Studies with 2-arylhydrazono-3-oxopropanals: routes for the synthesis of pyridazine-3,4-dicarboxylate and 3,5-diaroyl pyrazoles

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Abstract

The title compounds **3a-j** were synthesized via coupling of enaminones **2a-d** with aromatic diazonium salts. The reaction of **3b-f,h-j** with dimethyl acetylenedicarboxylate and triphenylphosphine afforded dimethyl 2-aryl-6-aroyl-2,3-dihydropyridazine-3,4-dicarboxylates **7b-f,h-j**. . The reaction of **3b,d,f,g** with phenacyl bromide afforded 3-aroyl-5-benzoylpyrazoles **9b,d,f,g**.,while compound **3i** condensed with benzoylacetonitrile to yield pyridazin-6-imine **11**.Reaction of **3c-e,h,j** with *p*-toluidine yielded the enamineazo **12c-e,h,j.** The structures of **7b,d,i** and **9b** were confirmed by X-ray crystal structure determination.

Keywords: 2-Arylhydrazonopropanals, enaminones, pyridazine-3,4-dicarboxylate, 3,5-diaroylpyrazoles

Introduction

The coupling reaction of functionally substituted enamines of type **2** with aromatic diazonium salts[1] has opened the route for the synthesis of 2-arylhydrazonals **3**. It was shown that derivatives of **3** are useful starting materials for a variety of heterocycles.[2-6] Therefore, in conjunction with this work, we report this study aimed at establishing, with certainty the previous conclusions. Our results were confirmed *via* X-ray crystal determinations and extended previously reported findings[6] in order to see if this constitutes a new general route for the preparation of dialkylpyridazine dicarboxylates as well as 3,5-diaroylpyrazoles.

Results and Discussion

Enaminones **2** were previously synthesized by condensing heteroaryl methyl ketones **1a,b** and arylmethyl ketones **1c-e** with dimethylformamide dimethylacetal DMFDMA in xylene following some literature procedures.[1,7] However, only moderate yields of the desired products **2a-e** were obtained. Consequently we have modified this synthetic approach and condensed these ketones with DMFDMA in absence of solvent. In this case, the required enaminones were obtained almost in better yield, and this method is more economic. Yields and reaction times for both methods are reported in Table1.

Table 1. Comparison between reaction time and yields obtained from conventional heating in solvent and without solvent

Sample NO.	Δ in xylene		Δ in excess DMFDMA	
	Time(min.)	Yield %	Time(min.)	Yield %
2a	450	70	480	80
2b	450	60	480	77
2c	450	60	480	85
2d	450	70	480	89
2e	450	61	480	88

Coupling enaminones **2** with aromatic diazonium salts afforded the products **3a-j** which were previously shown to exist, in the solid state, in the *anti* form according to the X-ray crystal structure determination of **3a,h** published recently by our group.[8] This agrees with a recent observation[9] that in the 2-arylhydrazonoketones stereoelectronic factors overweigh any possible lock of conformation that may occur due to hydrogen bonding. (Scheme 1). We observed in previous work[6] that other derivatives of **3** reacted with dimethyl acetylene dicarboxylate DMAD in the presence of triphenylphosphine to yield pyridazine-3,4-dicarboxylates. In the present work **3b-f,h-j** reacted with DMAD yielding **7b-f,h-j** (Scheme 1). Previously the mechanism for the formation of the end products[6] that was suggested could not be supported by evidence and the proposed structure did not seem completely convincing. By obtaining X-ray crystal structures for **7b,d,i** we could confirm our conclusions (cf. Figures 1-4).[10]

Recently,[11] it has been reported the first synthesis of 5-acetyl-3-aroylpyrazoles by mixing derivatives of **3** with chloroacetone. Now we have found that **3b,d,f,g** also react to yield colored products **9b,d,f,g,** of molecular formulae corresponding to their condensation with phenacyl bromide *via* hydrogen bromide and water elimination thus, the alternative furan structure **10** could be ruled out. X-ray crystal structure determination confirmed that the reaction products are in fact **9** (Scheme 1, Fig. 4) formed most likely via intermediacy of **8.** Compound **3g** condensed also with benzoylacetonitrile to yield pyridazin-6-imine **11,** based on spectral data.

