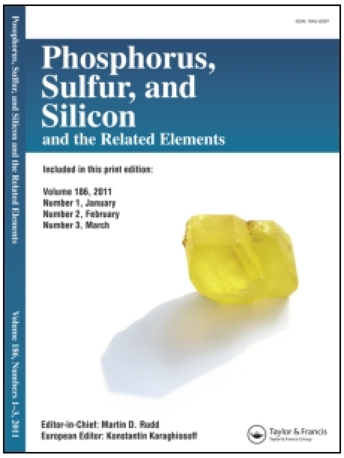

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SYNTHESIS AND REACTIONS OF 2-(HYDROXYIMINO)-2-PHENYLETHYL ARENEDITHIOCARBOXYLATES. A NEW SYNTHESIS OF 2,4-DIARYLTHIAZOLES

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Synthesis of 2-(hydroxyimino)-2-phenylethyl arenedithiocarboxylates and their reaction with triphenylphosphine dibromide have been investigated. The oxime, which was a mixture of syn and anti isomers (syn : anti = 90 : 10), was prepared by the reaction of the corresponding piperidinium arenedithiocarboxylate with 2-chloroacetophenone oxime in dichloromethane at room temperature in a high yield.

The oxime was added to a solution of 1.5 equivalent amounts of freshly prepared triphenylphosphine dibromide in acetonitrile at −10°C followed by stirring for 3 h at 25°C to give the corresponding thiazole in a moderate yield with a small amount of the hydrolyzed product, 2-(thioaroylthio)acetophenone. Beckmann rearrangement products such as amide, imidoyl bromide, or keteneimine were not detected.

The conditions for this procedure are markedly milder compared with those of previously reported methods.

INTRODUCTION

In the course of our research to develop a new application of dithiocarboxylic acid derivatives,[1–3] 2-(hydroxyimino)-2-phenylethyl arenedithiocarboxylates (**3**) attracted our attention, because of interest in the reactivity of the thiocarbonyl moiety and their applicability for the syntheses of heterocyclic compounds.[4–6] In our previous paper, we described a convenient synthesis of thiazoles (**4**) via 2-(thioaroylthio)acetophenones **5**.[6]

In this paper we describe the synthesis of the oximes **3** and their facile conversion to the thiazoles **4** by the treatment with triphenylphosphine dibromide.

RESULTS AND DISCUSSION

Addition of piperidinium arenedithiocarboxylate **1**[7] to a dichloromethane solution of 2-chloroacetophenone oxime **2**[8] at room temperature gave the oxime **3** in high yield as a mixture of syn and anti isomers (Eq. 1).[9] The yields and physical properties are summarized in Table I. Because of the difficulty of isolating each isomer, the following reactions were carried out without separation.

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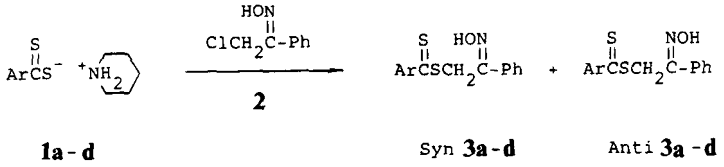
TABLE I

Syntheses of 2-(hydroxyimino)-2-phenylethyl arenedithiocarboxylates (**3**)

Product No.	Ar	Yield[a] [%]	m.p.[b] [°C]	IR [cm^{-1}][c] ν (C=N) ν (C=S)	UV. Vis.[d] λ_{max} [nm] (log ε)	^{1}H-NMR ($CDCl_3$) δ [ppm]	Isomer Ratio [%][e] Syn : Anti
3a	C_6H_5	86	99–101	1587 1238	300(4.24) 492(2.22)	4.55 (s, 2 H, CH_2-anti), 4.76 (s, 2 H, CH_2-syn), 7.08–8.05 (m, 10 H, Ar), 9.47 (br, 1 H, OH)	90 : 10
3b	4-CH_3—C_6H_4	86	122–124	1600 1225	316(4.32) 489(2.30)	2.32 (s, 3 H, CH_3), 4.52 (s, 2 H, CH_2-anti), 4.73 (s, 2 H, CH_2-syn), 6.96–8.00 (m, 9 H, Ar), 9.31 (br, 1 H, OH)	90 : 10
3c	4-CH_3O—C_6H_4	91	117–118	1600 1242	338(4.34) 489(2.39)	3.83 (s, 3 H, CH_3), 4.57 (s, 2 H, CH_2-anti), 4.78 (s, 2 H, CH_2-syn), 6.67–8.15 (m, 9 H, Ar), 9.29 (br, 1 H, OH)	90 : 10
3d	4-Cl—C_6H_4	74	98–100	1580 1215	311(4.32) 492(2.32)	4.52 (s, 2 H, CH_2-anti), 4.72 (s, 2 H, CH_2-syn), 7.10–8.00 (m, 9 H, Ar), 9.30 (br, 1 H, OH)	90 : 10

