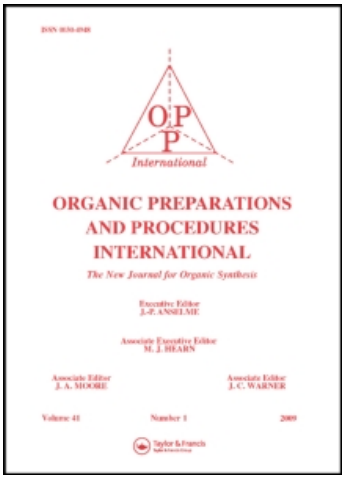

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A NOVEL SYNTHESIS OF 2,2,4,5-TETRASUBSTITUTED-1,3-DITHIOLES

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A NOVEL SYNTHESIS OF 2,2,4,5-TETRASUBSTITUTED-1,3-DITHIOLES

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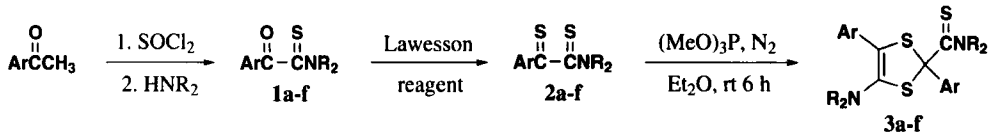
Organosulfur compounds such as α-carbonylthioformamides and α-keto hemithioacetals, are very useful intermediates for synthesis of heterocyclic compounds.[1-4] α-Thiocarbonylthioformamide represents a class of stable and little explored compounds.[5] This has prompted us to explore their reactivity and application in heterocyclic synthesis. Our present results show that α-thiocarbonylthioformamides can be used as precursors for the synthesis of the 1,3-dithiole ring system. 1,3-Dithioles are key intermediates for the preparation of well-known organic conductors such as tetrathiafulvalenes (TTF).[6] This has led to the development of synthetic methods for 1,3-dithioles. In general, dithioesters, dithiocarbamates,[6] dithiocarbonates[7] and trithiocarbonates[8] with a variety of functional groups can be cyclized to the corresponding 1,3-dithiole derivatives. The 1,3-dithiole ring system can also be prepared from [4+1] atom fragments; for example, condensation of acetic or benzoic esters with benzene-1,2-dithiol yields 2-methyl or 2-phenyl-1,3-benzodithiolylium salts, respectively.[9] Various 1,3-dithiolylium salts can be prepared by combining an excess of thioacids or thioesters with α-halo-, α-hydroxy-, α-mercaptoketones in the presence of hydrogen iodide or perchloric acid.[10] Carbon disulfide reacts with alkynes bearing electron-withdrawing substituents and benzyne to produce 1,3-dithioles.[11, 12] We now report a novel synthesis of new 2,2,4,5-tetrasubstituted-1,3-dithioles by the reaction of α-thiocarbonylthioformamides and trimethyl phosphite.

α-Thiocarbonylthioformamides (**2a-f**) were synthesized from the reaction of α-carbonylthioformamides (**1a-f**) and Lawesson's reagent.[13-15] In our initial experiments, the reaction of compounds **2a-f** with a variety of phosphorus reagents was explored. When trimethyl phosphite was added to an ethereal solution of α-thiobenzoylthioformamide (**2a**) with stirring under nitrogen atmosphere at room temperature, the violet-red color of **2a** faded gradually and a yellow solid began to appear after 1h; the reaction was complete after 10 h (TLC). The crude product was purified by silica gel column chromatography to afford pale yellow crystals of 2-morpholinothioformyl-2-phenyl-4-morpholino-5-phenyl-1,3-dithiole (**3a**). Similarly, the reaction of compounds **2b-f** and trimethyl phosphite gave analogous products **3b-f**. Their structures were determined by IR, NMR, MS, elemental analyses and X-ray analysis of **3a**.



a) Ar = Ph, NR_2 = $N(CH_2CH_2)_2O$ b) Ar = Ph, NR_2 = NMe_2 c) Ar = Ph, NR_2 = $N(CH_2CH_2)_2CH_2$
d) Ar = Ph, NR_2 = $N(CH_2Ph)_2$ e) Ar = *p*-CH_3O-C_6H_4, NR_2 = $N(CH_2CH_2)_2O$
f) Ar = *p*-Cl-C_6H_4, NR_2 = $N(CH_2CH_2)_2O$

In conclusion, 2,2,4,5-tetrasubstituted-1,3-dithioles (**3a-f**) can be synthesized readily from the reaction of trimethyl phosphite and α-thiocarbonylthioformamides (**2a-f**), which were obtained from the sulfurization of α-carbonylthioformamides (**1a-f**). The present methodology has the advantage of mild conditions, good yields and short procedures for synthesis of 2,2,4,5-tetrasubstituted-1,3-dithioles (**3a-f**).