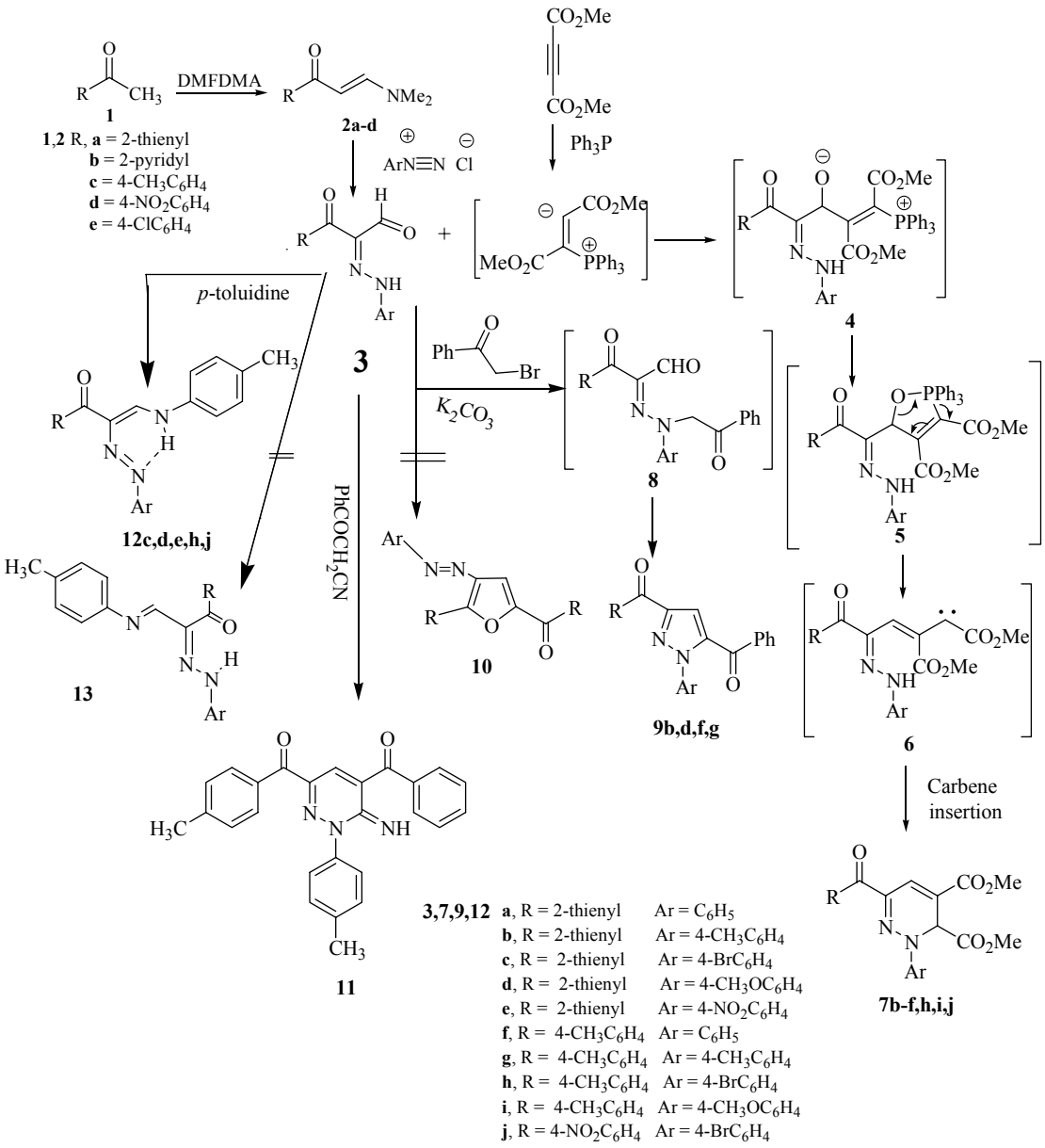
2-Arylhydrazono-3-propanals **3c-e,h,j** reacted with *p*-toluidine to yield products of condensation via water elimination. Two tautomeric forms are possible for these condensation products enamineazo **12** or iminohydrazone isomer **13**. ^{1}H NMR data clearly revealed that this condensation has involved the formyl carbon as the formyl proton has disappeared and also ^{1}H NMR spectra for condensation products of **3c-e,h,j** with *p*-toluidine revealed a doublet signal at δ = 8.6 ppm (J= 7.2 Hz) for *H*CNH proton and another signal at δ = 15.4 ppm for NH proton. The fact that the proton attached to the carbon atom linked to the amine nitrogen appeared as a doublet allowed us to suggest the enaminoazo structures **12** for these products(Scheme 1).

Conclusions

In conclusion, 2-arylhydrazonopropanals can serve as starting materials for the synthesis of a variety of heteroaromatic compounds with an interesting substitution pattern and the efficient synthesis of enaminones achieved in this work makes also these compounds economically acceptable as starting materials. Moreover, previously assigned studies could be unambiguously established.

Crystallographic Analysis

The crystals were mounted on a glass fiber. All measurements were performed on an ENRAF NONIUNS FR 590. The data were collected at temperature of 20$\pm$1 °C using the ω scanning technique to a maximum of a 20 of 27.12°. The structure was solved by the direct method using SIR 92[12]. Non-hydrogen atoms were refined anisotropically by full matrix least squares. Hydrogen atoms were located geometrically and were refined isotropically.[13]


DMFDMA
1
1,2 R, a = 2-thienyl
b = 2-pyridyl
c = 4-CH3C6H4
d = 4-NO2C6H4
e = 4-ClC6H4
2a-d
ArN≡N Cl
CO2Me
Ph3P
3
p-toluidine
12c,d,e,h,j
13
PhCOCH2CN
10
Ph
Br
K2CO3
8
9b,d,f,g
4
5
6
Carbene insertion
7b-f,h,i,j
11
3,7,9,12 a, R = 2-thienyl Ar = C6H5
b, R = 2-thienyl Ar = 4-CH3C6H4
c, R = 2-thienyl Ar = 4-BrC6H4
d, R = 2-thienyl Ar = 4-CH3OC6H4
e, R = 2-thienyl Ar = 4-NO2C6H4
f, R = 4-CH3C6H4 Ar = C6H5
g, R = 4-CH3C6H4 Ar = 4-CH3C6H4
h, R = 4-CH3C6H4 Ar = 4-BrC6H4
i, R = 4-CH3C6H4 Ar = 4-CH3OC6H4
j, R = 4-NO2C6H4 Ar = 4-BrC6H4