[a] Yields of mixtures of syn and anti isomers.
[b] Recrystallized from dichloromethane/*n*-hexane (1 : 5).
[c] KBr.
[d] Dichloromethane as a solvent.
[e] On the basis of ^{1}H-NMR.[9]



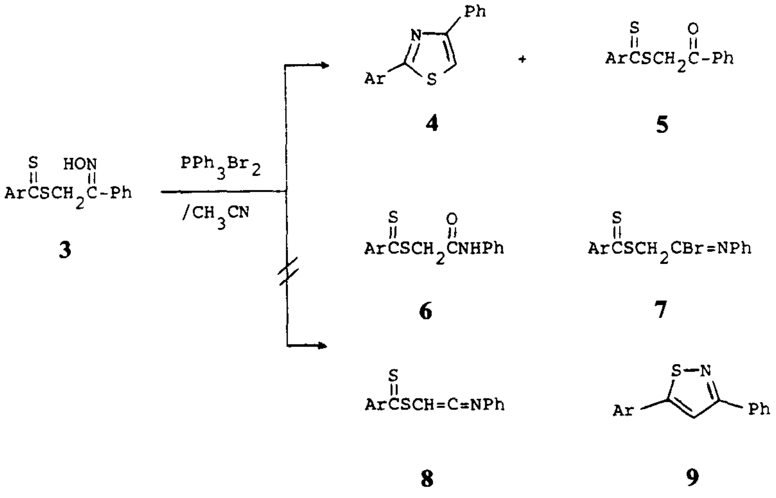
a; Ar = C_6H_5

b; Ar = $4\text{-}CH_3\text{-}C_6H_4$

c; Ar = $4\text{-}CH_3O\text{-}C_6H_4$

d; Ar = $4\text{-}Cl\text{-}C_6H_4$

The oxime **3** was added to a solution of 1.5 equivalent amounts of freshly prepared triphenylphosphine dibromide in acetonitrile at −10°C followed by stirring for 3 h at 25°C.[10] After the usual workup, the crystalline thiazole **4** was obtained in moderate yield with a small amount of the hydrolyzed product 2-(thioaroylthio)acetophenone **5**.[6] Addition of triethylamine as neutralizing reagent resulted in a poor yield (Table II). In all cases, Beckmann rearrangement products such as amide **6**, imidoylbromide **7**, or keteneimine **8** were not detected (Eq. 2).[11] The conditions for this procedure are markedly milder compared with those of previously reported methods.[6,12,13]



Absence of the corresponding isothiazoles **9** may suggest that the thiazole **4** proceeds from the nucleophilic attack of the hydroxyimino nitrogen on the thiocarbonyl carbon[14] to form the episulfide **10** followed by extrusion of sulfur (Scheme 1).[15]

The reactions of the oximes **3** with various reagents that activate the hydroxyimino moiety are now in progress.

TABLE II

Yields of 2,4-diarylthiazoles (**4**)

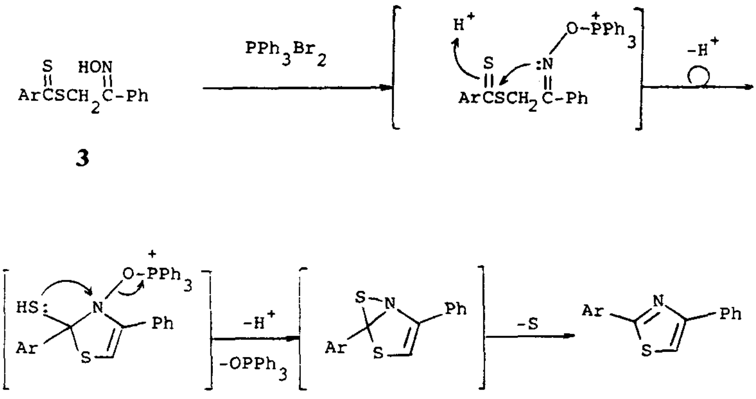
Entry No.	Ar	Yield [%][a,b,c] **4**	**5**
1	C_6H_5	37 (40)	10
2	$4\text{-}CH_3\text{—}C_6H_4$	74 (26)	11
3	$4\text{-}CH_3\text{—}C_6H_4$	14[d]	0
4	$4\text{-}CH_3O\text{—}C_6H_4$	60 (27)	13
5	$4\text{-}Cl\text{—}C_6H_4$	22 (37)	14

[a] Yields of pure isolated products.

[b] The spectral data and physical properties of **4a–d** and **5a–d** were well consistent with those of authentic samples.[6]

[c] Yields of **4a–d** reported in our previous report are in parentheses.[6]

[d] The reaction was carried out in the presence of triethylamine.



3

10

4

SCHEME 1

EXPERIMENTAL

Melting points were determined using a Yanagimoto micro melting point apparatus and are uncorrected. The IR spectra were measured on a JASCO grating IR spectrophotometer IR-G. The UV and visible spectra were obtained from a Hitachi 124 spectrometer. The ^1H-NMR spectra were recorded on a Hitachi R-22 (90 MHz) and R-24 (60 MHz) with tetramethysilane as an internal standard. The mass spectra were recorded on Hitachi RMU-6M mass spectrometer at an ionizing voltage 20 eV. Elemental analyses were performed by the Elemental Analyses Center of Osaka University.

