Substituted hydrazonals as building blocks in heterocyclic synthesis: a new route to arylhydrazonocinnolines

Mariam A. Al-Shiekh[a], Hanady Y. Medrassi[a], Mohamed H. Elnagdi[b] and Ebtisam A. Hafez[b]*

[a]*Department of Chemistry, Girls College of Education, Jeddah, P. O. Box 334 Jeddah 21341, Kingdom of Saudi Arabia*

[b]*Department of Chemistry, Faculty of Science, Cairo University, Giza-12611, Egypt*

2-heteroylhydrazonopropanals **2a–e** and 3-oxo-2-arylhydrazonopropanals **2f–k** were prepared via coupling of enaminones **1** with aromatic diazonium salts. Compounds **2a–c** condensed with hydrazine hydrate to yield the corresponding hydrazones **3a–c** which afford on cyclisation the cinnoline derivatives **6a–c**, while condensation of **2g, j** with hydrazine hydrate directly yielded the pyrazole derivatives **4g–j**. Condensation of **2a–c, f, g** with phenyl hydrazine gave the corresponding phenyl hydrazone derivatives **7a–c, f, g**. Structures of **2a, h** and **3a** were assessed by single crystal X-ray analyses.

Keywords*:* 2-arylhydrazonopropanals, enaminones, arylhydrazonopyrazoles, cinnoline

The coupling of enaminones **1** with aromatic diazonium salts to synthesise 3-oxo-2-aryl or 2-heteroylhydrazonopropanals **2a–k** has been previously reported.[1,2] The structure and chemistry of these novel arylhydrazones has attracted much attention with plenty of uses for these compounds being reported recently.[3,4] It has been noted that in DMSO these molecules exist as a mixture of two conformers *E* and *Z*.[2,5] Since 2-arylhydrazonopyrovales undergoes rearrangement into the 1-arylhydrazono-2-oxopropanes under mild conditions, we thought that it might be possible that such a rearrangement might also take place in the case of **2.** This would be a reasonable rationale for the existence of the equilibrium mixture in the ^{1}H NMR study.

Results and discussion

We have prepared the arylhydrazonals **2a–k** and obtained X-ray crystal structures for two of the reaction products, namely **2a, h**; which adopted an *anti*-form in the solid state. This agrees with the recent observation that within the 2-arylhydrazonoketones strereoelectronic factors overweigh any possible fixation that may occur due to hydrogen bonding.[6] Note that the most stable conformation of **2a** was found to be planar, whereas in **2h** the phenyl moiety rotates around a single bond. The planar orientation of the **2a** conformer is probably the result of stereoelectronic interaction between the oxygen and sulfur lone pairs. We thus believe that assumed fixation of hydrazones by hydrogen bonding in DMSO solution is least likely although we observed in almost every case of aroyl derivatives the presence of two NH signals integrating for a total of one proton with varying intensity in each case depending upon the nature of the substituent at the carbonyl moiety. This may point to the existence of an equilibrium between the two forms **2C** and **2D** in DMSO solution (Scheme 1).

Compounds **2a–c** refluxed with hydrazine hydrate in ethanol for 3 h gave the corresponding hydrazones **3a–c** while compounds **2g, j** reacted with hydrazine hydrate under the same conditions to yield the corresponding arylhydrazonopyrazole derivatives **4g–j** as based upon spectral data.[4] Compound **3a** was shown by X-ray crystallography to also adopt the *anti*-form **2C** where bond lengths and bond angles indicate the absence of hydrogen bonding (Fig. 3). The observed low field signal for NH in compounds **2** and **3** is thus a result of extensive delocalisation of hydrogen NH at both CH and CO. Selected bond lengths and bond angles for compounds **2a, h** and **3a** are listed in Tables 1 and 2.[7] It is apparent that as a result of lone pair delocalisation hydrazone nitrogens have bond angles corresponding to two sp^2 nitrogens. The N–N bond also appears as a double bond N=N, rather than a saturated N–NH bond. It is thus believed that in both structures **2** and **3** the resonance form **2D** contributes significantly to the actual state of the molecules. The dominant anti form structures of compounds **2** and **3** indicate that in these systems stereoelectronic factors overweigh possible fixation through hydrogen bonding (see Scheme 1).

The attempted cyclisation of **3a–c** into pyrazoles **4** resulted in the formation of the heteroylhydrazonocinnoline derivatives **6a–c** as indicated by their spectral data, in which the ^{1}H NMR spectra of compounds **6a–c** showed in every case the existence of hydrazone NH_2 at about δ 13.5–13.7 ppm. Compounds **6a–c** are assumed to be formed via initial enolisation of **3** to **5** with subsequent cyclisation through thermally induced 6π electrons.[5] The difference in behaviour between **2a–c** and **2g, j** is rationalised for in terms decrement of carbonyl nucleophilicity thus allowing for competiting electrocyclisation (Scheme 1). Reaction of compounds **2a–c, f, g** with phenylhydrazine afforded the hydrazones **7a–c, f, g**. The attempted cyclisation of **7a–c, f, g** into arylhydrazonopyrazoles **4** or heteroylhydrazonocinnoline **6** failed.

