ARTICLE

OBC
www.rsc.org/obc

3-Mercaptopropionic acid–nitrile imine adducts. An unprecedented cyclization into 1,3,4-thiadiazol-2(3*H*)-ones and -2(3*H*)-thiones

Jalal A. Zahra,[a] Bassam A. Abu Thaher,[b] Mustafa M. El-Abadelah*[a] and Roland Boese[c]

[a] *Chemistry Department, Faculty of Science, University of Jordan, Amman, Jordan. E-mail: mustelab@ju.edu.jo; Fax: 00962 6 534 8932*

[b] *Chemistry Department, Faculty of Science, Islamic University of Gaza, Gaza Strip*

[c] *Institut für Anorganische Chemie, Universität Duisburg-Essen, Campus Essen Universitätstrasse 3–5, D-45117, Essen, Germany*

Received 12th April 2005, Accepted 13th May 2005
First published as an Advance Article on the web 13th June 2005

3-Mercaptopropionic acid–nitrile imine acyclic adducts (**6a–c**) undergo cyclocondensation with 1,1′-carbonyldiimidazole to afford the respective 1,3,4-thiadiazol-2-(3*H*)-ones (**7a–c**). Corresponding 1,3,4-thiadiazol-2(3*H*)-thiones (**8a–c**) were likwise produced from **6a–c** and 1,1′-thiocarbonyldiimidazole, with consequent elimination of the propionate moiety. The constitution of these heterocyclic products follows from analytical and spectral data and is confirmed by single crystal X-ray structure determination for **7b**.

Introduction

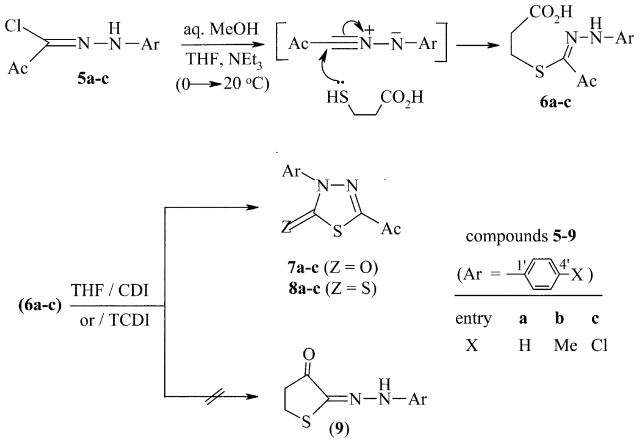
Recently we have reported on an unique transformation of 2-mercaptobenzoic acid–nitrile imine adducts (**1**), induced by 1,1′-carbonyldiimidazole (CDI) into the corresponding 2-(arylhydrazono)-1-benzothiophene-3-ones (**3**) (Scheme 1).[1] Likewise, CDI-induced cyclocondensation of 2-mercaptonicotinic acid-nitrile imine adducts (**2**) gave the corresponding 2-(arylhydrazono)-3-oxothieno[2,3-*b*]pyridines (**4**).[2]

1 (X = CH)
2 (X = N)

3 (X = CH)
4 (X = N)

Scheme 1

Following this route, we envisaged that the related 3-mercaptopropionic acid–nitrile imine acyclic adducts (**6**), under similar conditions, would produce the respective 2-(arylhydrazono)dihydrothiophen-3-ones (**9**, Scheme 2). However, this expectation was not realized in this study. Instead, the main isolable products from **6a–c** and CDI were identified as 5-acetyl-3-aryl-1,3,4-thiadiazol-2(3*H*)-ones (**7a–c**, Scheme 2). Interestingly, the corresponding -2(3*H*)-thiones (**8a–c**) were obtained from the respective **6a–c** when 1,1′-thiocarbonyldiimidazole (TCDI) was employed in placement of CDI. Hence, the present work deals with this unprecedented transformation mode of **6** as a new synthetic route towards 1,3,4-thiadiazol-2(3*H*)-ones (**7**) and the respective -2(3*H*)-thiones (**8**), for which a plausible mechanistic pathway is postulated (Scheme 3). In this context, it is worth noting that the chemistry and bio-properties of 1,3,4-thiadiazoles received considerable interest and the subject was occasionally reviewed.[3]



