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# Synthesis of mesoionic[1,2,3]triazolo[5,1-*d*][1,2,5]triazepines

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**Abstract**—Intramolecular cyclization of 1-amino-3-phenacyl-4-carbohydrazido-1,2,3-triazolium-5-olates has been shown to take place via selective interaction of the carbonyl group with the terminal amino function of the hydrazido group to form a 1,2,5-triazepine ring. Minor products, resulting from the interaction of the α-nitrogen atom of the hydrazido group with the carbonyl function, having a N-amino-pyridazine structure were also detected and isolated. A general method for the synthesis of novel mesoionic 2-amino-7-aryl-4-oxo-2,4,5,8-tetrahydro[1,2,3]triazolo[5,1-*d*][1,2,5]triazepin-9-ium-3-olates was developed.


## 1. Introduction

Fused 1,2,5-triazepines with a bridgehead nitrogen atom in the molecule exhibit interesting biological properties.[1] At the same time, there are no examples of mesoionic compounds among publications concerning the synthesis of fused triazepines,[2] although mesoionic 1,2,3-triazoles fused to six-membered rings are known to exhibit various biological effects.[3] The latter prompted M. Furber and colleagues[4] to elaborate an efficient method to prepare 1,2,3-triazoles of mesoionic structure fused to quinazoline, quinoxaline and benzotriazine rings. However, this method did not give access to 1,2,3-triazoles fused to triazepine ring.

In this connection, we would like to report our recent results of a new synthetic approach towards novel mesoionic [1,2,3]triazolo[5,1-*d*][1,2,5]triazepines.

## 2. Results and discussion

The basic idea of our approach consists in the synthesis of 3-phenacyl-4-carbohydrazido-1,2,3-triazolium-5-olates which in subsequent cyclization of carbonyl and hydrazide groups should form the 1,2,5-triazepine ring. Earlier we have shown,[5] that alkylation of 1-aryl- and 1-amino-5-hydroxy-1*H*[1,2,3]triazoles with substituted phenacyl bromides leads solely to *N*-3 alkylated products of type **1** (Scheme 1). We proposed that triazolotriazepines **4** could be obtained in cyclization of mesoionic hydrazides of 3-phenacyl-1,2,3-triazolio-5-olate-4-carboxylic acid **3** (Scheme 1). However, it was found that the ester group at the position 4 of the triazole ring did not react with hydrazine hydrate. An attempt to obtain 1,2,3-triazole-4-carbonyl chloride **2** starting from esters **1** completely failed. Unfortunately, in both experiments the ethyl 1-substituted 5-hydroxy-1,2,3-triazole-4-carboxylate **1** was recovered unchanged, demonstrating the low reactivity of the ester group due to extensive conjugation with the olate function.

Therefore, the preparation of the desired hydrazide of type **3** was performed by a three-step synthesis starting from the protected hydrazide **5** (Scheme 2). A diazo group transfer reaction with hydrazide **5** allowed us prepare sodium 1*H*-1,2,3-triazole-5-olate **6** in good yield by adapting a literature protocol.[5]

When the triazolate **6** was reacted with substituted phenacyl bromides (Scheme 3), *N*-3 alkylated products **7** were generated. After dilution with water, the hydrolysis of one of the azomethine groups took place to form 1-amino-3-(*p*-*R*-phenacyl)-4-(*iso*-propylidencarboxamido)-1,2,3-triazolium-5-olate **8**. We managed to isolate intermediate **7e** (R=$CH_3O$), in good yield and then transformed this compound to 1-aminotriazolium-5-olate **8e** by subsequent hydrolysis.

Heating of compounds **8a**-**e** in a 0.1 N HCl solution leads to the removal of the second isopropylidene group to result in