Scheme 1

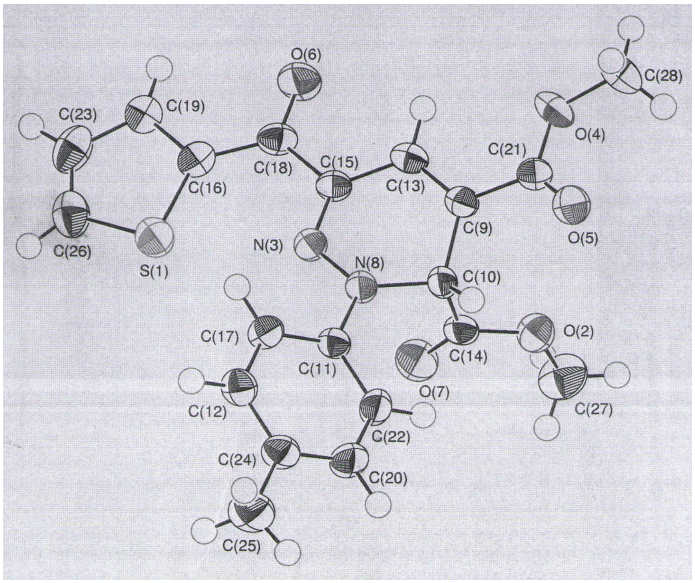


Figure 1. Thermal ellipsoid plots of the X-ray structure of **7b** (50 % probability).

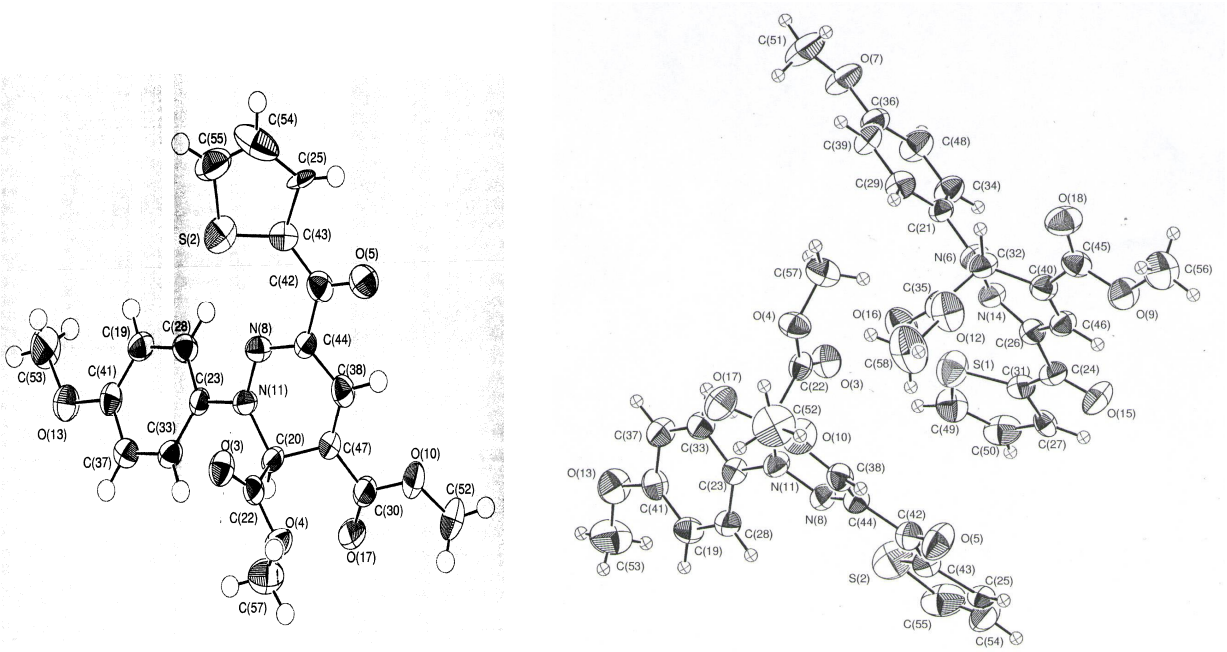


Figure 2. Thermal ellipsoid plots of the X-ray structure of **7d** (50 % probability).

