Synthesis and tautomeric structure of the azo-coupling products of 2-methyl-7-phenylpyrimido[1,2-*b*][1,2,4]triazepine-4,9(3*H*,5*H*)-dione

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A simple synthetic strategy is described for synthesis of 3-arylazo-2-methyl-7-phenylpyrimido[1,2-*b*][1,2,4]triazepine-4,9-diones **4a–j**. The acid dissociation constants were determined for the series prepared and were correlated by a Hammett-type equation using enhanced substituent constants. The results of such correlation together with the spectral data, including ^{15}N isotopic labelling, indicated that the studied compounds exist predominantly in the hydrazone tautomeric form.

Keywords: fused pyrimidines, 1,2,4-triazepines; arylazo compounds, tautomerism, N-15 labelling

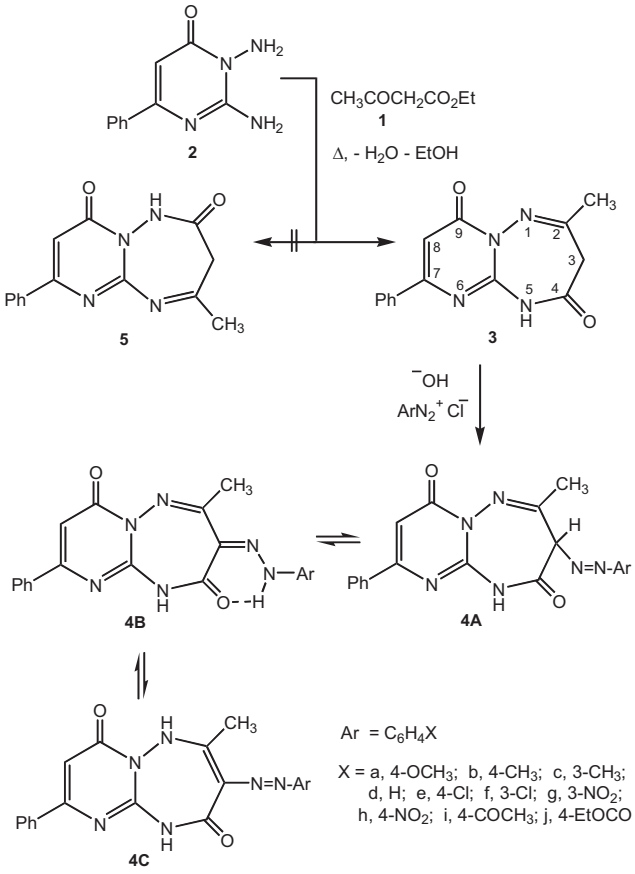
Our research group has recently been interested in the azo-hydrazone tautomerism of arylazo heterocycles in both ground and excited states as many of them are useful in the field of material sciences and theoretical chemistry.[1-7] In addition to these applications, azo compounds are used as photosensitive species in photographic or electrophotographic systems and are the dominant organic photoconductive materials in commercial copiers.[8]

To the best of our knowledge 2-methyl-7-phenyl-pyrimido[1,2-*b*][1,2,4]triazepine-4,9(3*H*,5*H*)-dione (**3**) has not been reported hitherto. In continuation of our previous studies, we report here on the coupling of the novel ring system **3** with diazonium salts in an attempt to synthesise the respective azo derivatives **4** (Scheme 1) and the elucidation of their tautomeric structures. (Scheme 1)

Results and discussion

The starting 2-methyl-7-phenylpyrimido[1,2-*b*][1,2,4]triazepine -4,9(3*H*,5*H*)-dione (**3**) was prepared by condensation of ethyl acetoacetate (**1**) with 2,3-diamino-6-phenylpyrimidin-4(3*H*)-one (**2**).[9] Although the reaction of **1** with **2** can lead theoretically to **3** and/or its isomer the 4-methyl-7-phenylpyrimido[1,2-*b*]triazepine-2,9(1*H*,3*H*)-dione **5**, the latter structure was ruled out on the basis of the fact that condensation reactions of ethyl acetoacetate with *C*,*N*-1,2-diaminoheterocycles thus far studied have been reported to be regioselective, leading to products that result from nucleophilic attack of the N–NH_2 and the C–NH_2 groups at the keto and ester carbonyl groups, respectively, of the β-keto ester to give the corresponding fused 4-oxo-1,2,4-triazepine derivatives.[10-13] This regioselectivity was substantiated by X-ray crystallographic analysis in some cases[13] and by spectral data.[10-13] The structure of the novel derivative **3** was confirmed by its spectra (MS, ^1H NMR and IR) together with its elemental analysis. The ^1H NMR spectra revealed five characteristic signals near δ 2.29, 4.52, 5.79, 7.51-8.06 and 13.00 assignable to CH_3, CH_2, CH, C_6H_5 and the ring NH protons, respectively. Its IR spectrum revealed bands at 3433 (NH), 1685, 1658 (CO) cm^{-1}. Its mass spectrum shows the molecular ion peak at *m/z* 268.

