Research Article

# Synthesis of Some Novel Monoazo Triazepine Derivatives Containing a Pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine Skeleton

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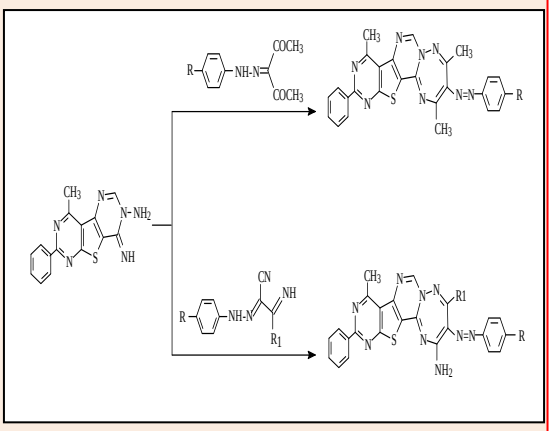
**Abstract**

The appropriate arylamines **6a-e** were diazotized and coupled with acetylacetone, 3-aminocrotonitrile **8** and β-amino-β-(pyrid-4-yl)-acrylonitrile **10** to give the corresponding arylazo-enaminonitriles (such as azobeneacetylacetones **7a-e**, 2-arylhydrazono-3-ketimino-butyronitriles **9a-e** and 3-amino-2-arylazo-3-(pyrid-4-yl)-acrylonitrile derivatives **11a-e)**. On the other hand, intramolecular cyclization of 7-amino-8-imino-pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine **5** with arylazo-enaminonitriles (**7a-e**, **9a-e**, and **11a-e**) under acidic condition afforded the corresponding monoazo triazepine derivatives **12a-e**, **13a-e** and **14a-e**, respectively. The structures of the newly synthesized compounds were characterized by IR, $^1$H NMR, mass, elemental analysis.



**Keywords:** Synthesis, diazotization, monoazo triazepine derivatives, arylazo-enaminonitriles, 7-amino-8-imino pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine

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## Introduction

Azo compounds are the largest group of colorants in terms of number and production volume of currently marketed dyes and pigments. A number of azo compounds have been prepared from amino heterocycles. Several patents describe the synthesis and technical importances of heterocyclic azo disperse dyes [1-6]. Azo compounds derived from heterocyclic ring systems have many advantages, such as color deepening effect as an intrinsic property of heterocyclic ring and result in good sublimation fastness of dyed fibers [7, 8]. Likewise, a number of triazepine derivatives with a bridgehead nitrogen atom have attracted considerable attention due to their wide range of pharmacological activities [9-14]. Recently, compounds with triazepine skeletons have attracted much attention as a result of their interesting biological properties [15-18]. Specially, it has been demonstrated that heterocycles attached to seven member rings show versatile biological activities such as anti-microbial, anti-cancer, anti-inflammatory [15, 16].

Various conventional methods for the synthesis of fused triazepines are exemplified in literature including cycloaddition and photochemical methods [19-21]. To the best of our knowledge, the synthesis of monoazo triazepine derivatives, those containing a pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine skeleton have not yet been reported. Therefore, base on our previous works [22-28], we report herein the use of 7-amino-8-imino-pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine **5** and arylazo-enaminonitriles for the synthesis of a series of monoazo triazepine derivatives containing a pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine skeleton.

## Experimental

**General**

All melting points are uncorrected and in ℃. IR spectra were recorded on a JASCO FTIR-3 spectrometer (KBr); $^1$H NMR spectra were obtained on a Bruker AM-300 WB FI-NMR spectrometer, and chemical shifts are expressed in δ ppm using TMS as an internal standard. Electron impact mass spectra were obtained at 70 eV using a Finingan Mat TSQ-46C spectrometer. Microanalyses for C, H, and N were performed on a Perkin-Elmer 240 elemental Analyzer. The intermediates **7a-e** [29], **9a, 9e** [30] and **11a** [31] were prepared according to known procedures.

**General procedures for the preparation of 2-arylhydrazono-3-ketimino-butyronitrile derivatives (9a-e)**

The appropriate arylamine **6a-e** (0.01 mol) was dissolved in aqueous hydrochloric acid (8 mL) and cooled to 0-5℃, prior to addition of a cold solution of sodium nitrite (0.7 g in 3 mL water) while maintaining the temperature at 0-5℃. The excess of nitrous acid was destroyed by addition of urea (0.5 g). The diazonium solution was then added dropwise to a cooled and stirred mixture of 3-aminocrotonitrile **8** (0.82 g, 0.01 mol) and sodium acetate (2.0 g, dissolved in 10 mL aqueous ethanol). Stirring was continued for 3 h and the resulting crystals collected, washed with water and recrystallised from chloroform.

**2-Phenylhydrazono-3-ketobutyronitrile (9a)**

Yellow crystals. Yield 1.73 g (93 %), mp 152℃ ; IR : ν 3233-3221 (NH), 2216 (C≡N), 1625 (N＝N) cm$^{-1}$ ; $^1$H NMR (DMSO-$d_6$): δ 2.30 (3H, s, $CH_3$), 7.71-7.70, 7.53-7.51 (5H, m, phenyl-H), 8.72 (1H, s, C＝NH), 12.19 (1H, br, NH－N＝); MS: 186(M$^+$,87), 144(5), 118(3), 105(19), 92(9), 77(100), 65(14), 51(8). Anal. Calcd. for $C_{10}H_{10}N_4$: C, 64.51; H, 5.37; N, 30.10. Found: C, 64.69; H, 5.66; N, 30.28 %.

**2-(4-Methylphenyl)hydrazono-3-ketobutyronitrile (9b)**

Yellow crystals. Yield 1.70 g (85 %), mp 142℃ ; IR : ν 3232-3220 (NH), 2210 (C≡N), 1628 (C＝N) cm$^{-1}$ ; $^1$H NMR (DMSO-$d_6$): δ 2.31 (3H, s, $CH_3$), 2.41 (3H, s, $CH_3$), 7.41 (2H, d, 3,5-H of phenyl), 7.61 (2H, d, 2,6-H of phenyl), 8.67 (1H, s, C＝NH), 12.15 (1H, br, NH－N＝); MS: 200(M$^+$,55), 157(3), 132(2), 119(16), 91(100), 77(12), 65(7).Anal. Calcd. for $C_{11}H_{12}N_4$: C, 66.00; H, 6.00; N, 28.00. Found: C, 66.14; H, 6.05; N, 28.05 %.