Scheme 2

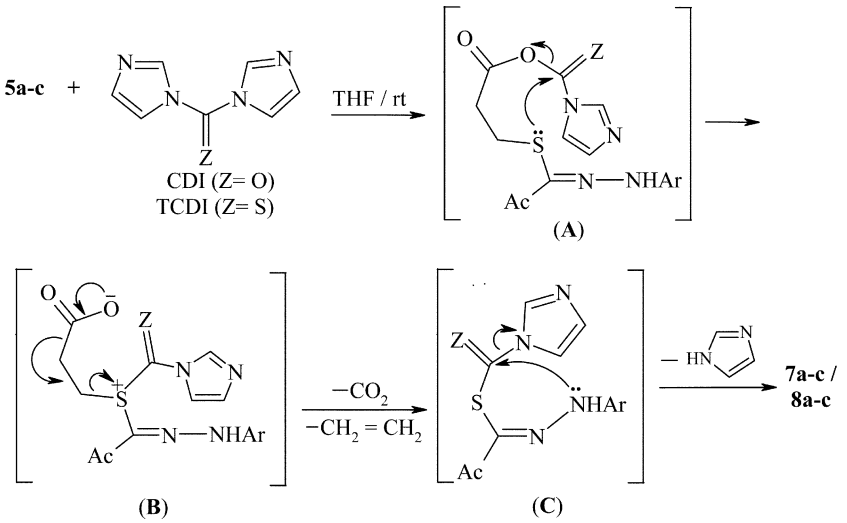
Results and discussion

3-Mercaptopropionic acid, acting as a strong sulfur nucleophile in basic medium, readily adds to nitrile imines (the reactive 1,3-dipolar species, generated *in situ* from their *N*-arylhydrazonoyl chloride precursors (**5a–c**)[4,5] in the presence of triethylamine) to produce the corresponding 3-[(2-oxo-1-arylhydrazonopropan-1-yl)mercapto]propanoic acids (**6a–c**, Scheme 2). The constitution of the latter acyclic adducts (**6a–c**) is based on elemental analyses, IR, MS and NMR spectral data that are given in the Experimental section. ^{1}H- and ^{13}C-signal assignments followed from DEPT and 2D (COSY, HMQC and HMBC) experiments. The α- and β-methylene carbon atoms in **6a–c** resonate at *ca.* 28 and 29 ppm, respectively, while their methylene hydrogens give rise to two distinct triplets centered at *ca.* 2.5 and 3.0 ppm.

Surprisingly, these methylene ^{1}H-/^{13}C-resonances are not observed in the NMR spectra of the corresponding cyclized products, isolated from the reaction of **6a–c** with CDI. This fact implies the loss of the α- and β-methylene groups in **6a–c** during the cyclization process and thus excludes the formation of the anticipated structure **9** (Scheme 2). Eventually, the cyclized products of **6a–c**/CDI were identified as 5-acetyl-3-aryl-1,3,4-thiadiazol-2-(3*H*)-ones **7a–c**, as evidenced from their elemental analyses, IR, MS, ^{1}H- and ^{13}C-NMR spectral data, given in the Experimental section, and confirmed by single crystal X-ray structure determination for **7b** (Table 1, Fig. 1and Fig. 2).†

On the other hand, activation of **6a–c** with TCDI led to the formation of the corresponding 1,3,4-thiadiazol-2(3*H*)-thiones (**8a–c**, Scheme 2), while none of **7a–c** was detected therein. This result indicates that the endocyclic 2-thione group in **8a–c** comes from 1,1′-thiocarbonyldiimidazole and that, by inference, the 2-one entity in **7a–c** originates from 1,1′-carbonyldiimidazole, and not from the carboxy group of **6a–c**. These *de facto* results suggest that the carboxy group is also eliminated from **6a–c**, together with the α- and β-methylenes (as gaseous CO_2 and CH_2=CH_2), during the cyclization process as induced by CDI

DOI: 10.1039/b505010c



Scheme 3

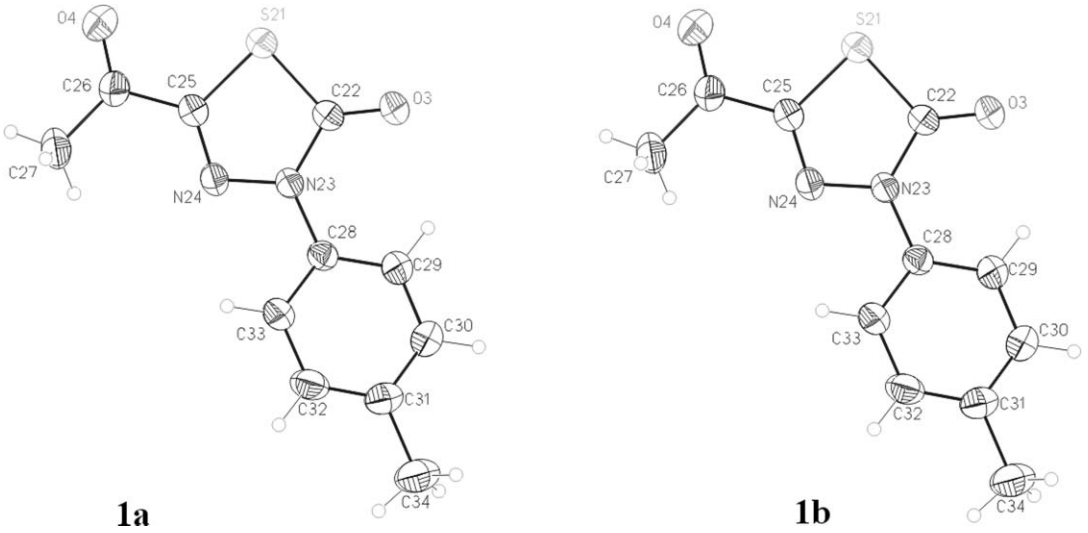


Fig. 1 ORTEP plot for both independent molecules of **7b**.