In aqueous ethanol in the presence of sodium hydroxide, compound **3** reacted with diazotised anilines giving the respective arylazo derivatives **4** (Scheme 1). The mass spectra of the latter products revealed the molecular ion peaks at the expected *m/z* values with relative intensities varying from 30 to 100% and their elemental analysis data were consistent with their assigned structures. Their infrared spectral data (see Experimental) appear consistent more with the hydrazone tautomeric structure **4B** than the CH- or NH-azo tautomeric



Scheme 1

forms, **4A** and **4C** respectively (Scheme 1). For example, all compounds exhibit two carbonyl bands in the regions 1699 –1659 and 1662–1611 cm^{-1} corresponding to the stretching vibrations of the pyrimidinone and the 1,2,4-triazepinone carbonyl groups, respectively. The observed low frequency of the latter CO band may be the result of possible strong chelation with the hydrazone NH and conjugation with the C=N double bond as required by the hydrazone form **4B** (Scheme 1).[14] The fact that the IR spectra of compounds **4** show evidence for strong intramolecular hydrogen bonding also excludes the azo form **4A** (Scheme 1).

To elucidate the actual tautomeric form of the studied compounds **4**, we examined first their electronic absorption spectra. The data are summarised in Table 1. As shown, each of compounds **4** in dioxan exhibits two characteristic absorption bands in the regions 389–349 and 295–286 nm. Such an absorption pattern is similar to that of a typical hydrazone

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Table 1 UV spectra and acid dissociation constants[a] of 3-arylazo-2-methyl-7-phenylpyrimido[1,2-*b*][1,2,4]triazepine-4,9(3*H*, 5*H*)-dione **4a–j** in dioxan

Compd.	λ_{max} (log ε)	$_pK_a$ (±s)	σ^-_x
4a	370 (3.71), 293 (3.60)	7.02 (0.04)	–0.27
4b	378 (3.62), 286 (4.01)	6.72 (0.03)	–0.17
4c	371 (3.58), 293 (3.44)	6.61 (0.05)	–0.07
4d[b]	370 (3.40), 293 (3.31)	6.48 (0.04)	0.0
4e	369 (3.56), 294 (3.42)	5.90 (0.03)	0.23
4f	363 (3.68), 295 (3.55)	5.63 (0.04)	0.37
4g	349 (3.77), 294 (3.80)	4.96 (0.05)	0.71
4h	389 (3.85), 293 (3.45)	3.85 (0.03)	1.28
4i	373 (3.94), 288 (3.68)	5.03 (0.03)	0.68
4j	377 (3.73), 302 (3.26)	4.68 (0.03)	0.84

[a]pK_a in dioxin–water (4:1 v/v) solution at 25°C and μ = 0.10.
[b]Solvent : λ_{max} (log ε) : acetic acid 371 (3.67), 287 (4.20) ; ethanol 369 (3.57), 286 (4.22); acetonitrile 362 (3.62), 286 (4.21); DMF 360 (3.40), 286 (4.27).

chromophore.[3,15] Furthermore, the spectrum of **4d**, taken as a typical example of the series studied, was recorded in solvents of different polarities. The spectra obtained showed little, if any, shift (Table 1). The small shifts in λ_{max} of **4d** in different solvents are due to solute-solvent interaction. In agreement with this conclusion is the observation that the spectra of arylhydrazones derived from the reaction of quinones with *N*-alkyl-*N*-phenylhydrazine, unlike those of *o*- and *p*-hydroxyazo compounds, are largely independent of the solvent polarity.[14] This finding excludes the azo tautomeric forms **A** and **C**, and supports the conclusion that each of compounds **4** exists in a single tautomeric form, namely **4B** (Scheme 1).