**2-(4-Acetamidophenyl)hydrazono-3-ketobutyronitrile (9c)**

Yellow crystals. Yield 2.18 g (90 %), mp 223℃ ; IR : ν 3226-3219 (NH), 2211 (C≡N), 1624 (C＝N) cm$^{-1}$ ; $^1$H NMR (DMSO-$d_6$): δ 2.07 (3H, s, $COCH_3$), 2.28 (3H, s, $CH_3$), 7.41 (2H, d, 3,5-H of phenyl), 7.60 (2H, d, 2,6-H of phenyl), 8.62 (1H, s, C＝NH), 10.10 (1H, s, CONH), 12.12 (1H, br, NH－N＝); MS: 243(M$^+$,100), 202(8), 161(2), 149(7), 134(11), 107(68), 92(2). Anal. Calcd. for $C_{12}H_{13}N_5O$: C, 59.25; H, 5.34; N, 28.80. Found: C, 59.24; H, 5.37; N, 28.85 %.

**2-(4-Chlorophenyl)hydrazono-3-ketobutyronitrile (9d)**

Light yellow crystals. Yield 1.83 g (83 %), mp 182℃ ; IR : ν 3233-3224 (NH), 2216 (C≡N), 1626 (C＝N) cm$^{-1}$ ; $^1$H NMR (DMSO-$d_6$): δ 2.30 (3H, s, $CH_3$), 7.42 (2H, d, 2,6-H of phenyl), 7.50 (2H, d, 3,5-H of phenyl), 8.86 (1H, s, C＝NH), 12.23 (1H, br, NH－N＝); MS: 220.5(M$^+$,100), 178(2), 152(3), 139(24), 126(6), 111(34), 99(9) 90(3), 75(8), 52(2).Anal. Calcd. for $C_{10}H_9N_4Cl$: C, 54.42; H, 4.08; N, 25.39. Found: C, 54.66; H, 4.11; N, 25.47 %.

**2-(4-Nitrophenyl)hydrazono-3-ketobutyronitrile (9e)**

Orange crystals. Yield 2.01 g (87 %), mp 237℃ ; IR : ν 3231-3225 (NH), 2217 (C≡N), 1623 (C＝N) cm$^{-1}$ ; $^1$H NMR (DMSO-$d_6$): δ 2.35 (3H, s, $CH_3$), 7.58 (2H, d, 2,6-H of phenyl), 8.17 (2H, d, 3,5-H of phenyl), 8.90 (1H, s, C＝NH), 12.39 (1H, br, NH－N＝); MS: 231(M$^+$,100), 205(1), 189(1), 163(2), 150(32), 122(49), 108(3) 92(5), 76(5), 63(4).Anal. Calcd. for $C_{10}H_9N_5O_2$: C, 51.94; H, 3.89; N, 30.30. Found: C, 51.99; H, 3.96; N, 30.41 %.

**General procedures for the preparation of 3-amino-2-arylazo-3-(pyrid-4-yl)-acrylonitrile (11a-e)**The appropriate arylamine **6a-e** (0.01 mol) was dissolved in aqueous hydrochloric acid (8 mL) and cooled to 0-5℃, prior to addition

of a cold solution of sodium nitrite (0.7 g in 3 mL water) while maintaining the temperature at 0-5℃. The excess of nitrous acid was destroyed by addition of urea (0.5 g). The diazonium solution was then added dropwise to a cooled and stirred mixture of β-amino-β-(pyrid-4-yl)-acrylonitrile **10** (1.45 g, 0.01 mol) in ethanol (50 mL) containing sodium acetate (2.0 g). The reaction mixture was than stirred in an ice bath for 1-2 h. The solid so formed, was collected by filtration and washed several times with water and recrystallized from ethanol.

**3-Amino-2-phenylazo-3-(pyrid-4-yl)-acrylonitrile (11a)**

Light yellow crystals. Yield 2.19 g (88 %), mp 226℃ ; IR : ν 3458, 3390 ($NH_2$), 2215 (C≡N), 1622 (C=N), 1551 (N=N) $cm^{-1}$ ; $^1H$ NMR (DMSO-$d_6$) :δ 7.02 (2H, s, $NH_2$), 7.58-7.54, 7.38-7.32 (5H, m, phenyl-H), 8.58 (1H, s, C=NH), 8.63(2H, d, 3,5-H of pyridyl), 8.81 (2H, d, 2,6-H of pyridyl), 9.12 (1H, s, NH−N=); MS: 249($M^+$,36), 220(5), 205(6), 166(2), 145(100), 130(11), 118(30), 105(46), 91(10), 77(62), 63(8), 51(24).Anal. Calcd. for $C_{14}H_{11}N_5$: C, 67.46; H, 4.41; N, 28.11. Found: C, 67.69; H, 4.52; N, 28.25 %.

**3-Amino-2-(4-methylphenyl)azo-3-(pyrid-4-yl)-acrylonitrile (11b)**

Yellow crystals. Yield 2.26 g (86 %), mp 192℃ ; IR : ν 3446, 3384 ($NH_2$), 2211 (C≡N), 1628 (C=N), 1550 (N=N) $cm^{-1}$ ; $^1H$ NMR (DMSO-$d_6$) : δ 2.35 (3H, s, $CH_3$), 7.02 (2H, s, $NH_2$), 7.54 (2H, d, 3,5-H of phenyl), 7.70 (2H, d, 2,6-H of phenyl), 8.48 (1H, s, C=NH), 8.64 (2H, d, 3,5-H of pyridyl), 8.76 (2H, d, 2,6-H of pyridyl), 9.01 (1H, s, NH−N=); MS: 263($M^+$,100), 256(3), 234(7), 220(4), 171(2), 157(3), 145(9), 129(6), 119(33), 105(11), 91(30), 78(14), 65(22). Anal. Calcd. for $C_{15}H_{13}N_5$: C, 68.44; H, 4.94; N, 26.61. Found: C, 68.56; H, 5.06; N, 26.78 %.

