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Design and synthesis of hydrazone incorporated pyrazoles and triazoles as possible antioxidants

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ABSTRACT

Novel series of hydrazone incorporated pyrazoles and 1,2,3-triazole were synthesized and evaluated for their antioxidant activity by DPPH scavenging assay. Title compounds were prepared from 5-methyl-1-(p-nitro phenyl)-1H-1,2,3-triazole-4-carbohydrazide ***(3)*** *by reaction with appropriate pyrazole aldehydes. Among the tested compounds, compound* ***11a****,* ***12d*** *and* ***12e*** *exhibited good scavenging activity.*

Key words: Hydrazones, pyrazoles, 1,2,3-triazoles, antioxidant activity.

INTRODUCTION

Hydrazones possessing an azomethine -NHN=CH- pharmacophore constitute an important class of compound for new drug development. This observation have been guiding for the synthesis of new hydrazones that possess varied biological activities. Hydrazones have been demonstrated to possess interesting bioactivity such as, antimicrobial [1], anticonvulsant [2], analgesic [3], anti-inflammatory [4], antiplatelet [5], antitubercular [6] and anticancer [7] activities.

1,2,3-Triazoles are attractive constructs, because of their unique chemical properties and they find many applications in organic and medicinal chemistry [8]. Not present in natural products, they are remarkably stable to metabolic transformations, such as oxidation, reduction, and both basic and acidic hydrolysis. The 1,2,3-triazole based derivatives have received much attention due to their wide coverage of biological properties including antiviral [9], anti-HIV [10], anticonvulsants [11], anti-allergic [12], antimicrobial [13], analgesic, anti-inflammatory [14]antioxidant and anticancer properties [15].Hydrazones derived from aroylhydrazides containing heterocyclic rings such as 1,2,3-triazole have attracted special attention.

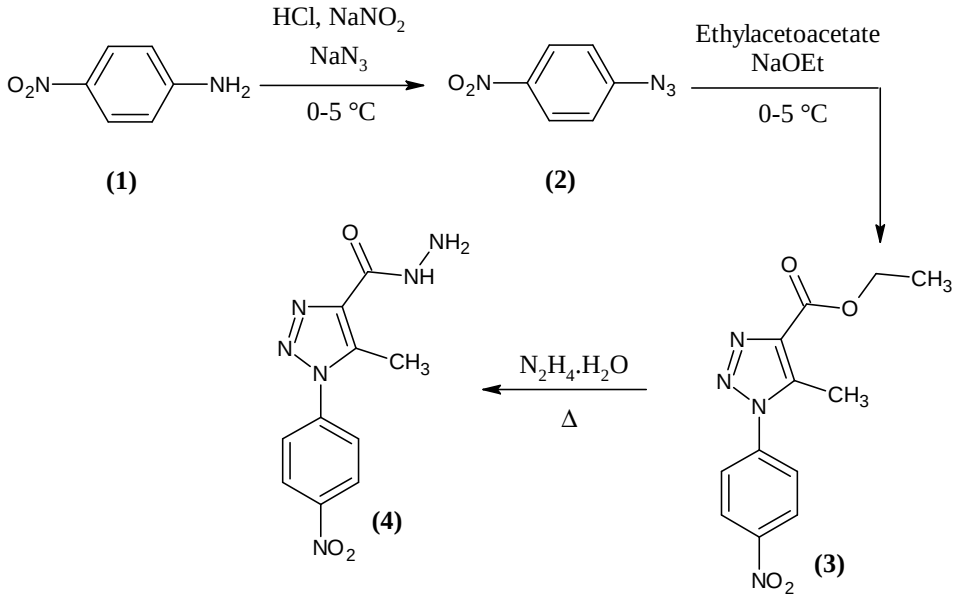
Pyrazole heterocycles occupy a prominent place in medicinal and pesticide chemistry because of their capability to exhibit a wide range of biological activities including antimicrobial [16], anti-inflammatory, analgesic [17], antioxidant [18], angiotensin antagonists, cytotoxic agents [19, 20] etc. A few of the pyrazole hydrazone derivatives have also been reported [21, 22] in the literature. However, there has been no report in the literature on the synthesis and biological evaluation of hydrazone derivatives incorporated with pyrazoles and 1,2,3- triazole moiety.Prompted by these observations and in continuation of our work on bioactive pyrazole derivatives[27,28], we herewith report a novel series of hydrazones incorporated with pyrazole moiety and their antioxidant activity.