*Keywords*: Fused mesoionic heterocycles; 1-Amino-1,2,3-triazolium-5-olate; [1,2,3]Triazolo[5,1-*d*][1,2,5]triazepine; [1,2,3]Triazolo[1,5-*a*]-pyrazine; Diazo group transfer; Alkylation.
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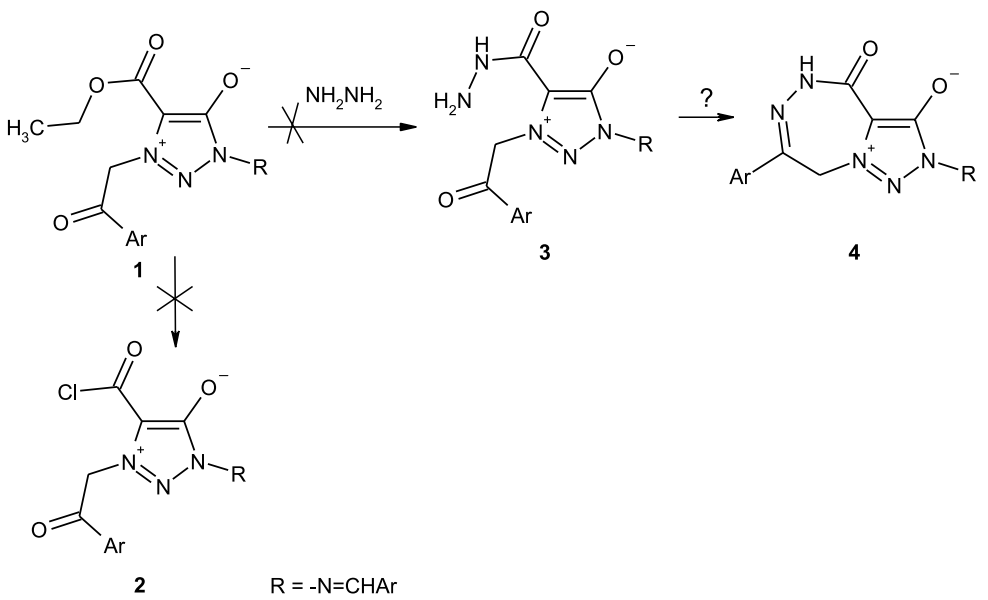
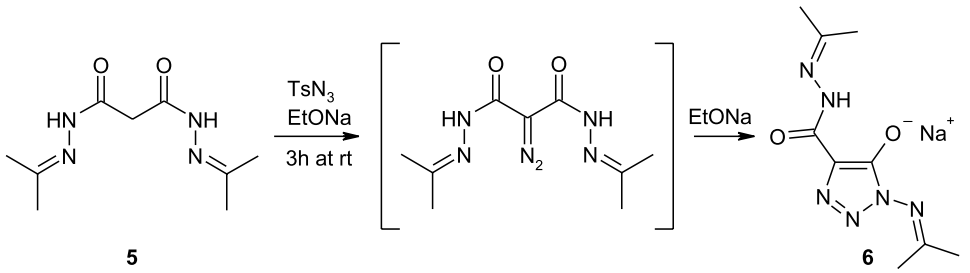
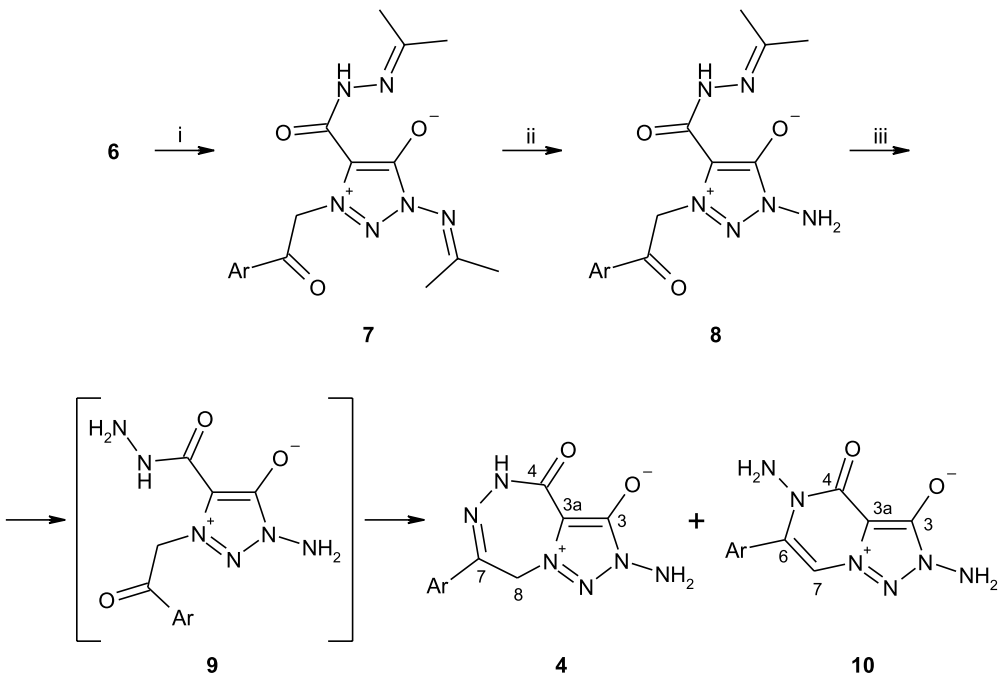



**Scheme 1.**




**Scheme 2.**




| 4, 7, 8, 9, 10 | a | b | c | d | e |
|---|---|---|---|---|---|
| Ar | $C_6H_5$ | p-$CH_3C_6H_4$ | p-$ClC_6H_4$ | p-$BrC_6H_4$ | p-$CH_3OC_6H_4$ |

**Scheme 3.** Reagents and conditions: (i), $ArCOCH_2Br$, DMF, 70 °C, 5 h; (ii) $H_2O$, rt, 1 h; (iii) 0.1 N HCl, 100 °C, 15 h.

