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Novel electrosynthesis of a condensed thioheterocyclic system containing a 1,2,4-triazole ring

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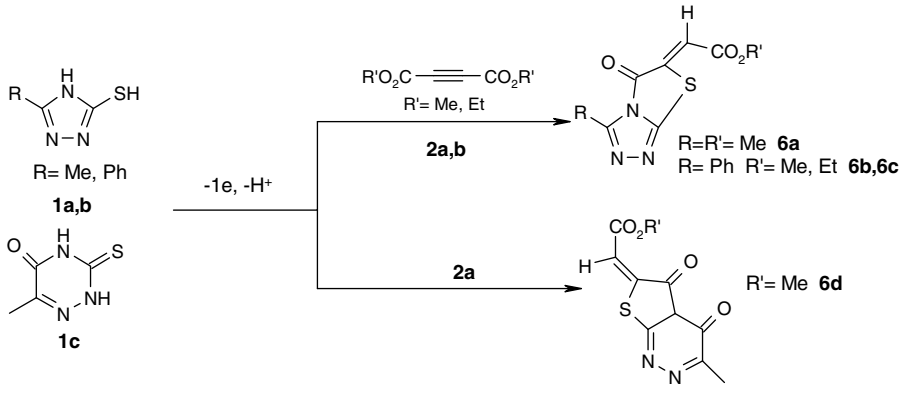
ABSTRACT

An efficient and convenient electrosynthesis of thioheterocyclic compounds **6a–d** is described via a one-pot, two-component condensation of triazoles (**1a,b**) or triazine (**1c**) with acetylenedicarboxylic acid esters (**2a,b**).

In recent years, the biological properties of 1,2,4-triazoles have been widely investigated. They were shown to be effective as anti-inflammatory, antibacterial, anticonvulsant, dephlogisticate, antidepressant, and antifungal agents.[1–5]

The encouraging biological activities of these heterocycles prompted us to investigate the synthesis of their novel thioheterocyclic derivatives using an electrochemical method. In our previous work, various chemical methods were used to synthesise thioheterocyclic derivatives,[6–8] but each of these methods has its own merits and drawbacks.

To the best of our knowledge, no reports have been published on the electrosynthesis of these thioheterocyclic compounds. In continuation of our program devoted to the electrosynthesis of heterocycles,[9–12] we have investigated the electrochemical reaction of triazoles **1a,b** and triazine **1c** with acetylenedicarboxylic acid esters **2a,b** at a constant controlled potential in order to obtain fused bicyclic derivatives (Scheme 1). In the present work, we report the preparation of new thioheterocyclic derivatives **6a–d** via electrooxidation of **1a–c** in the presence of **2a,b**.



Scheme 1.

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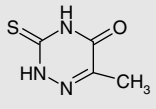
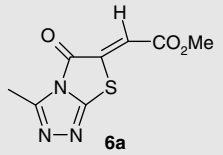
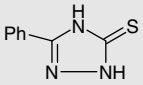
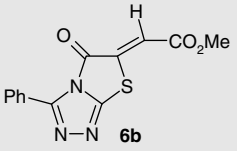
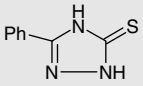
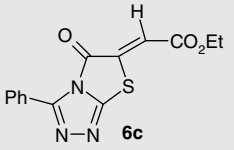
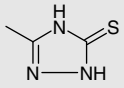
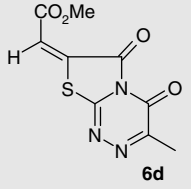
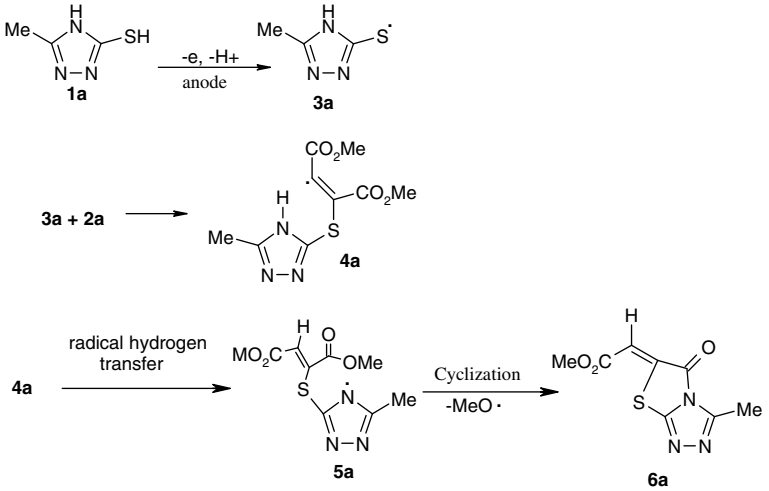
Table 1
Electrosynthesis of **6a–d** derivatives in ethanol-DMF[a]

Entry	Triazine and triazole compounds	Acetylenedicarboxylic acid ester compounds	Product	Yield (%)
1			 **6a**	90
2			 **6b**	86
3			 **6c**	89
4			 **6d**	95

[a] Refers to yield determined by GC analysis.

