Indian Journal of Chemistry
Vol. 41B, June 2002, pp. 1234-1237

A convenient synthesis of 3,5-diarylthieto[2,3-*d*]thiazole-2-thiones, and expansion of their thiete ring with carbon disulphide

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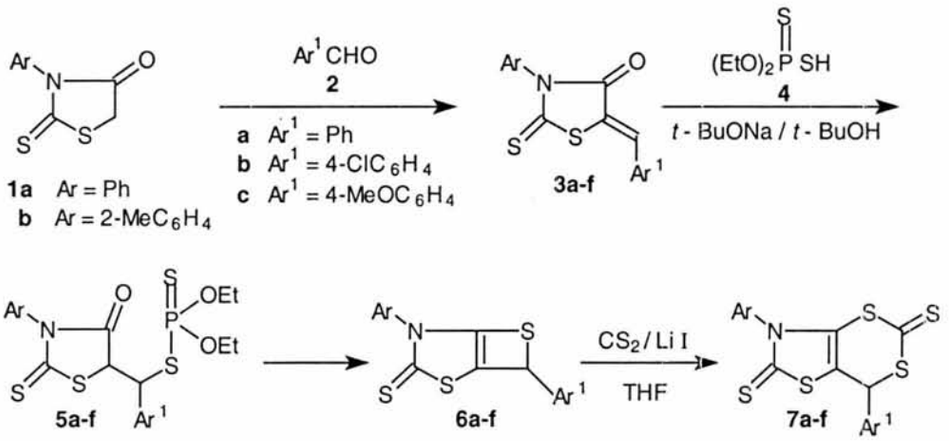
Received 28 February 2001; accepted (revised) 11 October 2001

3-Aryl-5-arylidenerhodanines **3a-f** react with *0,0*-diethyl hydrogen phosphorodithioate **4** to yield 3,5-diarylthieto[2,3-*d*]thiazole-2-thiones **6a-f** in a one-pot procedure. The compounds **6a-f** undergo expansion of their thiete ring by the reaction with carbon disulphide, catalysed by lithium iodide, to afford the corresponding 3,7-diarylthiazolo[4,5-*d*]-1,3-dithiin-2,5-dithiones **7a-f** in high yields under mild conditions.