**Table 1**. $^{13}C$ NMR (at 100 MHz in DMSO-$d_6$) chemical shifts (ppm) and coupling constants ($J$ (Hz))

| $\delta$ ($J$ (Hz)) | Compound | | | | |
|---|---|---|---|---|---|
| | **4a** | **4b** | **4c** | **4d** | **4e** |
| $C_3$ | 153.9 d<br>$^3J$=1.2 | 153.8 br. s<br>$\omega_{1/2}$=2.4 Hz | 153.9 d<br>$^3J$=1.2 | 153.9 d<br>$^3J$=1.3 | 153.8 s |
| $C_{3a}$ | 109.9 t<br>$^3J$=2.8 | 109.8 quintet<br>$^3J$=2.7 | 109.9 quintet<br>$^3J$=2.8 | 109.9 dt<br>$^3J$=3.1, $^3J$=3.5 | 109.9 quintet<br>$^3J$=3.1 |
| $C_4$ | 156.5 s | 156.5 s | 156.4 s | 156.3 s | 156.6 s |
| $C_7$ | 152.5 quintet<br>$^2J$=4.2 | 152.5 quintet<br>$^2J$=4.5 | 151.3 quintet<br>$^2J$=4.2 | 151.3 quintet<br>$^2J$=3.6 | 152.6 quintet<br>$^2J$=4.0 |
| $C_8$ | 48.9 t<br>$^1J$=147.4 | 48.8 t<br>$^1J$=147.5 | 48.8 t<br>$^1J$=147.5 | 48.7<br>$^1J$=148 | 48.8 t<br>$^1J$=147.5 |
| Arom. | 126.6, 128.9, 130.7, 133.9 | 126.5, 129.4, 131.0, 140.7 | 128.5, 128.9, 132.8, 135.5 | 128.6, 124.3, 124.3, 133.5 | 114.3, 126.0, 128.4, 161.4 |
| Subs. ($CH_3$) | — | 20.8 qt<br>$^1J$=126.6 | — | — | 55.4 q<br>$^1J$=144.8 |

the triazolohydrazides **9**, which undergo smooth cyclization in situ to the desired 2-amino-7-aryl-4-oxo-2,4,5,8-tetrahydro-[1,2,3]triazolo[5,1-*d*][1,2,5]triazepinium-3-olates **4a-e** in good yields. The $^1H$ and $^{13}C$ NMR spectral data for compound **4** corroborate the formation of the triazepine ring and are in a good accordance with its mesoionic structure[6] (Table 1).

Thus, for compounds **4**, splitting of signal $C_{3a}$ due to coupling with protons of the methylene group $C_8$ is observed. The carbon signals for the methylene group $C_8$ and $C_7$ of the triazepines **4** are shifted upfield in comparison with the signals of similar atoms of precursors **8**. The final structural proof for the compounds **4** prepared was given by X-ray diffraction data for crystals of **4d** grown from DMF (Fig. 1).[7]

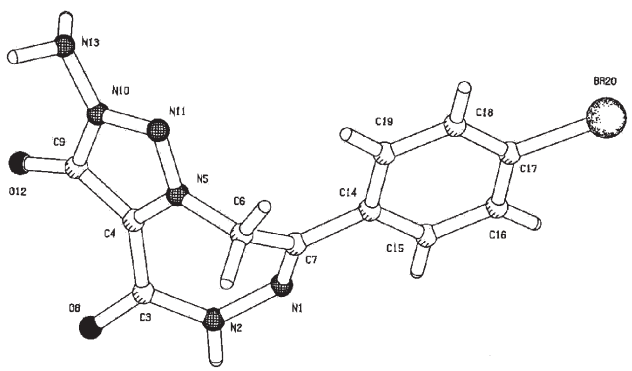



**Figure 1.** X-ray structure of **4d**.

The shape of molecule **4d** is determined by the boat conformation of the 7-membered ring. The phenyl ring makes an angle of 46.12(11)° with the 5-membered ring. The angle between the best planes through the 5- and 7-membered ring is 27.96(10)°. The asymmetric unit consists of one molecule **4d**, one DMF and one water molecules. These solvent molecules are involved in a hydrogen bond network with atoms N2, O8, N11, O12 and N13 (as numbered in Fig. 1).

It should be noted that the reaction described here represents the first example of the formation of the 1,2,5-triazepine ring due to intramolecular interaction of carbohydrazide and phenacyl functionalities.