Further and unambiguous evidence for the tautomeric form **4B** is provided by the ^{1}H NMR spectrum of the ^{15}N-isotopomer **4d',** taken as a typical example of the series. This material was prepared as follows. ^{15}N-Aniline was diazotised in the usual way and the resulting diazonium salt was coupled with **2**. It is known that diazonium nitrogen scrambling during diazotisation or coupling is negligible.[1,16] The ^{1}H NMR spectrum of **4d'** in deuterated dimethylsulfoxide contains a doublet centred at δ 9.86 with coupling constant J = 93.8 Hz. This indicates that the hydrazone proton is directly attached to the ^{15}N atom. Because of the magnitude of the ^{15}N–H coupling, and since the area of the ^{15}N–H signal relative to that of the methyl protons was in a good 1 : 3 ratio, compound **4d'** must exist entirely in the hydrazone form **4B** under these conditions. Furthermore, the presence of only one ^{15}NH doublet in the spectrum of the labelled **4d'** indicates the presence of only one geometric isomer of the hydrazone form, namely the E-isomer, in the solvent used.

To provide further evidence for the assignment of the tautomeric structure **4B** for the products **4**, their acid dissociation constants, K_a, were determined and their correlation by the Hammett equation was examined.[3-7] The acid dissociation constants for the series **4a–j** were determined potentiometrically at 25°C in 80% dioxan-water mixture (v/v). In all determinations the ionic strength was kept constant at 0.1. From the pH-titrant volume data, the acid dissociation constants of the compounds studied were calculated (see Experimental) and the results are summarised in Table 1.

When the pK_a values were plotted *versus* Hammett substituent constants σ_x,[17] all the substituents fall on the correlation line except the substituents with -R effect, namely the *p*-NO_2, *p*-CH_3CO and *p*-EtOCO groups, which are capable of direct interaction with the negatively charged reaction site. However, when the pK_a data were plotted versus σ_x^- constants,[17] a better correlation was obtained. The Hammett type equation of the regression line obtained is:

$$pK_a = 6.43 - 2.05\ \sigma_x^-;\ r = 0.998;\ s = \pm 0.04$$

This excellent correlation indicates that the parameter r in the Humffray–Ryan equation[18]: $pK_a = pK_a^o - \rho\{\sigma_x + r(\sigma_x^- - \sigma_x)\}$, which gives the contribution of the resonance effect of the substituent varied, is close to unity for the series **4a–j** studied.

The linear correlation between pK_a values and σ_x^- constants and the values of ρ and r found provide further evidence that the studied compounds **4** exist predominantly in the hydrazone form **4B**. This is because the values of ρ (2.05) and r = 1.00 are similar to those reported for ionisation of phenols (ρ = 2.67; r = 1.00) and anilinium ions (ρ = 2.77; r = 1.00) in 50% ethanol–water mixture.[19-21] This finding indicates that the negative charge in the anion formed by deprotonation of **4** is largely localised on the N-atom adjacent to the benzene ring bearing the substituent. This anion will take up a proton on the N-atom bearing the negative charge to give **4B** which is also stabilised by hydrogen bonding. Furthermore, if either form **4A** or **4C** were the predominant form for the studied compounds, the ρ values would have been less than 2.0 and will be similar to that reported for ionisation of 2-arylazophenols (ρ = 1.223; r = 0.286).[19] and this was not found to be the case. Thus, it is not unreasonable to conclude that the observed linear correlation of the dissociation constants with the Hammett equation indicates that the hydrazone tautomeric form **4B** prevails under the conditions of the measurement of pK_as.

In conclusion, we have encountered a novel series of 3-arylazo-2-methyl-7-phenylpyrimido[1,2-*b*][1,2,4]triazepine-4,9(3*H*, 5*H*)-diones **4** and their spectral data presented here indicate collectively that such compounds exist predominantly in the hydrazone tautomeric form **4B**.

