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NOTE

Use of 1,5-diaminotetrazole in the synthesis of some fused heterocyclic compounds

Mamdouh A. M. Taha

Department of Chemistry, Faculty of Science, Cairo University at Faiyoum, Egypt

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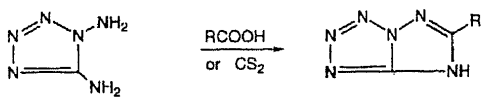
1,5-Diaminotetrazole was reacted in 'one-pot' with one carbon cyclizing reagents to afford the corresponding 1,2,4-triazolo[1,5-*d*]tetrazoles. Analogues reactions with nitrous acid, benzil, diethyl oxalate, pyruvic acid and ethyl acetoacetate afforded tetrazolo-heterocycles for biological interest.

Several publications have dealt with the synthesis of fused tetrazole derivatives[1-8]. Numerous biological properties were reported for tetrazoloheterocycles, such as being useful as antiallergic[9], antiulcer[9], antiinflammatory[10], analgesic[10], bronchodilating[10], bactericidal[10], hypotensive[11] and pesticidal[12] activities. In the light of these findings, the present work describes 'one-pot' construction of the novel tetrazoloheterocycles viz. 1,5-diaminotetrazole with the aim of developing certain fused heterocycles for potential pharmacological activities.

Results and discussion

The required 1,2,4-triazolotetrazoles were prepared via efficient synthetic routes[13,14]. In the present investigation, 'one-pot' construction of the 1,2,4-triazolotetrazoles from 1,5-diaminotetrazole[7] (**1**) in the first instance, is developed. Thus, **1** reacted with formic acid, acetic acid or aromatic acids to yield the 7*H*-1,2,4-triazolo[1,5-*d*]tetrazoles (**2-4**) through the dehydrative cyclization of the unisoluble intermediates. Similarly, the reaction of **1** with carbon disulfide in presence of pyridine afforded 6-mercapto-7*H*-1,2,4-triazolo[1,5-*d*]tetrazole (**5**) via H_2S elimination (Scheme 1). The structures of all new compounds were confirmed by elemental and spectroscopic data (IR, ^{1}H NMR and MS; *cf.* Experimental).

In many cases, the action of nitrous acid with hydrazino-heterocycles are well known. However, in some

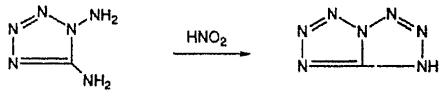


1 2-5

2 R = H; 3 R = CH_3; 4a R = C_6H_5, b R = *p*(Br)C_6H_4, c R = *p*(Cl)C_6H_4, d R = *p*(OCH_3)C_6H_4, e R = *p*(NO_2)C_6H_4, 5 R = SH

Scheme 1

of these reactions, it cannot be predicted with certainty whether the final product would involve the formation of a tetrazole ring system[15-17] or an azido function[18,19] may be considered as existing in a tautomeric equilibrium with tetrazole system[20]. Consequently, it was of interest to develop of synthetic methods for construction of tetrazolo nucleus. Compound **1** was readily coupled with sodium nitrite in HCl solution to yield structure **6**. The ^{1}H NMR spectrum of **6** revealed the disappearance of the signal at 5.6 ppm

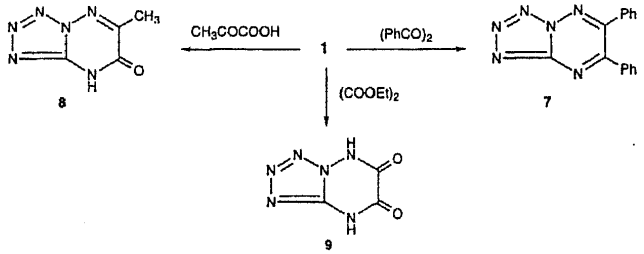


1 6

Scheme 2

characteristic of NH_2 protons of authentic sample **1** (Scheme 2).

