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A new ring transformation of 1,2,3-thiadiazoles into furan-2-carbothioamides

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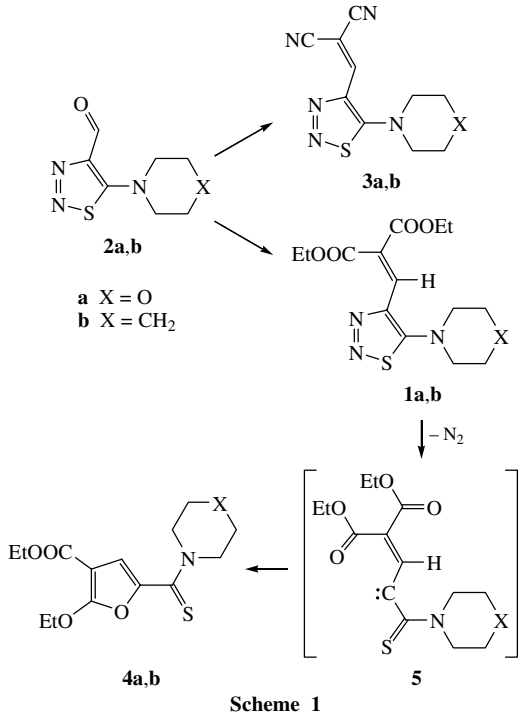
2-(5-Amino-1,2,3-thiadiazol-4-ylmethylene)malonates transform into furans containing thioamide groups.

Ring transformation reactions and rearrangements of 1,2,3-thiadiazoles leading to various heterocyclic compounds have been discovered.[1,2] These processes are governed by the following factors: (i) the facile cleavage of the weak N–S bond, (ii) the existence of an equilibrium between 1,2,3-thiadiazoles and α-diazo thiocarbonyl compounds and (iii) the capacity of both thiocarbonyl and diazo groups to cyclise onto electrophilic and nucleophilic functionalities. It was shown that 1,2,3-thiadiazoles could be transformed with the involvement of one (Dimroth type rearrangement),[3] two (Cornforth type),[4] three (L'abbé type)[5] or four[6] atoms of the side chain. Here, we report a new ring transformation of 1,2,3-thiadiazoles, where four atoms of the side chain take part in the process, into furan containing the thiocarbamoyl functional group.

Starting materials for this ring transformation {2-[(1,2,3-thiadiazol-4-yl)methylene]malonates **1a**,**b**} were obtained by the Knövenagel reaction from 1,2,3-thiadiazole-5-carbaldehydes **2a**,**b** (Scheme 1).† We found that compounds **1a**,**b** transformed to ethyl 2-ethoxy-5-(4-aminothiocarbonyl)furan-3-carboxylates **4a**,**b** in moderate yields on heating in a solvent. Among ethanol, *n*-butanol, xylenes and benzene, *n*-butanol was selected as a solvent of choice. The structure of products **4a**,**b** was assigned



Scheme 1

† *Diethyl 2-[(5-morpholino-1,2,3-thiadiazol-4-yl)methylene]malonate* **1a**. To a solution of aldehyde **2a**[6] (199 mg, 1 mmol) in ethanol (20 ml) malonic ester (0.154 ml, 1 mmol) was added at room temperature, and the resulting mixture was stirred for 9 h. The precipitate was filtered and crystallised from ethanol. Yield, 146 mg (43%), mp 104–106 °C. ^{1}H NMR ([$^2H_6$]DMSO) δ: 7.65 (s, 1H, CH), 4.23 (q, 2H, OCH_2, *J* 7.0 Hz), 4.19 (q, 2H, OCH_2, *J* 7.0 Hz), 3.78 [t, 4H, $O(CH_2)_2$, *J* 4.9 Hz], 3.41 [t, 4H, $N(CH_2)_2$, *J* 4.9 Hz], 1.25 (t, 3H, Me, *J* 7.0 Hz), 1.19 (t, 3H, Me, *J* 7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 170.14 [C(5)], 165.75 (C=O), 164.06 (C=O), 139.60 [C(4)], 128.36 (CH=), 126.29 (=C), 65.78 ($2OCH_2$), 61.65 (OCH_2), 61.53 (OCH_2), 54.59 ($2NCH_2$), 13.98 (Me), 13.80 (Me). MS, *m*/*z* (*I*, %): 341 $[M]^{+\cdot}$ (5). Found (%): N, 12.41; S, 9.44. Calc. for $C_{14}H_{19}N_3O_5S$ (%): N, 12.31; S, 9.39.

