Synthesis of new pyrazolone dyes

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New azo- and bisazo-5-pyrazolone dyes have been synthesised by azo coupling of various arylamines and aryl diamines with 5-pyrazolones: 1-methyl-3-phenyl-1*H*-pyrazol-5(4*H*)-one, 1-(4-chlorophenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one and 3-isopropyl-1-(4-methoxyphenyl)-1*H*-pyrazol-5(4*H*)-one, respectively. All new synthesised dyes have been characterised by FTIR, ^{1}H, ^{13}C NMR and UV-Vis spectral studies with GC/MS and LC/MS analyses. FTIR and ^{1}H NMR studies confirmed the existence of azo- and hydrazo-tautomeric forms of the dyes in the solid and liquid states, respectively.

Keywords: pyrazolone dyes, 5-pyrazolone derivatives, azo coupling

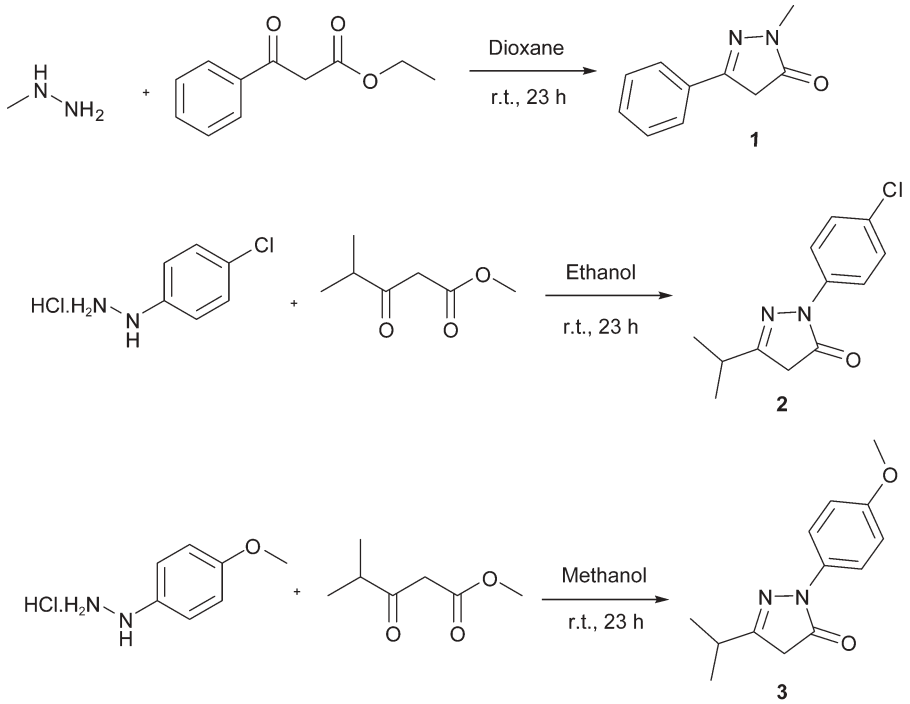
Disperse dyes are a popular class of dyes that are used with polyester fabrics because of their brilliance, wide range of hues and excellent fastness, in addition to environmental and economic reasons. Azo dyes derived from coupling diazonium salts with sulfur and/or nitrogen heterocyclic compounds are especially used in this context.[1–3] Many patents and papers describe the synthesis and dyeing properties of phenylazopyrazolone disperse dyes.[4–6]

In our previous work, we reported the synthesis of some pyrazolone derivatives.[7,8] The pyrazolone ring is an important pharmacophore which exhibits a wide range of pharmacological properties, such as anticancer, analgesic, anti-inflammatory, antipyretic, antioxidant, antiproliferative and antimicrobial activities.[9–11] Edaravone, (3-methyl-1-phenyl-1*H*-pyrazol-5-(4*H*)-one) has been found to be a promising drug for ischaemia and for the treatment of fatal neurodegenerative and cardiovascular diseases.[12,13] Many azo pyrazolone dyes have been used as chromogenic reagents for colourimetric determinations and as indicators for complexometric titration.[14] Some aryl azo pyrazolone dyes also have powerful antimicrobial activities.[15] Pyrazolone azomethine dyes are also important for the production of magenta dye images in various colour photographic processes.[16] Consequently, we decided to extend our study to the colouring and spectroscopic features of new pyrazolone derivatives with potential biological activity. First, we chose edaravone analogues as the starting materials since these are strong free radical scavengers for the treatment of cardiovascular diseases.[12,13] We now report on the successful synthesis of a series of dyes containing pyrazolone moiety and their spectroscopic data.

Results and discussion

1-Methyl-3-phenyl-1*H*-pyrazol-5(4*H*)-one (**1**)[14] and 1-(4-chlorophenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one (**2**),[17] which had been tested as inhibitors of *Mycobacterium tuberculosis* (MTB), were prepared according to the known procedures. 3-Isopropyl-1-(4-methoxyphenyl)-1*H*-pyrazol-5(4*H*)-one (**3**) was prepared by the reaction of methyl isobutyrylacetate with 4-methoxyphenylhydrazine in methanol (Scheme 1).

The coupling of **1**, **2** and **3** with the diazonium salt of 2-amino-4-chlorophenol produced compounds **4a–c**. Treatment of compounds **1–3** with the diazonium salt of 3-aminobenzensulfonic acid gave compounds **5a–c** (Scheme 2). The reactions were carried out in the presence of KOH due to the active



Scheme 1 Synthesis of pyrazol-5-ones **1**, **2** and **3**.