Results reported in the literature on the synthesis of tetrazole[1,5-*b*]1,2,4-triazines has usually been performed to be two routes. The first[15,21] was to fuse the tetrazole ring on 1,2,4-triazine nucleus and the second[6] was to fuse the 1,2,4-triazine to a tetrazole foundation. In addition, the structures of tetrazolo[1,5-*b*]1,2,4-triazines (**7-9**) was performed by the reaction of **1** with benzil, pyruvic acid, or diethyl oxalate (Scheme 3). The elemental analyses and spec-

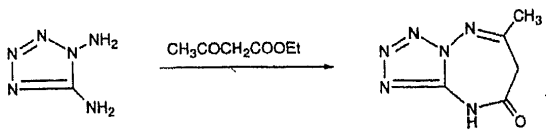


8 7 9

Scheme 3

troscopic techniques are consistent with the assigned structures.

Finally, the tetrazolo[1,5-*b*]1,2,4-triazepine has already been synthesized by Graponik and Karavai[7]. Accordingly, compound **1** reacted with ethyl acetoacetate to yield the 6-



1 10

Scheme 4

methyl-6-tetrazolo[1,5-*b*]triazepin-8(9*H*) one (**10**) (Scheme 4). The structure **10** was established on the basis of their elemental and spectroscopic data (*cf.* Experimental).

In conclusion, it seems that the results extend and broaden the knowledge in the synthesis of tetrazolo-heterocycles via 1,5-diaminotetrazole with different reagents. The obtained products are promising for biological evaluation studies.

Experimental

Melting points are uncorrected. IR spectra (KBr), Pye-Unicam SP 3-300, ν in cm^{-1}, ^1H NMR spectra (DMSO-d_6), Varian Mercury 300 MHz spectrometer, TMS as internal standard, chemical shifts in δ (ppm). Mass spectra, Shimadzu GCMS-QP 100 EX mass spectometer operating at 70 eV. All compounds gave satisfactory C, H and N analyses. 1,5-Diaminotetrazole[7] (**1**) was prepared according to the literature.

7H-1,2,4-Triazolo[1,5-d] (**2**) : A mixture of **1** (0.01 mol) and formic acid (10 ml) was refluxed for 1 h, then left to cool down to room temperature. The separated crystalline product was collected by filtration and dried then recrystallized from ethanol. Yield 0.8 g (73%), m.p. 195°C; IR 3256 (NH); ^1H NMR 12.8 (1H, s, NH), 4.2 (1H, s, CH triazole ring).

6-Methyl-7H-1,2,4-triazolo[1,5-d]tetrazole (**3**) : A solution of **1** (0.01 mol) in glacial acetic acid (10 ml) was boiled under reflux for 30 min and the solvent evaporated *in vacuo*. The reaction mixture was triturated with H_2O; the solid product was filtered off, washed with H_2O, dried and crystallized from ethanol. Yield 0.7 g (57%), m.p. 185°C; ^1H NMR 12.5 (1H, s, NH), 1.3 (3H, s, CH_3); MS *m/z* (%) = 125 (M^+ + 1, 16%).

General procedure for the preparation of 6-aryl-7H-1,2,4-triazolo[1,5-d]tetrazoles (**4a-e**) : A solution of **1** (0.01 mol) and the appropriate aromatic acid, namely, benzoic acid, *p*-bromo-, *p*-chloro-, *p*-methoxy- or *p*-nitro-benzoic acids (0.01 mol) in ethanol (20 ml) was boiled under reflux for 1 h. The reaction mixture was evaporated *in vacuo* and the crude product was recrystallized from ethanol to give the pure product. The following compounds were prepared according to this procedure : *6-Phenyl-7H-1,2,4-triazolo[1,5-d]tetrazole* (**4a**) : Yield 0.9 g (48%), m.p. 230°C; IR 3202 (NH); ^1H NMR 12.3 (1H, s, NH), 8.6-7.2 (5H, m, arom-H); MS *m/z* (%) = 186 (M^+, 20%). *6-(p-Bromophenyl)-7H-1,2,4-triazolo[1,5-d]tetrazole* (**4b**) : Yield 1.9 g (72%), m.p. 210°C; MS *m/z* (%) = 265 (M^+, 12%). *6-(p-Chlorophenyl)-7H-1,2,4-triazolo[1,5-d]tetrazole* (**4c**) : Yield 1.6 g (73%), m.p. 190°C; MS *m/z* (%) = 221 (M^+, 55.5%). *6-(p-Methoxyphenyl)-7H-1,2,4-triazolo[1,5-d]tetrazole* (**4d**) : Yield 1.4 g (64%), m.p. 225°C; ^1H NMR 12.5 (1H, s, NH), 8.6–7.1 (4H, m, arom-H), 1.7 (3H, s, OCH_3); MS *m/z* (%) = 216 (M^+, 12%). *6-(p-Nitrophenyl)-7H-1,2,4-triazolo[1,5-d]tetrazole* (**4e**) : Yield 1.5 g (65%), m.p. 240°C; MS *m/z* (%) = 231 (M^+, 6%).

