SHORT PAPER

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Regioselective synthesis of [1,2,4]triazolo[3,2-*b*][2,4]benzothiazepin-10(5*H*)-ones: a new heterocyclic ring system†

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[1,2,4]Triazolo[3,2-b][2,4]benzothiazepin-10(5H)-ones, members of a novel heterocyclic ring system, are synthesised in a regioselective manner *via* reaction of unsubstituted or substituted 1,2,4-triazole-3-thiones with 2-chloromethylbenzoyl chloride in good yields.

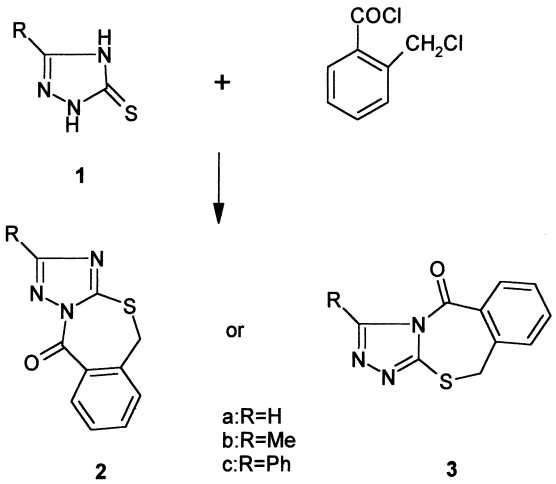
Keywords: fused 2,4-benzothiazepinones, 1,2,4 -triazole-3-thiones, regioselectivity

[1,2,4]Triazolobenzothiazepines are a class of fused heterocycles of considerable interest owing to the remarkable diversity of their biological activities.[1,2] A number of these compounds have been considered as potential CNS depressants[3,4], analgesics[5], anti-HIV-1 agents[6], tranquillisers and anti convulsants.[7]

Among the variety of triazolobenzothiazepine systems which have been prepared, the [1,2,4]triazolo[3,2-*b*][2,4]benzothiazepin-10(5*H*)-one (**2**) is notable by its absence. This paper describes the synthesis of some derivatives of this new heterocyclic system.

As shown in Scheme 1, 1,2,4 -triazole-3-thiones (**1a–c**) were used as starting materials. The reaction of 2-chloromethylbenzoyl chloride[8] with **1a** gave a product which may have had structure **2a** or **3a**.

An unequivocal decision between structures **2a** and **3a** was possible with the help of X-ray analysis made with the unsubstituted derivative, synthesised from the known 1,2,4-triazole-3-thione[9] (**1a**). Figure 1 shows the molecular structure and the atom labelling of the triazolobenzothiazepinone. The X-ray determination clearly shows the structure to be that of **2a**.



Scheme 1

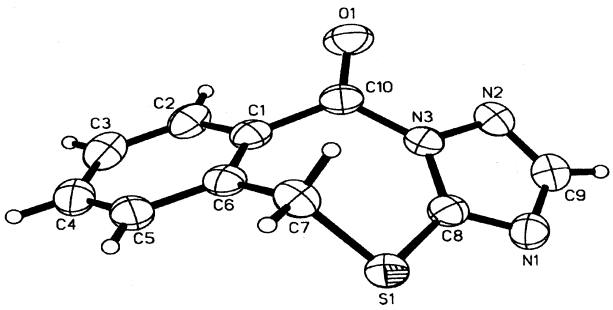


Fig. 1 ORTEP diagram for [1,2,4]triazolo[3,2-b][2,4]benzothiazepin-10(5H)-one **(2a)**. (The data are available from the authors on request.)

Repeating the above reaction with other 1,2,4-triazoles **1b**,**c**, led to **2b** and **2c** respectively, both representatives of the [1,2,4]triazolo[3,2-*b*][2,4]benzothiazepin-10(5*H*)-one system. The proof for the structures of the products was based on analogy with derivative **2a**. Thus, the thiazepinone ring was characterised by a CH_2 group in the ^1H NMR spectra at δ = 4.22–4.52 (in d_6-DMSO solution) and a C=O group in the IR spectra at 1718-1695 cm^{-1}.