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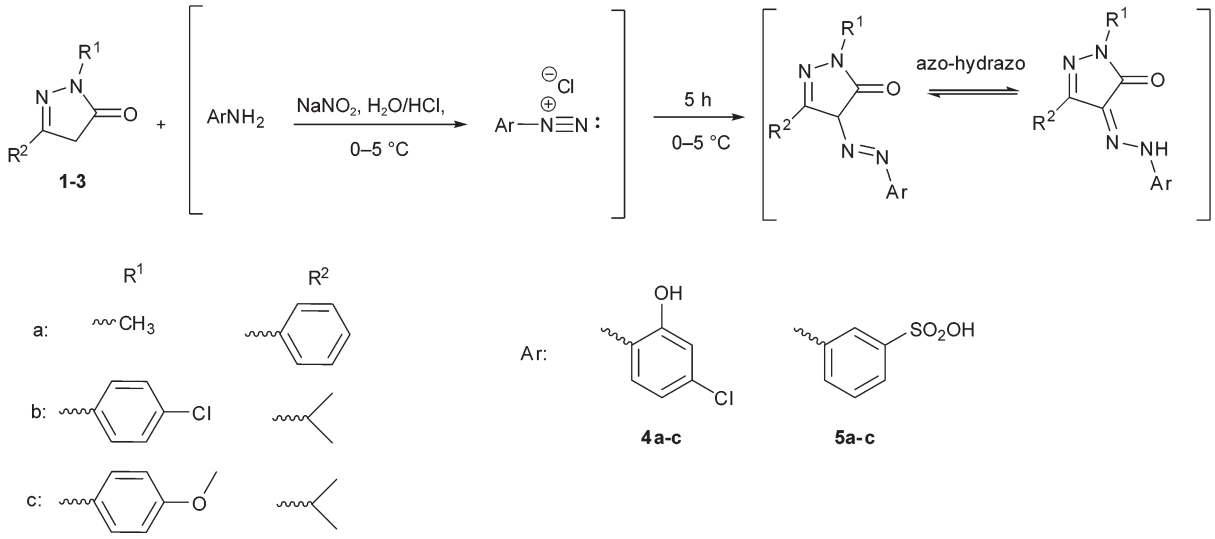


Scheme 2 Preparation of new azo pyrazol-5-ones.

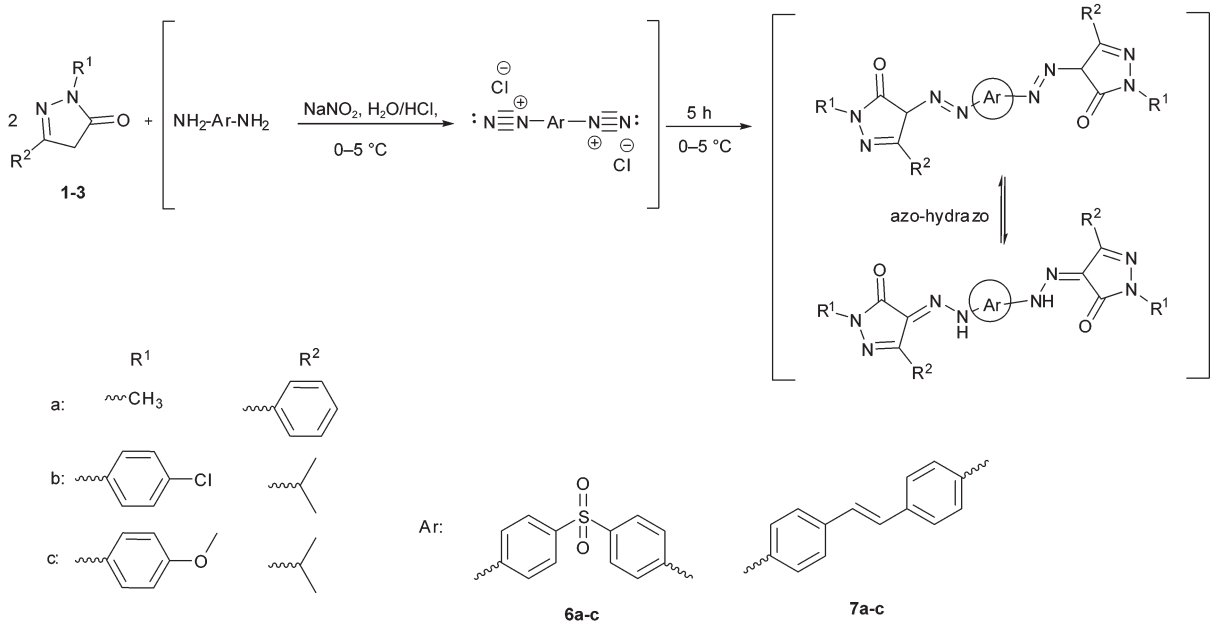
methylene protons of 5-pyrazolones. The products were purified either by chromatography or by rinsing the crystalline material with an appropriate solvent.