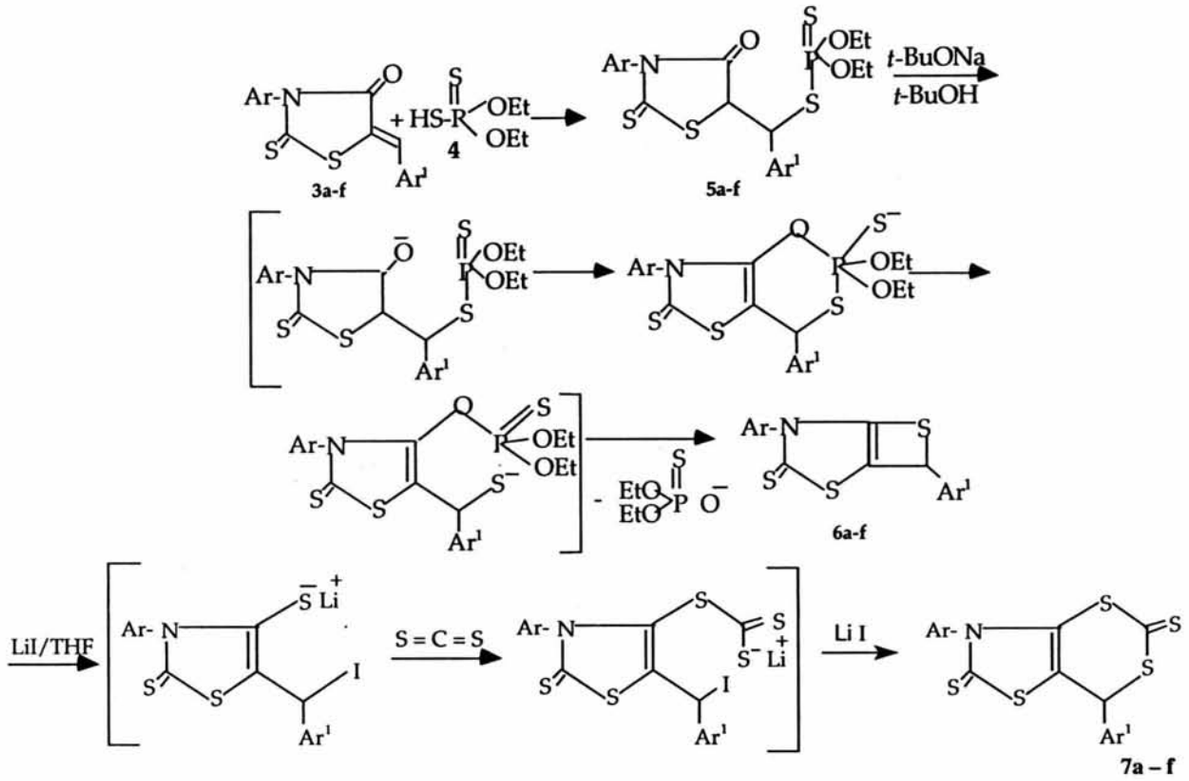
In general, the chemistry of four-membered heterocycles has been far less extensively studied than that of other heterocycles such as the three– and five–membered ones. We have previously reported the synthesis of 2,4-diarylthietanes starting from chalcones[1]. We now report a new, two-step, general method for the convenient synthesis of 3,5-diarylthieto[2,3-*d*]thiazole-2-thiones **6a-f** starting from 3-arylrhodanines **1a,b** along with expansion of the thiete ring of **6a-f** by their reaction with carbon disulphide, catalysed by alkali metal halides, to afford **7a-f**. The present synthesis was devised in view of the inherent toxicity of rhodanine derivatives to microorganisms[2-4], especially to fungi and bacteria, and the unexplored chemistry and bioactivity of the title compounds **6**.

The synthetic sequence leading to the formation of **7** is depicted in **Scheme I**. After some preliminary experimentation, it was found that the envisaged synthesis was successful with 5-arylidenerhodanines **3** and *O,O* - diethyl hydrogen phosphorodithioate **4** (**Scheme I**). Michael-type addition of **4** to **3** furnished the corresponding Michael adducts **5** which underwent cyclisation on treatment with *t*-BuONa/*t*-



3, 5-7	Ar	Ar^1	3, 5-7	Ar	Ar^1
a	Ph	Ph	d	2-MeC$_6$H$_4$	Ph
b	Ph	4-ClC$_6$H$_4$	e	2-MeC$_6$H$_4$	4-ClC$_6$H$_4$
c	Ph	4-MeOC$_6$H$_4$	f	2-MeC$_6$H$_4$	4-MeOC$_6$H$_4$

Scheme I



Scheme II

BuOH in the same vessel to yield the corresponding thieto-thiazoles **6** in 76-88% yield **(Scheme I)**.

The formation of thieto-thiazoles **6** is best explained by Michael-type addition of **4** to **3** to furnish the Michael adducts **5** which undergo intramolecular attack of the oxygen of the enolate ion on the phosphorus atom resulting in the formation of **6 (Scheme II)**. This conclusion is based on the observation that the representative intermediate compounds **5a** and **5e** were isolated in 81 and 86% yield, respectively and that these could be converted into the ccorresponding thieto-thiazoles **6a** and **6e** in 86 and 92% yield, respectively (Experimental Section). Further, the addition of a base, such as *t*-$BuON_a$, facilitates the formation of enolate ion resulting in 76-88% yield of **6**, otherwise poor yield (6-18%) of **6** was obtained even after a longer reaction time (9-12 hr).