**3-Amino-2-(4-acetamidophenyl)azo-3-(pyrid-4-yl)-acrylonitrile (11c)**

Brownish yellow crystals. Yield 2.72 g (89 %), mp 220℃ ; IR : ν 3445, 3385 ($NH_2$), 2210 (C≡N), 1621 (C=N), 1551 (N=N) $cm^{-1}$ ; $^1H$ NMR (DMSO-$d_6$) : δ 2.07 (3H, s, $CH_3$), 7.01 (2H, s, NH2), 7.55 (2H, d, 3,5-H of phenyl), 7.80 (2H, d, 2,6-H of phenyl), 8.43 (1H, s, C=NH), 8.63 (2H, d, 3,5-H of pyridyl), 8.78 (2H, d, 2,6-H of pyridyl), 8.93 (1H, s, CONH), 10.16 (1H, s, NH−N=); MS: 306($M^+$,100), 283(30), 278(5), 241(10), 219(4), 162(16), 150(20), 134(48), 108(16), 93(41). Anal. Calcd. for $C_{16}H_{14}N_6O$: C, 62.74; H, 4.57; N, 27.45. Found: C, 62.86; H, 4.77; N, 27.68 %.

**3-Amino-2-(4-chlorophenyl)azo-3-(pyrid-4-yl)-acrylonitrile (11d)**

Yellow crystals. Yield 2.49 g (88 %), mp 156℃ ; IR : ν 3501, 3391 ($NH_2$), 2213 (C≡N), 1631 (C=N), 1553 (N=N) $cm^{-1}$ ; $^1H$ NMR (DMSO-$d_6$) : δ 6.97 (2H, s, $NH_2$), 7.54 (2H, d, 3,5-H of phenyl), 7.87 (2H, d, 2,6-H of phenyl), 8.65 (1H, s, C=NH), 8.72 (2H, d, 3,5-H of pyridyl), 8.81 (2H, d, 2,6-H of pyridyl), 9.22 (1H, s, NH−N=); MS: 283.5($M^+$,100), 254(3), 220(2), 145(19), 139(34), 111(31), 70(2). Anal. Calcd. for $C_{14}H_{10}ClN_5$: C, 59.26; H, 3.52; N, 24.69. Found: C, 59.36; H, 3.66; N, 24.78 %.

**3-Amino-2-(4-nitrophenyl)azo-3-(pyrid-4-yl)-acrylonitrile (11e)**

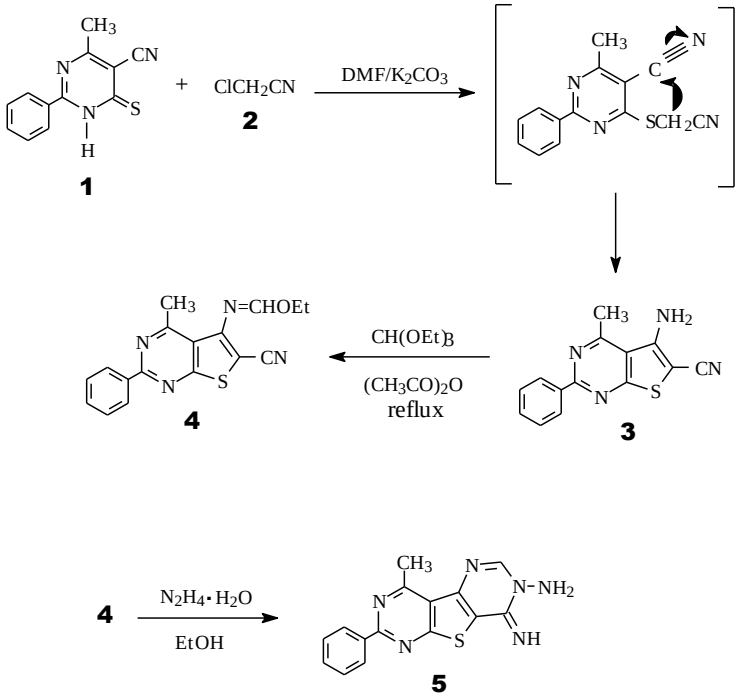
Reddish brown crystals. Yield 2.50 g (85 %), mp 280℃ ; IR : ν 3504, 3395 ($NH_2$), 2221 (C≡N), 1617 (C=N), 1554 (N=N) $cm^{-1}$ ; $^1H$ NMR (DMSO-$d_6$) : δ 7.41 (2H, s, $NH_2$), 7.44 (2H, d, 2,6-H of phenyl), 8.04 (2H, d, 3,5-H of phenyl), 8.29 (2H, d, 3,5-H of pyridyl), 8.84 (2H, d, 2,6-H of pyridyl), 9.22 (1H, s, C=NH), 9.68 (1H, s, NH−N=); MS: 294($M^+$,94), 266(8), 247(3), 219(5), 192(4), 172(3), 150(33), 144(26), 122(100), 90(17), 78(26), 63(16), 51(23).Anal. Calcd. for $C_{14}H_{10}N_6O_2$: C, 57.14; H, 3.40; N, 28.57. Found: C, 57.36; H, 3.56; N, 28.78 %.

**General procedures for the preparation of 2-phenyl-10-arylazo-9,11-disubstituted-pyrimido[3',2':4,5]-thieno[3,2:4,5]pyrimido[1,6-b][1,2,4]triazepines (12a-e, 13a-e and 14a-e)**

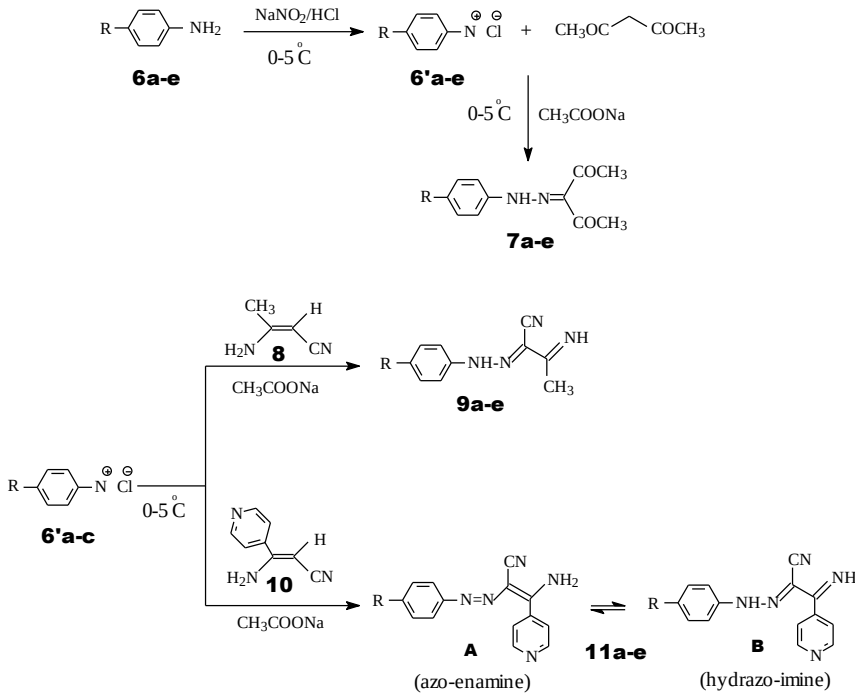
A mixture of compound **5** (0.308 g, 1 mmol) and azobenzeneacetylacetone **7a-e** and arylazo-enaminonitrile derivatives **9a-e** and **11a-e** (1 mmol) in glacial acetic acid (10 mL) was refluxed for 11 h. The solvent was removed by evaporation under reduced pressure and the remainder was left to cool. The solid formed was collected by filtration and recrystallized from chloroform/acetone. The physical constants and spectral data of compounds **12a-e**, **13a-e** and **14a-e** are record in Table 1, 2.