The structures of the prepared compounds were confirmed by spectroscopic techniques including UV, FTIR, NMR and mass spectroscopy. 5-Pyrazolones appear in solution in three different tautomeric forms (NH-form, CH-form and OH-form) which were easily identified in NMR spectra. The resulting azo dyes can exist in two possible tautomeric forms, namely the azo-hydrazo and the azo keto-enol forms. The FTIR spectra of compounds **4a–c** and **5a–c** are characterised by the presence of absorption bands for the N=N groups within the range 1550–1593 cm^{-1} and for the C=O groups of the pyrazolone moiety within the range 1630–1683 cm^{-1}. The IR spectra of these groups of dyes did not show NH absorption bands, although the NH group in the ^{1}H NMR spectra exhibited broad singlets between 13.80 and 14.04 ppm. This phenomenon is suggestive of the fact that these dyes do not exist as hydrazo-forms in the solid state. The presence of the C=O groups in the FTIR spectra and the absence of peaks for the OH protons in the ^{1}H NMR spectra indicate that the compounds do not prefer the azo-enol tautomeric form either in the solid or in the liquid state. The ^{1}H NMR spectra of these compounds showed the disappearance of the characteristic methylene single peaks of the 5-pyrazolone ring in **1**, **2** and **3** at 3.90, 3.41 and 3.33 ppm, respectively. In addition, the ^{13}C NMR spectra were in agreement with the proposed structures. The mass spectra of all the new compounds showed the expected molecular fragmentation.

New bisazo dyes **6a–c** and **7a–c** were prepared by the diazotisation with 4,4′-diaminodiphenylsulfone and 4,4′-diaminostilbene (Scheme 3), respectively.

The structures of **6a–c** and **7a–c** have been confirmed by FTIR, ^{1}H NMR, ^{13}C NMR and ESI MS data. In the FTIR spectra, compounds **6a**, **6c** and **7c** exist in the azo-form but their structures are in the hydrazo-form (NH at 13.74, 13.52 and 13.76 ppm, respectively) in solution as revealed from their respective ^{1}H NMR spectra. The ESI-MS spectra of the compounds showed the characteristic molecular ion peaks.

The absorption spectra of the examined dyes were recorded within the wavelength range 245–512 nm in MeOH (without 6c) at room temperature (Table 1).



Scheme 3 Preparation of new bisazo pyrazol-5-ones.

Table 1 Spectral data of dyes

Dye	Solvent	c/mol L^{-1}	λ_{max}/nm	Σ_{max}/mol^{-1} L cm^{-1}
2	CH_3OH	$4.64 \cdot 10^{-5}$	248	26939
3	CH_3OH	$1.43 \cdot 10^{-4}$	245	3706
4a	CH_3OH	$5.08 \cdot 10^{-5}$	431	984
4b	CH_3OH	$5.96 \cdot 10^{-4}$	431	413
4c	CH_3OH	$1.03 \cdot 10^{-4}$	417	2136
5a	CH_3OH	$1.86 \cdot 10^{-4}$	396	4194
5b	CH_3OH	$7.89 \cdot 10^{-4}$	393	963
5c	CH_3OH	$3.20 \cdot 10^{-4}$	423	3125
6a	CH_3OH	$2.15 \cdot 10^{-4}$	399	1860
6c	$CHCl_3$	$9.08 \cdot 10^{-5}$	407	19273
7a	CH_3OH	$1.72 \cdot 10^{-4}$	421	872
7b	CH_3OH	$5.67 \cdot 10^{-5}$	511.50	28536
7c	CH_3OH	$1.23.10^{-4}$	417	8443

Conclusion

In summary, new azo dyes containing the pyrazolone ring were synthesised from the pyrazolone **1-3**. All compounds were characterised and investigated for their dyeing characteristics and tautomeric equilibrium. The results show that dyes may exist as mixtures of two tautomeric forms in the solid or liquid state. It has been known that some azo compounds are used as acid-base indicators due to the different colours of their acid and salt forms. The new dyes may be used for this purpose as well. In addition, all the new synthesised molecules will be examined for their possible biological activity.

Experimental

Reactions were monitored using TLC. IR spectra were obtained with a Perkin Elmer, FT-IR and Shimadzu IR Affinity-1 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Melting points were determined with Gallenkamp digital thermometer equipment. All melting points are uncorrected. NMR spectra were determined with a Bruker Ac-400 MHz NMR, Varian-INOVA-500 MHz NMR and Varian Mercury-400 MHz NMR spectrometer. TMS (tetramethylsilane) was used as the internal standard and $CDCl_3$, CD_3OD, C_5D_5N and DMSO-d_6 were used as the solvents. Mass spectra were measured either with Agilent LC-MSD Trap SL and LC-Triple Quadrupole MS/MS system (Jet Stream electro spray ıonisation source), LC/MS, Thermo-Finnigan (Ion Trap) or Varian Saturn 2100T/GC3900 GC-MS. The UV-Vis spectra were measured using Agilent 8453 and Shimadzu UV-1800 spectrophotometers at a wavelength of maximum absorption (λ_{max}, nm). Elemental analyses were carried out on a Thermo Flash EA 1112 Series apparatus.

Synthesis of pyrazol-5-ones; general procedure

The hydrazine (methylhydrazine, 4-chlorophenylhydrazine or 4-methoxyphenylhydrazine) (3 mmol) was dissolved in suitable solvent (dioxane, ethanol, methanol respectively) (10 mL) and ethyl benzoylacetate or methyl isobutyrylacetate (3 mmol) were added. The mixture was stirred overnight at room temperature.

Synthesis of azo and bisazo pyrazol-5-ones;general procedure

KOH (40 mmol) was added to the stirred cold solution of compounds (**1**, **2** or **3**) (5mmol, for bisazo 10 mmol) in 10 mL suitable solvent (dioxane, methanol or ethanol respectively). In a separate flask, a diazonium chloride solution was prepared by adding concentrated HCl (1 mmol) to the arylamine (5 mmol) at 0–5 °C and then treating the resulting salt with a cold solution of $NaNO_2$ (7.5 mmol) in H_2O (5 mL) while stirring at 0–5 °C. The diazonium chloride solution (5 mmol) was added continuously to the reaction mixture and stirred in an ice bath for 5–7 hours. The solvents were evaporated under reduced pressure.