The strain inherent in the thiete ring serves as the driving force for its expansion through breaking of a relatively weak carbon-sulphur bond under mild conditions. Prompted by the reports that the ring expansion reaction of oxiranes with carbon dioxide as well as carbon disulphide is catalysed by alkali metal halides[5,6], we used them as catalyst for expansion of the thiete ring of compounds **6a-f** with carbon disulphide. Amongst LiCl, LiBr, LiI, NaI and KI, LiI was found to be the most effective catalyst. Thus, LiI-catalysed reaction of **6a-f** with carbon disulphide in THF at room temperature afforded the corresponding **7a-f** in high yields (79-92%). Under similar conditions but in the absence of the catalyst, compounds **7a-f** were obtained in <14% yield. The probable mechanism of this ring expansion reaction is shown in **Scheme II.** Compounds **5-7** were obtained as their racemic modifications.

Experimental Section

General. Melting points were determined in open glass capillaries and are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer 993 infrared spectrophotometer (ν_{max} in cm^{-1}) and PMR spectra on a Perkin-Elmer R-32 (90 MHz) spectrometer using DMSO-d_6 as solvent and TMS as internal reference (chemical shifts in δ, ppm and coupling constants *J* in Hz). Mass spectra were recorded on a JEOL D-300 mass spectrometer at 70 eV.

The requisite starting compounds 3-aryl-5-aryli-denerhoda-nines **3a-f** were prepared according to the method already reported in the literature[4].

Table I — Physical and analytical data for compounds **5 - 7**

Compd	Yield (%)	mp (°C)	Mol. formula ‡	δ_H (J in Hz)	MS (M^+)
5a†	81	112-113	$C_{20}H_{22}NO_3PS_4$	1.16 (t, 6H, J, 7.0, 2×Me), 4.11 (q, 4 H, *J*, 7.0, 2×CH_2), 4.80 (d, 1 H, *J*, 5.0, COCH), 5.31 (d, 1 H, *J*, 5.0, SCH), 7.13-7.79 (m, 10 H, ArH)	483
5e†	86	120-121	$C_{21}H_{23}ClNO_3PS_4$	1.18 (t, 6 H, *J*, 7.0, 2×Me), 2.33 (s, 3 H, Me), 4.14 (q, 4 H, *J*, 7.0, 2×CH_2), 4.85 (d, 1 H, *J*, 5.0, 5.33 (d, 1H, *J*, 5.0, SCH), COCH), 7.11 - 8.12 (m, 8 H, ArH)	497
6a	83	155-156	$C_{16}H_{11}NS_3$	5.84 (s, 1 H, SCH), 7.10 - 7.80 (m, 10 H, ArH)	313
6b	88	213-215	$C_{16}H_{10}ClNS_3$	5.89 (s, 1 H, SCH), 7.15 - 7.85 (m, 9 H, ArH)	347
6c	78	199-200	$C_{17}H_{13}NOS_3$	5.81 (s, 1H, SCH), 3.79 (s, 3 H, OMe), 7.11- 7.80 (m, 9 H, ArH)	343
6d	81	153-154	$C_{17}H_{13}NS_3$	5.82 (s, 1 H, SCH), 2.31 (s, 3 H, Me), 7.16 - 7.75 (m, 9 H, ArH)	327
6e	85	149-150	$C_{17}H_{12}ClNS_3$	5.88 (s, 1 H, SCH), 2.34 (s, 3 H, Me), 7.14 - 7.84 (m, 8 H, ArH)	361
6f	76	143-144	$C_{18}H_{15}NOS_3$	5.80 (s,1 H, SCH), 2.33 (s, 3 H, Me), 3.77 (s, 3 H, OMe), 7.19-7.81 (m, 8 H, ArH)	357
7a	85	140-141	$C_{17}H_{11}NS_5$	5.32 (s, 1 H, SCH), 7.12 - 7.78 (m, 10 H, ArH)	389
7b	92	190-191	$C_{17}H_{10}ClNS_5$	5.36 (s, 1 H, SCH), 7.17 - 7.85 (m, 9 H, ArH)	425
7c	80	189-191	$C_{18}H_{13}NOS_5$	5.30 (s, 1 H, SCH), 3.77 (s, 3 H, OMe), 7.13 - 8.81 (m, 9 H, ArH)	419
7d	82	139-140	$C_{18}H_{13}NS_5$	5.32 (s, 1 H, SCH), 2.30 (s, 3 H, Me), 7.14 - 7.77 (m, 9 H, ArH)	403
7e	88	142-143	$C_{18}H_{12}ClNS_5$	5.37 (s, 1 H, SCH), 2.31 (s, 3 H, Me), 7.12 - 7.86 (m, 8 H, ArH)	439
7f	79	132-133	$C_{19}H_{15}NOS_5$	5.31 (s, 1 H, SCH), 2.32 (s, 3 H, Me), 3.79 (s, 3 H, OMe), 7.16-7.83 (m, 8 H, ArH)	433