EXPERIMENTAL SECTION

All melting points were uncorrected. The elemental analyses of C, H, N and S were performed on a Carlo Erba 1110 elemental analyzer. The infrared spectra were determined on a Mattson Alpha-Centauri FT-IR spectrometer. The ^1H and ^{13}C NMR spectra were recorded on a INOVA-400 MHz NMR spectrometer. The mass spectra were measured on a Finigan 4021 mass spectrometer and Micromass OA-TOF-HRMS.

Preparation of α-Carbonylthioformamides (1a-f). Typical Procedure.- Acetophenone (12 g, 0.1 mol) was added dropwise into thionyl chloride (118 g, 1 mol), then pyridine (2 mL) was added and the mixture was stirred at room temperature for 48 h. After removal of excess of thionyl chloride, the residue was dissolved in chloroform, and the solution was added dropwise into a solution of sodium hydroxide (10%, 30 mL) and of the secondary amine (0.15 mol) dissolved in chloroform (15 mL) below 0°. After the mixture was stirred at room temperature for 2 h, it was poured into cold 5% hydrochloric acid. The mixture was stirred for a few minutes, the organic layer was separated and cooled, then diethyl ether was added. The precipitated solid was collected, washed with ether to afford yellow crystals, which were recrystallized from 95% ethanol to give pure α-carbonylthioformamides (**1a-f**). The mps, yields, elemental analyses, MS, IR and ^1H NMR spectral data are summarized in Tables 1 and 2.

Preparation of α-Thiocarbonylthioformamides (2a-f). General Procedure.- α-Carbonylthioformamides (**1a-f**) (21 mmol) and the Lawesson reagent[6] (12 mmol) were refluxed in dry toluene (40 mL) under the nitrogen atmosphere for 10h (TLC), after removing solvent under reduced pressure, the residue was purified by silica gel column using acetone/petroleum ether (1:5) as eluent to afford deep red-violet crystals **2a-f**. The mps, yields, elemental analyses, MS and ^1H NMR spectral data were presented in Tables 3 and 4.

Table 1. Mps, Yields, Elemental Analyses, HRMS Spectral Data of Compounds **1a-f**

Cmpd	mp. (°C)	Yield (%)	MS(M^+) *m/z* (%)		Analysis (Found)			
			Calcd	Found	C	H	N	S
1a	112-113 [a]	73	235.0668	235.0648 (70)	----	----	----	----
1b	84-85 [b]	72	193.0562	193.0546 (45)	----	----	----	----
1c	74-75	62	233.0876	233.0862 (72)	66.92 (66.79)	6.48 (6.46)	6.00 (5.99)	13.74 (13.77)
1d	120-122	80	345.1189	345.1150 (100)	76.49 (76.31)	5.54 (5.53)	4.05 (4.06)	9.28 (9.30)
1e	139-141	70	265.0774	265.0758 (100)	58.85 (58.73)	5.70 (5.71)	5.28 (5.29)	12.09 (12.11)
1f	156-158	60	269.0277	269.0264 (85)	53.43 (53.33)	4.48 (4.49)	5.19 (5.18)	11.89 (11.92)

a) *Lit.*[16] mp 114-115°; b) *Lit.*[15] mp 84.5°

Table 2. IR and ^{1}H NMR Spectral Data of Compounds **1c-f**

Cmpd	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS) (δ)
1c	1667 (C = O)	1.40-2.20 (m, 6H), 3.25-3.60 (m, 2H), 4.00-4.40 (m, 2H), 7.20-7.80 (m, 5H, C_6H_5)
1d	1669 (C = O)	4.51-5.30 (m, 4H), 6.50-8.00 (m, 15 H, 3 x C_6H_5)
1e	1658 (C = O)	3.50-3.70 (m, 4H), 3.80-3.92 (m, 5H, OCH_3 and CH_2), 4.30-4.40 (m, 2H), 6.90-8.00 (m, 4H, C_6H_4)
1f	1670 (C = O)	3.55-3.62 (m, 2H), 3.65-3.72 (m, 2H), 3.85-3.92 (m, 2H), 4.30-4.35 (m, 2H), 7.40-8.00 (m, 4H, C_6H_4)