To conclude, we can state that in 2-oxoarylhydrazones stereoelectronic effects overweigh any possible fixation that may be formed through hydrogen bonding. Moreover a novel cinnoline synthesis is reported.

Crystallographic analysis

The crystals were mounted on glass fibre. All measurements were performed on an ENRAF NONIUNS FR 590. The data were collected at a temperature of 20 ± 1°C using the ω scanning technique to a maximum of 20 of 27.12°. The structures were solved by the direct method using SIR 92.[8] Non-hydrogen atoms were refined anisotropically by full matrix least squares. Hydrogen atoms were located geometrically and were refined isotropically.[9]

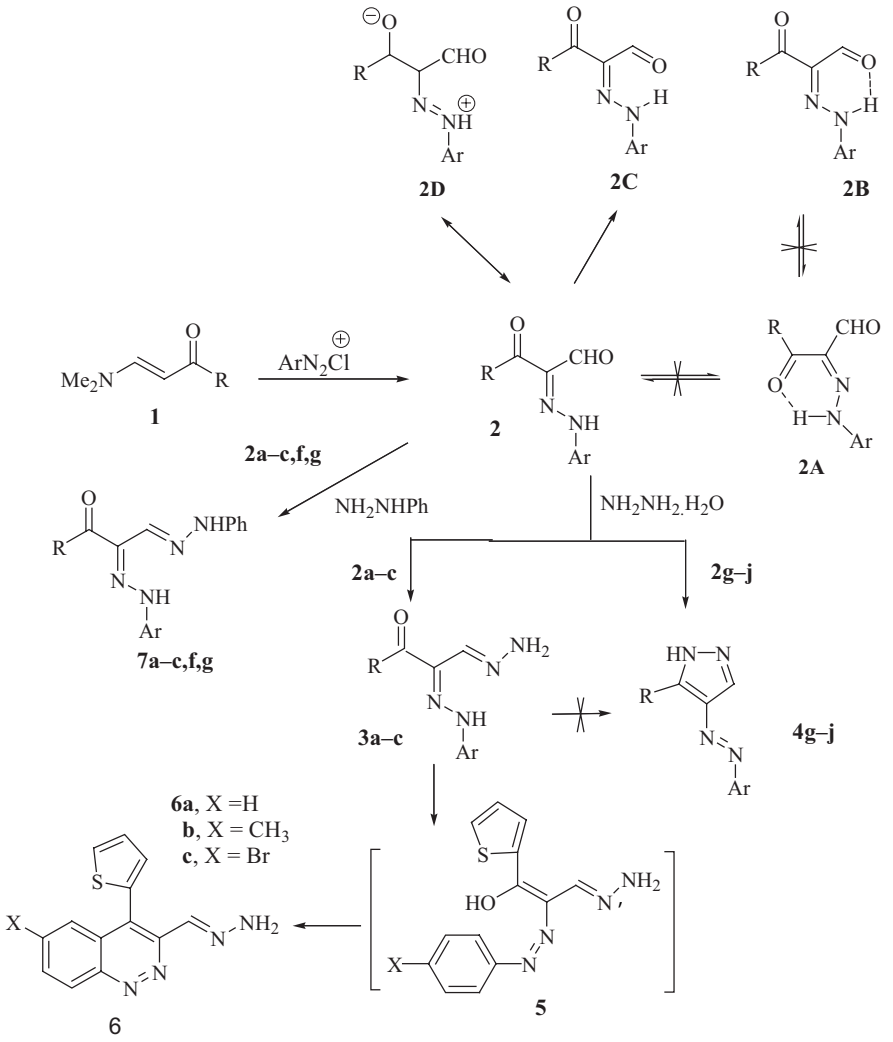
Experimental

All melting points were measured on a 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 deutrated chloroform ($CDCl_3$) at 200, 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 Microanalytical centre of Cairo University.