Experimental

Melting points were determined on a Gallenkamp apparatus. IR spectra were recorded in potassium bromide using Perkin Elmer FTIR 1650 and Pye-Unicam SP300 infrared spectrophotometers. ^{1}H NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 using a Varian Gemini 300 NMR spectrometer. Mass spectra were recorded on a GCMS-QP 1000 EX Shimadzu and GCMS 5988-A HP spectrometers. Electronic absorption spectra were recorded on a Perkin-Elmer Lambada 40 spectrophotometer. Elemental analyses were carried out at the Microanalytical Laboratory of Cairo University, Giza, Egypt. ^{15}N-Aniline (95% isotopic purity) was purchased from Merck & Co. Inc., Rahway, NJ, USA. 2,3-Diamino-6-phenyl-4(3*H*)-pyrimidinone **2** was prepared as previously described.[9]

2-Methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**3**): A mixture of 2,3-diamino-6-phenyl-4(3*H*)-pyrimidinone **2** (2.02 g, 10 mmol) and ethyl acetoacetate **1** (2.4 g, 3 ml, 20 mmol) in dioxan (20 ml) was refluxed for 2 h, then cooled. The solid that separated was collected and crystallised from ethanol to give compound **3** as a yellow crystalline solid (0.5 g, 19%), m.p. 242 – 244°C. IR (KBr): ν_{max} 3058 (NH), 1685, 1658 (CO) cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 2.29 (s, 3H, CH_3), 4.52 (s, 2H, CH_2), 5.79 (s 1H, =CH), 7.51-8.06 (m, 5H, Ph), 13.00 (s, 1H, NH). MS: *m/z* (%) 269 (M^+ + 1, 4), 268 (M^+, 12), 267 (13), 240 (10), 191 (1), 149 (1), 135 (1), 107 (2), 105 (100), 77 (58). Anal. Found: C, 62.89; H, 4.48; N, 20.63. Calcd for $C_{14}H_{12}N_4O_2$ (268.0): C, 62.69; H, 4.48; N, 20.90%.

3-Arylazo-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-diones (**4a-j**): To a stirred solution of compound **3** (1.34 g, 5 mmole) in ethanol (40 ml) was added sodium hydroxide (0.2 g, 5 mmole) and the mixture was cooled in an ice bath to 0–5°C. To the resulting solution, while stirred, was added dropwise over a period of 20 min a solution of the appropriate arenediazonium chloride, prepared as usual by diazotising the respective aniline (5 mmole) in hydrochloric acid (6 M, 3 ml) with sodium nitrite (1 M, 5 ml). The whole mixture was then left in a refrigerator overnight. The precipitated solid was collected, washed with water and finally crystallised from ethanol to give the respective hydrazone **4a–j**.

Coupling of **3** with diazotised ^{15}N-aniline under the same conditions gave **4d'**, the ^{15}N-isotopomer of **4d**. The physical constants of **4d'** proved identical with those of the unlabelled compound **4d** indicated below.

3-(4-Methoxyphenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4a**): Yellow crystals (yield 1.45 g, 72%), mp. 245°C. IR (KBr): ν_{max} 3450, 3053, 1699, 1653, 1244 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.38 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 5.96 (s 1H, CH), 7.13 (d, *J* = 8 Hz, 2H, ArH), 7.33–7.66 (m, 5H, ArH), 7.91 (d, *J* = 8 Hz, 2H, ArH), 11.67 (s, 1H, NH), 13.50 (s, 1H, NH). MS: *m/z* (%) 403 (M^+ + 1, 16), 402 (M^+, 100), 311 (21), 285 (25), 243 (31), 170 (17), 157 (41), 140 (15), 128 (22), 116 (15), 101 (17), 77 (21). Anal. Found: C, 62.67; H, 4.67; N, 20.68. Calcd for $C_{21}H_{18}N_6O_3$ (402.42): C, 62.68; H, 4.51; N, 20.88%.

3-(4-Methylphenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4b**): Yellow crystals (yield 1.45 g, 75%), m.p. 290–292°C. IR (KBr) ν_{max} 3425, 3055, 1689, 1655 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.25 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 5.96 (s 1H, CH), 7.03 (d, *J* = 8 Hz, 2H, ArH), 7.13 (d, *J* = 8 Hz, 2H, ArH), 7.52–7.92 (m, 5H, ArH), 11.68 (s, 1H, NH), 13.34 (s, 1H, NH). MS: *m/z* (%) 388 (M^+ + 2, 5), 387 (M^+ + 1, 26), 386 (M^+, 100), 371 (2), 357 (14), 309 (23), 266 (14), 183 (12), 176 (14), 136 (12), 105 (69), 91 (15), 77 (61). Anal. Found: C, 65.27; H, 4.59; N, 21.71. Calcd for $C_{21}H_{18}N_6O_2$ (386.4): C, 65.17; H, 4.70; N, 21.75%.

