s, 3H, CH_3), 7.15–8.04 (m, 10H, Ar–H), 8.63 (s, 1H, -N=C-H), 8.85 (s, 1H, -N=C-H), 12.25 (s, 1H, NH), 13.38 (s, 1H, NH), 9.21 (s, 1H, H of pyrazole ring); MS: m/z: 463.10 [M+1].

1-(p-Anisyl)-1H-pyrazol-3,4-bis(2-thiophenyl)-3,4-dicarbohydrazone (4l)

IR (KBr cm^{-1}) 3420–3499 (NH), 3010 (C–H, aromatic), 1670 (C=O), 1575 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 3.86 (s, 3H, OCH_3), 7.24–8.15 (m, 10H, Ar–H), 8.69 (s, 1H, -N=C-H), 8.9 (s, 1H, -N=C-H), 12.56 (s, 1H, NH), 13.49(s, 1H, NH), 9.25 (s, 1H, H of pyrazole ring); MS: m/z: 479.23 [M+1].

1-(Phenyl)-1H-pyrazol-3,4-bis(2,4-dichloro-5-thiazolyl)-3,4-dicarbohydrazone (4m)

IR (KBr cm^{-1}) 3153–3317 (NH), 2964 (C–H, aromatic), 1674 (C=O), 1589(C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.44-8.14 (m, 5H, Ar–H), 8.52 (s, 1H, -N=C-H), 8.9 (s, 1H, -N=C-H), 12.57 (s, 1H, NH), 13.55 (s, 1H, NH), 9.22 (s, 1H, H of pyrazole ring); MS: m/z: 589.85, 591.82, 593.85, 595.85 and 597.85 [M+1], [M+3], [M+5], [M+7] and [M+9].

1-(p-Tolyl)-1H-pyrazol-3,4-bis(2,4-dichloro-5-thiazolyl)-3,4-dicarbohydrazone (4n)

IR (KBr cm^{-1}) 3100–3310 (NH), 3000 (C–H, aromatic), 1675 (C=O), 1592 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 2.40 (s, 3H, CH_3), 7.36–7.99 (m, 4H, Ar–H), 8.51 (s, 1H, -N=C-H), 8.89 (s, 1H, -N=C-H), 12.6 (s, 1H, NH), 13.6 (s, 1H, NH), 9.17 (s, 1H, H of pyrazole ring); MS: m/z: 601, 603, 605, 607 and 609 [M+1], [M+3], [M+5], [M+7] and [M+9].

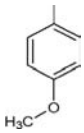
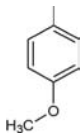
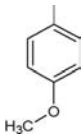
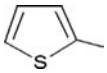
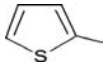
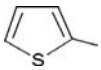
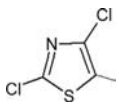
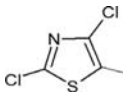
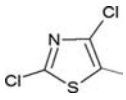
1-(p-Anisyl)-1H-pyrazol-3,4-bis(2,4-dichloro-5-thiazolyl)-3,4-dicarbohydrazone (4o)

IR (KBr cm^{-1}) 3212–3346 (NH), 2989 (C–H, aromatic), 1669 (C=O), 1596 (C=C); ^{1}H NMR (400 MHz, DMSO-*d6*) δ 2.89 (s, 3H, OCH_3), 7.39–8.3 (m, 4H, Ar–H), 8.61 (s, 1H, -N=C-H), 8.88 (s, 1H, -N=C-H), 12.62 (s, 1H, NH), 13.68 (s, 1H, NH), 9.15 (s, 1H, H of pyrazole ring); MS: m/z: 619.45, 621.45, 623.45, 625.45 and 627.45 [M+1], [M+3], [M+5], [M+7] and [M+9].