General procedure for preparation of 2-arylhydrazono-3-oxopropanal derivatives **2a–k**:

A cold solution of aryldiazonium salt (10 mmol) prepared by adding a cold solution of sodium nitrite (10 mmol) in water to a cold

* Correspondent. E-mail: ebtisam_hafez@hotmail.com



2,3,4,7: a, R = 2-thienyl Ar = C_6H_5
b, R = 2-thienyl Ar = 4-$CH_3C_6H_4$
c, R = 2-thienyl Ar = 4-BrC_6H_4
d, R = 2-thienyl Ar = 4-$CH_3OC_6H_4$
e, R = 2-thienyl Ar = 4-$NO_2C_6H_4$
f, R = 4-$CH_3C_6H_4$ Ar = C_6H_5
g, R = 4-$CH_3C_6H_4$ Ar = 4-$CH_3C_6H_4$
h, R = 4-$CH_3C_6H_4$ Ar = 4-BrC_6H_4
i, R = 4-$CH_3C_6H_4$ Ar = 4-$CH_3OC_6H_4$
j, R = 4-$NO_2C_6H_4$ Ar = 4-BrC_6H_4
k, R = 4-ClC_6H_4 Ar = 4-ClC_6H_4

Scheme 1

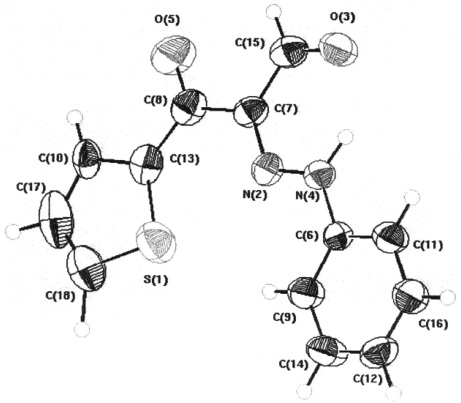


Fig. 1 Thermal ellipsoid plots of the X-ray structure of **2a** (50% probability).

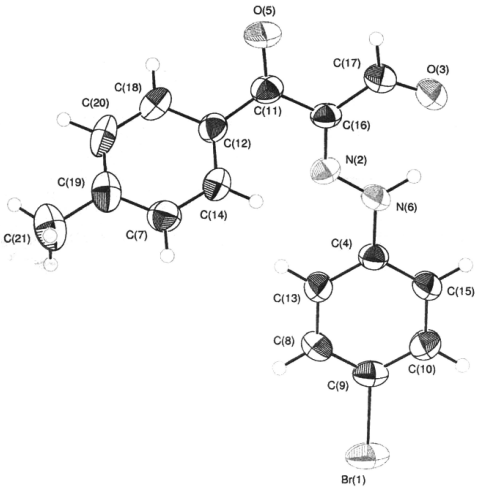


Fig. 2 Thermal ellipsoid plots of the X-ray structure of **2h** (50% probability).

Table 1 Crystal data and structure refinement for compounds **2a, h** and **3a**

	2a	**2h**	**3a**
	CCDC-617779	CCDC-617778	CCDC-629546
Empirical formula	$C_{13}H_{10}N_2O_2S$	$C_{16}H_{13}BrN_2O_2$	$C_{13}H_{12}N_4OS$
Formula weight	258.299	345.19	272.330
Crystal system	Monoclinic	Triclinic	Trigonal
Space group	'C2/c	'P-1	'R-3
Unit cell parameters			
a [Å]	26.0481(8)	6.5122(2)	36.9986(12)
b [Å]	5.4763(2)	7.3253(2)	36.9986(12)
c [Å]	21.0944(9)	16.6701(6)	5.2142(2)
α°	90.00	81.1963(13)	90.00
β°	127.115(2)	81.8713(11)	90.00
γ°	90.00	71.676(2)	120.00
Unit cell volume [Å^3]	2399.5(2)	742.32(4)	6181.4(4)
Z	8	2	18
R factor	0.053	0.043	0.064
Radiation	Mo*Ká*	*MoKá*	*MoKá*
Dx Mg m^{-3}	1.430	1.540	1.317
F(000)	1072 loop	346	2555
Absorption coefficient(mm^{-1})	0.26	2.77	0.23
Parameters	163	190	172

Table 2 Selected bond length [Å] and angles [°] for compounds **2a, h** and **3a**