Table 3. Mps, Yields, Elemental Analyses, HRMS Spectral Data of Compounds **2a-f**

Cmpd	mp. (°C)	Yield (%)	MS (M^+) *m/z* (%)		Analysis (Found)			
			Calcd	Found	C	H	N	S
2a	94-95	60	251.0439	251.0406 (6)	57.34 (57.20)	5.21 (5.20)	5.57 (5.56)	25.51 (25.57)
2b	79-81[c]	55	209.0333	209.0313 (11)	----	----	----	----
2c	100-102	50	249.0646	249.0690 (6)	62.61 (62.43)	6.06 (6.05)	5.61 (5.60)	25.71 (25.76)
2d	126-127	50	361.0959	361.0938 (4)	73.09 (72.90)	5.30 (5.31)	3.87 (3.86)	17.74 (17.78)
2e	136-137	65	281.0545	281.0487 (12)	55.49 (55.39)	5.37 (5.36)	4.98 (4.99)	22.79 (22.85)
2f	168-169	45	285.0049	284.9994 (18)	50.43 (50.35)	4.23 (4.24)	4.90 (4.91)	22.44 (22.50)

c) *Lit.*[15] mp 72°

Table 4. ^{1}H NMR Spectral Data of Compounds **2a-f**

Cmpd	^{1}H NMR ($CDCl_3$/TMS) (δ)
2a	3.00-3.40 (m, 4H), 3.41-3.60 (m, 4H), 7.30-8.20 (m, 5H, C_6H_5)
2c	1.30-2.00 (m, 6H), 3.40-3.80 (m, 2H), 4.20-4.50 (m, 2H), 7.30-8.20 (m, 5H, C_6H_5)
2d	4.40-5.20 (m, 4H), 6.40-8.10 (m, 15H, 3 x C_6H_5)
2e	3.40-3.61 (m, 2H), 3.62-3.80 (m, 2H), 3.81-4.00 (m, 5H, OCH_3 and CH_2), 4.20-4.60 (m, 2H), 6.80-8.20 (m, 4H, C_6H_4)
2f	3.40-4.00 (m, 6H), 4.30-4.50 (m, 2H), 7.30-8.10 (m, 4H, C_6H_4)

General Procedure for the Preparation of 2,2,4,5-Tetrasubstituted-1,3-dithioles (3a-f) Trimethyl phosphite (0.14 mL, 1.2 mmol) was added into a diethyl ether (10 mL) solution of α-thiocarbonylthioformamide (**2**) (0.8 mmol) and the mixture was stirred under nitrogen atmosphere at room temperature. The violet-red color of **2** faded gradually and a yellow solid appeared. Stirring was continued to complete the reaction (about 10 h). The solid was collected, washed with diethyl ether and purified with column chromatography on silica gel using a mixture of petroleum ether and acetone (6:1) as the eluent to afford pure 2,2,4,5-tetrasubstituted-1,3-dithioles (**3a-f**). The mps, yields, elemental analyses, IR, NMR, MS spectral data are summarized in Tables 5-7.

Table 5. Mps, Yields, Elemental Analyses, IR, MS Spectral Data of Compounds **3a-f**

Cmpd	mp. (°C)	Yield (%)	IR (cm^{-1})	MS (M^+) *m/z* (%)	Analysis (Found) C	H	N	S
3a	149-151	59	1615 1581 1481	470 (6.4)	61.24 (61.42)	5.57 (5.56)	5.95 (5.94)	20.44 (20.38)
3b	156-157	65	1619 1591 1505	386 (5.6)	62.13 (62.20)	5.74 (5.75)	7.25 (7.27)	24.88 (24.82)
3c	156-158	71	1619 1590 1506	466 (2.0)	66.90 (66.76)	6.48 (6.46)	6.00 (5.99)	20.61 (20.55)
3d	139-141	56	1623 1592 1498	691 (1.0)	76.48 (76.59)	5.54 (5.55)	4.05 (4.07)	13.92 (13.87)
3e	173-175	42	1617 1593 1512	530 (1.0)	58.84 (58.95)	5.70 (5.71)	5.28 (5.27)	18.12 (18.07)
3f	164-166	80	1617 1512 1480	539 (1.0)	53.42 (53.48)	4.48 (4.49)	5.19 (5.20)	17.83 (17.88)