Table 1 Selected bond lengths (Å) and angles (°) for **7b**

Bond	Length (Å)	Bond	Angle (°)
S(1)–C(2)	1.7772(18)	C(5)–S(1)–C(2)	88.91(8)
S(1)–C(5)	1.7321(18)	O(1)–C(2)–S(1)	125.91(15)
C(2)–N(3)	1.397(2)	O(1)–C(2)–N(3)	127.17(17)
N(3)–N(4)	1.3600(18)	N(4)–N(3)–C(2)	116.74(13)
N(4)–C(5)	1.291(2)	N(4)–N(3)–C(8)	117.14(13)
O(1)–C(2)	1.208(2)	C(5)–N(4)–N(3)	111.29(14)
C(5)–C(6)	1.486(2)	N(4)–C(5)–S(1)	116.01(13)
N(3)–C(8)	1.437(2)	C(6)–C(5)–S(1)	121.39(13)
S(21)–C(22)	1.7765(16)	C(25)–S(21)–C(22)	88.54(7)
S(21)–C(25)	1.7312(15)	O(3)–C(22)–S(21)	126.77(12)
C(22)–N(23)	1.4005(17)	O(3)–C(22)–N(23)	126.12(14)
N(23)–N(24)	1.3616(16)	N(24)–N(23)–C(22)	117.02(12)
N(24)–C(25)	1.2936(19)	N(24)–N(23)–C(28)	118.03(11)
O(3)–C(22)	1.2058(17)	C(25)–N(24)–N(23)	110.37(11)
C(25)–C(26)	1.483(2)	N(24)–C(25)–S(21)	116.92(11)
N(23)–C(28)	1.4347(18)	C(26)–C(25)–S(21)	120.29(11)

or TCDI and for which a plausible pathway is depicted in the annexed mechanism (Scheme 3). Intramolecular nucleophilic attack by the sulfur atom at the suitably situated *N*-carbonyl (thiocarbonyl) carbon of the mixed anhydride (Scheme 3, **A**) facilitates the initial displacement of the propionate anion (shown in Scheme 3, **B**) and its subsequent breakdown, with the ultimate formation of the respective thiocarbamate (dithiocarbamate)

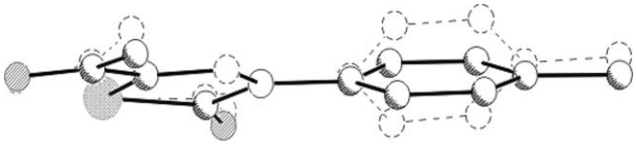
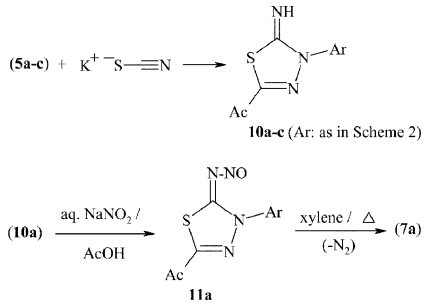


Fig. 2 Overlay of the two independent molecules, demonstrating the different conformations.

intermediate (Scheme 3, **C**). Subsequently, the aryl-NH hooks at the nearby *N*-carbonyl (thiocarbonyl) carbon in **C**, displacing the imidazole with consequent production of the corresponding thiadiazole derivatives (**7a–c**/**8a–c**). The imidazole nucleus in **A** probably participates cooperatively in the '*catalytic*' nucleophilic role of the sulfur atom that led to the expulsion of the propionate moiety from **B**/**C** (Scheme 3).

Conclusion

1,3,4-Thiadiazol-2-ones (*e.g.* **7**) are readily prepared by a two-step reaction involving the formation of 3-mercaptopropionic acid–nitrile imine acyclic adducts (**6**) and their cyclization with CDI under mild conditions (Scheme 2). This new method competes favorably with the reported route involving the preparation of 5-imino-1,3,4-thiadiazolines (*e.g.* **10a**) and their subsequent two-step transformation (*N*-nitrosation to **11**, followed by thermal decomposition) into **7** (Scheme 4).[6–8] Cyclization of adducts



Scheme 4

(**6**) with TCDI followed a similar course (as for CDI[9]), producing the respective 1,3,4-thiadiazol-2-thiones (**8**, Scheme 2) for which other procedures, based on hydrazonoyl chlorides (*e.g.* **1**), were described.[7,10,11]

Experimental

General

3-Mercaptopropionic acid, 3-chloro-2,4-pentanedione, 1,1′-carbonyldiimidazole (CDI) and 1,1′-thiocarbonyldiimidazole (TCDI) were purchased from Acros. Melting points (uncorrected) were determined on a Gallenkamp electrothermal melting temperature apparatus. ^{1}H- and ^{13}C -NMR spectra were measured on a Bruker DPX-300 instrument with Me_3Si as an internal reference. EIMS spectra were obtained using a Finnigan MAT TSQ-70 spectrometer at 70 eV; ion source temperature = 200 °C. High resolution MS-ESI data for **6a–c** were obtained with Bruker Bio TOF III, while HRMS data for **7a–c/8a–c** were obtained with a MAT 95(S) mass spectrometer. IR spectra were recorded as KBr discs on a Nicolet Impact-400 FT-IR spectrophotometer. Microanalyses were performed at the Microanalytical Laboratory-Inorganic Chemistry Department, Tübingen University, Germany.