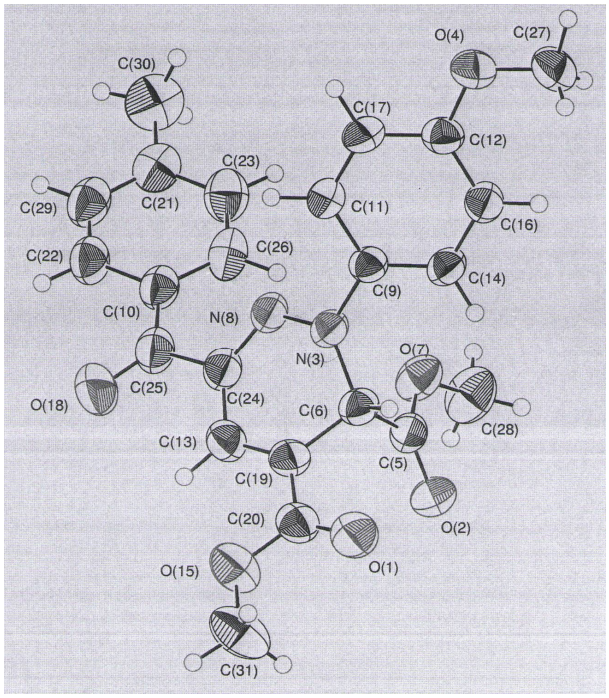


Figure 3. Thermal ellipsoid plots of the X-ray structure of **7i** (50 % probability.

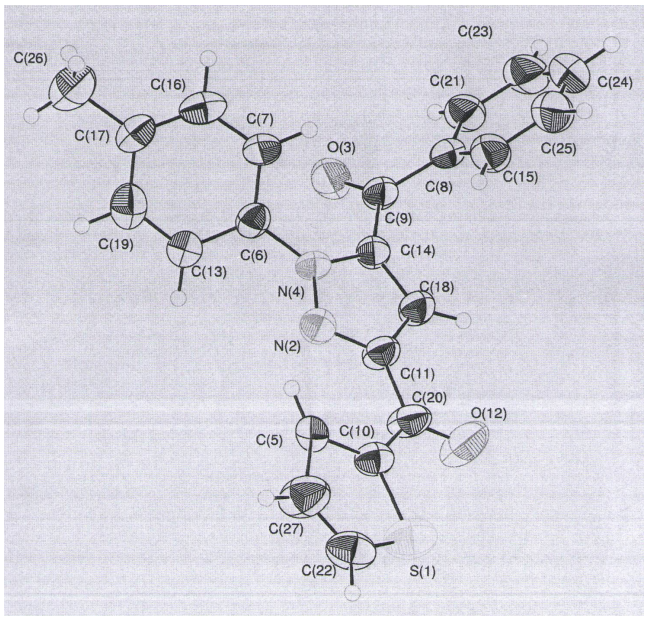


Figure 4. Thermal ellipsoid plots of the X-ray structure of **9b** (50 % probability).

Table 2. Crystal data and structure refinement for compounds **7b,d,i** and **9b**

	7b **CCDC 617787**	**7d** **CCDC 617786**	**7i** **CCDC 617788**	**9b** **CCDC 617777**
Empirical Formula	$C_{20}H_{18}N_2O_5S$	$C_{20}H_{18}N_2O_6S$	$C_{23}H_{22}N_2O_6$	$C_{22}H_{16}N_2O_2S$
Formula weight	398.437	414.436	453.407	372.446
Crystal System	Triclinic	Triclinic	Monoclinic	Triclinic
Space group	P-1	P-1	P21/c	P-1
Unit cell parameters				
a [Å]	7.9742(2)	9.7889(2)	8.0662(2)	8.5993(3)
b [Å]	9.5600(3)	13.3834(3)	21.1130(4)	10.9802(3)
c [Å]	13.4031(4)	16.8502(5)	12.3971(3)	11.1537(5)
α^o	79.5153(12)	69.6369(8)	90.00	116.9690(14)
β^o	73.4154(13)	76.0099(9)	95.7775(9)	91.8325(14)
γ^o	89.1275(11)	81.6577(8)	90.00	95.353(2)
Unit cell volume	962.18(5)	2003.66(9)	2100.52(8)	931.25(6)
Z	2	4	4	2
Temperature (K)	298	298	298	298
Radiation type	Mo*Ká*	Mo*Ká*	Mo*Ká*	Mo*Ká*
F(000)	416	864	944	388
Absorption coefficient (mm^{-1})	0.20	0.20	0.11	0.19
Parameters	253	523	280	239
R factor	0.050	0.061	0.048	0.089

Table 3. Selected bond length [Å] and angles [°] for compounds **7b,d,i** and **9b**

Bond lengths **7b**		*Bond lengths* **7d**		*Bond lengths* **7i**		*Bond lengths* **9b**	
N3 N8	1.332(3)	N8 N11	1.335(3)	N3 N8	1.328(2)	N2 N4	1.337(5)
N3 C15	1.313(3)	N8 C44	1.319(3)	N3 C6	1.468(2)	N2 C11	1.335(6)
N8 C10	1.474(3)	C44 C38	1.426(4)	C6 C19	1.503(3)	N4 C14	1.366 (6)
C10 C14	1.504(3)	N11 C23	1.431(3)	N3 C9	1.426(2)	C6 C7	1.375(6)
C10 H10	0.960(2)	C20 C47	1.518(3)	C13 C24	1.432(3)	C9 C14	1.485(6)
C13 C15	1.434(3)	N11 C20	1.464(3)	C9 C14	1.378(2)	C11 C18	1.394(7)
C13 C9	1.343(3)	C38 C47	1.336(3)	C14 C16	1.395(3)	C14 C18	1.363(6)