MATERIALS AND METHODS

Melting points of the new compounds were determined in open capillary tubes in Innovative DTC-967A digital melting point apparatus and are uncorrected. IR spectra were recorded by dispersing the compounds in KBr pellets on a Schimadzu FT-IR 157 spectrophotometer. ^{1}H NMR spectra were recorded on a 300 MHz / 400 MHz / 500 MHz BrukerAvance II NMR spectrometer and all the chemical shift values were reported as δ (ppm), downfield

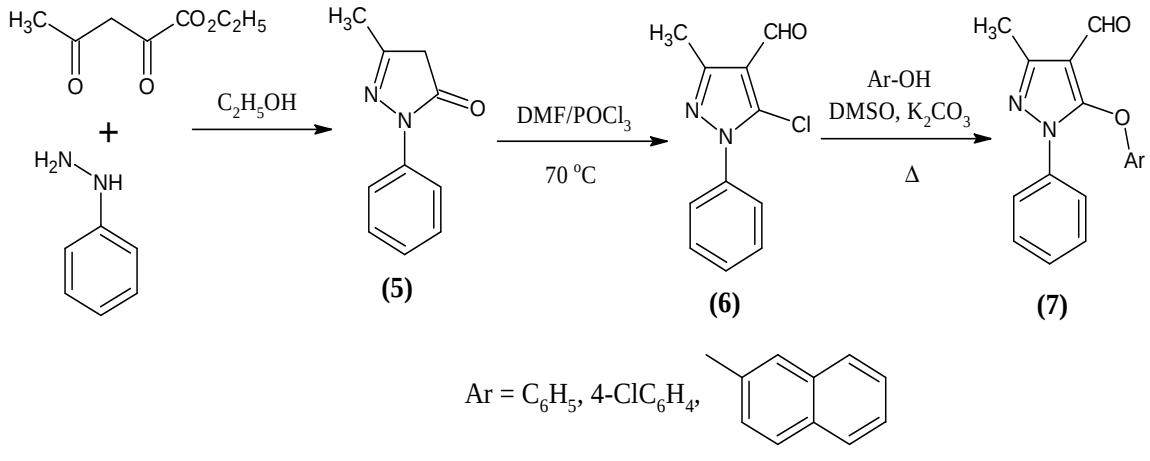
from TMS and proton signals are indicated as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectra were recorded either on a Waters UPLC-MS spectrometer or LCMS (API 3000, Applied Bio Systems) operating at 70eV. Elemental analysis was carried out on a Schimadzu ElementarVario EL III model. The purity of the compound was checked by thin layer chromatography (TLC) on silica gel plates.

The ethyl-5-methyl-1-(*p*-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylate **(3)** was prepared by the reaction of 1-azido-4-nitrobenzene **(2)** with ethylacetoacetate in presence of sodium ethoxide. The 1-azido-4-nitrobenzene **(2)** was in turn obtained by the diazotization of *p*-nitroaniline **(1)** followed by the reaction with sodium azide. The 5-methyl-1-(*p*-nitrophenyl)-1*H*-1,2,3-triazole-4-carbohydrazide**(4)** was prepared by hydrazinolysis of ethyl-5-methyl-1-(*p*-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylate**(3) (Scheme 1.1)**.