1-Arylhydrazono-1-chloropropanones 1a–c

These hydrazonoyl chlorides **5a**,[4,5] **5b**[4] and **5c**[4,5] were previously characterized and are prepared in this study *via* the Japp–Klingemann reaction,[12] that involves direct coupling of the appropriate arenediazonium chloride with 3-chloro-2,4-pentanedione following a standard procedure.[4]

3-{[2-Oxo-1-(phenylhydrazono)propan-1-yl]mercapto} propanoic acid 6a

To a stirred and cooled (0 °C) solution of 1-chloro-1-phenylhydrazonopropanone (**5a**) (3.1 g, 16 mmol) in tetrahydrofuran (40 cm^3) was added triethylamine (11 cm^3). To this solution was immediately added dropwise a solution of 3-mercaptopropionic acid (2.1 g, 20 mmol) in methanol–water (47:3 v/v) containing NaOH (1.6 g). The reaction mixture was further stirred at 0 °C for 20–30 min and then at rt for 3–4 h. The organic solvents were then removed *in vacuo* from the reaction mixture and the residual solution was directly acidified with glacial acetic acid (6 cm^3). Trituration of the resulting crude gum yielded a solid product which was collected, dried and recrystallized from methanol. Yield 2.8 g (66%); mp 133–134 °C; found C, 54.22; H, 5.18; N, 10.55; S, 11.86%. $C_{12}H_{14}N_2O_3S$ requires C, 54.12; H, 5.30; N, 10.52; S, 12.04%; ν_{max}(KBr)/cm^{-1} 3440, 3413, 3150, 3100, 3002, 2959, 2926, 1724, 1635, 1600, 1524, 1463, 1428, 1358, 1325, 1288, 1233 and 1028;^{1}H-NMR (300 MHz, DMSO-d$_6$): δ 2.40 (s, 3H, CH_3), 2.47 (t, J = 6.7 Hz, 2H, CH_2CO$_2$H), 2.94 (t, J = 6.7 Hz, 2H, CH$_2$–S), 6.96 (t, J = 7.2 Hz, 1H, H-4′), 7.29 (dd, J = 7.9 Hz, 7.2 Hz, 2H, H-3′/ H-5′), 7.41 (d, J = 7.9 Hz, 2H, H-2′/ H-6′), 10.55 (s, 1H, NH), 12.57 (br s, 1H, CO$_2$H); ^{13}C-NMR (75 MHz, DMSO-d$_6$): δ 26.0 (CH_3), 27.7 (CH$_2$–S), 35.5 (*C*H$_2$–CO$_2$H), 115.3 (C-2′/C-6′), 123.0 (C-4′), 129.7 (C-3′/C-5′), 133.7 (C=N), 143.4 (C-1′), 173.4 (CO$_2$H), 193.5 (O=*C*–Me); HRMS (ESI): found 289.0604 (M + Na$^+$), $C_{12}H_{14}N_2O_3SNa$ requires 289.0623; m/z (EI): 266 (M$^+$, 100%), 194 (13), 160 (28), 118 (88), 92 (53), 91 (82).

3-{[1-(4-Methylphenylhydrazono)-2-oxopropan-1-yl]mercapto}propanoic acid 6b

This compound was prepared from 3-mercaptopropionic acid (2.1 g, 20 mmol) and 1-chloro-1-(4-methylphenylhydrazono)-propanone (**5b**) (3.4 g, 16 mmol) by following the same procedure described above for obtaining **6a**. Yield 3.2 g (71%); mp 144–145 °C; found C, 55.49; H, 5.66; N, 9.85; S, 11.41%. $C_{13}H_{16}N_2O_3S$ requires C, 55.70; H, 5.75; N, 9.99; S, 11.44.%; ν_{max}(KBr)/cm^{-1} 3434 br, 3183, 2997, 2925, 1703, 1634, 1513, 1441, 1226, 1203 and 1081;^{1}H-NMR (300 MHz, DMSO-d$_6$): δ 2.22(s, 3H, Ar–CH_3), 2.38 (s, 3H, CH_3CO), 2.46 (t, J = 6.9 Hz, 2H, CH_2CO$_2$H), 2.92 (t, J = 6.9, Hz, 2H, CH$_2$–S), 7.10 (d, J = 8.0 Hz, 2H, H-3′/H-5′), 7.31 (t, J = 8.0 Hz, 2H, H-2′/ H6′), 10.38 (s, 1H, NH), 12.30 (br s, 1H, CO$_2$H);^{13}CNMR (75 MHz, DMSO-d$_6$): δ 20.9 (*C*H$_3$–Ar), 25.9 (*C*H$_3$CO), 27.7 (CH$_2$–S), 35.4 (*C*H$_2$–CO$_2$H), 115.3 (C-2′/C-6′), 130.1 (C-3′/C-5′), 132.0 (C-4′), 132.9 (C=N), 141.1 (C-1′), 173.4 (CO$_2$H), 193.4 (O=*C*–Me); HRMS (ESI): found 303.0780 (M + Na$^+$), $C_{13}H_{16}N_2O_3SNa$ requires 303.0779; m/z (EI): 280 (M$^+$, 100%), 208 (15), 174 (6), 132 (98), 106 (76), 91 (82).