Bond angles **7b**		*Bond angles* **7d**		*Bond angles* **7i**		*Bond angles* **9b**	
N8 N3 C15	118.4(2)	N8 N11 C20	121.6(2)	N8 N3 C9	116.13(14)	N4 N2 C11	105.1(4)
C9 C10 C14	111.1(2)	N11 C20 C22	110.3(2)	C6 N3 N8	120.95(14)	N2 N4 C14	112.1(4)
N8 C10 C9	108.5(2)	N11 C20 C47	109.1(2)	N3 C6 C19	107.3(13)	N4 C6 C7	121.0(4)
C10 C9 C13	117.7(2)	C44 C38 C47	120.3(2)	C25 C24 N8	116.8(2)	C7 C6 C13	119.6(4)
N8 C10 C14	110.6(2)	N8 C44 C38	121.9(2)	N3 N8 C24	117.6(2)	N2 C11 C18	110.9(4)
N3 N8 C10	121.8(2)	C20 C38 C47	120.3(2)			N2 C11 C20	124.0(4)

Experimental Section

All melting points were measured on Gallenkamp electrothermal melting point apparatus and are uncorrected. IR spectra were recorded as KBr pellets on a Pye Unicam SP 3-300 Spectrophotometer. ^{1}H NMR spectra were recorded in deuterated dimethylsulfoxide (DMSO-d_6) or deuterated chloroform ($CDCl_3$) at **300** MHz on a Varian Gemini NMR spectrometer using tetramethylsilane (TMS) as an internal reference and results are expressed as δ values. Mass spectra were performed on a Shimadzu GCMS-QP 1000 Ex mass spectrometer at 70 eV. Elemental analyses were carried out at the Micro analytical center of Cairo University. Compounds **3a-j** has been prepared as previously reported.[8]

General procedure for preparation of enaminones 2a-d

A mixture of heteroaryl ketones and methylaryl ketones **1a-d** (10 mmol) and dimethylformamide dimethylacetal DMFDMA (10 mmol) with little excess, or in xylene was heated under reflux for 8 hours, and then left to cool at room temperature. The solid products **2a-d** were collected by filtration, and then recrystallized form xylene.

3-Dimethylamino-1-(2-thienyl) propenone (**2a**), mp 122-124ºC (Lit[1] 132ºC).

3-Dimethylamino-1-(2-pyridyl) propenone (**2b**), mp 135-136ºC (Lit[1] 134ºC).

3-Dimethylamino-1-***p*** -tolyl propenone (**2c**), mp 94-96 ºC (Lit[14]93-95 ºC).

3-Dimethylamino-1-(4-nitrophenyl) propenone (**2d**), mp 152-154ºC (Lit[14] 153ºC).

3-Dimethylamino-1-(4-chlorophenyl) propenone (**2e**), mp 86-88 ºC (Lit[14] 81-83 ºC).

General procedure for preparation of pyridazine derivatives 7b-f,h-j

To a solution of Ph_3P (10 mmol) and each of hydrazones **3b-f,h-j** (10 mmol) in CH_2ClCH_2Cl (10 ml) was added drop wise to a solution of dimethylacetylene dicarboxylate (10 mmol). The mixture was left standing at room temperature for 24hrs and then treated with ethanol. The solid product was collected by filtration, then recrystallized from ethanol.

6-(Thiophene-2-carbonyl)-2-*p*-tolyl-2,3-dihydro-pyridazine-3,4-dicarboxylic acid dimethyl ester (7b). Orange crystals, yield (89%); mp 184-185°C. IR (KBr): ν = 1676 (CO), 1651 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.43(s, 3H, CH_3), 3.66 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.26 (s, 1H, HC-NAr) , 7.34-7.85(m, 7H, Ar-H), 7.81(s, 1H, H-5). MS (EI, 70eV): *m/z* = 398 (M^+). Anal. calcd for $C_{20}H_{18}N_2O_5S$ (398.43): C, 60.29; H, 4.55; N, 7.03. Found: C, 60.30; H, 4.56; N, 7.20.

2-(4-Bromophenyl)-6-(thiophene-2-carbonyl)-2,3-dihydropyridazine-3,4-dicarboxylic acid dimethyl ester (7c). Yellow crystals, yield (86%); mp 172-174°C. IR (KBr): ν = 1690 (CO), 1620 (CO) cm^{-1};- ^1H NMR (DMSO-d_6): δ = 3.66 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.26 (s, 1H, HC-NAr), 7.30-8.13 (m, 7H, Ar-H), 7.59 (s, 1H, H-5). - MS (EI, 70eV): *m/z* = 464 (M^++1). Anal. calcd for $C_{19}H_{15}BrN_2O_5S$ (463.30): C, 49.26; H, 3.26; N, 6.05. Found: C, 49.31; H, 3.25; N, 6.22.