## Results and Discussion

The required key intermediate 7-amino-8-imino-pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine **5** was prepared from our previous work [23, 28] (Scheme 1). Diazotization of appropriate arylamines **6a-e** in hydrochloric acid and sodium nitrite has been reported to afford the corresponding diazonium salts **6'a-e** which undergo coupling reaction with acetylacetone in sodium acetate buffered solution to yield the corresponding azobeneacetylacetone derivatives **7a-e**. Under same reaction conditions, diazonium salts **6'a-e** coupling reaction with 3-aminocrotonitrile **8** and β-amino-β-(pyrid-4-yl)-acrylonitrile **10** afforded the corresponding 2-arylhydrazono-3-ketimino-butyronitrile **9a-e** and 3-amino-2-arylazo-3-(pyrid-4-yl)-acrylonitrile derivatives **11a-e**, respectively (Scheme 2). The structures of the compounds **9a-e** and **11a-e** were established on the basis of their elemental analysis and spectral data. The IR absorption spectra of **9a-e** indicated absorption bands at ν ($cm^{-1}$): 2217-2210 (C≡N) and 3233-3219 (NH). The $^1$H NMR spectra of compounds **9a-e** revealed a singlet at δ 2.35-2.28 (3H, s), which were readily assigned to the methyl group and two singlets at δ 8.90-8.67 (1H, s) and 12.39-12.12 (1H, br), which were readily assigned to the C=NH and NH−N= protons, respectively. Furthermore, spectral data for **11a-e** indicate them to have a hydrazone configuration; the IR absorption spectra indicated absorption bands at ν ($cm^{-1}$): 2221-2210 (C≡N), 1554-1550 (N=N) and 3504-3384 ($NH_2$). This suggests that these intermediates are predominantly in azo-enamine form, in solid state. Moreover, $^1$H NMR spectra of compounds **11a-e** revealed three singlets at δ 7.41-6.97 (2H, s), 9.22-8.43 (1H, s) and 10.16-9.01 (1H, s), which were readily assigned to the $NH_2$, C=NH and NH−N=protons, respectively. These results suggest that intermediates **11a-e** are present as a mixture of two tautomeric forms in DMSO, namely the azo-enamine form **A** and the hydrazo-imine form **B** as shown in Scheme 2. Also, $^1$H NMR spectra of compounds **11a-e** revealed two doublets at δ 8.04-7.55 (2H, d) and 8.22-7.70 (2H, d), which were readily assigned to the hydrogen attached at $C_3$, $C_5$ and $C_2$, $C_6$ of the pyridyl ring, respectively. On the other hand, cyclocondensation of compound **5** with azobeneacetylacetone derivatives **7a-e** in glacial acetic acid under reflux afforded the corresponding 10-arylazo-4,9,11-trimethyl-pyrimido[3',2':4,5]thieno[3,2:4,5]pyrimido[1,6-*b*][1,2,4]triazepines **12a-e** (Scheme 3).

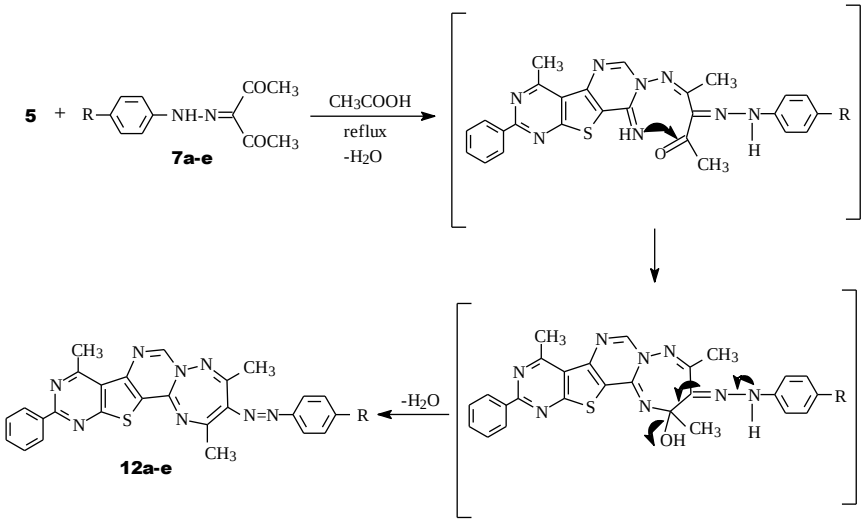



**Scheme 1**. Synthesis of key intermediate **5**




| 7, 9, 11 | a | b | c | d | e |
|---|---|---|---|---|---|
| R | H | $CH_3$ | $NHCOCH_3$ | Cl | $NO_2$ |