Bond lengths **2a**		Bond lengths **2h**		Bond lengths **3a**	
S1 C18	1.685(3)	C11 C16	1.476(4)	C8 C9	1.4.98(3)
N2 N4	1.300(2)	C11 C12	1.493(4)	N3 H5	1.9082(15)
N2 C7	1.319(2)	C18 C20	1.375(5)	C8 C9	1.498(3)
N4 C6	1.421(3)	C12 C18	1.388(4)	N5 C10	1.394(2)
C7 C8	1.483(3)	C12 C14	1.386(4)	C10 C13	1.392(3)
C7 C15	1.467(3)	N2 C16	1.317(3)	N4 C9	1.300(2)
C8 C13	1.474(3)	N2 N6	1.314(3)	N3 C11	1.271(2)
C11 C16	1.385(3)	C16 C17	1.453(3)	N4 N5	1.324(2)
Bond angles 2a		**Bond angles 2h**		**Bond angles 3a**	
C13 S1 C18	93.41(14)	C18 C20 C19	122.2(3)	C7 S1 C17	91.90(10)
N4 N2 C7	119.9(2)	C12 C18 C20	120.3(3)	N6 N3 C11	118.3(2)
N2 N4 C6	120.9(2)	C11 C16 C17	117.7(2)	N4 C9 C11	127.5(2)
N4 C6 C9	122.1(2)	N2 C16 C11	117.6(2)	N4 C5 C10	120.6(2)
N2 C7 C8	117.9(2)	N6 N2 C16	121.0(2)	N5 N4 C9	117.6(2)
N2 C7 C15	124.0(2)	N6 C4 C15	118.9(3)	S1 C17 C16	112.1(2)

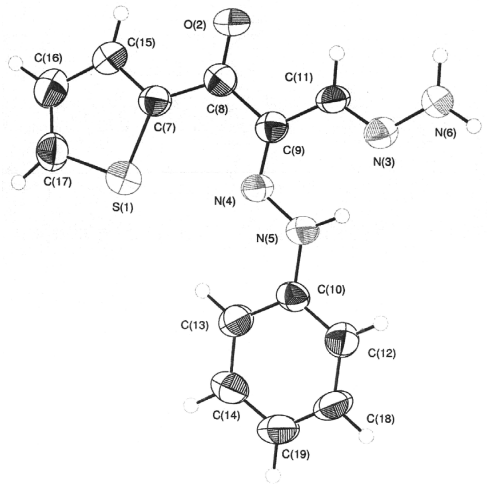


Fig. 3 Thermal ellipsoid plots of the X-ray structure of **3a** (50% probability).

solution of appropriate arylamine (10 mmol) in conc. HCl-was added with stirring to a cold solution of appropriate enaminones **1a–d** in ethanol (50 ml) containing sodium acetate (10 mmol). The reaction mixture was stirred at 0°C for 1 h, then ice cold water was added, the solid product, so formed was collected and recrystallised from ethanol.

3-Oxo-2-(phenylhydrazono)3-(thiophen-2-yl)propionaldehyde (**2a**): Obtained from ethanol as red crystals. m.p. 115°C (Lit.[1] 113–115°C). Yield 85.7%. IR (KBr): ν = 3448 (NH), 1643 (CO) cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 7.22 (m, 1H, H-4$_{thienyl}$), 7.26–7.68 (m, 5H, Ar–H), 8.03–8.07 (m, 1H, H-3 and H-5$_{thienyl}$), 10.0 (s, 1H, CHO) and 14.34 (s, 1H disappeared after D_2O exchange, NH) ppm. ^{13}C NMR: δ 118.95, 127.92, 129.59, 136.69 (phenyl carbons) 131.47, 133.51, 137.53, 140.57 (thienoyl carbons), 143.07 (*C=N*), 182.35 (thienoyl *C*O), 189.80 (*C*HO). MS: *m/z* 257 (M$^+$–1).

3-Oxo-3-(thiophen-2-yl)2-(p-tolylhydrazono)propionaldehyde (**2b**): Obtained from ethanol as yellow crystals. m.p. 134°C (Lit.[10] 132°C). Yield 82.4%. ^{1}H NMR (DMSO-d$_6$): δ 2.35(s, 3H, CH$_3$), 7.29–8.09 (m, 7H, 4H, Ar–H and 3H$_{thienyl}$), 10.02 (s, 1H, CHO) and 14.43 (s, 1H, NH). MS: *m/z* = 272 (M$^+$).

2-[(4-Bromophenyl)hydrazono]-3-oxo-3-(thiophen-2-yl)propionaldehyde (**2c**): Obtained from ethanol as yellow powder crystals. m.p. 162°C. Yield 88%. IR (KBr): ν = 3110–3760 (NH), 1640 (CO) cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 7.25–8.06 (m, 7H, 4H, Ar–H and 3H$_{thienyl}$) 9.98 (s, 1H, CHO) and 14.17 (s, 1H, NH). MS: *m/z* 336 (M$^+$–1). Found: C 46.50; H 2.67; N 8.44. $C_{13}H_9BrN_2O_2S$ (337.19) requires C 46.31; H 2.69; N 8.31.