*1-Methyl-3-phenyl-1*H*-pyrazol-5(4*H*)-one* (**1**): The title compound was synthesised from methylhydrazine (0.138 g, 3 mmol) and ethyl benzoylacetate (0.516 mL, 3 mmol) following the general method. White solid, yield 0.454 g (87%), m.p. 209–210 °C dec (lit.[18] 210–211 °C dec).

*1-(4-Chlorophenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one* (**2**): The title compound was synthesised from 4-chlorophenylhydrazine hydrochloride (0.537 g, 3 mmol) and methyl isobutyrylacetate (0.427 mL, 3 mmol) following the general method, and was purified by column chromatography (SiO_2; ethyl acetate/*n*-hexane 2:1). Cream solid, yield 0.482 g (68%), m.p. 168–169 °C dec. R_f 0.45 (SiO_2; ethyl acetate/*n*-hexane 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.24 (d, J = 6.91 Hz, 6H, CH_3), 2.72–2.83 (sep, J = 6.91 Hz, 1H, CH), 3.41 (s, 2H, CH_2), 7.32–7.35 (d, J = 8.94 Hz, 2H, ArH), 7.85 (d, J = 8.94 Hz, 2H, ArH) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.29 (CH_3), 30.99 (CH), 40.08 (CH_2), 120.06 (ArC), 129.03 (ArC), 130.14 (C–Cl), 137.01 (ArC), 164.81 (C=N), 170.72 (C=O) ppm; IR (ATR): ν = 1600 (C=O), 1531 (C=N) cm^{-1}; GC-MS *m/z*: 236 (M^+), 193, 125, 111; UV (CH_3OH, $c = 4.64 \times 10^{-5}$ mol L^{-1}): λ_{max} (Σ) 203.50 (27758), 248 (26939) nm (mol^{-1} L cm^{-1}).[19]

*3-Isopropyl-1-(4-methoxyphenyl)-1*H*-pyrazol-5(4*H*)-one* (**3**): The title compound was synthesised from 4-methoxyphenylhydrazine hydrochloride (0.524 g, 3 mmol) and methyl isobutyrylacetate (0.427 mL, 3 mmol) following the general method and was purified by column chromatography (SiO_2; ethyl acetate/*n*-hexane 2:1). Brown solid, yield 0.508 g (73%), m.p. 145–147 °C. R_f 0.60 (SiO_2; ethyl acetate/*n*-hexane 2:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.17 (d, J = 6.93 Hz, 6H, CH_3), 2.67–2.75 (sep, J = 6.93 Hz, 1H, CH), 3.33 (s, 2H, CH_2), 3.74 (s, 3H, OCH_3), 6.83 (d, J = 9.14 Hz, 2H, ArH), 7.66 (d, J = 9.14 Hz, 2H, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.18 (CH_3), 30.75 (CH), 39.67 (CH_2), 55.48 (OCH_3), 113.96 (ArC), 120.83 (ArC), 124.81 (C-Cl), 156.82 (ArC), 164.23 (C=N), 170.32 (C=O) ppm; IR (ATR): ν = 1707 (C=O), 1557 (C=N) cm^{-1}; GC-MS *m/z*: 232 (M^+), 217, 203, 189, 107, 77; UV (CH_3OH, $c = 1.43 \times 10^{-4}$ mol L^{-1}): λ_{max} (Σ) 200 (5594), 245 (3706) nm (L mol^{-1} cm^{-1}). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.01; H, 7.03; N, 11.94%.

*4-((4-Chloro-2-hydroxyphenyl)diazenyl)-1-methyl-3-phenyl-1*H*-pyrazol-5(4*H*)-one* (**4a**): The title compound was synthesised from **1** (0.870 g, 5 mmol) and 2-amino-5-chlorophenol (0.715 g, 5 mmol) following the general method and was purified by column chromatography (SiO_2; ethyl acetate/*n*-hexane 2:1). Orange solid, yield 0.442 g (27%), m.p. 210 °C dec. R_f 0.30 (SiO_2; ethyl acetate/*n*-hexane 3:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.44 (s, 1H, CH), 3.55 (s, 3H, CH_3), 7.39–7.41 (m, 2H, ArH), 7.44–7.50 (m, 4H, ArH), 7.94–7.96 (m, 2H, ArH) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 28.68 (CH_3), 44.82 (C–N=N), 112.93, 114.91, 126.08, 126.49, 127.06, 127.66, 128.14, 128.71, 128.97, 143.99, 157.51 (C=N), 169.69 (C=O) ppm; IR (ATR): ν = 3261 (OH), 1640 (C=O), 1538 (N=N) cm^{-1}; GC-MS *m/z*: 329 (M^+), 313, 294, 155, 127, 98; UV (CH_3OH, $c = 5.08 \times 10^{-5}$ mol L^{-1}): λ_{max} (Σ) 204 (34448), 253 (25984), 431 (984) nm (L mol^{-1} cm^{-1}). Anal. Calcd for $C_{16}H_{13}ClN_4O_2$: C, 58.45; H, 3.99; N, 17.04. Found: C, 58.27; H, 4.08; N, 16.97%.

