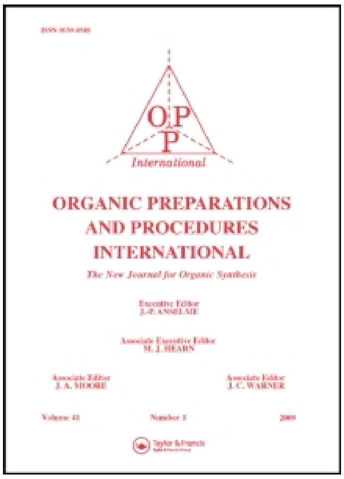

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Zhu Zheng-Hua[a]; Chen Shu-Ling[a]; Yao Zu-Guang[a]
[a] Research Institute of Fine Chemicals East China University of Chemical Technology, Shanghai, PEOPLE'S REPUBLIC OF CHINA

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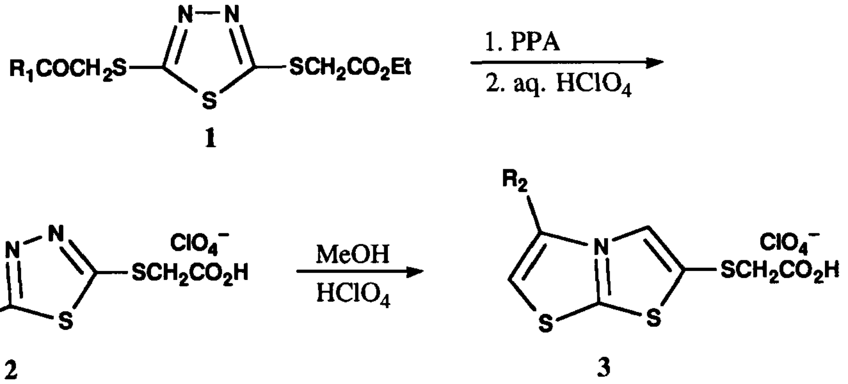
Submitted by (0313/91) Zhu Zheng-Hua*, Chen Shu-Ling and Yao Zu-Guang

Research Institute of Fine Chemicals
East China University of Chemical Technology
130 Meilong Road, Shanghai 200237
PEOPLE'S REPUBLIC OF CHINA

Thiazolo[2,3-b]-1,3,4-thiadiazolium salts have been prepared and studied as important synthetic intermediates of optically active heteroocines[1,2] and potential broad spectrum anthelmintics.[3] Recently, these heterocyclic quaternary salts have attracted much attention because of their importance as useful photographic development accelerators.[4,6] In continuation of our synthetic study on heterocyclic compounds as potential photographic development accelerators,[7] we now report the preparation of novel substituted thiazolo[2,3-b]-1,3,4-thiadiazolium salts **3**.

2-Ethoxycarbonylmethylthio-5-arylcarbonylmethylthio-1,3,4-thiadiazoles (**1**) are easily accessible products[7] and have been used as intermediates in the synthesis of photographic development-accelerator-releasing colorless couplers.[7] 2-Methoxycarbonylmethylthio-5-arylthiazolo[2,3-b]-1,3,4-thiadiazolium perchlorates (**3**) were obtained by the cyclodehydration of **1**



a) $R_1 = R_2 = C_6H_5$, b) $R_1 = R_2 = 4\text{-}BrC_6H_4$, c) $R_1 = R_2 = 4\text{-}ClC_6H_4$, d) $R_1 = R_2 = 4\text{-}MeC_6H_4$,
e) R_1 $R_2 = 4\text{-}HOC_6H_4$, f) $R_1 = 4\text{-}MeOC_6H_4$, $R_2 = 4\text{-}HOC_6H_4$ g) $R_1 = 4\text{-}BuOC_6H_4$, $R_2 = 4\text{-}HOC_6H_4$

in polyphosphoric acid (PPA) at 160-170° under reduced pressure, followed by treatment with hot aqueous perchloric acid and by acid-catalyzed esterification of the resulting carboxylic acids (**2**) with methanol. The overall yields were 34-70% (Table 1). When compounds (**1e-1g**) were used as starting materials, the same product (**3e**) was obtained. The methoxy group in **1f** and the butoxy group in **1g** were probably hydrolyzed by aqueous phosphoric acid in the reaction of the first step.

TABLE 1. Yields, mp and Elemental Analyses for **3a-3e**

Compd.	Yield[a] (%)	mp °C (MeOH)	Analysis Found(Calculated) C	H	N
3a	57	148-150	36.69 36.94	2.61 2.62	6.58 6.62
3b	57	203-204	31.01 31.12	2.14 2.01	5.64 5.58
3c	51	196-197	33.99 34.14	2.31 2.20	6.21 6.10
3d	70	182-184	38.33 38.49	3.04 3.00	6.50 6.41
3e	45[b] 38[c] 34[d]	127-129	35.77 35.58	2.61 2.52	6.11 6.38

a) Isolated yield of **3** based on **1**. b) Using **1e** as starting material. c) Using **1f** as starting material. d) Using **1g** as starting material.

The presence of an OH group (3460 cm^{-1}) in **3e** was established by its IR spectrum and ^{1}H NMR spectrum. The chemical shift of the OH proton of **3e** which appears at 8.32 ppm, disappears in the presence of deuterium oxide.