2-[(4-Methoxyphenyl)hydrazono]-3-oxo-3-(thiophen-2-yl)propionaldehyde (**2d**): Obtained from ethanol as pale orange crystals. m.p. 249°C. Yield 84.7%. IR (KBr): ν = 3108–3751 (NH), 1636 (CO) cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 3.78 (s, 3H, OCH$_3$), 7.03–8.08 (m, 7H, 4H, Ar–H and 3H$_{thienyl}$), 10.85 (s, 1H, CHO) and 13.49 (s, 1H, NH) MS: *m/z* 288 (M$^+$). Found: C 58.25; H 4.19; N 9.69.$C_{14}H_{12}N_2O_3S$ (288.32) requires C 58.32; H 4.20; N 9.72.

2-[(4-Nitrophenyl)hydrazono]-3-oxo-3-(thiophen-2-yl)propionaldehyde (**2e**): Obtained from ethanol as yellow crystals.

m.p. 255°C (Lit.[1] 256–258). Yield 77%. IR (KBr): ν = 3447 (NH), 1652 (CO) cm^{-1}. MS: *m/z* 302 (M^+–1).

3-Oxo-2-(phenylhydrazono)3-(p-tolyl)propionaldehyde (**2f**): Obtained from ethanol as red crystals. m.p. 154°C. Yield 88%. IR (KBr): ν = 3112–3755 (NH), 1635 (CO) cm^{-1}. ^1H NMR (DMSO-d_6): δ. 2.39 (s, 3H, CH_3), 7.08–7.85 (m, 9H, Ar–H), 9.53, 9.98 (2 s, ^1H, CHO) and 12.01, 14.21 (2 s, 1H, NH) ppm. *Z, E* isomers. MS: *m/z* 265 (M^+–1). Found C 72.21, H 5.29, N 10.41. $C_{16}H_{14}N_2O_2$ (266.29) requires C 72.16, H 5.30, N 10.52.

3-Oxo-3(p-tolyl)2-(p-tolylhydrazono)propionaldehyde (**2g**): Obtained from ethanol as red crystals. m.p. 165°C. Yield 77.24%. IR (KBr): ν = 3425 (NH) and 1635 (CO) cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.30 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 7.19–7.84 (m, 8H, Ar–H), 9.53, 9.99 (2 s, 1H, CHO) and 12.18, 14.32 (2 s, 1H, NH) ppm, *Z, E* isomers. MS: *m/z* 280 (M^+). Found: C 72.75; H 5.77; N 10.09. $C_{17}H_{16}N_2O_2$ (280.32) requires C 72.84; H 5.75; N 9.99.

2-[(4-Bromophenyl)hydrazono]-3-oxo-3(p-tolyl)propionaldehyde (**2h**): Obtained from ethanol as orange crystals. m.p. 181°C. Yield 76.82%. IR (KBr): ν = 3417 (NH) and 1635 (CO) cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.42 (s, 3H, CH_3), 7.34–7.85 (m, 8H, Ar–H), 9.55, 9.99 (2s, 1H, CHO) and 11.94, 14.10 (2 s, 1H, NH) ppm. *Z, E* isomers. MS: *m/z* 346 (M^++1). Found: C 55.74; H 3.79; N 8.35. $C_{16}H_{13}BrN_2O_2$ (345.19) requires C 55.67; H 3.80; N 8.12.

2-[(4-Methoxyphenyl)hydrazono]3-oxo-3(p-tolyl)propionaldehyde (**2i**):Obtained from ethanol as orange crystals. m.p. 165°C. Yield (70.42%). IR (KBr): ν = 3440 (NH) and 1645 (CO) cm^{-1}.^1H NMR (DMSO-d_6): δ 2.38 (s, 3H, CH_3), 3.75 (s, 3H, OCH3) 6.73–8.36 (m, 8H, Ar–H), 9.51, 9.99 (2s, 1H, CHO) and 12.21, 14.43 (2s, 1H, NH) ppm. *Z, E* isomers. MS: *m/z* 296 (M^+). Found: C, 68.92; H, 5.42; N, 9.50 $C_{17}H_{16}N_2O_3$ (296.32): requires C, 68.91; H, 5.44; N, 9.45.

2-[(4-Bromophenyl)hydrazono]-3-(4-nitrophenyl)3-oxo-propionaldehyde (**2j**): Obtained from ethanol as pale orange crystals. m.p. 195°C. Yield 75.86%. IR (KBr): ν = 3446 (NH) and 1650 (CO) cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.60–8.41 (m, 8H, Ar–H), 9.54, 9.96 (2s, 1H, CHO) and 13.82, 14.89 (2s, 1H, NH) ppm, *Z, E* isomers. MS: *m/z* 375 (M^+–1). Found: C 47.78; H 2.64; N 11.42. $C_{15}H_{10}BrN_3O_4$ (376.16) requires C 47.89; H 2.68; N 11.17.