It is known that both α- and β-nitrogen atoms of thiocarbohydrazide group can react with the phenacyl moiety leading to the formation of both seven- and six-membered heterocyclic compounds.[8] Careful study of the mother liquid of the reaction of compound **8** with HCl allowed us also to detect the presence of by-products, that were isolated in two cases. On the basis of elemental analyses and $^1H$ and $^{13}C$ NMR data (Table 2) the structures of the minor products were assigned as 2,5-diamino-6-aryl-4-oxo-4,5-dihydro-[1,2,3]triazolo[1,5-*a*]pyrazinium-3-olates **10c** and **10e**.

It is known that 1,4-dihydro-5*H*-[1,3,4]-benzo- and azolotriazepin-5-ones are capable of rearranging to isomeric benzopyrimidin-4(3*H*)-ones.[9] To determine the formation mechanism of triazolo[1,5-*a*]pyrazinium-3-olates **10**, we have treated triazepines **4** with diluted

**Table 2**. $^1H$, $^{13}C$ NMR (at 400 and 100 MHz in DMSO-$d_6$) chemical shifts (ppm) and coupling constants ($J$ (Hz))

| Atom/group | $^{13}C$ | | $^1H$ | |
|---|---|---|---|---|
| | **10c** | **10e** | **10c** | **10e** |
| $C_3$ | 154.4 s | 154.4 s | — | — |
| $C_{3a}$ | 107.3 d, $^3J$=5.3 | 107.2 d, $^3J$=4.3 | — | — |
| $C_4$ | 151.7 d, $^3J$=0.8 | 151.7 br. s, $\omega_{1/2}$=2.4 | — | — |
| $C_6$ | 139.1 dt, $^2J$=6.8 $^3J$=3.4 | 139.9 dt, $^2J$=6.3 $^3J$=3.2 | — | — |
| $C_7$ | 104.5 d, $^1J$=200.4 | 103.6 d, $^1J$=200 | 7.61, s | 7.52, s |
| Arom. | 127.7, 129.9, 131.6, 134.1 | 113.2, 123.2, 131.2, 160.1 | 7.53, d ($J$=8.7), 7.6, d ($J$=8.7) | 7.01, d ($J$=8.7), 7.53, d ($J$=8.7) |
| $CH_3$ | — | 55.3 q, $^1J$=144.6 | — | 3.81, s |
| $NH_2$ | — | — | 5.21, s[a] | 5.23, s[a] |
| $NH_2$ | — | — | 6.28, s[a] | 6.26, s[a] |

[a] Disappeared after adding of $D_3CCOOD$.

HCl. Triazepines **4** were found to be stable even after prolonged heating at reflux in a solution of 0.1 N HCl, and this confirms the formation of compounds **10** directly from hydrazide **9** and rejects the rearrangement mechanism for their formation.

In conclusion, intramolecular cyclization of 1-amino-3-phenacyl-4-carbohydrazido-1,2,3-triazolium-5-olates has been shown to take place via selective interaction of the carbonyl group with the terminal amino function of the hydrazido group to form a 1,2,5-triazepine ring. Minor products resulting from the interaction of the α-nitrogen atom of the hydrazido group with the carbonyl function, namely the N-amino-pyridazines were also detected. A general method for the synthesis of novel mesoionic 2-amino-7-aryl-4-oxo-2,4,5,8-tetrahydro[1,2,3]triazolo [5,1-*d*][1,2,5]triazepin-9-ium-3-olates was developed.

## 3. Experimental

### 3.1. General

Melting points are uncorrected. The $^1$H and $^{13}$C NMR spectra were recorded in DMSO-$d_6$ solution with Bruker DRX-400, 400 MHz or Bruker WM-250, 250 MHz for $^1$H and 100 MHz for $^{13}$C, using TMS as internal standard. Infrared spectra were recorded in KBr on a UR-20 spectrometer. Mass spectra were recorded using Finnigan MAT 8200 instrument.

**3.1.1. Bis(1-methylethylidene)malonhydrazide (5).** A suspension of 10 g (0.76 mol) of malonhydrazide in 100 ml of acetone was refluxed for 2 h. The solid compound **5** was filtered off and washed with 15 ml of ethanol and dried in vacuum. Yield 15.5 g (98%); mp 163–5 °C. [Found C, 50.85, H, 7.53, N, 26.15. $C_9H_{16}N_4O_2$ requires: C, 50.93, H, 7.60, N, 26.40].