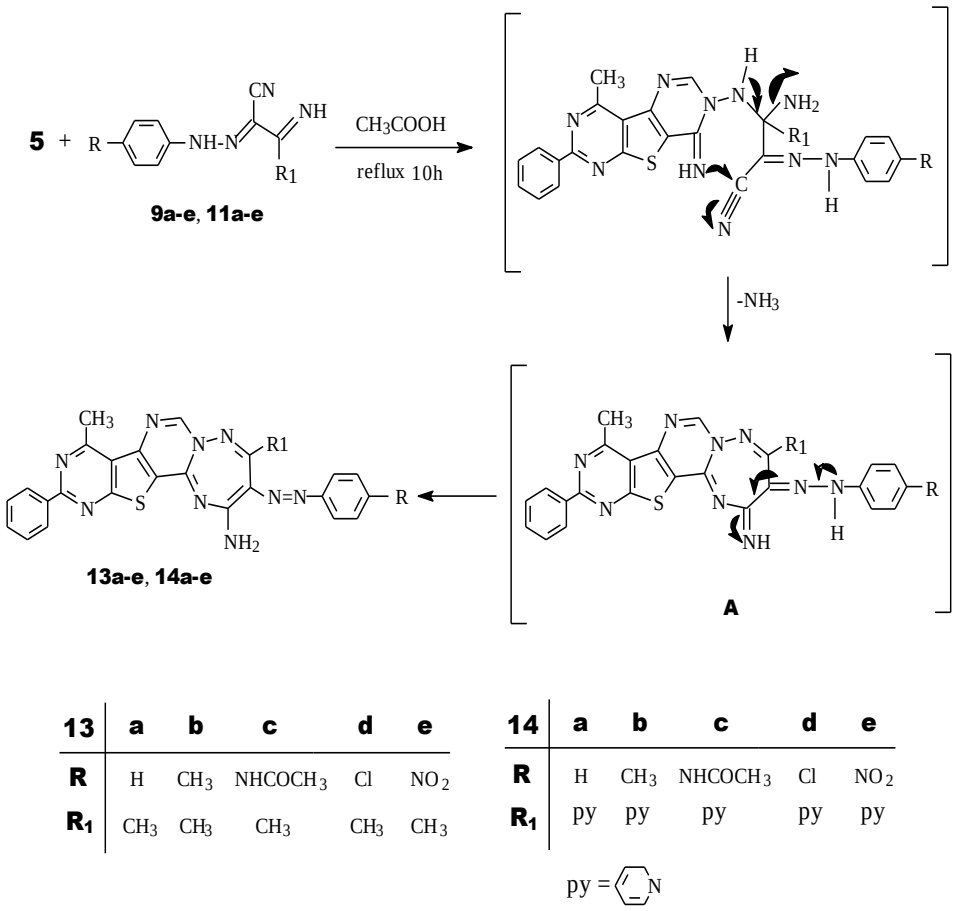
**Scheme 2**. Synthesis of intermediates **7a-e**, **9a-e** and **11a-e**




| 7, 12 | a | b | c | d | e |
|---|---|---|---|---|---|
| R | H | $CH_3$ | $NHCOCH_3$ | Cl | $NO_2$ |

**Scheme 3**. Synthesis of monoazo-triazepine derivatives **12a-e**

The mechanism involves the condensation of the 7-$NH_2$ of the compound **5** with the carbonyl group of the compound **12a-e**, followed by dehydration, subsequent cyclization, with loss of water [32]. The IR spectra of **12a-e** indicated the absence of the $NH_2$ and NH groups and appearance of the azo band at 1554-1549 $cm^{-1}$ confirms that all the derivatives contain the azo group in the solid state. In particular, the $^1H$ NMR spectra of compounds **12a-e** revealed two additional singlet at δ 2.98-2.62 (3H, s) and 3.14-2.71 (3H, s), which were readily assigned to the methyl group attached at $C_{11}$ and $C_9$ of the triazepine ring, respectively.




| 13 | a | b | c | d | e |
|---|---|---|---|---|---|
| R | H | $CH_3$ | $NHCOCH_3$ | Cl | $NO_2$ |
| $R_1$ | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ |

| 14 | a | b | c | d | e |
|---|---|---|---|---|---|
| R | H | $CH_3$ | $NHCOCH_3$ | Cl | $NO_2$ |
| $R_1$ | py | py | py | py | py |

py = 

**Scheme 4**. Synthesis of monoazo-triazepine derivatives **13a-e** and **14a-e**

Also, these structures get further support from mass spectroscopy. It has been observed that electron impact (EI) spectral has many common features. Compounds **12a-e** exhibited m/z 399, m/z 371, m/z 343, m/z 332, m/z 293, m/z 278, m/z 250 and m/z 240 piece peaks. Under same reaction conditions, cyclization of compound **5** with 2-arylhydrazono-3-ketimino-butyronitrile **9a-e** and 3-amino-2-arylazo-3-(pyrid-4-yl)-acrylonitrile derivatives **11a-e** afforded the corresponding monoazo-triazepine derivatives 11-amino-10-arylazo-9-substituted-pyrimido-[3',2':4,5]thieno[3,2:4,5]pyrimido[1,6-*b*][1, 2,4]triazepines **13a-e** and **14a-e**, respectively (Scheme 4).

The structures of compounds **13a-e** and **14a-e** were established on the basis of their elemental analysis and spectral data. The mechanism involves the condensation of the 7-$NH_2$ of the compound **5** with the imino group of **9a-e** and **11a-e**, then an internal nucleophilic attack by 8-NH group of compound **5** on the cyano group takes place and accompanied by deamination to yield the nonisolable intermediate **A**, which tautomerizes to the final isolable **13a-e** and **14a-e** (Scheme 4).