*4-((4-Chloro-2-hydroxyphenyl)diazenyl)-1-(4-chlorophenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one* (**4b**): The title compound was synthesised from **2** (1.183 g, 5 mmol) and 2-amino-5-chlorophenol (0.715 g, 5 mmol) following the general method and was purified by column chromatography (SiO_2; chloroform). Orange solid, yield 1.153 g (59%), M.p. 279 °C dec. R_f 0.37 (SiO_2; chloroform); ^{1}H NMR (400 MHz, d_6-DMSO): δ 1.42 (d, J = 6.73 Hz, 6H, CH_3), 3.19–3.29 (sep, J = 6.73 Hz, 1H, CH), 7.11–7.18 (m, 2H, ArH), 7.57–7.59 (m, 3H, ArH), 8.02 (d, J = 8.02 Hz, 2H, ArH), 11.34 (br s, 1H, OH), 13.58 (br s, 1H, NH) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 20.53 (CH_3), 28.59 (CH), 119.34, 125.55 (C=N–NH), 129.08, 141.65, 141.85, 143.67, 143.69, 148.19, 149.44, 150.86, 154.57, 164.26 (C=N), 169.67 (C=O) ppm; IR (ATR): ν = 3210 (OH), 1639 (C=O), 1537 (N=N) cm^{-1}; GC-MS (*m/z*): 390 (M^+–1), 281, 249, 233, 111; UV (CH_3OH, $c = 5.96 \times 10^{-4}$ mol L^{-1}): λ_{max} (Σ) 200 (1085), 251 (582), 431 (413) nm (L mol^{-1} cm^{-1}). Anal. Calcd for $C_{18}H_{16}Cl_2N_4O_2$: C, 55.26; H, 4.12; N, 14.32. Found: C, 54.99; H, 4.25; N, 17.93%.

*4-((4-Chloro-2-hydroxyphenyl)diazenyl)-3-isopropyl-1-(4-methoxyphenyl)-1*H*-pyrazol-5(4*H*)-one* (**4c**): The title compound was synthesised from **3** (1.160 g, 5 mmol) and 2-amino-5-chlorophenol (0.715 g, 5 mmol) following the general method and was purified by column chromatography (SiO_2; ethyl acetate/*n*-hexane 1:1). Red solid, yield 1.069 g (58%), m.p. 275 °C dec. R_f 0.56 (SiO_2; ethyl acetate/*n*-hexane 2:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.25 (d, J = 7.80 Hz, 6H, CH_3), 3.04–3.09 (sep, J = 7.80 Hz, 1H, CH), 3.74 (s, 3H, OCH_3), 5.27 (br s, 1H, OH), 6.83–6.91 (m, 4H, ArH), 7.67–7.75 (m, 3H, ArH), 11.71 (br s, 1H, NH) ppm; IR (ATR): ν = 3263 (OH), 1713 (C=O), 1574 (N=N) cm^{-1}; GC-MS (*m/z*): 386 (M^+), 373, 343, 329, 279, 123, 107, 43; UV (CH_3OH, $c = 1.03 \times 10^{-4}$ mol L^{-1}): λ_{max} (Σ) 204 (17961), 247 (12864), 334 (1942), 417 (2136) nm (L mol^{-1} cm^{-1}). Anal. Calcd for $C_{19}H_{19}ClN_4O_3$: C, 58.99; H, 4.95; N, 14.48. Found: C, 59.06; H, 4.83; N, 14.55%.

*3-((1-Methyl-5-oxo-3-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)diazenyl) benzenesulfonic acid* (**5a**): The title compound was synthesised from **1** (0.870 g, 5 mmol) and 3-aminobenzen sulfonic acid (0.866 g, 5 mmol) following the general method. The reaction mixture was poured into ice-water and the solid precipitate was filtered and washed with cold ether to obtain the pure product. Orange solid, yield 0.753 g (42%), m.p. 260 °C dec. R_f 0.39 (SiO_2; ethyl acetate/*n*-hexane 2:1); ^{1}H NMR (500 MHz, CD_3OD): δ 2.68 (s, 1H, SO_2OH), 3.41 (s, 3H, CH_3), 3.51 *(*s, 1H, CH), 7.33–7.51 (m, 5H, ArH), 7.58 (d, *J* = 7.55 Hz, 1H, ArH), 7.91 (s, 1H, ArH), 8.01 (d, *J* = 8.45 Hz, 2H, ArH) ppm; APT (125 MHz, C_5D_5N): δ 31.76 (CH_3), 33.29 (CH), 115.30 (ArCH), 117.51 (ArCH), 124.50 (ArCH), 127.98 (ArCH), 128.38 (ArC–S), 128.92 (ArCH), 129.45 (ArCH), 129.68 (ArCH), 131.80 (ArC–N), 142.34 (ArC), 154.58 (C=N), 159.27 (C=O) ppm; IR (ATR): ν = 3429 (OH), 1652 (C=O), 1599 (N=N) cm^{-1}; GC-MS (*m*/*z*): 360 (M^+ + 2), 345, 201, 174, 103, 80, 77; UV (CH_3OH, $c = 1.86 \times 10^{-4}$ mol L^{-1}): λ_{max} (Σ) 204 (7957), 241 (3871), 396 (4194) nm (L mol^{-1} cm^{-1}). Anal. Calcd for $C_{16}H_{14}N_4O_4S$: C, 53.62; H, 3.94; N, 15.63; S, 8.95. Found: C, 53.69; H, 4.07; N, 15.52; S 8.88%.