**3.1.2. Synthesis of sodium 1-[(1-methylethylidene) amino]-4-{[2-(1-methylethylidene) hydrazino]carbonyl}-1*H*-1,2,3-triazol-5-olate (6).** The N′$^1$,N′$^3$-bis(1-methylethylidene)-malonohydrazide **5** (9.96 g, 0.047 mol) was suspended in a solution of sodium ethoxide (3.196 g, 0.047 mol) in 20 ml of dry ethanol, and tosyl azide (9.26 g, 0.047 mol) was added in a dropwise manner at 0–5 °C. The reaction mixture was stirred for 2 h. After cooling, the precipitate **6** was filtered off, washed with chloroform and dried. Yield 11.45 g (75%); mp 202–204 °C; $\nu$ (cm$^{-1}$): 1650, 1610 (CO). [Found: C 40.17, H 5.33, N 32.84. $C_9H_{13}N_6NaO_2$. requires: C 41.54, H 5.04, N 32.29]; $^1$H NMR (250 MHz) $\delta$: 11.27 (1H, br. s, NH), 2.13 (3H, s, Me), 1.96 (3H, s, Me), 1.94 (3H, s, Me), 1.84 (3H, s, Me).

### 3.2. Synthesis of 1-amino-3-(*p*-*R*-phenacyl)-4-{[2-(1-methylethylidene)hydrazino]carbonyl}-[1,2,3]-triazolium-5-olates (8a-d)

*General procedure*. A solution of sodium salt **6** (16 mmol) and an equivalent amount of the corresponding phenacyl bromide in 10 ml of DMF was heated at 70° for 3 h, cooled to room temperature and diluted with 15 ml of water. After 1 h, the solid of **8a-d** was filtered off, washed with water, dried and crystallized from chloroform (**8b**), from toluene (**8c**, **d**) or from ethanol (**8a**).

**3.2.1. 1-Amino-4-{[2-(1-methylethylidene)hydrazino]-carbonyl}-3-phenacyl-1*H*-1,2,3-triazol-3-ium-5-olate (8a).** Yield 2.28 g (45%); mp 234–236 °C; MS, *m*/*z*: 316 (54%, M$^+$). [Found: C 53.10, H 4.97, N 26.55. $C_{14}H_{16}N_6O_3$. requires: C 53.16, H 5.10, N 26.57]; $^1$H NMR (250 MHz) $\delta$: 1.92 (3H, s, $CH_3$), 1.98 (3H, s, $CH_3$), 6.2 (2H, s, $COCH_2$), 6.4 (2H, s, $NH_2$), 7.57 (2H, t, *J*=7.3 Hz, Ph), 7.67 (1H, t, *J*=7.3 Hz, Ph), 8.04 (2H, d, *J*=7.3 Hz, Ph), 10.89 (1H, s, NH).

**3.2.2. 1-Amino-4-{[2-(1-methylethylidene)hydrazino]-carbonyl}-3-(4-methylphenacyl)-1*H*-1,2,3-triazol-3-ium-5-olate (8b).** Yield 2.96 g (56%); mp 225–228 °C; MS, *m*/*z*: 330 (16%, M$^+$); $\nu$ (cm$^{-1}$): 3272, 3175 (NH), 3060, 3030, 2990, 2940 (CH), 1660, 1640 (CO), 1600, 1550. [Found: C 54.27, H 5.38, N 25.64. $C_{15}H_{18}N_6O_3$. requires: C 54.53, H 5.49, N 25.44]; $^1$H NMR (250 MHz) $\delta$: 1.90 (3H, s, $CH_3$), 1.95 (3H, s, $CH_3$), 2.43 (3H, s, $CH_3$Ar), 6.22 (2H, s, $CH_2$), 6.54 (2H, s, $NH_2$), 7.42 (2H, d, *J*=8.1 Hz, ArH), 7.94 (2H, d, *J*=8.1 Hz, ArH), 10.93 (1H, br. s., NH). $^{13}$C NMR (100 MHz) $\delta$: 16.5 (qq, $CH_3$, *J*=127 Hz), 21.2 (q, $CH_3$-*p*, *J*=131 Hz), 24.4 (qq, $CH_3$, *J*=127.5 Hz), 58.7 (t, $CH_2$, *J*=144.9 Hz), 110.1 (quint, C(4), *J*=1.7 Hz), 128.3 (dd, Ar, *J*=161.8 ,6.4 Hz), 129.4 (dm, Ar, *J*=161.4, 5.8 Hz), 131.5 (t, Ar, *J*=7.4 Hz), 144.9 (m, Ar), 153.6 (d, NCO, *J*=6.8 Hz), 154.2 (s, C(5)), 154.3 (m, C=N), 189.9 (d, CO, *J*=4.2 Hz).