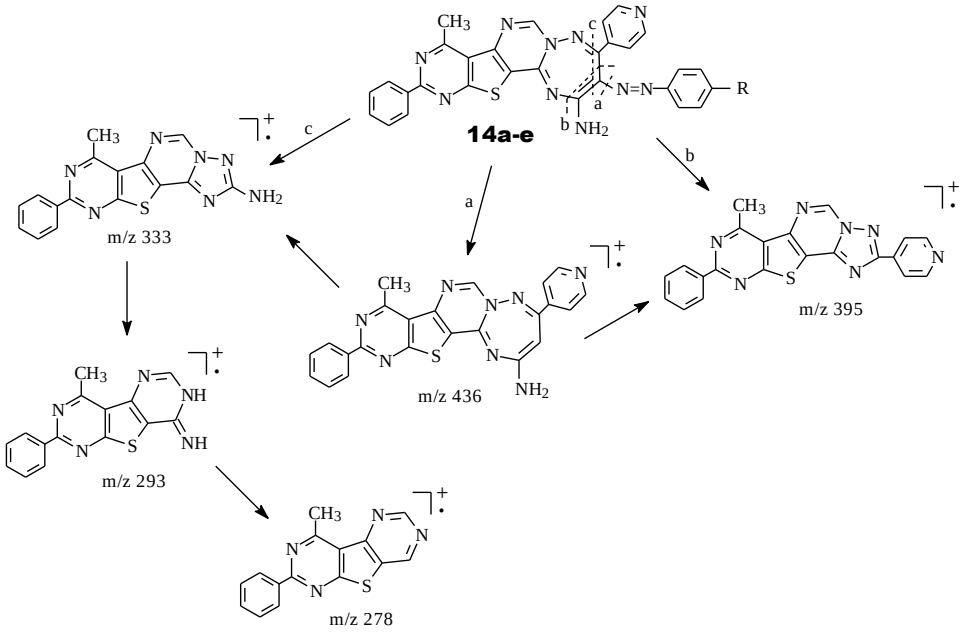



**Chart 1**. The possible mass fragmentation pathway of derivatives **14a-e**

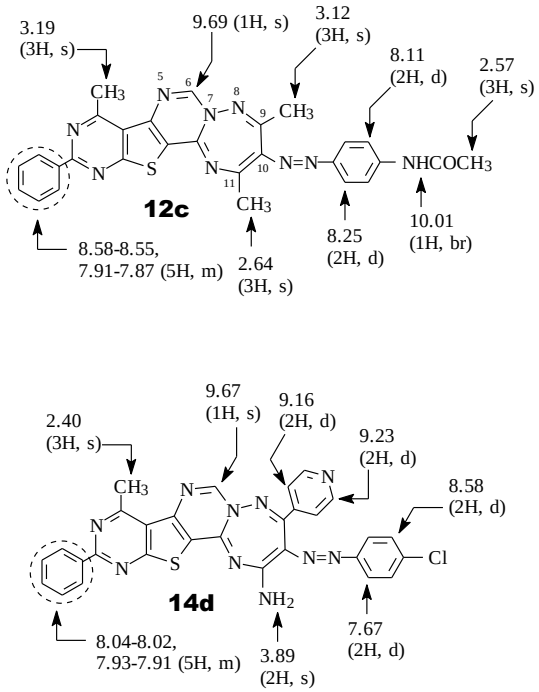



**Figure. 1**. Structural assignments of typical protons in **12c** and **14d** by $^1$H NMR

The IR spectra of compounds **13a-e** and **14a-e** showed the characteristic absorption band at 3247-3223 and 3246-3225 cm$^{-1}$ for the $NH_2$ group, respectively. Moreover, the $^1$H NMR spectra of dyes **13a-e** revealed two additional singlets at δ 2.98-2.60 (3H, s) and 4.18-3.17 (2H, s), which were readily assigned to the methyl and $NH_2$ groups attached at $C_9$ and $C_{11}$ of the triazepine ring, respectively. In addition, the $^1$H NMR spectra of compounds **14a-e**

revealed an additional singlet at δ 4.29-3.80 (2H, s), which were readily assigned to the $NH_2$ group attached at $C_{11}$ of the triazepine ring and two doublets at δ 9.34-8.88 (2H, d) and 9.53-9.05 (2H, d), which were readily assigned to the hydrogen attached at $C_3$, $C_5$ and $C_2$, $C_6$ of the pyridyl ring, respectively. These structures get further support from mass spectroscopy. It is noteworthy that Electron Impact (EI) spectral has many common features. Compounds **13a-e** exhibited m/z 400, m/z 372, m/z 332, m/z 293, m/z 278, m/z 190 and m/z 163 piece peaks. Nevertheless, because of the molecular ion m/z 540 of compound **14a** is unstable and could not be recorded in the electron impact mass spectra, but showed the presence of the ion peaks m/z 436[M-N=N—$C_6H_5$], m/z 395, m/z 333, m/z 293, m/z 278, m/z 190 and m/z 163 piece peaks. Similar results are observed in the case of compounds **14b-e**. The possible mass fragmentation pathway of derivatives **14a-e** is shown in Chart 1. Typical assignments for compounds **12c** and **14d** by $^1$H NMR are shown in Figure 1. Physical and spectral data of compounds **12a-e**, **13a-e** and **14a-e** are given in Table 1 and 2.

**Table 1** Physical and analytical data of 2-phenyl-10-arylazo-9,11-disubstituted- pyrimido[3',2':4,5]thieno-[3,2:4,5]pyrimido[1,6-*b*][1,2,4]triazepines (12a-e, 13a-e and 14a-e)

| Compound | Appearance | M.P. (°C)a | Yield (%) | Molecular formula | Elemental Analysis (%) Calcd/Found. | | |
|---|---|---|---|---|---|---|---|
| | | | | | C | H | N |
| **12a** | Pale yellow | 250 | 39 | $C_{26}H_{20}N_8S$ | 65.55<br>65.41 | 4.20<br>4.41 | 23.53<br>23.55 |
| **12b** | Light yellow | 292 | 41 | $C_{27}H_{22}N_8S$ | 66.12<br>66.14 | 4.49<br>4.89 | 22.86<br>22.69 |
| **12c** | Pale yellow | 335 | 46 | $C_{28}H_{23}N_9OS$ | 63.04<br>63.11 | 4.32<br>4.12 | 23.64<br>23.69 |
| **12d** | Yellow | 272 | 43 | $C_{26}H_{19}N_8ClS$ | 61.12<br>61.15 | 3.72<br>4.04 | 21.94<br>21.55 |
| **12e** | Yellow | 212 | 79 | $C_{26}H_{19}N_9O_2S$ | 59.88<br>59.99 | 3.65<br>3.59 | 24.18<br>24.38 |
| **13a** | Orange | 278 | 52 | $C_{25}H_{19}N_9S$ | 62.89<br>62.59 | 3.98<br>4.21 | 26.42<br>26.01 |
| **13b** | Orange | 269 | 47 | $C_{26}H_{21}N_9S$ | 63.54<br>63.28 | 4.28<br>4.33 | 25.66<br>25.58 |
| **13c** | Orange | 275 | 49 | $C_{27}H_{22}N_{10}OS$ | 60.67<br>60.79 | 4.12<br>4.14 | 26.22<br>26.33 |
| **13d** | Orange | 259 | 58 | $C_{25}H_{18}N_9ClS$ | 58.65<br>58.79 | 3.52<br>3.99 | 24.63<br>24.25 |
| **13e** | Light orange | 251 | 66 | $C_{25}H_{18}N_{10}O_2S$ | 57.47<br>57.25 | 3.45<br>3.65 | 26.82<br>26.67 |
| **14a** | Brownish orange | 254 | 37 | $C_{29}H_{20}N_{10}S$ | 64.44<br>64.36 | 3.70<br>3.59 | 25.93<br>25.77 |
| **14b** | Reddish orange | 307 | 60 | $C_{30}H_{22}N_{10}S$ | 64.98<br>65.01 | 3.97<br>4.13 | 25.27<br>25.58 |
| **14c** | Orange | ＞330 | 39 | $C_{31}H_{23}N_{11}OS$ | 62.31<br>60.59 | 3.85<br>4.04 | 25.80<br>25.63 |
| **14d** | Orange | 324 | 45 | $C_{29}H_{19}N_{10}ClS$ | 60.57<br>60.79 | 3.31<br>3.45 | 24.37<br>24.45 |
| **14e** | Brown | 281 | 51 | $C_{29}H_{19}N_{11}O_2S$ | 59.49<br>59.66 | 3.25<br>3.66 | 26.32<br>26.57 |