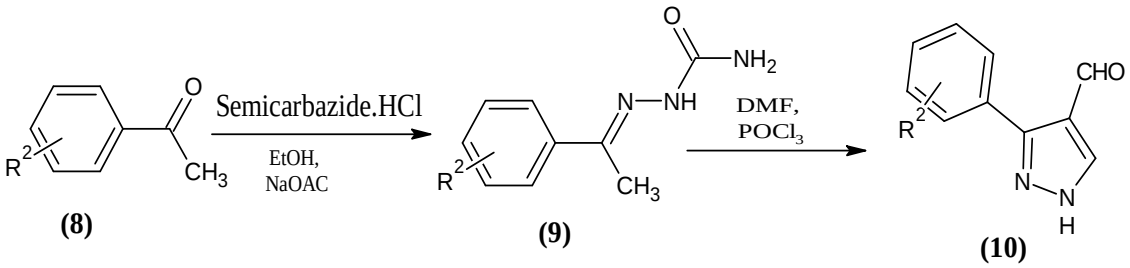


Scheme 1.1

3-Methyl-5-substituted-1-phenyl-1*H*-4-formyl-pyrazole (**6/7**) was prepared following the literature method [22,23]**(Scheme 1.2)**.3-Substituted-1*H*-pyrazole-4-carbaldehydes **(10)** were synthesized by the Vilsmayer Haack reaction of semicarbazones. The starting material semicarbazones**(9)** in turn were synthesized by refluxing equimolar amount of substituted carbonyl compounds **(8)** with semicarbazide hydrochloride in the presence of anhydrous sodium acetate in ethanol medium **(Scheme 1.3)**.



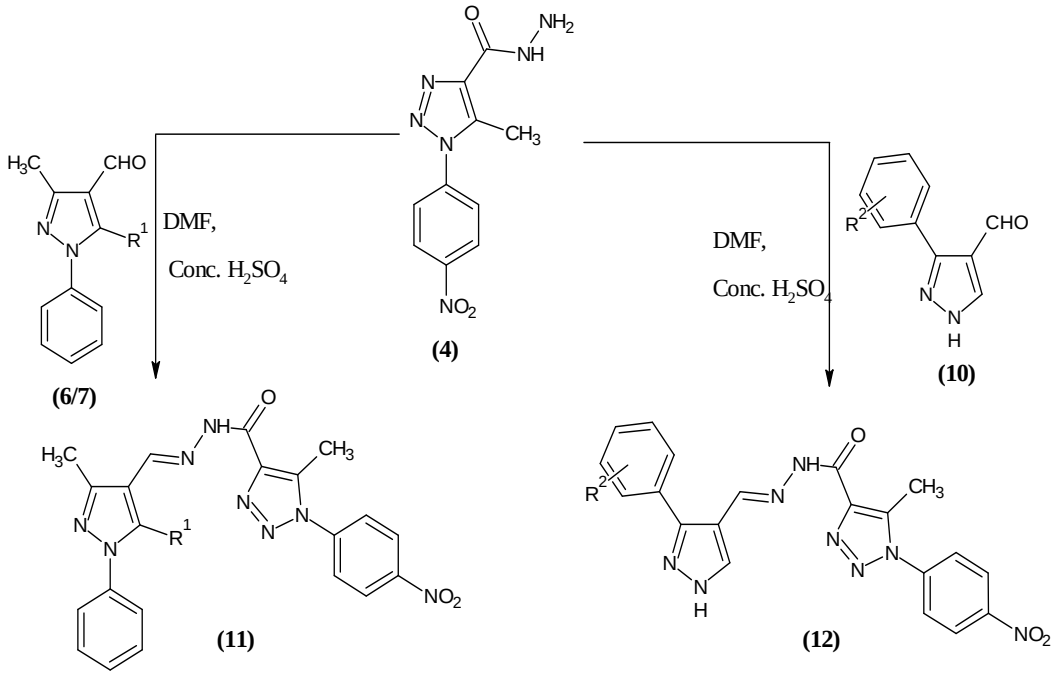
Scheme 1.2



R^2 = 4-chloro, 4-OCH_3, 4-CH_3, 2,4- dichloro, H, 4-NO_2, 3-NO_2

Scheme 1.3

1,2,3-Triazole hydrazide **(4)** upon condensation with substituted pyrazole aldehydes (6/7)in presence of conc. H_2SO_4 as catalyst in DMF-ethanol medium gave the corresponding hydrazones **(11/12) (Scheme 1.4)**.



Scheme 1.4

RESULTS AND DISCUSSION

The required intermediate pyrazole-4-carbaldehydes **(6/7)** were prepared as per the literature procedure [23, 24]. 3-Substituted-1*H*-pyrazole-4-carbaldehydes **(10)** were prepared as per the procedures reported in the literature [25, 26]. Characterization data of pyrazole-4-carbaldehydes are given in **Table 1.** The hydrazones **(11/12)** were prepared by the condensation of equimolar amounts of 5-methyl-1-(*p*-nitrophenyl)-1*H*-1,2,3-triazole-4-carbohydrazide**(4)** with different substituted pyrazole-4-carbaldehydes in DMF-ethanol medium using conc. H_2SO_4 as catalyst **Scheme 1.4**. All these hydrazones were isolated in satisfactory yields (68-85%) and the structures of newly synthesized compounds were confirmed on the basis of spectral and analytical data. Characterization data of hydrazones are given in **Table 2.**