**3.2.3. 1-Amino-3-(4-chlorophenacyl)-4-{[2-(1-methylethylidene)hydrazino]-carbonyl}-1*H*-1,2,3-triazol-3-ium-5-olate (8c).** Yield 4.32 g (77%); MS, *m*/*z*: 350 (36%, M$^+$). [Found: C 47.90, H 5.08, N 23.88. $C_{14}H_{15}ClN_6O_3$. requires: C 47.94, H 4.31, Cl 10.11, N 23.96]; $^1$H NMR (250 MHz) $\delta$: 1.91 (3H, s, $CH_3$), 1.97 (3H, s, $CH_3$), 6.19 (2H, s, $CH_2$), 6.46 (2H, s, $NH_2$), 7.63 (2H, d, *J*=8.5 Hz, ArH), 8.05 (2H, d, *J*=8.5 Hz, ArH), 10.88 (1H, br. s., NH). $^{13}$C NMR (100 MHz) $\delta$: 16.5 (q, $CH_3$, *J*=127.7, 3.1 Hz), 24.8 (q, $CH_3$, *J*=127.5, 2.9 Hz), 58.8 (t, $CH_2$, *J*=144.8 Hz), 109.9 (m, C(4), *J*=1.4 Hz), 129.1 (dd, Ph, *J*=169.1, 5.1 Hz), 130.1 (dd, Ph, *J*=164.5, 6.9 Hz), 132.8 (t, Ph, *J*=7.4 Hz), 139.2 (t, Ar, *J*=10.9, 3.03 Hz), 153.5 (d, NCO, *J*=7.1 Hz), 154.2 (s, C(5)), 154.3 (m, C=N, *J*=6.6, 3.7 Hz), 189.8 (t, CO, *J*=4.2 Hz).

**3.2.4. 1-Amino-3-4-bromophenacyl)-4-{[2-(1-methylethylidene)hydrazino]-carbonyl}-1*H*-1,2,3-triazol-3-ium-5-olate (8d).** Yield 4.43 g (79%); MS, *m*/*z*: (%, M$^+$). [Found: C, 42.58, H, 3.84, N, 21.22. $C_{14}H_{15}BrN_6O_3$. requires: C, 42.55, H, 3.83, N, 21.26]; $^1$H NMR (250 MHz) $\delta$: 1.92 (3H, s, $CH_3$), 1.97 (3H, s, $CH_3$), 6.17 (2H, s, $CH_2$), 6.45 (2H, s, $NH_2$), 7.66 (2H, d, *J*=8.3 Hz, ArH), 8.12 (2H, d, *J*=8.3 Hz, ArH), 10.87 (1H, br. s., NH). $^{13}$C NMR (100 MHz) $\delta$: 16.5 (q, $CH_3$, *J*=127.7, 3.1 Hz), 24.8 (q, $CH_3$, *J*=127.5, 2.9 Hz), 58.8 (t, $CH_2$, *J*=144.8 Hz), 109.9 (m, C(4), *J*=1.4 Hz), 129.1 (dd, Ph, *J*=169.1, 5.1 Hz), 130.1 (dd, Ph, *J*=164.5, 6.9 Hz), 132.8 (t, Ph, *J*=7.4 Hz), 139.2 (t, Ar, *J*=10.9, 3.03 Hz), 153.5 (d, NCO, *J*=7.1 Hz), 154.2 (s, C(5)), 154.3 (m, C=N, *J*=6.6, 3.7 Hz), 189.8 (t, CO, *J*=4.2 Hz).

### 3.3. Synthesis of 7e, 8e

A solution of sodium salt **6** (9.03 g, 35 mmol) and *p*-methoxyphenacyl bromide (8.15 g, 35 mmol) in DMF (5 ml) was heated at 70° for 3 h, cooled to room temperature and **7e** was filtered off from the reaction mixture, washed with DMF, dried and crystallized from ethanol. The filtrate was mixed with of water (20 ml). After 1 h, the solid **8e** was filtered off, washed with water, dried and crystallized from chloroform (Method A). Alternatively, a suspension of **7e** (6.02 g) in 50 ml water was heated at reflux for 0.5 h and evaporated under reduced pressure (Method B). The crude **8e** was purified as for method A.

**3.3.1. 3-[(3-Methoxyphenacyl)-1-[(1-methylethylidene) amino]-4-{[2-(1-methylethylidene)hydrazino]carbonyl}-1*H*-1,2,3-triazol-3-ium-5-olate (7e).** Yield 6.62 g (49%); mp 165–168 °C; MS, *m*/*z*: 386 (34%, $M^{+\cdot}$). [Found: C, 56.02, H, 5.56, N, 21.59. $C_{18}H_{22}N_6O_4$ requires: C, 55.96, H, 5.70, N, 21.76]; $^1$H NMR (250 MHz) $\delta$: 1.91 (3H, s, $CH_3$), 1.98 (3H, s, $CH_3$), 2.07 (3H, s, $CH_3$), 2.31 (3H, s, $CH_3$), 3.89 (3H, s, $OCH_3$), 6.20 (2H, s, $CH_2$), 7.06 (2H, d, ArH, *J*=8.8 Hz), 8.1 (2H, d, ArH, *J*=8.8 Hz), 10.83 (1H, s, NH).