3-(4-Chlorophenyl)2-](4-Chlorophenyl)hydrazono[-3-oxopropionaldehyde (**2k**): Obtained from ethanol as orange crystals. m.p. 165°C. Yield 70.42%. IR (KBr): ν = 3423 (NH) and 1648 (CO) cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.31–7.94 (m, 8H, Ar–H), 9.53, 9.99 (2s, 1H, CHO) and 13.60, 14.07 (2s, 1H, NH) ppm, *Z, E* isomers. ^{13}C NMR: δ 119.07, 129.51, 130.16, 130.59, 132.47, 132.97, 136.29, 137.78 (phenyl carbons) 141.15 (*C*=*N*), 188.75 (*C*O), 190.18 (*C*HO). MS: *m/z* 320 (M^+–1). Found: C 56.22; H 3.15; N 8.75.$C_{15}H_{10}Cl_2N_2O_2$ (321.16) requires C 56.10; H 3.14; N 8.72.

General procedure for preparation of compounds **3a–c** *and* **4a, b**

A mixture of each compound **2a–c, g, j** (10 mmol) and hydrazine hydrate (10 mmol) was refluxed for 3 hours in ethanol. The solid product so formed, was collected by filtration, then recrystallised from the proper solvents.

3-Hydrazono-2-phenylhydrazono-1-(thiophen-2-yl)propan-1-one (**3a**): Obtained from ethanol as pale orange crystals. m.p. 206°C. Yield 85.11%. IR (KBr): ν = 1612 (CO) and 3733 (NH_2) cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.04–8.05(m, 10H, 5H, Ar–H, 3$H_{thienyl}$ and NH_2), 8.21 (s, 1H, HC=N) and 13.78 (s, 1H disappeared after D_2O exchange, NH). MS: *m/z* 272 (M^+). Found: C 57.33; H 4.45; N 20.32. $C_{13}H_{12}N_4OS$ (272.33) requires C 57.34; H 4.44; N 20.57.

3-Hydrazono-1-(thiophen-2-yl)2-(p-tolylhydrazono)propan-1-one (**3b**): Obtained from ethanol as red crystals. m.p 261°C. Yield 89.33% IR (KBr): ν = 1612 (CO) and 3393 (NH_2) cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.37 (s, 3H, CH_3), 7.20–8.19 (m, 7H, 4H, Ar–H, and 3$H_{thienyl}$), 7.51 (s, 2H, NH_2), 8.19 (s, 1H, HC=N) and 13.73 (s, 1H, NH). MS: *m/z* 286 (M^+). Found: C 58.66; H 4.92; N 19.60.$C_{14}H_{14}N_4OS$ (286.36) requires C 58.72; H 4.93; N 19.57.

2-[(4-Bromophenyl)hydrazono]-3-hydrazono-1-(thiophen-2-yl) propan-1-one (**3c**): Obtained from ethanol as orange crystals. m.p. 205°C. Yield 79.58%. IR (KBr): ν = 1653 (CO) and 3392 (NH_2) cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.22–8.00 (m, 9H, 4H, Ar–H, 3$H_{thienyl}$ and NH_2), 8.15 (s, 1H, HC=N) and 13.75 (s, 1H, NH). MS: *m/z* 352 (M^++1). Found: C, 44.51; H, 3.14; N, 16.01.$C_{13}H_{11}BrN_4OS$ (351.22) requires C, 44.46; H, 3.16; N, 15.95.

3-(p-Tolyl)4-(p-tolylazo)pyrazole (**4g**): Obtained from ethanol as orange crystals. m.p. 163°C. Yield 79%. IR (KBr): ν = 3447 (NH) cm^1. ^1H NMR (DMSO-d_6): δ 2.36 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 7.34–7.96 (m, 8H, Ar–H), 8.3 (s, 1H, pyrazole H-5), 13.63 (s, 1H, NH). MS: *m/z* 276 (M^+). Found: C 73.77; H 5.82; N 20.30. $C_{17}H_{16}N_4$ (276.34) requires C 73.89; H 5.84; N 20.27;

4-(4-Bromophenyl)3-(4-Nitrophenylazo)pyrazole (**4j**): Obtained from ethanol as yellowish brown crystals. m.p. 244°C. Yield 68%. IR (KBr): ν = 3440 (NH) cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.70–8.32 (m, 8H, Ar–H), 8.38 (s, 1H, pyrazole H-5), 13.84 (s, 1H, NH). MS: *m/z* 371 (M^+–1). Found: C 48.25; H 2.73; N 18.89 $C_{15}H_{10}BrN_5O_2$ (372.18) requires C 48.41; H 2.71; N 18.82.