A cyclic voltammogram of either **1a** or **2a** in ethanol–DMF solution (1 mM) containing 0.1 M tetraethylammonium perchlorate shows one anodic peak at 1.7 V, but no cathodic peak on reverse scan. Therefore, the electrosynthesis at a constant potential of 1.7 V of 1 mmol of **1a–c** and 1 mmol of **2a,b** was conducted in an undivided cell containing a carbon electrode as anode, a Pt sheet as cathode and saturated KCl Ag/AgCl as the reference electrode. The progress of the reactions was monitored by TLC and produced the expected products under mild conditions in good to excellent yields (Table 1). All the products were characterized by physical and spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR, and MS).

We conclude that the triazole **1a** is oxidized in a one-electron oxidation process to a radical **3a** (anodic reaction), which is attacked by **2a** to form **4a** as an intermediate. After one-electron



Scheme 2.

oxidation of **4a** at the anode, **5a** is obtained. Finally, cyclization with expulsion of a methoxy group yields the final product **6a** (Scheme 2).

Electroorganic synthesis of **6a–d***:* In a typical procedure, 1 mmol of **1a–c** and 1 mmol of **2a,b** in a 1:1 solution of EtOH–DMF (50 ml) and tetraethylammonium perchlorate (0.1 M) as supporting electrolyte were subjected to electrolysis at a constant potential (1.7 V) in an undivided cell. An assembly of three graphite rods (8 mm diameter and 4 cm length) and a Pt sheet were used as working and auxiliary electrodes, respectively. All potentials are quoted versus a standard Ag/AgCl/saturated KCl reference electrode. All potentiostatic electrolysis was conducted at room temperature by stirring with a magnetic stirrer. The reaction equipment was described in an earlier paper.[13] Upon completion of the reaction (4–5 h), the reaction mixture was quenched by pouring into water, and the product was extracted twice with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$. Evaporation of the solvent gave **6a–d**. The products, in certain cases, were purified by column chromatography using petroleum ether/ethyl acetate (1:1).

(3-Methyl-5-oxothiazolo[2,3-c][1,2,4]triazol-6-ylidene)acetic acid methyl ester **(6a)**: Mp 158 °C. FT-IR (KBr) ν cm^{-1}: 1718, 1707, 1584. ^1H NMR (300 MHz, DMSO-d_6, δ):2.4 (3H, s), 3.9 (3H, s), 7.4 (1H, s). ^{13}C NMR (75 MHz, DMSO-d_6, δ): 12.1 (CH_3), 51.61 (OCH_3), 126.3 (C=C(=*C*–CO_2Me)), 137 (N=*C*–N), 142.5 (N=*C*–S), 145.6 (C=C(=*C*–S)), 162.4 (C=O(*C*O_2Me)), 165.8 (C=O (in five-membered ring)) ppm. MS: *m/z* 225[M^+].

(5-Oxo-3-phenylthiazolo[2,3-c][1,2,4]triazol-6-ylidene)acetic acid methyl ester **(6b)**: Mp 196 °C. FT-IR (KBr) ν cm^{-1}: 1713, 1653, 1592, 1522. ^1H NMR (300 MHz, DMSO-d_6, δ): 3.9 (3H, s), 7.2–7.5 (5H, m), 7.4 (1H, s) ppm. ^{13}C NMR (75 MHz, DMSO-d_6, δ): 50.5 (CH_3), 126.3 (C=C(=*C*–CO_2Me)), 122.1 (Ar), 128.4 (Ar), 131.2 (Ar), 134.0 (Ar), 142.5 (N=*C*–S), 142.9 (Ph–*C*=N), 150.8 (C=C(=*C*–S)), 162.1 (C=O(*C*O_2Me)), 165.5 (C=O (in five-membered ring)) ppm. MS: *m/z* 287 [M^+].