a.: recrystallization from DMF/ethanol.

**Table 2** Spectral data of 2-phenyl-10-arylazo-9,11-disubstituted-pyrimido[3',2':4,5]thieno[3,2:4,5]pyrimido[1,6-*b*][1,2,4]triazepines (12a-e, 13a-e and 14a-e)

| Compound | MS (m/e $M^+$) | IR (KBr) ν ($cm^{-1}$) | $^1$H-NMRa ($CDCl_3$) δ (ppm) |
|---|---|---|---|
| **12a** | 476($M^+$94), 461(35), 443(10), 399(29), 371(12), 343(100), 332(8), 293(18), 278(68), 250(12), 240(50), 238(30), 174(17), 147(12), 120(10), 104(55), 77(83) | 1608 (C=N), 1548 (N=N) | 2.62 (3H, s, 11-$CH_3$), 2.71 (3H, s, 9-$CH_3$), 3.19 (3H, s, 4-$CH_3$), 8.62-8.58, 7.52-7.42 (10H, m, phenyl-H), 9.34 (1H, s, 6-H). |
| **12b** | 490($M^+$63), 475(22), 457(6), 399(16), 371(9), 343(62), 332(100), 293(25), 278(68), 250(8), 240(20), 229(23), 174(8), 104(4), 65(4). | 1603(C=N), 1549 (N=N) | 2.44 (3H, s, 4-$CH_3$ of phenyl), 2.66 (3H, s, 11-$CH_3$), 2.93 (3H, s, 9-$CH_3$), 3.09 (3H, s, 4-$CH_3$), 7.66 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 8.07 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 7.98-7.97, 7.87-7.84 (5H, m, phenyl-H), 9.97 (1H, s, 6-H). |
| **12c** | 533($M^+$40), 518(12), 500(8), 488(15), 399(14), 387(17), 371(24), 343(74), 332(45), 293(37), 278(100), 250(8), 240(24), 225(15), 170(9), 107(5), 104(5), 54(5). | 1693 (C=O), 1601 (C=N), 1551 (N=N) | 2.57 (3H, s, COCH3), 2.64 (3H, s, 11-$CH_3$), 3.12 (3H, s, 9-$CH_3$), 3.19 (3H, s, 4-$CH_3$), 8.11 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 8.25 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.58-8.55, 7.91-7.87 (5H, m, phenyl-H), 9.69 (1H, s, 6-H), 10.01 (1H, br, NH). |
| **12d** | 510($M^+$68), 495(28), 441(2), 417(10), 399(18), 371(11), 343(70), 332(19), 308(53), 293(24), 278(100), 250(10), 240(22), 235(9), 175(23), 127(8), 111(19), 77(8). | 1600(C=N), 1552 (N=N) | 2.98 (3H, s, 11-$CH_3$), 3.14 (3H, s, 9-$CH_3$), 3.20 (3H, s, 4-$CH_3$), 7.84 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.17 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 8.60-8.57, 7.92-7.89 (5H, m, phenyl-H), 9.71 (1H, s, 6-H). |
| **12e** | 521($M^+$18), 506(5), 399(2), 387(4), 371(2), 343(18), 332(68), 308(39), 293(28), 278(100), 250(5), 240(8), 190(5), 175(24), 104(4). | 1602 (C=N), 1551 (N=N) | 2.77 (3H, s, 11-$CH_3$), 2.83 (3H, s, 9-$CH_3$), 3.03 (3H, s, 4-$CH_3$), 7.87 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.33 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 8.51-8.45, 7.81-7.79 (5H, m, phenyl-H), 9.92 (1H, s, 6-H). |
| **13a** | 477($M^+$58), 407(1), 400(18), 385(10), 372(11), 332(11), 308(17), 304(19), 293(45), 278(65), 250(15), 239(10), 201(4), 190(24), 163(16), 120(6), 104(42), 77(100) | 3227 ($NH_2$), 1611 (C=N), 1549 (N=N) | 2.74 (3H, s, 9-$CH_3$), 2.99 (3H, s, 4-$CH_3$), 3.72 (2H, s, $NH_2$), 8.47-8.40, 7.90-7.54 (10H, m, phenyl-H), 9.45 (1H, s, 6-H). |