*3-((1-(4-Chlorophenyl)-3-isopropyl-5-oxo-4,5-dihydro-1*H*-pyrazol-4-yl)diazenyl)benzenesulfonic acid* (**5b**): The title compound was synthesised from **2** (1.183 g, 5 mmol) and 3-aminobenzene sulfonic acid (0.866 g, 5 mmol) following the general method. Crude product was recrystallised in water/methanol (1:1). Dark yellow solid, yield 1.410 g (67%), m.p.>300 °C. R_f 0.76 (SiO_2; methanol); ^{1}H NMR (400 MHz, d_6-DMSO): δ 0.90 (d, *J* = 6.89 Hz, 6H, CH_3), 2.65–2.75 *(*sep, *J* = 6.89 Hz, 1H, CH), 6.93–7.08 (m, 6H, ArH), 7.37 (s, 1H, OH), 7.50 (d, *J* = 8.78 Hz, 2H, ArH), 13.30 (br s, 1H, NH) ppm; ^{13}C NMR (100 MHz, d_6-DMSO): δ 20.80 (CH_3), 27.15 (CH), 113.17, 117.0, 119.50, 123.24, 126.75, 128.85, 129.24, 129.35, 137.07 (C=N), 141.0, 150.14, 156.26 (C=N), 157.07 (C=O) ppm; IR (ATR): ν = 3444 (OH), 1651 (C=O), 1539 (N=N) cm^{-1}; GC-MS (*m*/*z*): 421 (M^+), 407, 376, 306, 205, 111, 43; UV (CH_3OH, $c = 7.89 \times 10^{-4}$ mol L^{-1}): λ_{max} (Σ) 202 (1719), 255 (1073), 393 (963) nm (L mol^{-1} cm^{-1}). Anal. Calcd for $C_{18}H_{17}ClN_4O_4S$: C, 51.37; H, 4.07; N, 13.31; S, 7.62. Found: C, 51.31; H, 4.18; N, 13.17; S, 7.43%.

*3-((3-Isopropyl-1-(4-methoxyphenyl)-5-oxo-4,5-dihydro-1*H*-pyrazol-4-yl)diazenyl)benzenesulfonic acid* (**5c**): The title compound was synthesised from **3** (1.160 g, 5 mmol) and 3-aminobenzene sulfonic acid (0.866 g, 5 mmol) following the general method and was purified by column chromatography (SiO_2; ethyl acetate/*n*-hexane 1:1). Orange solid, yield 1.270 g (61%), m.p. 264–265 °C. R_f 0.60 (SiO_2; ethyl acetate/*n*-hexane 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.35 (d, *J* = 6.91 Hz, 6H, CH_3), 3.11–3.19 *(*sep, *J* = 6.91 Hz, 1H, CH), 3.77 (s, 3H, OCH_3), 6.97 (d, *J* = 9.14 Hz, 1H, ArH), 7.03 (d, *J* = 9.14 Hz, 2H, ArH), 7.09 (d, *J* = 2.54 Hz, 1H, ArH), 7.11 (d, *J* = 2.54 Hz, 1H, ArH), 7.52 (d, *J* = 2.54 Hz, 1H, ArH), 7.77 (d, *J* = 9.09 Hz, 2H, ArH), 11.11 (br s, 1H, OH), 13.49 (br s, 1H, NH) ppm; APT (125 MHz, d_6-DMSO): δ 21.44 (CH_3), 21.50 (CH), 56.04 (OCH_3), 114.29 (ArCH), 114.89 (ArCH), 117.92 (ArCH), 120,69 (ArCH), 122.20 (ArCH), 124.66 (C=N–NH), 126.06 (ArCH), 128.60 (ArC), 130.91 (ArC–NH), 131.73 (ArC), 155.70 (C=N), 157.31 (C=O), 157.50 (ArC–OCH_3) ppm; IR (ATR): ν = 3352 (OH), 1636 (C=O), 1599 (N=N) cm^{-1}; GC-MS (*m*/*z*): 417 (M^+ + 1), 232, 217, 189, 81, 43; UV (CH_3OH, $c = 3.20 \times 10^{-4}$ mol L^{-1}): λ_{max} (Σ) 204 (5859), 249 (3750), 423 (3125) nm (L mol^{-1} cm^{-1}). Anal. Calcd for $C_{19}H_{20}N_4O_5S$: C, 54.80; H, 4.84; N, 13.45; S, 7.70. Found: C, 54.89; H, 4.95; N, 13.11; S, 7.59%.

*4,4′-(4,4′-Sulfonylbis(4,1-phenylene))bis(1-methyl-3-phenyl-1*H*-pyrazol-5(4*H*)-one)* (**6a**): The title compound was synthesised from **1** (1.740 g, 10 mmol) and 4,4′-sulfonyldianiline (1,241 g, 5 mmol) following the general method and was purified by column chromatography (SiO_2; ethyl acetate/*n*-hexane 2:1). Red solid, yield 1.392 g (45%), m.p.>300 °C. R_f 0.70 (SiO_2; ethyl acetate/*n*-hexane 2:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.45 (s, 6H, CH_3), 7.39–7.46 (m, 10H, ArH), 7.87–7.94 (m, 8H, ArH), 13.74 (br s, 2H, NH) ppm; APT (125 MHz, $CDCl_3$): δ 44.83 (N-CH_3), 75.75 (C–N=N), 112.91 (ArCH), 114.92 (ArCH), 126.07 (ArCH), 126.51 (ArCH), 128.72 (ArC), 140.73 (ArC), 144.11 (ArC), 157.51 (C=N), 157.59 (ArC=N), 169.76 (C=O) ppm; IR (ATR): ν = 1733 (C=O), 1556 (N=N) cm^{-1}; ESI$^{(-)}$-MS (*m*/*z*): 731 [M^- + (TFA – H]; UV (CH_3OH, $c = 2.15 \times 10^{-4}$ mol L^{-1}): λ_{max} (Σ) 202 (8418), 257 (2790), 399 (1860) nm (L mol^{-1}cm^{-1}). Anal. Calcd for $C_{32}H_{26}N_8O_4S$: C, 62.12; H, 4.24; N, 18.11; S, 5.18. Found: C, 62.01; H, 4.29; N, 17.99; S, 5.10.