In conclusion: we describe a simple one-pot regioselective transformation of 1,2,4-triazole-3-thiones to [1,2,4]triazolo[2,4]benzothiazepin-10(5*H*)-ones which is surely capable of extension to other heterocyclic systems.

Experimental

Melting points were recorded on an Electrothermal type 9100 melting point apparatus. The IR spectra were obtained on a 4300 Shimadzu spectrometer. The ^1H NMR (100 MHz) spectra were recorded on a Bruker AC 100 spectrometer. Mass spectra were scanned on a Varian Mat CH-7 instrument at 70 ev. Microanalyses were performed at Tarbiat Modares University, Tehran, Iran. Compounds **1a**, **1b** and **1c** were prepared by the published procedures of refs 9, 10 and 11 respectively.

General procedure for the preparation of triazolobenzothiazepinones **2a–c**: 2-Chloromethylbenzoyl chloride (0.4 ml) was added dropwise to a suspension of 1,2,4-triazole-3-thiones **1a–c** (3 mmol) in boiling acetonitrile. The mixture was refluxed for 3 hours. The solution was filtered while hot and the filtrate then refrigerated. The precipitate was collected and recrystallised from a suitable solvent, to give **2a–c** in 65, 70 and 58% yields respectively.

[1,2,4]Triazolo[3,2-b][2,4]benzothiazepin-10(5H)-one (**2a**): This compound was obtained as white crystals (acetone), m.p. 214–216 °C. ^1H NMR: δ (d_6-DMSO), 4.56 (s, 2H, S-CH_2), 7.65 (m, 4H, C_6H_4), 8.24 (s, 1H, N=CH). IR (KBr disc):$\nu_{C=O}$ 1718 cm^{-1}. MS: *m/z*

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(%) 217 (2), 216 (7), 215 (13), 214 (88), 186 (25), 185 (63), 118 (50), 90 (100), 89 (50), 71 (44).

Anal: Calcd.for $C_{10}H_7N_3OS$: C, 55.28; H,3.25; N, 19.34; S, 14.76. Found: C, 55.2; H, 3.17; N, 19.38; S, 14.80%.

2-Methyl[1,2,4]triazolo[3,2-b][2,4]benzothiazepin-10(5H)-one (**2b**): white crystals (acetonitrile), m.p. 249–251 °C. ^{1}H NMR (d_6-DMSO): 2.28 (s, 3H, Me), 4.53 (s, 2H, S-CH_2), 7.62 (m, 4H, C_6H_4). IR (KBr disc): $\nu_{C=O}$ 1695 cm^{-1}. MS: *m*/*z* (%) 231 (3), 230 (7), 229 (36), 201 (48), 200 (100), 133 (21), 118 (38), 91 (91), 90 (54).

Anal: Calcd. for $C_{11}H_9N_3OS$: C, 57.13; H, 3.92; N, 18.17; S, 13.86. Found: C, 57.34; H, 3.91; N, 18.25; S, 13.92%.

2-Phenyl[1,2,4]triazolo[3,2-b][2,4]benzothiazepin-10(5H)-one (**2c**): white crystals (acetonitrile), m.p. 176–178 °C. ^{1}H NMR: (d_6-DMSO), δ 4.62 (s, 2H, S-CH_2), 7.4–8.0 (m, 9H, Ph and C_6H_4). IR (KBr disc): $\nu_{C=O}$, 1710 cm^{-1}. MS: *m*/*z* (%) 293 (3), 292 (8), 291 (20), 290 (100), 262 (38), 151 (95), 124 (65), 88 (48), 36 (83).

Anal: Calcd.for $C_{16}H_{11}N_3OS$: C, 65.51; H, 3.78; N, 14.32; S, 10.93. Found: C, 65.54; H, 3.74;N, 14.33; S, 10.96%.

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