In the ^{1}H-NMR spectrum of 5-methyl-1-(*p*-nitrophenyl)-1*H*-1,2,3-triazole-4-carbohydrazide**(4)**,the signal due to methyl proton of 1,2,3-triazole appeared as a singlet at δ 2.6178 integrating for three protons. The NH_2 protons appeared as a singlet at δ 4.5167 integrating for two protons. Meta and ortho protons of *p*-nitrophenyl appeared as two doublets in the region δ 7.9816-8.0041 (J = 9 Hz) and δ 8.4677-8.4901 (J = 8.96 Hz) integrating for two protons each. The signal due to -NH proton appeared as a singlet at δ 9.8498 integrating for one proton.

In the IR spectrum of 5-Methyl-1-(*p*-nitrophenyl)-*N*'-[(5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylidene]-1*H*-1,2,3-triazole-4-carbohydrazone**(11a),**the absorption bands corresponding to the N-H stretching frequency is observed at 3427.5 cm^{-1} and the C-H stretching was observed at 3089.9 cm^{-1}. Characteristic C=O stretching

frequency was observed at 1678 cm^{-1} and C=N stretching was observed at 1570.0 cm^{-1}. Asymmetric and symmetric stretching for the nitro group is observed at 1517.3 cm^{-1} and 1335.6 cm^{-1} respectively. The spectral data of these hydrazones are given below.

5-Methyl-1-(*p*-nitrophenyl)-*N*'-[(5-chloro-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylidene]-1*H*-1,2,3-triazole-4-carbohydrazone**(11a):** ^{1}H-NMR (500MHz) (DMSO-d_6) δ: 2.64 (s, 3H, pyrazole CH_3), 2.79 (s, 3H, triazole CH_3), 7.52 (m, 3H, Ar-H), 7.57 (d, 2H, J = 8.5 Hz, ortho protons of phenyl), 7.78 (d, 2H, J = 8.5 Hz, meta protons of *p*-nitrophenyl), 8.27 (s, 1H, imine proton), 8.49 (d, 2H, J = 8.5 Hz, ortho protons of *p*-nitrophenyl), 10.19 (s, 1H, NH).LC Mass m/z: 465.1, (M^++1), (M.F. $C_{21}H_{17}N_8O_3Cl$). The isotope peak was observed at m/z 467.1.

5-Methyl-1-(*p*-nitrophenyl)-*N*'-[(5-(phenyloxy)-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylidene]-1*H*-1,2,3-triazole-4-carbohydrazone**11b:** IR KBr(cm^{-1})**:** 3323.2 (N-H), 2968.3 (C-H), 1679.0(C=O), 1548.4 (C=N), 1512.8 (asym. NO_2), 1368.2 (sym. NO_2),1130.0 (C-O-C);^{1}H-NMR (500MHz) (DMSO-d_6) δ: 2.62 (s, 6H, CH_3 of pyrazole and triazole), 7.65-7.79 (m, 10H, Ar-H), 7.83 (s, 1H, imine proton), 7.81 (d, 2H, J=9Hz, meta protons of *p*-nitrophenyl), 7.96 (d, 2H, J = 9 Hz, ortho protons of *p*-nitrophenyl), 9.42 (s, 1H, NH).LC Mass m/z: 523.2 (M^++1) (M.F. $C_{27}H_{22}N_8O_4$).

5-Methyl-1-(*p*-nitrophenyl)-*N*'-[(5-(β-naphthyloxy)-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methylidene]-1*H*-1,2,3-triazole-4-carbohydrazone**11c**: IR KBr (cm^{-1})**:** 3473.8 (N-H), 3086.1 (C-H), 1687.7 (C=O), 1560.4 (C=N), 1521.8 (asym. NO_2), 1342.4 (sym. NO_2), C-O-C (1136.0). 5^{1}H-NMR (500MHz) (DMSO-d_6) δ: 2.73 (s, 6H, CH_3 of pyrazole and triazole), 7.85-7.23 (m, 12H, Ar-H), 7.96 (s, 1H, imine proton), 7.71 (d, 2H, J=9Hz, meta protons of *p*-nitrophenyl), 8.46 (d, 2H, J = 9 Hz, ortho protons of *p*-nitrophenyl), 9.90 (s, 1H, NH). LC Mass m/z: 573.2 (M^++1) (M.F. $C_{31}H_{24}N_8O_4$).