Typical procedures for the synthesis of the oxime **3** *and the 2,4-diarylthiazole* **4** *are described below.*

2-(Hydroxyimino)-2-phenylethyl dithiobenzoate (**3a**). Piperidinium dithiobenzoate (**1a**) (1.20 g, 5.0 mmol) and 2-chloroacetophenone oxime (**2**) (0.85 g, 5.0 mmol) were stirred in dichloromethane (100 ml) at room temperature for 1 h. After washing of the mixture with water, the dichloromethane layer was dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure followed by recrystallization from dichloromethane/*n*-hexane (1 : 5) gave 1.24 g (86%) of the oxime **3a** as orange needles; m.p.

TABLE III

Elemental analyses of 2-(hydroxyimino)-2-phenylethyl arenedithiocarboxylate (3)

Product No.	Ar	Formula (mol. weight)	Elemental Analyses [%]			
				C	H	N
3a	C_6H_5	$C_{15}H_{13}NOS_2$	Calcd.	62.69	4.56	4.87
		(287.4)	Found	62.36	4.61	4.78
3b	4-CH_3—C_6H_4	$C_{16}H_{15}NOS_2$	Calcd.	63.76	5.02	4.65
		(301.4)	Found	63.76	4.96	4.66
3c	4-CH_3O—C_6H_4	$C_{16}H_{15}NO_2S_2$	Calcd.	60.54	4.76	4.41
		(317.4)	Found	60.51	4.59	4.12
3d	4-Cl—C_6H_4	$C_{15}H_{12}NOS_2Cl$	Calcd.	55.98	3.76	4.35
		(321.8)	Found	55.89	3.81	4.27

99–101°C; (syn : anti = 90 : 10). $C_{15}H_{13}NOS_2$ (287.4): Calcd.: C, 62.95; H, 4.56; N, 4.87. Found: C, 62.36; H, 4.61; N, 4.78.

2,4-Diphenylthiazole (**4a**). To a suspension of triphenylphosphine dibromide, prepared from triphenylphosphine (0.393 g, 1.5 mmol) and bromine (0.24 g, 1.5 mmol) in acetonitrile (50 ml), a solution of the oxime **3a** (0.287 g, 1.0 mmol) in acetonitrile (50 ml) was added dropwise with stirring at the temperature between −15 and −10°C (ice-salt cooling) under argon atmosphere. Then, the deep purple reaction mixture was stirred at 25°C for 3 h and concentrated under reduced pressure. The residue was diluted with dichloromethane (100 ml) and washed with saturated sodium carbonate (30 ml) and with water (30 ml × 3). The dichloromethane layer was dried over anhydrous sodium sulfate. After removal of the solvent, the residue was chromatographed on silica-gel (Fuji Davison BW-820 MH, benzene as eluant) and purified by preparative TLC (Wako Gel B-5F, 0.75 mm, dichloromethane/*n*-hexane = 1/1 as eluant) to give 88.3 mg (37%, Rf = 0.60) of the thiazole **4a** as pale yellow crystals: m.p. 91–92°C (Lit; m.p. 91–92°C,[16] m.p. 95–95.5°C[6]) and 26.1 mg (10%, Rf = 0.43) of **5a**: m.p. 76–77°C (Lit; m.p. 78.5–79.5°C[6]).

4a: ^{1}H-NMR ($CDCl_3$, δ) 7.00–7.55 (m, 6 H, Ar), 7.41 (s, 1 H, ring proton), 7.76–8.12 (m, 4 H, Ar); IR (KBr) 1467 cm^{-1} (C═N); mass spectra (m/e) 237 (M^+). The spectral data and physical properties of **4a** and **5a** were well consistent with those of the authentic samples.[6]

2-(4-Methylphenyl)-4-phenylthiazole (**4b**); *in the presence of triethylamine*. To a suspension of freshly prepared triphenylphosphine dibromide (0.75 mmol) in acetonitrile (25 ml) was added triethylamine (0.152 g, 1.5 mmol). Then, a solution of the oxime **3b** in acetonitrile (30 ml) was added dropwise to the reaction mixture at the same conditions described for the synthesis of **4a**. After similar workup, the thiazole **4b** was obtained in the yield of 14% (17 mg). **4b**: m.P. 128–129°C (Lit; m.p. 129.5–130°C[6]); ^{1}H-NMR($CDCl_3$, δ) 2.36 (s, 3 H, CH_3), 7.05–7.58 (m, 5 H, Ar), 7.35 (s, 1 H, ring proton), 7.58–8.22 (m, 4 H, Ar); IR (KBr) 1482 cm^{-1} (C═N); mass spectra (m/e) 251 (M^+). These spectral data and physical property of **4b** were well consistent with those of the authentic sample.[6]

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