2-(4-Methoxyphenyl)-6-(thiophene-2-carbonyl)-2,3-dihydro-pyridazine-3,4-dicarboxylic acid dimethyl ester (7d). Orange crystals, yield (85%); mp 168-170°C, IR (KBr): ν = 1695 (CO), 1628 (CO) cm^{-1};^1H NMR (DMSO-d_6): δ = 3.68 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3) , 3.90 (s, 3H, OCH_3), 6.26 (s, 1H, HC-NAr), 6.99 (d, 2H, *J* = 9 Hz, Ar-H), 7.09 (d, 2H, *J* = 9 Hz, Ar-H), 7.63 (s, 1H, H-5), 7.71 (m, 1H, thiophene H-4), 8.01 (d, 1H, thiophene H-3), 8.40 (d, 1H, thiophene H-5); - MS (EI, 70eV): *m/z* = 414 (M^+). Anal. calcd for $C_{20}H_{18}N_2O_6S$ (414.43): C, 57.96; H, 4.38; N, 6.76. Found: C, 58.00; H, 4.36; N, 6.83.

2-(4-Nitrophenyl)-6-(thiophene-2-carbonyl)-2,3-dihydro-pyridazine-3,4-dicarboxylic acid dimethyl ester (7e). Orange crystals, yield (90%); mp 286-288°C, IR (KBr): ν = 1708 (CO), 1635 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 3.65 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3) 6.38 (s, 1H, HC-NAr), 7.29-7.32 (m, 1H, thiophene H-4), 7.71 (s, 1H, H-5), 7.90 (d, 2H, *J* = 9 Hz, Ar-H), 8.10-8.14 (m, 2H, thiophene H-3,5), 8.35 (d, 2H, *J* = 9 Hz, Ar-H); ^{13}C NMR (DMSO-d_6): δ = 52.76 (CH_3), 53.30 (CH_3), 88.50 (C-3), 118.04 (C-2`,6`, Ar), 125.22 (C-3`,5`, Ar), 128.95 (C-4, thiophene), 133.20 (C-5, thiophene), 135.64 (C-3, thiophene), 136.88 (C-4`, Ar), 143.56 (C-2, thiophene), 144.60 (C-4), 146.05 (C-1`, Ar), 149.20 (C-5), 162.56 (CO), 168.90 (CO), 175.60 (CO). - MS (EI, 70eV): *m/z* = 429 (M^+). Anal. calcd for $C_{19}H_{15}N_3O_7S$ (429.40): C, 53.14; H, 3.52; N, 9.79. Found: C, 53.18; H, 3.50; N, 9.82.

6-(4-Methylbenzoyl)-2-phenyl-2,3-dihydro-pyridazine-3,4-dicarboxylic acid dimethyl ester (7f). Orange crystals, yield (81%); mp 156-157°C; IR (KBr): ν = 1700 (CO), 1624 (CO) cm^{-1};- ^1H NMR (DMSO-d_6): δ = 2.39 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3) , 3.85 (s, 3H, OCH_3), 6.25 (s, 1H, HC-NAr), 7.22-7.89 (m, 9H, Ar-H) and 7.60 (s, 1H, H-5). - MS (EI, 70eV): *m/z* =333 (M^+-

59). Anal. calcd for $C_{22}H_{20}N_2O_5$ (392.40): C, 67.34; H, 5.14; N, 7.14. Found: C, 67.70; H, 5.20; N, 7.22.

2-(4-Bromophenyl)-6-(4-methylbenzoyl)-2,3-dihydro-pyridazine-3,4-dicarboxylic acid dimethyl ester (7h). Orange crystals, yield (82%); mp 201-203°C; IR (KBr): ν = 1699 (CO), 1629 (CO) cm^{-1};- ^1H NMR (DMSO-d_6): δ = 2.41 (s, 3H, CH_3), 3.67 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.26 (s, 1H, HC-NAr), 7.34-7.85 (m, 8H, Ar-H), 7.81(s, 1H, H-5). - MS (EI, 70eV): *m/z* =413 (M^+-58). Anal. calcd for $C_{22}H_{19}BrN_2O_5$ (471.30): C, 56.07; H, 4.06; N, 5.94. Found: C, 56.20; H, 4.00; N, 6.00.

2-(4-Methoxyphenyl)-6-(4-methylbenzoyl)-2,3-dihydro-pyridazine-3,4-dicarboxylic acid dimethyl ester (7i). Orange crystals, yield (79%); mp 212-214°C; IR (KBr): ν = 1690 (CO), 1635 (CO) cm^{-1};^1H NMR (DMSO-d_6): δ = 2.39 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3) , 3.76 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.24 (s, 1H, HC-NAr), 6.96 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.22 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.27 (d, 2H, *J* = 9 Hz, Ar-H), 7.59 (s, 1H, H-5), 7.85 (d, 2H, *J* = 9 Hz, Ar-H), - MS (EI, 70eV): *m/z* =422 (M^+). Anal. calcd for $C_{23}H_{22}N_2O_6$ (422.43): C, 65.39; H, 5.25; N, 6.63. Found: C, 65.45; H, 5.32; N, 6.45.