*Diethyl 2-[(5-*N*-pyrrolidino-1,2,3-thiadiazol-4-yl)methylene]malonate* **1b**. Yield, 211 mg (65%), mp 88–90 °C. ^{1}H NMR ([$^2H_6$]DMSO) δ: 7.85 (s, 1H, CH), 4.21 (q, 2H, OCH_2, *J* 7.1 Hz), 4.19 (q, 2H, OCH_2, *J* 7.1 Hz), 3.55 [t, 4H, $N(CH_2)_2$, *J* 6.5 Hz], 2.03 [t, 4H, $(CH_2)_2$, *J* 6.5 Hz], 1.23 (t, 3H, Me, *J* 7.1 Hz), 1.19 (q, 3H, Me, *J* 7.1 Hz). MS, *m*/*z* (*I*, %): 325 $[M]^{+\cdot}$ (55). Found (%): N, 12.77; S, 9.74. Calc. for $C_{14}H_{19}N_3O_4S$ (%): N, 12.91; S, 9.85.

*2-[(5-*N*-Morpholino-1,2,3-thiadiazol-4-yl)methylene]malononitriles* **3a**. To a solution of 199 mg (1 mmol) of aldehyde **2a** in 20 ml of ethanol 66 mg (1 mmol) of malononitrile was added at room temperature and stirred for 9 h. The precipitate was filtered and crystallised from ethanol. Yield, 165 mg (67%), mp 150 °C. ^{1}H NMR ([$^2H_6$]DMSO) δ: 8.41 (s, 1H, CH), 3.75–3.84 [m, 4H, $O(CH_2)_2$], 3.57–3.61 [m, 4H, $N(CH_2)_2$]. IR (ν/cm^{-1}): 3430, 3560, 2900, 2860, 2200 (CN), 1555, 1490. MS, *m*/*z* (*I*, %): 247 $[M]^{+\cdot}$ (3). Found (%): N, 28.14; S, 12.41. Calc. for $C_{10}H_9N_5OS$ (%): N, 28.32; S, 12.97.

*Ethyl 2-ethoxy-5-(*N*-morpholinothiocarbonyl)furan-3-carboxylate* **4a**. A solution of 170 mg (0.5 mmol) of 1,2,3-thiadiazole **1a** in 2 ml of *n*-butanol was heated. The reaction mixture was stirred for 5 h at 120 °C. The completion of the reaction was judged from TLC. Then, the solvent was removed *in vacuo*, and the product was isolated by chromatography (eluent, CH_2Cl_2). Yield, 114 mg (73%), mp 92 °C. ^{1}H NMR ([$^2H_6$]DMSO) δ: 7.16 (s, 1H, CH), 4.50 (q, 2H, OCH_2, *J* 7.0 Hz), 4.18 (q, 2H, OCH_2, *J* 7.0 Hz), 4.09 [t, 4H, $O(CH_2)_2$, *J* 4.9 Hz], 3.70 [t, 4H, $N(CH_2)_2$, *J* 4.9 Hz], 1.39 (t, 3H, Me, *J* 7.0 Hz), 1.23 (t, 3H, Me, *J* 7.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 183.97 (C=S), 161.88 (C=O), 161.59 [C(2)], 140.30 [C(5)], 120.30 [C(4)H], 94.97 [C(3)], 68.36 ($2OCH_2$), 67.64 ($2OCH_2$), 60.12 ($2NCH_2$), 14.64 (Me), 14.15 (Me). MS, *m*/*z* (*I*, %): 313 $[M]^{+\cdot}$ (100). Found (%): C, 53.65; H, 5.94; N, 4.20. Calc. for $C_{14}H_{19}NO_5S$ (%): C, 53.66; H, 6.11; N, 4.47.