(5-Oxo-3-phenylthiazolo[2,3-c][1,2,4]triazol-6-ylidene)acetic acid ethyl ester **(6c)**: Mp 166 °C. FT-IR (KBr) ν cm^{-1}: 1711, 1634, 1587, 1522. ^1H NMR (300 MHz, DMSO-d_6, δ): 1.30 (t, J = 7.18 Hz, 3H), 4.19 (q, J = 7.18 Hz, 2H,), 7.2–7.5 (5H, m), 7.4 (1H, s) ppm. ^{13}C NMR (75 MHz, DMSO-d_6, δ): 14.4 (CH_3), 60.1 (CH_2), 127.0 (C=C(=*C*–CO_2Et)), 122.1 (Ar), 128.3 (Ar), 131.2 (Ar), 134.0 (Ar) 142.3 (N=*C*–S), 142.6 (Ph–*C*=N), 150.7 (C=C(=*C*–S)), 162.1 (C=O(*C*O_2Et)), 165.3 (C=O (in five-membered ring)) ppm. MS: *m/z* 301 [M^+].

(3-Methyl-4,6-dioxo-4H-thiazolo[2,3-c][1,2,4]triazin-7-ylidene)acetic acid methyl ester **(6d)**: Mp = 210–211 °C. FT-IR (KBr) ν cm^{-1}: 1759, 1701, 1597, 1560. ^1H NMR (300 MHz, DMSO-d_6, δ): 2.20 (3H, s), 3.84 (3H, s), 7.28 (1H, s) ppm. ^{13}C NMR (75 MHz, DMSO-d_6, δ): 13.6 (CH_3), 51.6 (OCH_3), 130.1 (C=C(=C–CO_2Me)), 142.4 (C=*C*–S)), 144.5 (C(N=*C*–S), 151.1 (C=O (in [1,2,4]triazine)), 155.4 (C=O (in five-membered ring)), 163.4 (C(N=*C*–CO)), 166.2 (C=O(*C*O_2Me)) ppm. MS: *m/z* 253 [M^+].

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References and notes

1. Boschelli, D. H.; Connor, D. T.; Bornemeier, D. A.; Dyer, R. D.; Kennedy, J. A.; Kuipers, P. J.; Okonkwo, G. C.; Schrier, D. J.; Wright, C. D. *J. Med. Chem.* **1993**, *36*, 1802–1810.
2. Mullican, M. D.; Wilson, M. W.; Connor, D. T.; Kostlan, C. R.; Schrier, D. J.; Dyer, R. D. *J. Med. Chem.* **1993**, *36*, 1090–1099.
3. Bozo, E.; Szilagyi, G.; Janaka, J. *Arch. Pharm.* **1989**, *322*, 583–587.
4. Palaska, E.; Sahin, G.; Kelicen, P.; Tugba Durlu, N.; Altinok, G. *IL FARMACO* **2002**, *57*, 101–107.
5. Odds, F. C.; Abbott, A. B. *J. Antimicrob. Chemother.* **1984**, *14*, 105–114 and references cited therein.
6. Heravi, M. M.; Beheshtiha, Y. S.; Shoar, R. H.; Nami, N. *Phosphorus, Sulfur Silicon Relat. Elem.* **2000**, *165*, 285–289.
7. Heravi, M. M.; Tajbakhsh, M.; Ramezanian, N. *Indian J. Heterocycl. Chem* **1998**, *7*, 309–310.
8. Heravi, M. M.; Bakherad, M.; Rahimzadeh, M.; Bakavoli, M. *Phosphorus, Sulfur Silicon Relat. Elem.* **2002**, *177*, 2403–2407.
9. Fotouhi, L.; Mosavi, M.; Heravi, M. M.; Nematollahi, D. *Tetrahedron Lett.* **2006**, *47*, 8553–8557.
10. Fotouhi, L.; Nematollahi, D.; Heravi, M. M.; Tammari, E. *Tetrahedron Lett.* **2006**, *47*, 1713–1716.
11. Fotouhi, L.; Taghavi Kiani, S.; Heravi, M. M.; Nematollahi, D. *Int. J. Chem. Kinet.* **2007**, 340–345.
12. Fotouhi, L.; Khakpour, M.; Nematollahi, D.; Heravi, M. M. *Arkivoc* **2008**, 43–52.
13. Fotouhi, L.; Nematollahi, D.; Heravi, M. M. *J. Chin. Chem. Soc.* **2007**, *54*, 1163–1166.