2-(4-Bromophenyl)-6-(4-nitrobenzoyl)-2,3-dihydro-pyridazine-3,4-dicarboxylic acid dimethyl ester (7j). Yellow crystals, yield (91%); mp 204-206°C; IR (KBr): ν = 1705 (CO), 1638 (CO) cm^{-1}; ^1H NMR; (DMSO-d_6): 3.78 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.25 (s, 1H, HC-NAr), 7.04-8.75 (m, 8H, Ar-H), 7.07 (s, 1H, H-5). MS; *m/z* 503 (M^++1). Anal. calcd for $C_{21}H_{16}BrN_3O_7$ (502.27): C, 50.22; H, 3.21; N, 8.37. Found: C, 50.23; H, 3.22; N, 8.24.

General procedure for preparation of pyrazole derivatives 9b,d,f,g

Each of 2-arylazopropanals **3b,d,f,g** (10 mmol), $PhCOCH_2Br$ (10 mmol) and potassium carbonate anhydrous (10 mmol) in acetone was heated under reflux for 6hrs in water bath. The reaction mixture was filtered, and then left to cool at room temperature. The solid product was collected by filtration and crystallized from ethanol.

(5-Benzoyl-1-*p*-tolyl-1*H*-pyrazol-3-yl)-thiophen-2-yl-methanone (9b). Orange crystals, yield (88%); mp 206-208ºC; IR (KBr): ν = 1680 (CO), 1648 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.37 (s, 3H, CH_3), 7.29-7.32 (m, 3H, Ar-H), 7.38 (s, 1H, pyrazole H-4), 7.44 (d, 2H, *J* = 8.5 Hz, Ar-H), 7.59 (t, 2H, *J* = 7.8Hz, Ar-H), 7.71-7.77 (m, 1H, thiophene H-4), 7.94 (d, 2H, *J* = 8.5 Hz, Ar-H),8.11 (d, 1H, thiophene H-3), 8.48 (d, 1H, thiophene H-5); ^{13}C NMR (DMSO-d_6): δ = 20.59 (CH_3), 114.21 (C-4), 120.81 (C-5), 124.62, 128.25, 128.86, 129.53, 129.65 (C-4, thiophene), 134.17, 136.04 (C-3, thiophene), 136.25, 136.96, 138.54 (C-5, thiophene), 140.26, 141.32 (C-2, thiophene), 149.21 (C-3), 177.47 (CO), 184.82 (CO). MS (EI, 70eV): *m/z* = 372 (M^+). Anal. calcd for $C_{22}H_{16}N_2O_2S$ (372.44): C, 70.95; H, 4.33; N, 7.52. Found: C, 71.00; H, 4.35; N, 7.55.

]5-Benzoyl-1-(4-methoxyphenyl)-1*H*-pyrazol-3-yl[-thiophen-2-yl-methanone (9d). Orange crystals, yield (81%); mp 237-239ºC; IR (KBr): ν = 1671 (CO), 1639 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 3.71 (s, 3H, OCH_3), 6.91 (s, 1H, H-4 pyrazole), 7.57-8.21 (m, 12H, 9 Ar-H and

3H-thienyl). - MS (EI, 70eV): *m/z* = 388 (M^+). Anal. calcd for $C_{22}H_{16}N_2O_3S$ (388.44): C, 68.02; H, 4.15; N, 7.21. Found: C68.21; H, 4.16; N, 7.33

(5-Benzoyl-1-phenyl-1*H*-pyrazol-3-yl)-*p*-tolylmethanone (9f). Yellow crystals, yield (90 %); mp 158-159ºC; IR (KBr): ν = 1675 (CO), 1625 (CO) cm^{-1};- ^1H NMR (DMSO-d_6): δ = 2.40 (s, 3H, CH_3), 7.36 (s, 1H, H-4 pyrazole), 7.39-8.19 (m, 14H, Ar-H). MS (EI, 70eV): *m/z* = 366 (M^+). Anal. calcd for $C_{24}H_{18}N_2O_2$ (366.41): C, 78.67; H, 4.95; N, 7.65 Found: C, 78.60; H, 5.00; N, 7.50.

(5-Benzoyl-1-*p*-tolyl-1*H*-pyrazol-3-yl)-*p*-tolylmethanone(9g). Orange crystals, yield (89%); mp 164-166ºC; IR (KBr): ν = 1679 (CO), 1629 (CO) cm^{-1};- ^1H NMR (DMSO-d_6): δ = 2.36 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 7.28 (s, 1H, H-4 pyrazole), 7.30-8.19 (m, 13H, Ar-H). - MS (EI, 70eV): *m/z* = 380 (M^+). Anal. calcd for $C_{25}H_{20}N_2O_2$ (380.44): C, 78.93; H, 5.30; N, 7.36. Found: C, 78.81; H, 5.47; N, 7.12.

5-(Benzoyl-6-imino-1- *p*-tolyl-1,6-dihydropyridazin-3-yl)-*p*-tolyl-methanone (**11**).