| | | | |
|---|---|---|---|
| **13b** | 491 ($M^+$65), 476(5), 463(5), 400(10), 372(8), 332(24), 317(7), 308(12), 293(100), 278(31), 245(12), 228(4), 190(29), 163(12), 147(11), 104(9), 91(11), 77(6). | 3223 ($NH_2$), 1606 (C=N), 1548 (N=N) | 2.50 (3H, s, 4-$CH_3$ of phenyl), 2.98 (3H, s, 9-$CH_3$), 3.02 (3H, s, 4-$CH_3$), 3.81 (2H, s, $NH_2$), 7.44 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 7.66 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.46-8.44, 7.79-7.76 (5H, m, phenyl-H), 9.46 (1H, s, 6-H). |
| **13c** | 534($M^+$31), 503(8), 491(8), 461(4), 400(4), 372(7), 332(20), 293(100), 278(42), 261(10), 190(28), 163(12), 104(9), 92(4). | 3241 ($NH_2$), 1690 (C=O), 1603 (C=N), 1553 (N=N) | 2.71 (3H, s, $COCH_3$), 2.81 (3H, s, 9-$CH_3$), 2.95 (3H, s, 4-$CH_3$), 4.18 (2H, s, $NH_2$), 8.34-8.30, 8.23-8.19 (7H, m, phenyl-H), 8.88 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 9.90 (1H, s, 6-H), 10.33 (1H, br, NH). |
| **13d** | 512($M^+$43), 438(4), 400(10), 372(8), 332(20), 293(100), 278(35), 255(9), 250(4), 190(28), 163(10), 111(10), 104(7), 66(4). | 3244 ($NH_2$), 1604 (C=N), 1554 (N=N) | 2.91 (3H, s, 9-$CH_3$), 2.95 (3H, s, 4-$CH_3$), 3.17 (2H, s, $NH_2$), 7.51 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 7.82 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 8.38-8.37, 7.72-7.66 (5H, m, phenyl-H), 9.39 (1H, s, 6-H). |

**Table 2 (continued)**

| **Compound** | **MS (m/e $M^+$)** | **IR (KBr) ν ($cm^{-1}$)** | **$^1$H-NMRa ($CDCl_3$) δ (ppm)** |
|---|---|---|---|
| **13e** | 522($M^+$25), 493(5), 410(1), 400(11), 385(16), 372(10), 341(11), 332(32), 293(84), 278(100), 251(18), 223(13), 212(5), 199(22), 190(22), 104(15), 566(8). | 3247 ($NH_2$), 1604 (C=N), 1554 (N=N) | 2.60 (3H, s, 9-$CH_3$), 3.10 (3H, s, 4-$CH_3$), 3.75 (2H, s, $NH_2$), 8.08 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.48 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 8.54-8.52, 7.87-7.82 (5H, m, phenyl-H), 9.56 (1H, s, 6-H). |
| **14a** | 436($M^+$20), 395(4), 350(6), 333(22), 308(12), 293(100), 278(9), 233(9), 243(6), 228(2), 212(8), 190(23), 163(11), 136(2), 104(5), 77(3). | 3225 ($NH_2$), 1606 (C=N), 1549 (N=N) | 2.76 (3H, s, 4-$CH_3$), 4.29 (2H, s, $NH_2$), 8.96-8.84, 8.41-8.26 (10H, m, phenyl-H), 9.34 (2H, d, J = 1.0 Hz, 3,5-H of pyridy), 9.53 (2H, d, J = 1.0 Hz, 2,6-H of pyridyl), 10.02 (1H, s, 6-H). |
| **14b** | 554($M^+$8), 436(60), 395(4), 333(11), 308(6), 293(100), 278(15), 251(5), 218(7), 190(30), 163(12), 104(5). | 3233 ($NH_2$), 1603 (C=N), 1551 (N=N) | 2.30 (3H, s, 4-$CH_3$ of phenyl), 2.75 (3H, s, 4-$CH_3$), 3.80 (2H, s, $NH_2$), 7.92 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.49-8.41, 7.81-7.79 (7H, m, phenyl-H), 8.88 (2H, d, J = 1.0 Hz, 3,5-H of pyridy), 9.05 (2H, d, J = 1.0 Hz, 2,6-H of pyridyl), 9.56 (1H, s, 6-H). |

| | | | |
|---|---|---|---|
| **14c** | 436($M^+$100), 395(22), 367(5), 333(7), 308(4), 293(67), 278(14), 265(7), 218(10), 190(15), 163(6), 103(4), 106(7). | 3241 ($NH_2$), 1691 (C=O), 1605 (C=N), 1553 (N=N) | 2.38 (3H, s, $COCH_3$), 3.10 (3H, s, 4-$CH_3$), 3.87 (2H, s, $NH_2$), 8.03-8.00, 7.91-7.88 (7H, m, phenyl-H), 8.49 (1H, br, NH), 8.56 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.95 (2H, d, J = 1.0 Hz, 3,5-H of pyridy), 9.14 (2H, d, J = 1.0 Hz, 2,6-H of pyridyl), 9.64 (1H, s, 6-H). |
| **14d** | 575($M^+$5), 436(100), 395(20), 350(8), 333(29), 308(24), 293(84), 278(37), 251(12), 218(9), 190(28), 163(9), 129(232), 104(11), 77(4). | 3239 ($NH_2$), 1606 (C=N), 1552 (N=N) | 2.40 (3H, s, 4-$CH_3$), 3.89 (2H, s, $NH_2$), 7.67 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.58 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 8.04-8.02, 7.93-7.91 (5H, m, phenyl-H), 9.16 (2H, d, J = 1.0 Hz, 3,5-H of pyridy), 9.23 (2H, d, J = 1.0 Hz, 2,6-H of pyridyl), 9.67 (1H, s, 6-H). |
| **14e** | 585($M^+$3), 436(41), 395(10), 380(4), 333(20), 308(12), 293(100), 278(28), 250(10), 243(6), 228(2), 190(30), 163(8), 138(9), 104(7), 77(3). | 3246 ($NH_2$), 1608 (C=N), 1553 (N=N) | 3.00 (3H, s, 4-$CH_3$), 3.83 (2H, s, $NH_2$), 7.89 (2H, d, J = 1.0 Hz, 2,6-H of phenyl), 8.03 (2H, d, J = 1.0 Hz, 3,5-H of phenyl), 8.44-8.32, 7.93-7.76 (5H, m, phenyl-H), 9.06 (2H, d, J = 1.0 Hz, 3,5-H of pyridy), 9.30 (2H, d, J = 1.0 Hz, 2,6-H of pyridyl), 9.51 (1H, s, 6-H). |

a Abbreviations : s, singlet; d, doublet; m, multiplet.

## Conclusions

In conclusion, a series of novel monoazo triazepine derivatives **12a-e**, **13a-e** and **14a-e** containing a pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine skeleton were obtained by the cyclization of 7-amino-8-imino-pyrimido[3,2:4,5]thieno[2,3-*d*]pyrimidine **5** with azobenzeneacetylacetones **7a-e** and arylazoenaminonitrile derivatives **9a-e** and **11a-e**, respectively. The structures of monoazo-triazepine derivatives **12a-e**, **13a-e** and **14a-e** were characterized by IR, $^1$H NMR, Mass, elemental analysis.

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