3-(3-Methylphenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4c**): Orange crystals (yield 1.55 g, 80%), m.p. 305–307 °C. IR (KBr): ν_{max} 3447, 3054, 1659, 1611 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.26 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 5.96 (s 1H, CH), 6.83-7.93 (m, 9H, ArH), 11.69 (s, 1H, NH), 13.40 (s, 1H, NH). MS: *m/z* (%) 388 (M^+ + 2, 6), 387 (M^+ + 1, 25), 386 (M^+, 78), 385 (77), 371 (3), 267 (12), 176 (22), 136 (22), 105 (100), 91 (24), 77 (84). Anal. Found: C, 64.94; H, 4.83; N, 21.51. Calcd for $C_{21}H_{18}N_6O_2$ (386.42): C, 65.28; H, 4.70; N, 21.75%.

3-Phenylazo-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4d**): Orange crystals (yield 1.47 g, 79%), m.p. 300–302°C. IR (KBr) ν_{max} 3436, 3055, 1690, 1655 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.38 (s, 3H, CH_3), 5.96 (s 1H, CH), 6.99-7.94 (m, 10 H, ArH), 11.70 (s, 1H, NH), 13.41 (s, 1H, NH). MS: *m/z* (%) 374 (M^+ + 2, 6), 373 (M^+ + 1, 34), 372 (M^+, 82), 371 (100), 343 (18), 267 (15), 252 (12), 176 (23), 169 (15), 136 (22), 105 (82), 92 (15), 77 (76). Anal. Found: C, 64.50; H, 4.53; N, 22.25. Calcd for $C_{20}H_{16}N_6O_2$ (372.39): C, 64.51; H, 4.33; N, 22.57%.

3-(4-Chlorophenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4e**): Orange solid (yield 1.69 g, 83%), m.p. 302–304°C. IR (KBr) ν_{max} 3451, 3054, 1698, 1653 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.38 (s, 3H, CH_3), 5.96 (s 1H, CH), 7.13 (d, *J* = 9 Hz, 2H, ArH), 7.37 (d, *J* = 9 Hz, 2H, ArH), 7.52–7.94 (m, 5H, ArH), 11.65 (s, 1H, NH), 13.41 (s, 1H, NH). MS: *m/z* (%) 409 (M^+ + 2, 12), 408 (M^+ + 1, 34), 407 (M^+, 55), 406 (100), 405 (90), 376 (15), 267 (12), 176 (31), 136 (17), 111 (11), 105 (98), 91 (4), 77 (73). Anal. Found: C, 59.29; H, 3.85; N, 20.22. Calcd for $C_{20}H_{15}ClN_6O_2$ (406.83): C, 59.05; H, 3.72; N, 20.66%.

3-(3-Chlorophenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4f**): Orange solid (yield 1.58 g, 78%), m.p. 310°C. IR (KBr) ν_{max} 3448, 3157, 3060, 1673, 1646 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.37 (s, 3H, CH_3), 5.95 (s 1H, CH), 7.01–7.97 (m, 9H, ArH), 12.83 (s, 1H, NH), 13.20 (s, 1H, NH). MS: *m/z* (%) 409 (M^+ + 2, 11), 408 (M^+ + 1, 25), 407 (M^+, 54), 267 (12), 252 (12), 176 (38), 134 (18),105 (100), 91 (4), 77 (73). Anal. Found: C, 59.50; H, 3.62; N, 20.33. Calcd for $C_{20}H_{15}ClN_6O_2$ (406.83): C, 59.05; H, 3.72; N, 20.66%.

3-(3-Nitrophenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4g**): Orange solid (yield 1.58 g, 78%), m.p. 318°C. IR (KBr) ν_{max} 3459, 3060, 1699, 1647 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.39 (s, 3H, CH_3), 5.98 (s, 1H, CH), 7.53–7.98 (m, 9H, ArH), 11.72 (s, 1H, NH), 13.50 (s, 1H, NH). MS: *m/z* (%) 418 (M^+ + 1, 24), 417 (M^+, 38), 416 (34), 176 (25), 136 (17),105 (100), 91 (6), 77 (83). Anal. Found: C, 57.05; H, 3.74; N, 23.08. Calcd for $C_{20}H_{15}N_7O_4$ (417.39): C, 57.55; H, 3.62; N, 23.49%.