5-Methyl-1-(*p*-nitrophenyl)-*N*'-[(3-(*p*-anisyl)-1*H*-pyrazol-4-yl)methylidene]-1*H*-1,2,3-triazole -4-carbohydrazone **12b:**IR KBr (cm^{-1})**:** 3245.5 (N-H), 2965.1 (C-H), 1675.3 (C=O), 1563.5 (C=N), 1513.4 (asym. NO_2), 1365.1 (sym. NO_2). ^{1}H-NMR (500MHz) (DMSO-d_6) δ: 2.56 (s, 3H, triazole CH_3), 3.02 (s, 3H, anisyl OCH_3),7.25 (d, 2H, J=7.8Hz, meta protons of *p*-anisyl), 7.36 (d, 2H, J = 7.5Hz, ortho protons of *p*-anisyl), 7.55 (d, 2H, J= 8.2Hz, ortho protons of *p*-nitrophenyl), 8.02 (s, 1H, imine –CH), 8.16 (s, 1H, pyrazole 5-H), 8.38 (d, 2H, J = 8.5 Hz, meta protons of *p*-nitro phenyl), 9.76 (s, 1H, NH), 10.32 (s, 1H, pyrazole NH).LC Mass m/z: 447.2 (M^++1) (M.F. $C_{21}H_{18}N_8O_4$).

5-Methyl-1-(*p*-nitrophenyl)-*N*'-[(3-(*p*-tolyl)-1*H*-pyrazol-4-yl)methylidene]-1*H*-1,2,3-triazole-4-carbohydrazone **12c**: IR KBr (cm^{-1})**:** 3265.4 (N-H), 3086.1 (C-H), 1676.0 (C=O), 1583.5 (C=N), 1523.7 (asym. NO_2), 1346.3 (sym. NO_2).^{1}H-NMR (500MHz) (DMSO-d_6) δ: 2.45 (s, 3H, tolyl CH_3), 2.79 (s, 3H, triazole CH_3), 7.35 (d, 2H, J=7.5Hz, meta protons of *p*-tolyl), 7.45 (d, 2H, J = 8Hz, ortho protons of *p*-tolyl), 7.76 (d, 2H, J= 8.5Hz, ortho protons of *p*-nitrophenyl), 8.23 (s, 1H, imine –CH), 8.32 (s, 1H, pyrazole 5-H), 8.50 (d, 2H, J = 8.5 Hz, meta protons of *p*-nitro phenyl), 9.90 (s, 1H, NH), 10.08 (s, 1H, pyrazole NH).LC Mass m/z: 430.5 (M^+) (M.F. $C_{21}H_{18}N_8O_3$).

5-Methyl-1-(*p*-nitrophenyl)-*N*'-[(3-(*p*-chlorophenyl)-1*H*-pyrazol-4-yl)methylidene]-1*H*-1,2,3-triazole-4-carbohydrazone**12d**: IR KBr (cm^{-1})**:** 3217.2 (N-H), 3093.8 (C-H), 1670.3 (C=O), 1585.4 (C=N), 1527.6 (asym. NO_2), 1346.3 (sym. NO_2).^{1}H-NMR (500MHz) (DMSO-d_6) δ: 2.79 (s, 3H, triazole CH_3), 7.25 (d, 2H, J=8Hz, meta protons of *p*-chlorophenyl), 7.32 (d, 2H, J = 8Hz, ortho protons of *p*-chlorophenyl), 7.46 (d, 2H, J= 8.2Hz, ortho protons of *p*-nitrophenyl), 7.96 (s, 1H, imine –CH), 8.02 (s, 1H, pyrazole 5-H), 8.21 (d, 2H, J = 8.2 Hz, meta protons of *p*-nitro phenyl), 8.96 (s, 1H, NH), 9.21 (s, 1H, pyrazole NH).LC Mass m/z: 451.6 (M^++1) (M.F. $C_{20}H_{15}ClN_8O_3$).