3-{[1-(4-Chlorophenylhydrazono)-2-oxopropan-1-yl]mercapto} propanoic acid 6c

This compound was prepared from 3-mercaptopropionic acid (2.1 g, 20 mmol) and 1-chloro-1-(4-chlorophenylhydrazono)-propanone (**5c**) (3.7 g, 16 mmol) by following the same procedure described above for obtaining **6a**. Yield 3.1 g (65%); mp 155–156 °C; found C, 48.12; H, 4.50; N, 9.18; S, 10.41%. $C_{12}H_{13}ClN_2O_3S$ requires C, 47.92; H, 4.36; N, 9.31; S, 10.66%; ν_{max}(KBr)/cm^{-1} 3441, 3410, 3178, 3120, 3094, 3074, 2999, 2931, 1702, 1645, 1595, 1514, 1455, 1408, 1362, 1324, 1230, 1089 and 1030;^{1}H-NMR (300 MHz, DMSO-d$_6$): δ 2.39 (s, 3H, CH_3), 2.46 (t, J = 6.6 Hz, 2H, CH_2–CO$_2$H), 2.95 (t, J = 6.6 Hz, 2H CH$_2$–S), 7.41 (d, J = 8.3 Hz, 2H, H-2′/ H-6′), 7.80 (d, J = 8.3 Hz, 2H, H-3′/ H-5′), 10.57 (s, 1H, NH), 12.34 (s, 1H, CO$_2$H); ^{13}C-NMR (75 MHz, DMSO-d$_6$): δ 26.0 (CH_3), 27.7 (CH$_2$–S), 35.6 (*C*H$_2$–CO$_2$H), 116.8 (C-2′/C-6′), 126.5 (C-4′), 129.5 (C-3′/C6′), 134.6 (C=N), 142.5 (C-1′), 173.5 (CO$_2$H), 193.5 (O=*C*–Me); HRMS (ESI): found 323.0225 (M + Na$^+$), $C_{12}H_{13}ClN_2O_3SNa$ requires 323.0233; m/z (EI): 300 (M$^+$, 84%), 228 (18), 194 (9), 152 (100), 126 (66), 111 (15).

5-Acetyl-3-phenyl-1,3,4-thiadiazol-2(3*H*)-one 7a

To a mixture of 1,1′-carbonyldiimidazole (2.0 g, 12.5 mmol) and compound **6a** (2.7 g, 10 mmol) was added dry tetrahydrofuran (50 cm^3) and the resulting solution was stirred at rt for 2–3 h. The solvent was then removed *in vacuo*, the residue was immediately treated with water (40 cm^3) and extracted with chloroform (2 × 40 cm^3). The combined organic extracts were dried (Na_2SO_4), the solvent was evaporated and the residual solid product was recrystallized from hot methanol. Yield 1.3 g (59%); mp 72–73 °C (lit.[6] 57 °C); found C, 54.33; H, 3.58; N, 12.61; S, 14.52%. $C_{10}H_8N_2O_2S$ requires C, 54.53; H, 3.66; N, 12.72; S, 14.56%; ν_{max}(KBr)/cm^{-1} 3113, 3068, 3010, 2965, 2920, 1692 br, 1654, 1592, 1527, 1487, 1418, 1362, 1274 br, 1144, 1089 and 1018;^{1}H-NMR (300 MHz, DMSO-d$_6$): δ 2.53 (s, 3H, CH_3), 7.42 (t, J = 7.3 Hz, 1H, H-4′), 7.52 (dd, J = 8.2 Hz, 7.3 Hz, H-3′/H-5′), 7.72 (d, J = 8.2 Hz, 2H, H-2′/H-6′); ^{13}C NMR (75 MHz, DMSO-d$_6$): δ 25.1 (CH_3), 123.2 (C-2′/C-6′), 128.8 (C-4′), 129.8 (C-3′/ C-5′), 137.3 (C-1′), 150.6 (C-5), 169.0 (C-2), 190.4 (Me–*C*=O); HRMS (EI): found 220.028431 (M$^+$), $C_{10}H_8N_2O_2S$ requires 220.030631; m/z (EI): 220 (M$^+$, 38%), 160 (20), 118 (73), 91 (100) and 77 (63).