General procedure for cyclisation of compounds **3a–c** *into cinnoline derivatives* **6a–c**

Each of the compounds **3a–c** (10 mmol) in pyridine (15 ml) was refluxed for 4 hours. Then the reaction mixture was left to cool at room temperature. The solid product, so formed, was collected by filtration, and then recrystallised from ethanol.

{[4-(Thiophen-2-yl)cinnolin-3-yl]methylene}hydrazine (**6a**): Obtained from ethanol as reddish-brown crystals. m.p. 205°C. Yield 78.32%. IR (KBr): ν = 3442 (NH_2) cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.25–7.98(m, 7H, 4H, Ar and 3$H_{thienyl}$), 8.32 (s, 1H, C*H*=*N*), 13.67, 14.02 (2s, 2H, NH_2).^{13}C NMR: δ 123.90, 128.32, 128.45, 128.63 120.74, 129.52, 154.49 and 130.19, 131.21, 132.18, 177.36 (thienyl carbons). MS: *m/z* 254 (M^+). Found: C 61.28; H 3.95; N 22.15. $C_{13}H_{10}N_4S$ (254.31) requires C 61.40; H 3.96; N 22.03.

[6-Methyl-4-(thiophen-2-yl)cinnolin-3-ylmethylene]hydrazine (**6b**): Obtained from ethanol as dark brown crystals. m.p. 202°C. Yield 80.36%. IR (KBr): ν = 3448 (NH_2)cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.38 (s, 3H, CH_3), 7.20–7.88 (m, 6H, 3H, Ar and 3$H_{thienyl}$) 8.21 (s, 1H, CH=N), 13.54, 13.89 (2s, 2H, NH_2). MS: *m/z* 268 (M^+). Found: C 62.58; H 4.50; N 20.76 $C_{14}H_{12}N_4S$ (268.34) requires C 62.66; H 4.51; N 20.88.

[6-Bromo-4-(thiophen-2-yl)cinnolin-3-ylmethylene]hydrazine (**6c**): Obtained from ethanol as reddish brown crystals. m.p. 226°C. Yield 78.39%. IR (KBr): ν = 3447 (NH_2)cm^{-1}. ^1H NMR (DMSO-d_6): δ 7.18–7.90 (m, 6H, 3H, Ar and 3$H_{thienyl}$), 8.24 (s, 1H, C*H*=*N*), 13.56, 13.90 (2s, 2H, NH_2). MS: *m/z* 332 (M^+–1). Found: C 46.74; H 2.70; N 16.83.$C_{13}H_9N_4BrS$ (333.21) requires C 46.86; H 2.72; N 16.81.

General procedure for preparation of compounds **7a–c, f, g**

A mixture of each compound of **2a–c, f, g** (10 mmol) and phenyl hydrazine (10 mmol) was refluxed for 3 h in ethanol. The solid product so formed, was collected by filtration, and then recrystallised from the proper solvents.

2, 3-Bis(phenylhydrazono)1-(thiophen-2-yl) propan-1-one (**7a**): Obtained from ethanol/dioxan as orange crystals. m.p. 222°C. Yield 81.78%. IR (KBr): ν = 1612 (CO) and 3263, 3417 (NH) cm^{-1}. ^1H NMR (DMSO-d_6): δ 6.89–6.96 (s, 1H, H-4$_{thienyl}$), 7.10–7.50 (m, 10H, Ar–H), 8.05–8.12 (m, 2H, H-3 and H-5$_{thienyl}$), 8.40 (s, 1H, HC=N), 11.02 (s, 1H disappear after D_2O exchange, $NH_{hydrazone}$) and 13.47 (s, 1H disappear after D_2O exchange, $NH_{hydrazone}$). ^{13}C NMR: δ 114.07, 117.05, 122.15, 125.23, 129.16, 131.39, 131.67, 133.65 (phenyl carbons), 134.16, 136.64, 137.80, 140.21 (thienoyl carbons), 144.33 (H*C*=*N*), 145.36 (C=N) and 182.13 (thienoyl *C*O). MS: *m/z* 348 (M^+). Found: C 65.61; H 4.65; N 16.20. $C_{19}H_{16}N_4OS$ (348.43) requires C 65.50; H 4.63; N 16.08.