5-Methyl-1-(*p*-nitrophenyl)-*N*'-[(3-(2,4-dichlorophenyl)-1*H*-pyrazol-4-yl)methylidene]-1*H*-1,2,3-triazole-4-carbohydrazone**12e**:IR KBr (cm^{-1})**:** 3227.2 (N-H), 3002.2 (C-H), 1686.6 (C=O), 1564.4 (C=N), 1523.2 (asym. NO_2), 1326.6 (sym. NO_2).^{1}H-NMR (400MHz) (DMSO-d_6) δ: 2.66 (s, 3H, CH_3), 6.86 (d, 1H, J= 8.0Hz, 6-H of 2,4-dichlorophenyl), 7.08 (d, 1H, J= 8.1Hz, 5-H of 2,4-dichlorophenyl), 8.51-7.30 (m, 7H, Ar-H and imine proton), 11.04 (s, 1H, NH), 12.04 (s, 1H, pyrazole NH).LC Mass m/z: 487.3 (M^++2) (M.F. $C_{20}H_{14}ClN_8O_3$).

4.1 Antioxidant studies

The newly synthesized hydrazones**(11/12)** were evaluated for antioxidant study by DPPH scavenging assay according to the method of Brand-Williams *et al*. [27].

100 mg/mL of each test sample and standard BHT was taken in different test tubes and the volume was adjusted to 1mL using MeOH. Freshly prepared 3mL of 0.1 mM DPPH solution was mixed and vortexed thoroughly and left in dark for 30 min. The absorbance of stable DPPH radical was measured at 517 nm. The DPPH control (containing no

sample) was prepared using the same procedure. Radical scavenging activity was expressed as the inhibition percentage and was calculated using the equation of DPPH radical scavenging activity.

$$\text{DPPH radical scavenging activiy (\%)} = \frac{\text{(Abs Control - Abs Sample)}}{\text{(Abs Control)}} * 100$$

Where Abs Control is the absorbance of DPPH radical + methanol; Abs Sample is the absorbance of DPPH radical + test sample/standard BHT. The antioxidant study results are tabulated in **Table 3.**

The DPPH scavenging activity for tested compounds showed activity ranging from 72.0% to 51.8%, whereas standard drug BHT showed 90.42% inhibition Compound **11a, 12d** and **12e** displayed significant radical scavenging activity i.e. 70.6%, 70.2% and 72.0% respectively among the set of compounds tested in the present study. This can be accounted due to the presence of chlorine substituent's in all the cases. Whereas compounds **12f** and **12g** with 4-nitro and 3-nitro groups showed moderate antioxidant activity i.e. 69.1 and 64.1% respectively. Also hydrazone with 4-methoxy group showed significant activity compared to other derivatives.

General procedure for the preparation of 1-azido-4-nitrobenzene (3)
p-Nitroaniline **(1)** (13.8g, 0.1mol) was dissolved in 1:1 ratio of HCl and water and taken in a round bottom flask equipped with stirrer. The reaction was agitated at 0-5 ^{o}C, sodium nitrite (6.9g, 0.1mol) was dissolved in ice-cold water and added drop wise, sodium azide (6.5g, 0.1mol) dissolved in water (20mL) was added drop wise, then stirring was continued for another 30 min. The resultant precipitate separated was extracted with chloroform and washed successively with water. The organic layer was dried over anhydrous sodium sulphate, and the solvent was removed under vacuum to get 4-nitroazidobenzene, yield 93.5%, m.p. 65-68 ^{o}C(Lit.[30] 63-66^{o}C).

General procedure for the preparation of ethyl-5-methyl-1-(*p*-nitrophenyl)-1H-1,2,3-triazole-4-carboxylate (3)
1-Azido-4-nitrobenzene **(2)** (1.6g, 0.01mol) was treated with ethyl acetoacetate (1.27mL, 0.01mol) in methanol (7.5 mL) and the mixture was cooled to 0^{o}C. Sodium ethoxide (0.7g, 0.01mol) was added under inert atmosphere to the above mixture and stirred at ambient temperature for 8 hr. Progress of the reaction was monitored by TLC (ethyl acetate/petroleum ether, 2:3, v/v). After completion of the reaction, the mixture was poured on to ice cold water and neutralized. The precipitated solid was filtered, washed with water and recrystallized from ethanol. Yield 75%, m.p. 166-168^{o}C (Lit.[28] 165-170^{o}C). Analysis for $C_{12}H_{12}N_4O_4$: C; 52.14 (Calcd. 52.17), H; 4.34 (Calcd. 4.38), N; 20.28 (Calcd. 20.28).