5-Acetyl-3-(4-methylphenyl)-1,3,4-thiadiazol-2(3*H*)-one 7b

This compound was prepared from **6b** (2.8 g, 10 mmol) and 1,1′-carbonyldiimidazole (2.0 g, 12.5 mmol) by following the same procedure described above for **7a**. Yield 1.5 g (64%); mp 87–88 °C (ethanol); found C, 56.28; H, 3.21; N, 11.75; S, 13.44%. $C_{11}H_{10}N_2O_2S$ requires C, 56.40; H, 4.30; N, 11.96; S, 13.68%; ν_{max}(KBr)/cm^{-1} 3100, 3023, 2914, 2849, 1693 br, 1609, 1524, 1508, 1452, 1365, 1274, 1153, 1087 and 1059;^{1}H- NMR (300 MHz, DMSO-d_6): δ 2.32 (s, 3H, Ar–CH_3), 2.52 (s, 3H, CH_3–C=O), 7.32 (d, J = 7.4 Hz, 2H, H-3′/ H-5′), 7.59 (d, J = 7.4 Hz, 2H, H-2′/H-6′);^{13}C-NMR (75 MHz, DMSO-d_6): δ 21.2 (Ar–*C*H$_3$), 25.1 (*C*H$_3$–CO), 123.2 (C-2′/C-6′), 130.2 (C-3′/C-5′), 134.2 (C-4′), 138.4 (C-1′), 150.3 (C-5), 169.0 (C-2), 190.4 (Me–*C*=O); HRMS (EI): found 234.046179 (M$^+$), $C_{11}H_{10}N_2O_2S$ requires 234.046281; *m/z* (EI): 234 (M$^+$, 24%), 174 (16), 132 (64), 105 (100), 104 (23) and 91 (11).

5-Acetyl-3-(4-chlorophenyl)-1,3,4-thiadiazol-2(3*H*)-one 7c

This compound was prepared from **6c** (3.0 g, 10 mmol) and 1,1′-carbonyldiimidazole (2.0 g, 12.5 mmol) by following the same procedure described above for **7a**. Yield 1.6 g (63%); mp 102–103 °C ($CHCl_3$–pet. ether); found C, 46.92; H, 2.58; N, 10.87; S, 12.44%. $C_{10}H_7ClN_2O_2S$ requires C, 47.16; H, 2.77; N, 11.00; S, 12.59%; ν_{max}(KBr)/cm^{-1} 3094, 2914, 1692, 1525, 1486, 1371, 1268, 1146 and 1088;^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.45 (s, 3H, CH_3), 7.58 (d, J = 8.0 Hz, 2H, H-3′/H-5′), 7.63 (d, J = 8.0 Hz, 2H, H-2′/H-6′); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 25.0 (CH_3), 124.6 (C-2′/C-6′), 129.4 (C-3′/C-5′), 132.8 (C-4′), 136.1 (C-1′), 150.8 (C-5), 169.0 (C-2), 190.4 (Me–*C*=O); HRMS (EI): found 253.990925 (M$^+$), $C_{10}H_7ClN_2O_2S$ requires 253.991655; *m/z* (EI): 254 (M$^+$, 33%), 194 (29), 152 (88), 125 (100) and 90 (24).

5-Acetyl-3-phenyl-1,3,4-thiadiazol-2(3*H*)-thione 8a

To a mixture of 1,1′-thiocarbonyldiimidazole (2.2 g, 12.5 mmol) and compound **6a** (2.7 g, 10 mmol) was added dry tetrahydrofuran (50 cm^3) and the resulting solution was stirred at rt for 4–5 h. The solvent was then removed *in vacuo*, the residue was immediately treated with water (40 cm^3) and extracted with chloroform (2 × 40 cm^3) The combined organic extracts were dried (Na_2SO_4), the solvent was evaporated and the residual solid product was purified by column chromatography (silica gel), using dichloromethane as eluent, to afford the *title compound* **8a** as yellow solid. Yield 1.51 g (64%); mp 117–118 °C; found 50.64; H, 3.28; N, 11.74; S, 27.02%. $C_{10}H_8N_2OS_2$ requires C, 50.83; H, 3.41; N, 11.85; S, 27.13%; ν_{max}(KBr)/cm^{-1} 3055, 3004, 2959, 2920, 2849, 1686, 1503, 1498, 1360, 1332, 1288, 1203, 1060 and 1018;^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.52 (s, 3H, CH_3), 7.57 (m, 3H, H-3′/H-5′, H-4′), 7.69 (dd, J = 8.2 Hz, 1.5 Hz, 2H, H-2′/H-6′); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.0 (CH_3), 126.9 (C-2′/C-6′), 129.8 (C-3′/C-5′), 130.4 (C-4′), 138.4 (C-1′), 156.3 (C-5), 188.9 (C(2)=S), 189.1 (Me–*C*=O); HRMS (EI): found 236.003228 (M$^+$), $C_{10}H_8N_2OS_2$ requires 236.007792; *m/z* (EI): 236 (M$^+$, 64%), 235 (27), 193 (3), 160 (9), 135 (48), 118 (57), 91 (100) and 77 (64).