**3.3.2. 1-Amino-3-(4-methoxyphenacyl)-4-{[2-(1-methylidene)hydrazino]-carbonyl}-1*H*-1,2,3-triazol-3-ium-5-olate (8e).** Yield 4.34 g (36%); mp 200–205 °C (subl.); MS, *m*/*z*: 346 (32%, $M^+$). [Found: C, 52.16, H, 5.06, N, 24.20. $C_{15}H_{18}N_6O_4$ requires: C, 52.02, H, 5.20, N, 24.28]; $^1$H NMR (250 MHz) $\delta$: 1.91 (3H, s, $CH_3$), 1.97 (3H, s, $CH_3$), 3.88 (3H, s, $OCH_3$), 6.14 (2H, s, $CH_2$), 6.40 (2H, s, NH), 7.04 (2H, d, ArH, *J*=8.9 Hz), 7.95 (2H, d, ArH, *J*=8.9 Hz), 10.90 (1H, s, NH). $^{13}$C NMR (100 MHz) $\delta$: 16.5 (q, $CH_3$, *J*=127.5 Hz), 24.8 (q, $CH_3$, *J*=127.3 Hz), 55.7 (q, $OCH_3$, *J*=145.6 Hz), 58.5 (t, $CH_2$, *J*=144.8 Hz), 110.2 (s, C(4)), 114.2 (dd, C(m), *J*=162.8, 4.6 Hz), 126.8 (t, C(i), *J*=7.3 Hz), 130.6 (dd, C(o), *J*=161.6, 7.1 Hz), 153.5 (d, NCO, *J*=6.9 Hz), 154.3 (m, C=N), 154.8 (s, C(5)), 188.7 (q, CO).

### 3.4. Synthesis of triazolotriazepines 4a-e

*General procedure*. A suspension of hydrazone **8** (1.0 mmol) in diluted HCl (100 ml, 0.1 N) was heated at reflux for 15 h, and then the reaction mixture was concentrated at reduced pressure to 5 ml. After cooling, product **4** was filtered off and washed with water up to neutral pH.

**3.4.1. 2-Amino-4-oxo-7-phenyl-2,4,5,8-tetrahydro[1,2,3]-triazolo[5,1-*d*][1,2,5]triazepin-9-ium-3-olate (4a).** Yield 0.24 g (93%); mp 273–276 °C (decomp.); MS, *m*/*z*: 258 (57%, $M^+$). [Found: C, 51.13, H, 3.88, N, 32.52. $C_{11}H_{10}N_6O_2$ requires: C, 51.16, H, 3.90, N, 32.54]; $^1$H NMR (250 MHz) $\delta$: 5.57 (2H, s, $CH_2$), 6.06 (2H, br. s, $NH_2$), 7.45 (3H, m, Ph), 7.86 (2H, m, Ph), 11.01 (1H, s, NH).

**3.4.2. 2-Amino-7-(4-methylphenyl)-4-oxo-2,4,5,8-tetrahydro[1,2,3]triazolo[5,1-*d*][1,2,5]-triazepin-9-ium-3-olate (4b).** Yield 0.30 g (88%); mp 294–296 °C; MS, *m*/*z*: 272 (49%, $M^+$); $\nu$ ($cm^{-1}$): 3440, 3330, 3225, 3122 (NH), 3070, 3047, 3010, 2917 (CH), 1690, 1641 (CO), 1600. [Found: C, 52.72, H, 4.53, N, 30.78. $C_{15}H_{18}N_6O_4$ requires: C, 52.94, H, 4.44, N, 30.87]; $^1$H NMR (250 MHz) $\delta$: 2.35 (3H, s, $CH_3$), 5.59 (2H, s, $CH_2$), 6.16 (2H, s, $NH_2$), 7.30 (2H, d, *J*=8.2 Hz, ArH), 7.77 (2H, d, *J*=8.2 Hz, ArH), 11.04 (1H, s, NH).

**3.4.3. 2-Amino-7-(4-chlorophenyl)-4-oxo-2,4,5,8-tetrahydro[1,2,3]triazolo[5,1-*d*][1,2,5]-triazepin-9-ium-3-olate (4c).** Yield 0.26 g (90%); mp 268–271 °C (decomp.); MS, *m*/*z*: 292 (54%, $M^+$). [Found: C, 45.08, H, 3.08, N, 28.68. $C_{11}H_9ClN_6O_2$ requires: C, 45.14, H, 3.10, N, 28.71]; $^1$H NMR (250 MHz) $\delta$: 5.58 (2H, s, $CH_2$), 6.09 (2H, s, $NH_2$), 7.47 (2H, d, *J*=8.5 Hz, ArH), 7.88 (2H, d, *J*=8.5 Hz, ArH), 11.07 (1H, s, NH).