General procedure for the preparation of 5-methyl-1-(*p*-nitrophenyl)-1*H*-1,2,3-triazole-4-carbohydrazide (4)
Ethyl-5-methyl-1-(*p*-nitrophenyl)-1*H*-1,2,3-triazole-4-carboxylate **(3)** (2.8g, 0.01mol) in DMF (5mL) and hydrazine hydrate (99 %, 0.5mL, 0.01mol) were taken in a round bottomed flask equipped with reflux condenser. The contents were refluxed for 6 hours. Precipitated solidwas filtered, dried and recrystallised from ethanol. Yield 80%, m.p. 210-212^{o}C (Lit.[28]210-214^{o}C); Analysis for $C_{10}H_{10}N_6O_3$: C; 45.82 (Calcd. 45.80), H; 3.86 (Calcd. 3.84), N; 32.06 (Calcd. 32.05).

General procedure for the synthesis of 2-(1-arylethylidene)hydrazine carboxamide (9)
A solution of semicarbazide hydrochloride (1.07 mmol) in 20 mL of water was added drop wise to a round bottom flask containing mixture of substituted carbonyl compounds **35** (1.0 mmol), sodium acetate (1.3 mmol) and ethanol (20 mL). The reaction mixture was stirred at 80^{o}C for 8 hours. After completion of the reaction, the separated solid was filtered, washed with water and dried. The crude product **(9)** was as such taken for next stage preparation without further purification.

General procedure for the synthesis of 3-substituted-1*H*-pyrazole-4-carbaldehyde (10):
3-Substituted-1*H*-pyrazole-4-carbaldehydes **(10)**were synthesized by Vilsmayer-Haack reaction. To an ice cold solution of 2-(1-arylethylidene)hydrazine carboxamide **(9)** (0.1 mmol) in DMF (20 mL), $POCl_3$ (8 mL)was added drop wise. After the addition, the reaction mixture was stirred for 30 minutes at ambient temperature and then stirred at 60-65^{o}C for 6 hours. The reaction mixture was quenched into ice cold water and was adjusted to pH 7 using 25% sodium hydroxide solution. The solid thus precipitated was filtered and dried. Crude product was recrystallized from ethyl acetate. Compounds prepared according to this procedure and their characterization data are given in **Table 1**.

Table 1: Characterization data of 3-Substituted-1*H*-pyrazole-4-carbaldehydes(6/7/10)

Com. no	R^1/R^2	Molecular formula (Mol. wt.)	M.p. (°C) (Yield %)	% Analysis Found (Calculated)		
				C	H	N
3	Cl	$C_{11}H_9N_2OCl$ (221)	138-39 {Lit.[23]135} (79)	59.90 (59.88)	4.13 (4.11)	12.72 (12.70)
4a	OC_6H_5	$C_{17}H_{14}N_2O_2$ (279)	89-90 {Lit.[24] 86-89} (75)	73.35 (73.37)	5.09 (5.07)	10.09 (10.07)
4b	$OC_{10}H_7$	$C_{21}H_{16}N_2O_2$ (328)	99-101 {Lit.[24] 100} (78)	76.84 (76.81)	4.89 (4.91)	8.58 (8.53)
4c	OC_6H_4Cl	$C_{17}H_{13}ClN_2O_2$ (312)	106-108 (73)	65.31 (65.29)	4.21 (4.19)	8.98 (8.96)
10a	H	$C_{10}H_8N_2O$ (172.18)	144-46 {Lit.[27] 145} (79)	69.78 (69.76)	4.71 (4.69)	16.29 (16.27)
10b	4-OCH_3	$C_{11}H_{10}N_2O_2$ (202.20)	163-64 {Lit.[28] 162-64} (77)	65.32 (65.34)	4.96 (4.98)	13.87 (13.85)
10c	4-CH_3	$C_{11}H_{10}N_2O$ (186.20)	124-26 {Lit.[27] 123-25} (82)	70.97 (70.95)	5.43 (5.41)	15.07 (15.04)
10d	4-Cl	$C_{10}H_7ClN_2O$ (206.62)	143-44 {Lit.[28] 142-44} (80)	57.15 (57.13)	5.16 (5.14)	9.54 (9.52)
10e	2,4-dichloro	$C_{10}H_6Cl_2N_2O$ (241.07)	113-115 {Lit.[28] 114-16} (79)	47.35 (47.33)	4.28 (4.26)	7.88 (7.89)
10f	4-NO_2	$C_{10}H_9N_3O_2$ (203.19)	197-198 {Lit.[27] 198-99} (81)	59.13 (59.11)	4.48 (4.46)	20.70 (20.68)
10g	3-NO_2	$C_{10}H_9N_3O_2$ (203.19)	154-155 {Lit.[27] 156-58} (83)	59.09 (59.11)	4.44 (4.46)	20.66 (20.68)