5-Acetyl-3-(4-methylphenyl)-1,3,4-thiadiazol-2(3*H*)-thione 8b

This compound was prepared from **6b** (2.8 g, 10 mmol) and 1,1′-thiocarbonyldiimidazole (2.2 g, 12.5 mmol) by following the same procedure described above for **8a**. Yield 1.53 g (61%); mp 76–77 °C; found C, 52.46; H, 3.88; N, 11.05; S, 25.36%. $C_{11}H_{10}N_2OS_2$ requires C, 52.78; H, 4.03; N, 11.19; S, 25.61%; ν_{max}(KBr)/cm^{-1} 3056, 3023, 2997, 2965, 2920, 2856, 1696, 1486, 1358, 1274, 1204, 1056 and 1017; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.36 (s, 3H, CH_3–Ar), 2.52 (s, 3H, CH_3–CO), 7.36 (d, J = 8.2 Hz, 2H, H-3′/H-5′), 7.55 (d, J = 8.2 Hz, 2H, H-2′/H-6′); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 21.3 (*C*H$_3$–Ar), 26.0 (*C*H$_3$CO), 126.6 (C-2′/C-6′), 130.2 (C-3′/C-5′), 136.0 (C-1′), 140.2 (C-4′), 156.2 (C-5), 188.9 (C(2)=S), 189.1 (Me–*C*=O); HRMS (EI): found 250.021512 (M$^+$), $C_{11}H_{10}N_2OS_2$ requires 250.023442; *m/z* (EI): 250 (M$^+$, 26%), 207 (2), 174 (3), 149 (86), 148 (30), 132 (32), 105 (65) and 91 (100).

5-Acetyl-3-(4-chlorophenyl)-1,3,4-thiadiazol-2(3*H*)-thione 8c

This compound was prepared from **6c** (3.0 g, 10 mmol) and 1,1′-thiocarbonyldiimidazole (2.2 g, 12.5 mmol) by following the same procedure described above for **8a**. Yield 1.84 g (68%); mp 122–123 °C; found C, 44.12; H, 2.52; N, 10.13; S, 23.51%. $C_{10}H_7ClN_2OS_2$ requires C, 44.36; H, 2.61; N, 10.35; S, 23.68%; ν_{max}(KBr)/cm^{-1} 3094, 3061, 2965, 2914, 2850, 1692, 1500, 1484, 1367, 1333, 1280, 1205, 1091, 1053 and 1015; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.53 (s, 3H, CH_3), 7.65 (d, J = 8.4 Hz, 2H, H-3′/H-5′), 7.75 (d, J = 8.4 Hz, 2H, H-2′/ H-6′); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.0 (CH_3), 128.8 (C-2′/C-6′), 129.9 (C-3′/C-5′), 134.8 (C-4′), 137.1 (C-1′), 156.5 (C-5), 189.0 (C(2)=S), 189.1 (Me–*C*=O); HRMS (EI): found 269.968284 (M$^+$), $C_{10}H_7ClN_2OS_2$ requires 269.968816; *m/z* (EI): 270 (M$^+$, 69%), 227 (1), 194 (10), 169 (100), 152 (71), 125 (65), 111 (42) and 90 (12).

Collection of X-ray diffraction data and structure analysis of 7b

Yellow block crystals were grown by allowing a clear solution of **7b** in hot ethanol to evaporate slowly at rt such that its volume was reduced by about 20% over 2–3 days. Crystal data collection was made with a Siemens SMART CCD diffractometer [Mo–Kα-radiation, graphite monochromator] operating in the omega scan mode (0.3°). The data were reduced with the Siemens-Bruker program suite XSCANS[13] and the structure was solved by the direct method using SHELXTL PLUS programs.[14] All non-hydrogen atoms were refined anisotropically by full-matrix, least-squares procedure based on F^2 using all unique data.

Crystal structure determination of 7b

Crystal data. C_{11} H_{10} N_2 O_2 S, M = 234.27, monoclinic, a = 11.9376(16), b = 14.0036(19), c = 13.9101(19) Å, β = 107.916(2)°, D_{calcd} = 1.407 g cm^{-3}, U = 2212.6(5) Å^3, T = 203(2) K, space group $P2_1/c$, Z = 8, μ(Mo–K$_\alpha$) = 0.278 mm^{-1}, 27 847 reflections measured ($2\theta_{max}$ = 56.52°), 5545 unique [R_{int} (F^2) = 0.0279] which were used in all calculations. The final R_1 was 0.0388 ($F_o > 4\sigma(F)$, 4467 data, 289 parameters), and wR_2 (F^2) = 0.1141 (all data), maximum residual electron density 0.39 e Å^{-3}. Hydrogen atoms were placed in calculated positions and treated as riding groups, with the 1.2 fold (1.5 fold for methyl groups) isotropic displacement parameters of the equivalent Uij of the corresponding carbon atom.

With two independent molecules, one has close O···S contacts *via* the inversion centres (O3–S21′ 2.925 Å, C22–O3–S21′ 140.6°), while the other does not exhibit significant intermolecular contacts. The heterocycles adopt almost planar conformations, the interplanar angles are 22.2 and 24.9°, respectively, for (S1, C2, N3, N4, C5)/(C8–C13) and (S21, C22, N23, N24, C25)/(C28–C33). However, the torsion direction is reversed as evident by the torsion angles N4–N3–C8–C9 −158.4° and N24–N23–C28–C29 156.1° as demonstrated by the graphical overlay of both independent molecules (Fig. 2), where the heterocycles are fitted best to each other.