**3.4.4. 2-Amino-7-(4-bromophenyl)-4-oxo-2,4,5,8-tetrahydro[1,2,3]triazolo[5,1-*d*][1,2,5]-triazepin-9-ium-3-olate (4d).** Yield 0.27 g (93%); mp 272–274 °C (decomp.); MS, *m*/*z*: 336 (59%, $M^{-1}$), 338 (58%, $M^{+1}$). [Found: C, 39.15, H, 2.66, N, 24.90. $C_{11}H_9BrN_6O_2$ requires: C, 39.19, H, 2.69, N, 24.93]; $^1$H NMR (250 MHz) $\delta$: 5.57 (2H, s, $CH_2$), 6.07 (2H, br. s, $NH_2$), 7.61 (2H, d, *J*=8.8 Hz, ArH), 7.81 (2H, d, *J*=8.8 Hz, ArH), 11.07 (1H, s, NH).

**3.4.5. 2-Amino-7-(4-methoxyphenyl)-4-oxo-2,4,5,8-tetrahydro[1,2,3]triazolo[5,1-*d*][1,2,5]-triazepin-9-ium-3-olate (4e).** Yield 0.25 g (87%); mp 283–286 °C (decomp.); MS, *m*/*z*: 288 (89%, $M^+$). [Found: C, 49.98, H, 4.12, N, 29.13. $C_{12}H_{12}N_6O_3$ requires: C, 50.00, H, 4.20, N, 29.15]; $^1$H NMR (250 MHz) $\delta$: 3.82 (3H, s, $OCH_3$), 5.50 (2H, s, $CH_2$), 5.98 (2H, br. s, $NH_2$), 6.97 (2H, d, *J*=9.0 Hz, ArH), 7.80 (2H, d, *J*=9.0 Hz, ArH), 10.71 (1H, s, NH).

### 3.5. Isolation of triazolopyrazines 10c,e

The water filtrate from **4c**,**e** was concentrated under reduced pressure to yield crude **10c**,**e**, which was than purified by crystallization from ethanol.

**3.5.1. 2,5-Diamino-6-(4-chlorophenyl)-4-oxo-4,5-dihydro-2*H*-[1,2,3]triazolo[1,5-*a*]pyrazin-8-ium-3-olate (10c).** Yield 0.022 g (7%); mp >250 °C (decomp.); MS, *m*/*z*: 292 (27%, $M^+$). [Found: C, 45.17, H, 3.14, N, 28.64. $C_{11}H_9ClN_6O_2$ requires: C, 45.14, H, 3.10, N, 28.71].

**3.5.2. 2,5-Diamino-6-(4-methoxyphenyl)-4-oxo-4,5-dihydro-2*H*-[1,2,3]triazolo[1,5-*a*]pyrazin-8-ium-3-olate (10e).** Yield 0.015 g (5%); mp >250 °C (decomp.); MS, *m*/*z*: 288 (30%, $M^+$). [Found: C, 50.11, H, 4.29, N, 29.13. $C_{12}H_{12}N_6O_3$ requires: C, 50.00, H, 4.20, N, 29.15].

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7. Crystal structure determination of triazolotriazepine **4d**. The compound $C_{11}H_9BrN_6O_2$ was recrystallized from DMF. Crystal data: crystal dimensions 0.30×0.20×0.10 mm, triclinic, *P*-1, $a$=6.6964(5), $b$=9.0098(6), $c$=15.6736(9) Å, $\alpha$=78.936(4), $\beta$=79.551(6), $\gamma$=76.967(6)°, $V$=894.68(11) Å$^3$, $Z$=2, $\rho_{calcd}$=1.590 g cm$^{-3}$, $2\theta_{max}$=142.2°, $\mu$(Cu $_{K\alpha}$)=3.464 cm$^{-1}$, Bruker SMART 6000 detector, $Cu_{K\alpha}$ ($\lambda$=1.54178 Å), crossed Göbel mirrors, $T$=100 K, 7789 measured reflections, 3242 independent reflections. The data were corrected for Lorentz and polarization effects. Structure solved by direct methods, asymmetric unit contains also one DMF and one water molecule. Full-matrix least-squares refinement based on $|F^2|$, 252 parameters, OH and NH hydrogen atoms located from difference density map, other hydrogen atoms placed at calculated positions and refined in riding mode with temperature factors 20% higher than parent atom, $R1$=0.0467 (for 2901 data with $I>2\sigma(I)$), $wR2$=0.1264, max./min. residual electron density 0.61/−0.84 e$^-$ Å$^{-3}$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-227138. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

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