(TFA: Trifluoroacetic acid).

*4,4′-(4,4′-Sulfonylbis(4,1-phenylene))bis(1-(4-chlorophenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one)* (**6b**): The title compound was synthesised from **2** (2.366 g, 10 mmol) and 4,4′-sulfonyldianiline (1,241 g, 5 mmol) following the general method. The crude product was recrystallised in acetone/DMSO (1:2) because of the solubility problem. Red solid, yield 2.305 g (62%), m.p.>300 °C. R_f 0.74 (SiO_2; DMSO); IR (ATR): ν = 1662 (C=O), 1546 (N=N) cm^{-1}; GC-MS (*m*/*z*): 403 ($C_{18}H_{16}ClN_4O^{\cdot}$, 22.72), 339 ($C_{18}H_{16}ClN_4O_3^{\cdot}$ - SO_2, 31.81), 296 ($C_{15}H_{19}ClN_4O^{\cdot}$, 20), 221 ($C_9H_5ClN_4O^{\cdot}$, 50.90), 207 ($C_{10}H_8ClN_2O^{\cdot}$, 100), 193 ($C_9H_5ClN_2O^{\cdot}$, 8.18), 111 ($C_6H_4Cl^{\cdot}$, 15.45), 43 (isopropyl$^{\cdot}$, 16.36); ESI$^{(-)}$-MS (*m*/*z*): 744 ($M^-$); UV (DMSO): 287.38 (not 100% soluble) nm. Anal. Calcd for $C_{36}H_{32}Cl_2N_8O_4S$: C, 58.14; H, 4.34; N, 15.07; S, 4.31. Found: C, 57.98; H, 4.48; N, 15.11; S, 4.39%.

*4,4′-(4,4′-Sulfonylbis(4,1-phenylene))bis(3-isopropyl-1-(4-methoxyphenyl)-1*H*-pyrazol-5(4*H*)-one)* (**6c**): The title compound was synthesised from **3** (2.320 g, 10 mmol) and 4,4′-sulfonyldianiline (1,241 g, 5 mmol) following the general method. The reaction mixture was poured into ice-water, the solid phase was filtered, then washed with cold ethanol and ether. Red solid, yield 1.469 g (40%), m.p.>300 °C. R_f 0.81 (SiO_2; ethyl acetate/*n*-hexane 2:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.33 (d, *J* = 6.71 Hz, 12H, CH_3), 3.04–3.19 *(*sep, *J* = 6.71 Hz, 2H, CH), 3.76 (s, 6H, OCH_3), 6.88 (d, *J* = 8.72 Hz, 4H, ArH), 7.40 (d, *J* = 8.72 Hz, 4H, ArH), 7.74 (d, *J* = 8.72 Hz, 4H, ArH), 7.90 (d, *J* = 8.72 Hz, 4H, ArH), 13.52 (br s, 2H, NH) ppm; APT (125 MHz, $CDCl_3$): δ 19.67 (CH_3), 26.62 (CH), 54.49 (OCH_3), 113.12 (ArCH), 114.71 (ArCH), 119.51 (ArCH), 128.51 (C=N–NH), 129.16 (ArCH), 130.03 (ArC), 136.36 (ArC), 144.23 (ArC), 154.78 (ArC), 156.05 (C=N), 156.32 (C=O) ppm; IR (ATR): ν = 1658 (C=O), 1560 (N=N) cm^{-1}; ESI$^{(-)}$-MS (*m*/*z*): 735 (M^- + 1); UV (chloroform, $c = 9.08 \times 10^{-5}$ mol L^{-1}): λ_{max} = 255 (17070), 407 (19273) nm (mol^{-1} L cm^{-1}). Anal. Calcd for $C_{38}H_{38}N_8O_6S$: C, 62.11; H, 5.21; N, 15.25; S, 4.36. Found: C, 61.99; H, 5.32; N, 15.11; S, 4.23%.

*4,4′-(4,4′-(Ethene-1,2-diyl)bis(4,1-phenylene))bis(1-methyl-3-phenyl-1*H*-pyrazol-5(4*H*)-one)* (**7a**): The title compound was synthesised from **1** (1.740 g, 10 mmol) and 4,4′-(ethane-1,2-diyl)dianiline dihydrochloride (1.416 g, 5 mmol) following the general method. The reaction mixture was poured into ice-water, the solid was filtered and then washed with cold ether twice. Red solid, yield 1.451 g (50%), m.p. 260–261 °C. R_f 0.61 (SiO_2; ethyl acetate/*n*-hexane 1:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.50 (s, 6H, CH_3), 7.23 (d, *J* = 8.78 Hz, 4H, ArH), 7.30 (d, *J* = 8.78 Hz, 4H, ArH), 7.59 (d, *J* = 8.78 Hz, 2H, =CH), 8.06–8.14 (m, 10H, ArH), 13.80 (br s, 2H, NH) ppm; APT (125 MHz, $CDCl_3$): δ 28.68 (CH_3), 109.01 (ArCH), 114.48 (ArC), 114.50 (ArCH), 126.04 (ArC), 126.11 (ArCH), 127.46 (=CH), 127.54 (C=N–NH), 126.86 (ArCH), 128.71 (ArCH), 133.08 (ArC), 142.97 (C=N), 157.76 (C=O) ppm; IR (ATR): ν = 1651 (C=O), 1550 (N=N) cm^{-1}; ESI$^{(+)}$-MS (*m*/*z*): 563 [(M^+ - 2) - CH_3]; UV (CH_3OH, $c = 1.72 \times 10^{-4}$ mol L^{-1}): λ_{max} (Σ) 204 (9593), 252 (7326), 421 (872) nm (L mol^{-1}cm^{-1}). Anal. Calcd for $C_{34}H_{28}N_8O_2$: C, 70.33; H, 4.86; N, 19.30. Found: C, 70.18; H, 4.93; N, 19.12%.