*Ethyl 2-ethoxy-5-(*N*-pyrrolidinothiocarbonyl)furan-3-carboxylate* **4b**. Yield, 115 mg (77%), mp 52–54 °C. ^{1}H NMR ([$^2H_6$]DMSO) δ: 7.28 (s, 1H, CH), 4.53 (q, 2H, OCH_2, *J* 7.0 Hz), 4.19 (q, 2H, OCH_2, *J* 7.0 Hz), 3.96 (t, 2H, NCH_2, *J* 6.1 Hz), 3.84 (t, 2H, NCH_2, *J* 6.1 Hz), 2.07 (q, 2H, CH_2, *J* 6.1 Hz), 1.98 (q, 2H, CH_2, *J* 6.1 Hz), 1.46 (t, 3H, Me, *J* 7.0 Hz), 1.30 (t, 3H, Me, *J* 7.0 Hz). MS, *m*/*z* (*I*, %): 297 $[M]^{+\cdot}$ (100). Found (%): C, 56.35; H, 6.24; N, 4.71. Calc. for $C_{14}H_{19}NO_4S$ (%): C, 56.55; H, 6.44; N, 4.71.

on the basis of elemental analyses, mass spectra, NMR spectra† and X-ray crystallography (for **4a**)‡ (Figure 1).

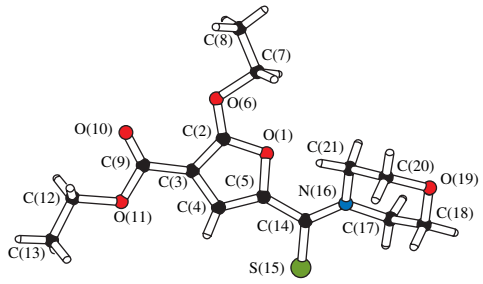


Figure 1 X-ray structure of furan **4a**.

‡ *Crystal structure of* **4a**. $C_{14}H_{19}NO_5S$ was crystallised from ethanol. Crystal data: crystal dimensions, 0.30×0.30×0.30 mm; monoclinic; $P2_1/c$, $a = 7.6831(2)$, $b = 24.5339(8)$ and $c = 8.1948(3)$ Å, $\beta = 100.196(2)°$, $V = 1520.30(8)$ Å^3, $Z = 4$, $d_{calc} = 1.369$ g cm^{-3}, $2\theta_{max} = 143.0°$, μ(CuKα) = = 2.087 mm^{-1}, Bruker SMART 6000 CCD detector, CuKα ($\lambda = 1.54178$ Å), crossed Göbel mirrors, $T = 100$ K, 15439 measured reflections, 2930 independent reflections. The data were corrected for Lorentz and polarization effects. Structure was solved by direct methods, full-matrix least-squares refinement based on $|F^2|$, 192 parameters, hydrogen atoms placed at calculated positions and refined in a riding mode with temperature factors 20% higher than parent atom (50% for methyl groups), $R_1 =$ = 0.0362 [for 2696 data with $I > 2\sigma(I)$], $wR_2 = 0.0951$, $S = 1.07$, max/min residual electron density 0.30/–0.34 eÅ^{-3}.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 292435. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2006.

The rearrangement probably involves a ring opening process, the subsequent formation of carbene **5** and a cyclisation reaction between the oxygen atoms of carboxylate groups and the carbene carbon atoms.

We found that 2-[(1,2,3-thiadiazol-4-yl)methylene]malononitriles **3** did not undergo this kind of reaction under the same conditions. Starting compound **3** was isolated in all of the experiments.

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