Solvent for recrystallization: Ethyl acetate

Table 2: Characterization data of hydrazones(11/12)

Comp. No.	R' / R^2	M.p. °C (Yield %)	Molecular Formula (Mol. Wt)	% Analysis Found (Calculated)		
				C	H	N
11a	Cl	210-212 (80)	$C_{21}H_{17}ClN_8O_3$ (464.86)	54.28 (54.26)	3.67 (3.69)	24.12 (24.10)
11b	Phenyloxy	235-238 (76)	$C_{27}H_{22}N_8O_4$ (522.51)	62.03 (62.06)	4.26 (4.24)	21.43 (21.45)
11c	β-Naphthyloxy	258-260 (78)	$C_{31}H_{24}N_8O_4$ (572.57)	65.05 (65.03)	4.20 (4.22)	19.59 (19.57)
11d	4-Chloro phenyloxy	240-242 (75)	$C_{27}H_{21}ClN_8O_4$ (556.95)	58.24 (58.22)	3.78 (3.80)	20.09 (20.12)
12a	H	120-124 (76)	$C_{20}H_{16}N_8O_3$ (416.39)	57.71 (57.69)	3.89 (3.87)	26.89 (26.91)
12b	4-OCH_3	150-154 (82)	$C_{21}H_{18}N_8O_4$ (446.41)	56.52 (56.50)	4.08 (4.06)	25.12 (25.10)
12c	4-CH_3	215-217 (80)	$C_{21}H_{18}N_8O_3$ (430.41)	58.62 (58.60)	4.20 (4.22)	26.05 (26.03)
12d	4-Chloro	256-258 (78)	$C_{20}H_{15}ClN_8O_3$ (450.83)	53.30 (53.28)	3.37 (3.35)	24.87 (24.85)
12e	2,4-Dichloro	258-260 (79)	$C_{20}H_{14}Cl_2N_8O_3$ (485.28)	49.52 (49.50)	2.93 (2.91)	23.11 (23.09)
12f	4-NO_2	230-232 (75)	$C_{20}H_{15}N_9O_5$ (461.39)	52.08 (52.06)	3.30 (3.28)	27.34 (27.32)
12g	3-NO_2	245-248 (80)	$C_{20}H_{15}N_9O_5$ (461.39)	52.08 (52.06)	3.30 (3.28)	27.30 (27.32)

Solvent for recrystallization: Ethanol + DMF mixture.

Table 3: DPPH radical assay of hydrazones(11/12)

Comp. No.	**11a**	**11b**	**11c**	**11d**	**12a**	**12b**
DPPH Assay in %	**70.6**	60.9	61.8	59.6	51.8	64.5
Comp. No.	**12c**	**12d**	**12e**	**12f**	**12g**	**BHT**
DPPH Assay in %	63.5	**70.2**	**72.0**	69.1	64.1	90.42

General procedure for the synthesis 5-methyl-1-(*p*-nitrophenyl)-N'-(aryl methylidene)-1*H*-1,2,3-triazole-4-carbohydrazone(11/12)

To a solution of 5-methyl-1-(*p*-nitrophenyl)-1*H*-1,2,3-triazole-4-carbohydrazide**(4)** (2.6g, 0.01mol) taken in a mixture of DMF and ethanol (25mL), was added appropriate substituted pyrazole aldehydes **(6/7/10)** (0.01mol). Concentrated sulphuric acid (0.5mL) was added to this reaction mixture. The contents were refluxed for about 1-2 hours. The solid product separated was collected by filtration. It was dried and recrystallized from DMF-ethanol mixture. The characterization data of these compounds are given in **Table 2**.

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