Crystallographic data for the structural analysis of **7b** have been deposited with the Cambridge Crystallographic Data Center under the depository No. CCDC-260037. Copies of information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: (deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).†

† CCDC reference numbers 260037. See http://www.rsc.org/suppdata/ob/b5/b505010c/ for crystallographic data in CIF or other electronic format.

Acknowledgements

We thank the Deanship of Scientific Research-Jordan University (Amman) for financial support.

References

1 J. A. Zahra, B. A. Abu Thaher, M. M. El-Abadelah and R. Boese, *Org. Biomol. Chem.*, 2003, **1**, 822–825.
2 J. A. Zahra, B. A. Abu Thaher, M. M. El-Abadelah and H.-H. Otto, *Monatsh. Chem.*, 2005, **136**, 567–570.
3 (*a*) G. I. Kornis, in *Comprehensive Heterocyclic Chemistry I*, ed. A. R. Katritzky and C. W. Rees, Pergamon Press, London, 1984, vol. 6, pp. 545–577; (*b*) G. I. Kornis, in *Comprehensive Heterocyclic Chemistry II*, ed. R. C. Storr, Elsevier, Oxford, 1996, vol. 4, pp. 379–408 and pp. 905–1006; (*c*) M. R. Grimmett and B. Iddon, *Heterocycles*, 1995, **41**, 1525–1574; (*d*) G. Mloston, in *Nitrogen, Oxygen and Sulfur Ylide Chemistry*, ed. J. S. Clark, Oxford University Press, 2002, pp. 271–278; (*e*) S. J. Collier, *Science of Synthesis, Houben-Weyl Methods of Molecular Transformations*, 2003, **13**, 349–414.
4 (*a*) M. M. El-Abadelah, A. Q. Hussein and B. A. Abu Thaher, *Heterocycles*, 1991, **32**, 1879–1895 and references cited therein; (*b*) N. F. Eweiss and A. Osman, *J. Heterocycl. Chem.*, 1980, **17**, 1713–1717.
5 R. Fusco and R. Romani, *Gazz. Chim. Ital.*, 1946, **76**, 419–438.
6 N. F. Eweiss and A. A. Osman, *Tetrahedron Lett.*, 1979, 1169–1170.
7 R. Fusco and C. Musante, *Gazz. Chim. Ital.*, 1938, **68**, 147–156 and 665–681.
8 (*a*) M. A. A. Elneairy, A. A. Abbas and Y. N. Mabkhout, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2003, **178**, 1747–1757; (*b*) A. M. Farag, H. M. Hassaneen, I. M. Abbas, A. S. Shawali and M. S. Algharib, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1988, **40**, 243–249; (*c*) A. O. Abdelhamid and F. A. Attaby, *Sulfur Lett.*, 1988, **7**, 239–247; (*d*) H. M. Hassaneen, A. O. Abdelhamid, A. S. Shawali and R. Pagni, *Heterocycles*, 1982, **19**, 319–326; (*e*) A. S. Shawali and A. O. Abdelhamid, *J. Heterocycl. Chem.*, 1976, **13**, 45–49.
9 CDI and TCDI are frequently used as carboxy group activators; these reagents, in their reactions with nucleophiles, are well-known to act as phosgene/thiophosgene equivalents, whereby their C=O/C=S groups reside in the substitution products: (*a*) H. A. Staab, *Angew. Chem., Int. Ed. Engl.*, 1962, **74**, 407–423; (*b*) N. S. Simpkins, *100 Modern Reagents*, The Royal Society of Chemistry, Nottingham, UK, 1989, p. 4–6; (*c*) A. Armstrong, in *Handbook of Reagents for Organic Synthesis: Activating Agents and Protecting Groups*, ed. A. J. Pearson and W. J. Roush, Wiley, New York, 1999, pp. 93–97.
10 A. Alemgna, P. Del Buttero, E. Licandro, S. Maiorana and R. Trave, *Tetrahedron*, 1984, **40**, 971–976.
11 M. R. H. El-Moghayar, M. H. Elnagdi, M. K. A. Ibrahim and M. M. M. Sallam, *Helv. Chim. Acta*, 1977, **60**, 2171–2176.
12 (*a*) R. R. Phillips, *Org. React.*, 1959, **10**, 143–178; (*b*) H. C. Yao and P. Resnick, *J. Am. Chem. Soc.*, 1962, **84**, 3514–3517; (*c*) G. C. Barrett, M. M. El-Abadelah and M. K. Hargreaves, *J. Chem. Soc. C*, 1970, 1986–1989.
13 Bruker AXS SADABS program multiscan V2.03.
14 G. M. Sheldrick, *SHELXTL PLUS System of computer programs for the determination of crystal structure from the X-ray diffraction data*, V.5.10.DOS/WIN 95/NT.