3-Phenylhydrazono-1-(thiophen-2-yl)2-(p-tolylhydrazono)propan-1-one (**7b**): Obtained as orange crystals from ethanol/dioxan. m.p. 241°C. Yield 86.45%; IR (KBr): ν = 1651 (CO), 3263–3425 (NH) cm^{-1}. ^1H NMR; (DMSO-d6): δ 2.30 (s, 3H, CH_3), 6.87–8.08 (m, 12H, 9H, Ar–H and 3H $_{thienyl}$), 8.38 (s, 1H, HC=N), 10.87 (s, 1H, $NH_{hydrazone}$) and 13.43 (s, 1H, $NH_{hydrazone}$).ppm ^{13}C NMR: δ 21.14 (*C*H_3), 112.93, 115.97, 120.95, 127.96, 130.23, 130.96, 136.43, 139.32) phenyl carbons), 132.58, 132.75, 133.39, 135.35 (thienoyl carbons), 140.94 (H*C*=*N*), 144.34 (H*C*=*N*) and 180.94 (thienoyl *C*O). MS: *m/z* 362 (M^+). Found: C 66.32; H 5.10; N 15.51 $C_{20}H_{18}N_4OS$ (362.46) requires C 66.28; H 5.01; N, 15.46.

2-](4-Bromophenyl)hydrazono[-3-(phenylhydrazono)1-(thiophen-2-yl)propan-1-one (**7c**): Obtained from ethanol/dioxan as orange crystals, m.p. 255°C. Yield 86%; IR (KBr): ν = 1610 (CO), 3258, 3475 (2NH) cm^{-1}. ^1H NMR; (DMSO-d_6) 6.97–7.76 (m, 12H, 9H$_{aromatic}$ and 3$H_{thienyl}$), 8.36 (s, 1H, HC=N), 10.97 (s, 1H, $NH_{hydrazone}$) and 13.36 (s, 1H, $NH_{hydrazone}$). MS: *m/z* 428 (M^++1). Found: C, 53.26; H, 3.53; N, 13.05. $C_{19}H_{15}BrN_4OS$ (427.32) requires C, 53.40; H, 3.54; N, 13.11.

2, 3-Bis(phenylhydrazono)1-(p-tolyl)propan-1-one (**7f**): Obtained from ethanol/dioxan as canary yellow crystals. m.p. 242°C. Yield 84.33%. IR (KBr): ν = 1628 (CO) and 3260, 3446 (NH) cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.43 (s, 3H, CH_3), 6.91–7.83 (m, 14H, Ar–H), 8.37 (s, 1H, HC=N), 10.94 (s, 1H, $NH_{hydrazone}$) and 13.35 (s, 1H, $NH_{hydrazone}$) ppm. MS: *m/z* 357 (M^++1). Found: C 74.31; H 5.69; N 15.84. $C_{22}H_{20}N_4O$ (356.42) requires C 74.14; H 5.66; N 15.72.

3-(Phenylhydrazono)1-p-tolyl-2-(p-tolylhydrazono)propan-1-one (**7g**): Obtained from ethanol/dioxan as yellow crystals. m.p. 241°C.

Yield 78.75%. IR (KBr): ν = 1628 (CO) and 3259, 3447 (NH) cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.33 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 6.95–7.0 (m, 13H, Ar–H), 8.42 (s, 1H, HC=N), 10.88 (s, 1H, $NH_{hydrazone}$) and 13.38 (s, 1H, $NH_{hydrazone}$) ppm. MS: *m/z* 370 (M^+). Found: C 74.63; H 5.97; N 15.40. $C_{23}H_{22}N_4O$ (370.45) requires C 74.57; H 5.99; N 15.12.

Received 21 April 2007; accepted 13 July 2007
Paper 07/4616 doi: 10.3184/030823407X234617

References

1 F. Al-Omran, M.M. Abdel-Khalik, A.A. El-Khair and M.H. Elnagdi, *Synthesis,* 1997, 91.
2 K.M. Al-Zaydi, E.A. Hafez and M.H. Elnagdi, *J. Chem. Res. (S)*, 2000, 154, *(M)* 2000, 510.
3 R.M. Abdel-Motaleb, A.A. Makhloof, H.M. Ibrahim and M.H. Elnagdi, *J. Het. Chem*., 2006, **43**, 931.
4 M.A. Al-Shiekh, A.M. Salaheldin, E.A. Hafez, M.H. Elnagdi, *J. Het. Chem*., 2004, **41**, 647.
5 N.A. Al-Awadi, M.H. Elnagdi, Y.A. Ibrahim, K. Kaul and A. Kumar, *Tetrahedron,* **2001**, **57**, 1609.
6 I.M. Kenawi and M.H. Elnagdi, *Spectrochim. Acta (A)*, 2006, 805.
7 CCDC 617778, 617779 and 629546 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.ac.uk/data_request/cif..
8 A. Altomare, G. Cascarano, C. Giacorazzo, A. Guaghardi, M.C. Burla, G. Polidori and M. Camalli, *J. Appl. Gryst*., 1994, ***27***, 435.
9 C.K. Jackson, ORTEP-11, Oak Ridge National Laboratory, Tennessee, USA, 1976.
10 S.M. Agamy, *J. Chem. Res. (S)*, 2001, 349, *(M)* 2001, 901