3-(4-Nitrophenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4h**): Orange solid (yield 1.66 g, 80%), m.p. 314–316°C. IR (KBr) ν_{max} 3436, 3178, 1697, 1662 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.38 (s, 3H, CH_3), 5.98 (s 1H, CH), 7.28 (d, *J* = 9 Hz, 2H, ArH), 7.56–7.99 (m, 5H, ArH), 8.22 (d, *J* = 9 Hz, 2H, ArH), 11.95 (s, 1H, NH), 13.45 (s, 1H, NH). MS: *m/z* (%) 417 (M^+, 30), 416 (41), 176 (32), 136 (17),105 (87), 91 (5), 77 (100). Anal. Found: C, 57.21; H, 3.62; N, 23.06. Calcd for $C_{20}H_{15}N_7O_4$ (417.39): C, 57.55; H, 3.62; N, 23.49%.

3-(4-Acetylphenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4i**): Pale yellow solid (yield 1.7 g, 82%), m.p. 310°C. IR (KBr) ν_{max} 3450, 1698, 1674, 1655 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.38 (s, 3H, CH_3), 2.60 (s, 3H, $COCH_3$), 5.98 (s 1H, CH), 7.21 (d, *J* = 8 Hz, 2H, ArH), 7.55–7.57 and 7.66–7.96 (m, 5H, ArH), 8.57 (d, *J* = 8 Hz, 2H, ArH), 11.82 (s, 1H, NH), 13.45 (s, 1H, NH). MS: *m/z* (%) 415 (M^+ + 1, 22), 414 (M^+, 100), 413 (67), 267 (16), 134 (12), 120 (12), 105 (96), 91 (9), 77 (67). Anal. Found: C, 63.64, H, 4.24, N, 20.18.. Calcd for $C_{22}H_{18}N_6O_3$ (414.43): C, 63.76; H, 4.38; N, 20.28%.

3-(4-Ethoxycarbonylphenylazo)-2-methyl-7-phenylpyrimido[1,2-b][1,2,4]triazepine-4,9(3H,5H)-dione (**4j**): Orange solid (yield 1.78 g, 80%), m.p. 285°C. IR (KBr) ν_{max} 3454, 1700, 1655, 1650 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 1.30 (t, *J* = 7 Hz, 3H, CH_3), 2.38 (s, 3H, CH_3), 4.26 (q, *J* = 7 Hz, 2H, CH_2), 5.97 (s 1H, CH), 7.19 (d, *J* = 6 Hz, 2H, ArH), 7.22-7.57 and 7.66 –7.97 (m, 5H, ArH), 7.58 (d, *J* = 6 Hz, 2H, ArH), 11.82 (s, 1H, NH), 13.45 (s, 1H, NH). MS: *m/z* (%) 444 (M^+, 20), 400 (18), 360 (18), 271 (20), 201 (20), 149 (20), 134 (20), 105 (100), 89 (18), 72 (53). Anal. Found: C, 67.04, H, 4.52, N, 18.65. Calcd for $C_{23}H_{20}N_6O_4$ (444.45): C, 67.16; H, 4.54; N, 18.91%.

Determination of pKa of compounds **4a–j**

The acid dissociation constants of the compounds **4** were determined potentiometrically in 80% dioxan–water mixtures at 25±0.1°C and ionic strength (KNO_3) of 0.1. A Meetrohm 686 titroprocessor equipped with 665 Dosimat was used. The electrode and the titroprocessor were calibrated with standard Beckman buffer solutions of pH 4.01 and 7.00. The pH metre reading B recorded in dioxin–water solution was converted to hydrogen ion concentration [H^+] by means of the relation of van Uitert and Hass,[22] namely:

$$-\log [H^+] = B + \log U_H$$

where log U_H is the correction factor for the solvent composition and ionic strength used for which B is read. The value of log U_H was found to be 0.48. A carbonate-free sodium hydroxide titrant was prepared and standardised against potassium hydrogen phthalate solution.

The experimental procedure followed in the determination of pK_a values and their calculations, by the method of least squares, from the titrant volume-pH data using the relation: $pK_a = pH_i - \log V_i/(V_e - V_i)$, is similar to that previously described.[4,6,23] In this equation, pH_i is the corrected pH value of the solution when the volume of the added titrant is V_i and V_e is the volume of the titrant at the equivalence point. The calculations of the pK_a values were carried out using computer program MINIQUAD-75.[24] The pK_a values obtained were reproducible to within ± 0.02 pK_a unit. The results are summarised in Table 1.

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