CONCLUSION

A series of novel fluorescent 1-(aryl)-1*H*-pyrazol-3,4-bis (aryl)-3,4-dicarbohydrazones was synthesized

Table 3: Characterization data of 1-(aryl)-1*H*-pyrazol-3,4-bis (aryl)-3,4-dicarbohydrazones (4a-o)

Comp No.	R	R^1	m.p (°C) (Yield %)	Molecular formula (Mol. Wt)	Color and crystal nature	Halochromism with sulfuric acid	% Analysis found (calculated)		
							C	H	N
4a	H		250 (88)	$C_{25}H_{20}N_6O_2$ (436)	Gray solid	Pale yellow	68.83 (68.80)	4.58 (4.62)	19.31 (19.25)
4b	CH_3		286 (79)	$C_{26}H_{22}N_6O_2$ (450)	White solid	Yellow	69.28 (69.32)	4.90 (4.92)	18.64 (18.66)
4c	OCH_3		255 (76)	$C_{26}H_{22}N_6O_3$ (466)	Yellow needles	Yellow	66.92 (66.94)	4.72 (4.75)	18.0 (18.02)
4d	H		231 (78)	$C_{27}H_{24}N_6O_4$ (496)	Pale yellow solid	Orange	65.2 (65.31)	4.86 (4.87)	16.88 (16.93)
4e	CH_3		267 (73)	$C_{28}H_{26}N_6O_4$ (510)	White solid	Yellow	65.84 (65.87)	5.10 (5.13)	16.42 (16.46)
4f	OCH_3		253 (78)	$C_{28}H_{26}N_6O_5$ (526)	White silky needles	Yellow	65.84 (65.87)	4.94 (4.98)	15.91 (15.96)
4g	H		270 (81)	$C_{23}H_{18}N_8O_2$ (438)	Gray solid	Pale yellow	62.98 (63.01)	4.10 (4.14)	25.52 (25.56)
4h	CH_3		289 (85)	$C_{24}H_{20}N_8O_2$ (452)	White solid	Yellow	63.68 (63.71)	4.42 (4.46)	24.72 (24.76)
4i	OCH_3		282 (84)	$C_{24}H_{20}N_8O_3$ (468)	Gray solid	Yellow	61.50 (61.53)	4.28 (4.30)	23.88 (23.92)
4j	H		265–266 (93)	$C_{21}H_{16}N_6O_2S_2$ (448)	White crystals	Yellow	56.21 (56.23)	3.54 (3.60)	18.71 (18.74)
4k	CH_3		251 (95)	$C_{22}H_{18}N_6O_2S_2$ (462)	Gray needles	Dark yellow	57.10 (57.13)	3.89 (3.92)	18.12 (18.17)
4l	OCH_3		244 (89)	$C_{22}H_{18}N_6O_3S_2$ (478)	Pale yellow needles	Yellow	55.20 (55.22)	3.74 (3.79)	17.54 (17.56)
4m	H		280 (94)	$C_{19}H_{10}Cl_4N_8O_2S_2$ (588)	Yellow solid	Pale yellow	38.74 (38.79)	1.68 (1.71)	19. 0 (19.05)
4n	CH_3		291 (88)	$C_{20}H_{12}Cl_4N_8O_2S_2$ (600)	Pale yellow solid	Yellow	39.84 (39.88)	1.98 (2.01)	18.58 (18.60)
4o	OCH_3		300 (91)	$C_{20}H_{12}Cl_4N_8O_3S_2$ (618)	Pale yellow solid	Dark yellow	39.84 (39.86)	1.97 (2.01)	18.54 (18.58)

Solvent of crystallization: Ethanol-DMF mixture.

under non-hazardous eco-friendly conditions, and their structures were determined by ^{1}H NMR, IR, LCMS, X-ray diffraction, and CHN analysis. The UV-visible absorption and photoluminescence spectra were measured. The absorption and emission were found to be influenced by substituents. Some of the compounds have potential for use as optical whiteners.

SUPPLEMENTARY INFORMATION

Crystallographic data for the compound 64 have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1578554, respectively. Copies of this information may be obtained free of charge through www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

ACKNOWLEDGMENTS

Authors are thankful to SAIF, Panjab University, PURSE laboratory, Mangalore University for providing the facility for spectral analysis. One of the authors Asma is grateful to UGC, New Delhi, for Senior Research Fellowship.

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Received: 10 Oct 2017; Accepted: o3 Jun 2018