EXPERIMENTAL SECTION

Melting points are uncorrected. Elemental analyses were obtained using a Carlo Erba 11600R element analyzer. Mass spectra were recorded on a Hitachi M-80 spectrometer using either FD or EI ionization. IR spectra were recorded on a Nicolet FT-IR 20SX spectrometer. ^{1}H NMR spectra were recorded on a Bruker NP-100SY spectrometer. All reagents were of commercial quality from freshly opened containers. 2-Ethoxycarbonylmethylthio-5-arylcarbonylmethylthio-1,3,4-thiadiazoles (**1a-1d**) and (**1f**) and 2-bromo-4'-hydroxyacetophenone were prepared according to the reported procedures.[7,8]

TABLE 2. Spectral Data of Compounds **3**

Compd.	IR (KBr) (cm^{-1})	FDMS m/z	^{1}H NMR (DMSO-d$_6$, TMS) δ (ppm)
3a	1724 (CO) 1600 (C=N) 1085 (ClO_4)	323 (M-ClO_4)	3.60 (s, 3H, CH_3), 4.30 (s, 2H, CH_2), 7.53-7.94 (m, 5H, Ar-H), 8.38 (s, 1H, -CH=)
3b	1730 (CO) 1590 (C=N) 1080 (ClO_4)	404/402 ($M^{+}1$-ClO_4)	3.60 (s, 3H, CH_3), 4.28 (s, 2H, CH_2), 7.78 (s, 4H, Ar-H), 8.42 (s, 1H, -CH=)
3c	1728 (CO) 1598 (C=N) 1080 (ClO_4)	359/357 (M-C1O4)	3.60 (s, 3H, CH_3), 4.30 (s, 3H, CH_3), 7.58-7.96 (m, 4H, Ar-H), 8.42 (s, 1H, -CH=)
3d	1730 (CO) 1615 (C=N) 1098(ClO_4)	338 ($M^{+}1$-ClO_4)	2.44 (s, 3H, ArCH_3), 3.67 (s, 3H, OCH_3), 4.32 (s, 2H, CH_2), 7.36-7.86 (m, 4H, Ar-H), 8.35 (s, 1H, -CH=)
3e	3460 (OH) 1730 (CO) 1610 (C=N) 1100 (ClO_4)	339 (M-ClO_4)	3.61 (s, 3H, CH_3), 4.28 (s, 2H, CH_2), 6.84-7.75 (m, 4H, Ar-H), 8.15 (s, 1H, -CH=), 8.32 (s, 1H, OH)

2-Ethoxycarbonylmethylthio-5-(4-hydroxyphenyl)carbonylmethylthio-1,3,4-thiadiazole (1e).- To a solution of 2-ethoxycarbonylmethylthio-5-mercapto-1,3,4-thiadiazole (23.6 g, 100 mmol) in ethanol (200 ml) solid potassium hydroxide (5.6 g, 100 mmol) was added at room temperature, and stirring was continued for 15 min. 2-Bromo-4'-hydroxyacetophenone (21.5 g, 100 mmol) was then added and the mixture was refluxed with vigorous stirring for 30 min. Then it was filtered and the filtrate chilled overnight. The crystalline solid which formed was collected to give 23 g (63%) of **1e** as colorless needles, mp. 157-159° (EtOH).

MS (70 ev), m/z (%): 370 (3, M^+), 325 (I), 250 (2), 236 (3), 121 (100), 107 (7), 65 (9), 45 (4), 32 (18), 29 (14).

Anal. Calcd. for $C_{14}H_{14}N_2O_4S_3$: C, 45.39; H, 3.81; N, 7.56. Found: C, 45.40; H, 3.75; N, 7.64

2-Ethoxycarbonylmethylthio-5-(4-butoxyphenyl) carbonylmethylthio-1,3,4-thiadiazole (1g).- To a solution of **1e** (11.1 g, 30 mmol) in ethanol (100 ml) solid potassium hydroxide (1.7 g, 30 mmol) was added at room temperature, and stirring was continued for 15 min. Butyl bromide (4.1 g, 30 mmol) was then added and the mixture was refluxed with stirring for 8 hrs. Then it was filtered and the filtrate chilled overnight. The crystalline solid which formed was collected to give 6.0 g (47%) of **1g** as colorless needles, mp. 100-102°(EtOH).

FDMS, m/z: 426 (M^+).

IR (KBr), ν (cm^{-1}): 1740 (EtOC=O), 1675 (ArC=O), 1600 (C=N)cm^{-1}.

^{1}H NMR (DMSO-d_6, TMS): δ 0.92-1.88 (m, 10H, $2CH_3$ + $2CH_2$, 3.98-4.22 (m, 6H, $3CH_3$), 5.00 (s, 2H, $ArCOCH_2$), 6.98-7.00 (m, 4H, Ar-H).

Anal. Calcd. for $C_{18}H_{22}N_2O_4S_3$: C, 50.68; H, 5.20; N, 6.56. Found: C, 50.61; H, 5.22; N, 6.46

2-Methoxycarbonylmethylthio-5-arylthiazolo[2,3-b]-1,3,4-thiadiazolium Perchlorates (3). General Procedure.- Compound **1** (2 mmol) was added to freshly prepared PPA[9] (20 g). The reaction mixture was heated in an oil bath at 160-170° and at 50 mmHg for 8 hrs. It was cooled to room temperature and taken up in hot water (50 ml). After filtration it was treated with perchloric acid (70%, 2 ml) and cooled. The solid which separated was collected and dissolved in methanol (10 ml). Perchloric acid (70%, 0.5 ml) was added to the solution and the mixture was refluxed for 30 min. After filtration the filtrate was chilled overnight. A crystalline solid was formed. It was separated by filtration and washed several times with cold methanol to give pure product **3**. The yields, melting points and analytical data are shown in Tables 1 and 2.

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