† IR : 1705 (C=O), this IR band was absent in case of compounds **6** and **7**.

‡ All compounds are new and gave satisfactory elemental analyses : (C, H and N within ± 0.32% of calcd values).

3,5-Diarylthieto[2,3-*d*]thiazole-2-thiones 6. To a solution of 5-arylidenerhodanine **3** (10 mmole) in dry *t*–BuOH (20 mL) was added a solution of *O,O* - diethyl hydrogen phosphorodithioate (10 mmole) in dry *t*-BuOH (10 mL) at room temperature and the reaction mixture was refluxed for 3 hr. Now, *t*-BuONa (10 mmole) in *t*-BuOH (20 mL) was added to the above reaction mixture at room temperature and it was refluxed for 4 hr. The solvent was evaporated, the residue thus obtained was washed well with water and recrystallised from ethanol as shining yellowish needles of **6** (**Table I**).

Isolation of the Michael adducts 5a and 5e and their conversion into the corresponding products 6a and 6e. As representatives of the intermediates **5**, the Michael adducts **5a** and **5e** were isolated. Thus, to a solution of **3** (10 mmole) in dry *t*-BuOH (20 mL) was added a solution of **4** (10 mmole) in dry *t*-BuOH (10 mL) at room temperature and the reaction mixture was refluxed for 3 hr. The solvent was evaporated and the residue was recrystallised from ethanol to give a mixture of diastereoisomers (>96 : < 4, determined by PMR spectroscopy) which on the second recrystallisation from ethanol furnished the analytical sample of a single diastereoisomer **5** (**Table I**). On the basis of PMR spectra and general literature precedent[6-9], the adducts **5a** and **5e** were assigned the *erythro (syn)* stereochemistry, as their PMR spectra exhibited a lower value of coupling constant, $J_{COCH,SCH}$ = 5 Hz than that for the very minor (< 3%) diastereoisomer (*threo* or *anti*), $J_{COCH,\ SCH}$ = 10 Hz. The adducts **5a** and **5e** were refluxed with equimolar amount of *t*-BuONa in *t*-BuOH for 4 hr to give the corresponding compounds **6a** and **6e** in 86 and 92% yield, respectively.

3,7-Diarylthiazolo[4,5-*d*]-1,3-dithiin-2,5-dithiones 7. To a solution of LiI (0.25 mmole) and compound **6** (5 mmole) in THF (25 mL) was added carbon disulphide (6 mmole), and the reaction mixture was refluxed for 5 hr. The solvent and excess of carbon disulphide were evaporated, the residue thus obtained was washed well with water and recrystallised from THF as shining yellow crystals of **7** (**Table I**).

Acknowledgement

The authors sincerely thank RSIC, Lucknow for recording elemental analyses and spectra, and UGC, New Delhi for financial support.

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