Table 6. ^{1}H NMR Spectral Data of Compounds **3a-f**

Cmpd	^{1}H NMR (DMSO-d_6) (δ)
3a	7.90-7.10 (m, 10H, ArH), 4.40 (b, 2H, CH_2), 3.70 (b, 2H, CH_2), 3.67-3.55 (m, 4H, 2 x CH_2), 3.45 (b, 2H, CH_2), 3.15 (b, 2H, CH_2), 2.90-2.70 (m, 4H, 2 x CH_2)
3b	8.00-7.00 (m, 10H, ArH), 3.42 (s, 3H, CH_3), 3.00 (s, 3H, CH_3), 2.50 (s, 6H, 2 x CH_3)
3c	7.18-7.90 (m, 10H, ArH), 4.26 (b, 2H, NCH_2), 3.42 (b, 2H, NCH_2), 2.70-2.88 (m, 4H, $2CH_2$), 1.40-1.72 (m, 10H, $5CH_2$), 0.98-1.18 (b, 2H, CH_2)
3d	6.59-7.87 (m, 30H, ArH), 4.54-5.17 (b, 4H, $2NCH_2$), 3.68-3.87 (m, 4H, $2NCH_2$)
3e	7.80-6.80 (m, 8H, ArH), 4.26 (b, 2H, CH_2), 3.75 (s, 6H, 2 x OCH_3), 3.68-3.55 (m, 4H, 2 x CH_2), 3.49 (b, 2H, CH_2), 3.34 (b, 2H, CH_2), 3.10 (b, 2H, CH_2), 2.88-2.60 (m, 4H, 2 x CH_2)
3f	7.90-7.20 (m, 8H, ArH), 4.25 (b, 2H, CH_2), 3.62 (b, 2H, CH_2), 3.60-3.50 (m, 4H, 2 x CH_2), 3.45 (b, 2H, CH_2), 3.10 (b, 2H, CH_2), 2.90-2.60 (m, 4H, 2 x CH_2)

Table 7. ^{13}C NMR Spectral Data of Compounds **3a-f**

Cmpd	^{13}C NMR (DMSO-d_6) (δ)
3a	196.77 (C = S), 141.45, 139.78, 133.67, 128.89, 128.39, 128.26, 128.23, 127.34, 124.79, 117.21, 78.11, 66.76, 66.00, 53.36, 52.04
3b	195.45 (C = S), 141.68, 141.55, 133.97, 129.01, 128.51, 128.42, 128.00, 127.16, 124.68, 114.97, 77.61, 47.19, 44.54, 43.99
3c	196.31 (C = S), 142.70, 140.73, 134.96, 129.00, 128.64, 128.53, 128.21, 127.24, 125.32, 116.34, 79.02, 54.73, 53.71, 26.43, 24.34, 24.12
3d	197.82 (C = S), 140.30, 140.20, 137.02, 134.53, 133.92, 128.74, 128.32, 128.24, 128.13, 127.62, 127.53, 127.24, 127.11, 126.92, 125.53, 114.25, 79.33, 56.61, 55.90
3e	195.11 (C = S), 159.03, 158.43, 137.31, 133.46, 129.37, 125.83, 125.14, 118.87, 114.11, 113.76, 77.10, 65.94, 65.55, 65.12, 55.17, 55.15, 55.10, 53.66, 52.82, 51.82
3f	194.16 (C = S), 140.64, 140.45, 133.36, 132.03, 131.86, 129.75, 129.25, 128.70, 126.58, 116.19, 77.44, 66.12, 65.71, 53.88, 53.07, 52.09

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TETRAHYDROFURAN RING-OPENING WITH ACYLOXYPHOSPHONIUM IODIDE CATALYZED BY SAMARIUM TRIIODIDE

Submitted by Yunkui Liu[†] and Yongmin Zhang* [†,††]
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Tetrahydrofuran ring opening with acyl halides or acid anhydrides is a useful method for preparation of 4-halobutyl esters.[1] Several methods have been reported for this purpose, e.g. the reaction of tetrahydrofuran with sodium iodide and acid chlorides,[2] the tetrahydrofuran ring–opening with acid chlorides or acid anhydrides catalyzed by samarium triiodide[3,4] to give 4-iodobutyl esters; the