6-Mercapto-7H-1,2,4-triazolo[1,5-d]tetrazole (**5**) : A mixture of **1** (0.01 mol), pyridine (3 ml) and carbon disulfide (5 ml) was refluxed for 3 h, then the reaction mixture was poured onto ice H_2O. The formed crystalline product was collected by filteration, dried and recrystallized from ethanol. Yield 0.8 g (57%), m.p. 240°C; MS *m/z* (%) = 142 (M^+, 9%).

1H-Tetrazolo[1,5-d]tetrazole (**6**) : A solution of sodium nitrite (0.01 mol) in water (5 ml) was added dropwise to a stirred solution of compound **1** (0.01 mol) in conc. HCl (5 ml). The reaction mixture was kept at 0°C for 30 min and the precipitated solid was filtered, washed with water, dried and crystallized from ethanol. Yield 0.6 g (55%), m.p. 210°C; IR 3202 (NH); ^1H NMR 1206 (1H, s, NH).

6,7-Diphenyl-tetrazolo[1,5-d]1,2,4-triazine (**7**) : A mixture of **1** (0.01 mol), benzil (0.01 mol), concentrated hydrochloride acid (1 ml) and ethanol (20 ml) was refluxed for 20 min. The solvent was evaporated and crude product was collected and recrystallized from ethanol. Yield 2.2 g (80%), m.p. 200°C ([15] 198°C, [18] 201°C); MS *m/z* (%) = 274 (M^+, 23%).

6-Methyl-tetrazolo[1,5-b]1,2,4-triazin-7(8H) one (**8**) : A mixture of **1** (0.01 mol) and pyruvic acid (0.01 mol) in ethanol (20 ml) was heated under reflux for 30 min. The reaction mixture was cooled to room temperature and the precipitated solid was collected by filteration and crystallized from ethanol. Yield 1 g (66%), m.p. 210°C; IR 3341 (NH), 1674 (CON); ^1H NMR 12.3 (1H, s, NH), 1.8 (1H, s, CH_3); MS *m/z* (%) = 152 (M^+, 13%).

Tetrazolo[1,5-b]1,2,4-triazine-6,7(5H,8H) dione (**9**) : A

mixture of **1** (0.01 mol) and diethyl oxalate (0.01 mol) in ethanol (20 ml) was boiled under reflux for 30 min. The reaction mixture was left to cool at ambient temperature. The separated solid was filtered, and crystallized from ethanol. Yield 0.8 g (53%), m.p. 240°C; IR 3341, 3294 (NH), 1659 (CON); ^{1}H NMR 12.5, 11.5 (1H, 2s, each, 2NH); MS *m/z* (%) = 154 (M^+, 6%).

6-Methyl-tetrazolo[1,5-b]1,2,4-triazepin-8(9H)one (**10**) : A mixture of **1** (0.01 mol) and ethyl acetoacetate (0.01 mol) in ethanol (20 ml) was refluxed for 30 min. The solid separated after concentration and recrystrallized from ethanol. Yield 1.1 g (66%), m.p. 180°C; IR 3203 (NH), 1668 (CON); ^{1}H NMR 12.2 (1H, s, NH), 4.5 (2H, s, CH_2), 1.9 (3H, s, CH_3); MS *m/z* (%) = 166 (M^+, 9%).

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