*4,4′-(4,4′-(Ethene-1,2-diyl)bis(4,1-phenylene))bis(1-(4-chlorophenyl)-3-isopropyl-1*H*-pyrazol-5(4*H*)-one)* (**7b**): The title compound was synthesised from **2** (2.366 g, 10 mmol) and 4,4′-(ethane-1,2-diyl)dianiline dihydrochloride (1.416 g, 5 mmol) following the general method. The solid phase was filtered, the solid phase washed with cold ethanol and ether to obtain the pure product. Red solid, yield 2.363 g (67%), m.p. 228 °C dec. R_f 0.87 (SiO_2; chloroform/*n*-hexane 2:1); ^{1}H NMR (500 MHz, d_6-DMSO): δ 1.27 (d, *J* = 6.93 Hz, 12H, CH_3), 3.19–3.28 *(*sep, *J* = 6.93 Hz, 2H, CH), 7.31 (d, *J* = 8.83 Hz, 2H, =CH), 7.36 (d, *J* = 8.83 Hz, 4H, ArH), 7.52 (d, *J* = 8.47 Hz, 4H, ArH), 7.57 (d, *J* = 8.47 Hz, 4H, ArH), 8.14 (d, *J* = 8.47 Hz, 4H, ArH), 13.02 (br s, 2H, NH) ppm; ^{13}C NMR (125 MHz, d_6-DMSO): δ 20.77 (CH_3), 29.96 (CH), 118.25, 118.67, 120.18, 125.64, 126.72 (=C), 128.07 (C=N–NH), 128.66, 131.89, 146.62, 149.97, 157.06 (C=N), 160.42 (C=O); IR (ATR): ν = 1651 (C=O), 1539 (N=N) cm^{-1}; ESI$^{(+)}$-MS (*m*/*z*): 721 (M^+ + 15); UV (CH_3OH, $c = 5.67 \times 10^{-5}$ mol L^{-1}): λ_{max} (Σ) 235.50 (70546), 269.50 (17777), 323.50 (5943), 511.50 (28536) nm (mol^{-1} L cm^{-1}). Anal. Calcd for $C_{38}H_{34}Cl_2N_8O_2$: C, 64.68; H, 4.86; N, 15.88. Found: C, 64.44; H, 4.98; N, 15.67%.

*4,4′-(4,4′-(Ethene-1,2-diyl)bis(4,1-phenylene))bis(3-isopropyl-1-(4-methoxyphenyl)-1*H*-pyrazol-5(4*H*)-one)* (**7c**): The title compound was synthesised from **3** (2.320 g, 10 mmol) and 4,4′-(ethane-1,2-diyl)dianiline dihydrochloride (1.416 g, 5 mmol) following the general method and was purified by column chromatography (SiO_2; ethyl acetate/*n*-hexane 2:1). Red solid, yield 2.125 g (61%), m.p. 283–284 °C dec. R_f 0.84 (SiO_2; ethyl acetate/*n*-hexane 2:1); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.45 (d, *J* = 6.93 Hz, 12H, CH_3), 3.17–3.25 *(*sep,

J = 6.93 Hz, 2H, CH), 3.86 (s, 6H, OCH_3), 6.99 (d, J = 8.95 Hz, 2H, =CH), 7.36–7.60 (m, 10H, ArH), 7.77–7.96 (m, 6H, ArH), 13.76 (br s, 2H, NH) ppm; APT (125 MHz, C_5D_5N): δ 23.00 (CH_3), 29.74 (CH), 57.51 (OCH_3), 116.35 (ArCH), 116.49 (ArCH), 117.38 (ArCH), 119.72 (=CH), 122.42 (ArCH), 134.61 (ArC–N), 157.47 (C=N), 159.29 (ArC-OCH_3), 159.97 (ArC), 160.30 (C=O) ppm; IR (ATR): ν = 1655 (C=O), 1554 (N=N) cm^{-1}; ESI$^{(-)}$-MS (m/z): 695 (M^- - H); UV(CH_3OH, c = 1.23 × 10^{-4} mol L^{-1}): λ_{max} (Σ) 227 (32434), 417 (8443) nm (L $mol^{-1}cm^{-1}$). Anal. Calcd for $C_{40}H_{40}N_8O_4$: C, 68.95; H, 5.79; N, 16.08. Found: C, 68.78; H, 5.83; N, 15.89%.

We gratefully acknowledge financial support of this work by the Yildiz Technical University Scientific Research Projects' Coordination Department (Project No. 29-01-02-ODAP01) and TUBITAK, the Scientific and Technological Research Council of Turkey (Project No: 110T549).

Received 20 December 2012; accepted 11 February 2013
Paper 1201691 doi: 10.3184/174751913X13636169962208
Published online: 19 April 2013

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