To a solution of **3g** (10 mmol) and benzoylacetonitrile (10 mmol) in ethanol (50 ml) were added a few drops of piperidine. The reaction mixture was heated under reflux for 2 hours. Then the solvent was evaporated and the solid so formed, was collected by filtration and then recrystallized from ethanol. Orange crystals, yield (89%); mp 213-215ºC; IR (KBr): ν = 3244 (NH), 1660 (CO), 1625 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.36 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 7.22-8.01 (m, 14H, Ar-H, NH and 4H pyridazine). - MS (EI, 70eV): *m/z* = 407 (M^+). Anal. calcd for $C_{26}H_{21}N_3O_2$ (407.46): C, 76.64; H, 5.19; N, 10.31. Found: C, 76.60; H, 5.25; N, 10.44.

General method for preparation of 12c-e,h,j *via* reaction with *p*-toluidine

A mixture of compound **3c-e,h,j** (10 mmol) and *p*-toluidine (10 mmol, 1.07 g) in ethanol was refluxed for 3 hours. The solvent was evaporated and the solid so formed, was collected by filtration and then recrystallized from ethanol.

2-(4-Bromophenylazo)-1-thiophen-2-yl-3-*p*-tolylaminopropenone (12c). Orange crystals, yield (34 %), mp. 197-199ºC. IR (KBr): ν = 3258 (NH), 1626 (CO) cm^{-1};- ^1H NMR (DMSO-d_6): δ = 2.35 (s, 3H, CH_3), 7.25-8.09 (m, 11H, Ar-H), 8.76 (d, 1H, *J* = 6.9 Hz, *H*C-NH), 15.14 (d, 1H, *J* = 6.9 Hz, NH). MS (EI, 70eV): *m/z* = 425 (M^+-1). - Anal. calcd for $C_{20}H_{16}BrN_3OS$ (426.33): C 56.34, H 3.78, N 9.86. Found C 56.33, H 3.79, N 9.65.

2-(4-Methoxyphenylazo)-1-thiophen-2-yl-3-*p*-tolylaminopropenone (12d). Orange crystals, yield (40 %), mp. 164-166ºC; IR (KBr): ν = 3263 (NH), 1651 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.34 (s, 3H, CH_3), 3.75 (s, 3H, OCH_3), 7.08-8.08 (m, 11H, Ar-H), 8.63 (d, 1H, *J* = 7.2 Hz, *H*C-NH), 14.73 (d, 1H, *J* = 7.2 Hz, NH) - MS (EI, 70eV): *m/z* = 377 (M^+). Anal. calcd for $C_{21}H_{19}N_3O_2S$ (377.46): C 66.82, H 5.07, N 11.13. Found C 66.59, H 5.06, N 11.27.

2-(4-Nitrophenylazo)-1-thiophen-2-yl-3-*p*-tolylaminopropenone (12e). Orange crystals, yield (43%), mp. 225-227ºC; IR (KBr): ν = 3297 (NH), 1652 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.38 (s, 3H, CH_3), 7.31-8.37 (m, 11H, Ar-H), 8.90 (d, *J* = 6.9 Hz, 1H, *H*C-NH), 15.56 (d**,** *J* = 6.9 Hz, 1H, NH) - MS (EI, 70eV): *m/z* = 392 (M^+). Anal. calcd for $C_{20}H_{16}N_4O_3S$ (392.43): C 61.21, H 4.11, N 14.28. Found C 61.34, H 4.10, N 14.33.

2-(4-Bromophenylazo)-1-*p*-tolyl-3-*p*-tolylaminopropenone (12h). Orange crystals, yield (66%), mp. 166-168ºC. IR (KBr): ν = 3417 (NH), 1635 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.35 (s, 3H,CH_3), 2,41 (s, 3H,CH_3),7.28-8.30 (m, 12H, Ar-H), 8.79 (d , *J* = 6.7 Hz, 1H, *H*C-NH), 15.14 (d, 1H, *J* = 6.7 Hz, NH) - MS (EI, 70eV): *m/z* = 434 (M^+). - Anal. calcd for $C_{23}H_{20}BrN_3O$ (434.33): C 63.60, H 4.64, N 9.67. Found C 63.61, H 4.62, N 9.49.

2-(4-Bromophenylazo)-1-(4-nitrophenyl)-3-*p*-tolylaminopropenone (12j). Orange crystals, yield (40%), mp. 234-236ºC. IR (KBr): ν = 3417 (NH), 1643 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ = 2.36 (s, 3H, CH_3), 7.27 (d, 2H, *J* = 8.1 Hz, Ar-H), 7.44 (d, 2H, *J* = 8.1 Hz, Ar-H), 7.52 (d, 2H, *J* = 8.4 Hz, Ar-H), 7.69 (d, 2H, *J* = 8.4 Hz, Ar-H), 8.05 (d, 2H, *J* = 8.7 Hz, Ar-H), 8.36 (d, 2H, *J* = 8.7 Hz, Ar-H), 8.77 (d , *J* = 7 Hz, 1H, *H*C-NH), 14.94 (d, 1H, *J* = 7 Hz, NH) - MS (EI, 70eV): *m/z* = 464 (M^+-1). - Anal. calcd for $C_{22}H_{17}BrN_4O_3$ (465.30): C 56.79, H 3.68, N 12.04. Found C 56.88, H 3.67, N 12.30.

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10. CCDC 617786, 617787, 617788 and 617777 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via.* http://www.ccdc.ac.uk/data_request/cif.
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