

## A Facile Synthesis of Thiophenacylketene S,N-Acetals from Treatment of 2-Alkyl-3-alkylthio-5-phenylisothiazolium Salts with Sodium Borohydride

Sung Hoon Kim<sup>†</sup>, Youn Young Lee<sup>†</sup>, Kyongtae Kim<sup>\*†</sup>,  
and Jung-Hyup Kim<sup>‡</sup>

<sup>†</sup>Department of Chemistry,  
Seoul National University, Seoul 151-742  
<sup>‡</sup>Division of Applied Science,  
Korea Institute of Science and Technology,  
P.O. Box 131, Cheongryang, Seoul 130-650

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Thiophenacylketene S,N-acetal (**1**) is an analog of phenacylketene S,N-acetal, which has been known as a potential intermediate for the preparation of various heterocyclic compounds.<sup>1</sup> In comparison with the utility of phenacylketene S,N-acetal, **1** has been rarely studied. Only 1-methylamino-1-methylthio-3-phenylpropene-3-thione (**1a**) was reported to be isolated from the reactions of 2-methyl-3-methylthio-5-phenylisothiazolium iodide (**2**,  $R = \text{Me}$ ,  $R' = \text{Me}$ ,  $X = \text{I}$ ) with benzylamine in 12% yield,<sup>2</sup> with benzoyl acetate in 10% yield,<sup>3</sup> and with ethanolic sodium hydrosulfide in 32% yield.<sup>3</sup>

In the previous paper,<sup>4</sup> we reported that the reaction of 2-alkyl-3-(carbethoxyacetylmethylthio)-5-phenylisothiazolium chlorides (**2**,  $R' = \text{MeCOCHCO}_2\text{Et}$ ,  $X = \text{Cl}$ ) with  $\text{NaBH}_4$  in a mixture of chloroform and ethanol at room temperature underwent easily S-N bond cleavage to give ring-opened intermediates **1** ( $R' = \text{MeCOCHCO}_2\text{Et}$ ) which then immediately cyclized to afford 3-alkyl-5-carbethoxy-4-methyl-2-thiophenacylidene-1,3-thiazole (**3**) as shown in Scheme 1. A similar reaction was obtained from the reaction of 2,3,5-trimethyl-4-substituted isothiazolium tetrafluoroborate with either  $\text{NaBH}_4$  or  $\text{LiAlH}_4$  at  $-78^\circ\text{C}$ .<sup>5</sup>

We have found that the reactions of 2-alkyl-5-phenylisothiazolium halides (**2**,  $X = \text{Br}$ ,  $\text{I}$ ) having simple alkylthio group at C-3 with  $\text{NaBH}_4$  in ethanol at room temperature gave **1** in good to excellent yields. Compound **1**, to the best of our knowledge, is not currently accessible by the reported methods. Typical experimental procedure: To the suspension of 3-ethylthio-2-methyl-5-phenylisothiazolium iodide (**2b**)

**Table 1.** Yields and Physical Properties of Thiophenacylketene S,N-Acetals (**1**)

<b>1</b>	<i>R</i>	<i>R'</i>	Yield(%) <sup>a</sup>	mp <sup>b</sup>	Color
<b>a</b>	Me	Me	83	91.5-92.5	yellow
<b>b</b>	Me	Et	98	148-149	yellow
<b>c</b>	Me	allyl	91	liq	yellow
<b>d</b>	Et	Me	94	74-75	yellow
<b>e</b>	Et	Et	95	73-74	yellow
<b>f</b>	Et	allyl	98	liq	yellow
<b>g</b>	allyl	Me	93	liq	brown
<b>h</b>	allyl	$\text{C}_6\text{H}_5\text{CH}_2$	89	95-96	yellow
<b>i</b>	cyclohexyl	Me	100	70-71	yellow
<b>j</b>	cyclohexyl	Et	87	liq	yellow
<b>k</b>	cyclohexyl	allyl	98	148-149	yellow
<b>l</b>	phenylethyl	Me	93	112-113	yellow
<b>m</b>	phenylethyl	$\text{C}_6\text{H}_5\text{CH}_2$	96	106-107	yellow
<b>n</b>	$\text{C}_6\text{H}_5\text{CH}_2$	Me	80	112.5-113.5	yellow
<b>o</b>	$\text{C}_6\text{H}_5\text{CH}_2$	Et	96	liq	yellow
<b>p</b>	$\text{C}_6\text{H}_5\text{CH}_2$	allyl	96	liq	yellow
<b>q</b>	4-Me- $\text{C}_6\text{H}_4\text{CH}_2$	Me	93	102-103	yellow
<b>r</b>	4-MeO- $\text{C}_6\text{H}_4\text{CH}_2$	Me	97	120.0-121.5	yellow
<b>s</b>	2-Cl- $\text{C}_6\text{H}_4\text{CH}_2$	Me	86	83-84	scarlet
<b>t</b>	3-Cl- $\text{C}_6\text{H}_4\text{CH}_2$	Me	97	99-100	orange
<b>u</b>	4-Cl- $\text{C}_6\text{H}_4\text{CH}_2$	Me	90	98-99	yellow
<b>v</b>	4-Cl- $\text{C}_6\text{H}_4\text{CH}_2$	$\text{C}_6\text{H}_5\text{CH}_2$	94	160.5-162	yellow

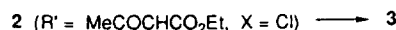
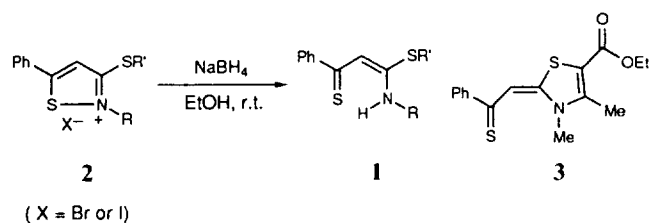
<sup>a</sup>Isolated yields. <sup>b</sup>All melting points are uncorrected.

(0.490 mmol) in 95% ethanol (2 ml) was added portionwise  $\text{NaBH}_4$  (0.490 mmol). Upon addition of  $\text{NaBH}_4$ , the solid dissolved and the solution turned to dark yellow. The reaction was monitored by TLC until all of **2b** had disappeared. The solvent was evaporated to dryness *in vacuo*. The residue was purified by column chromatography (Merck, silica gel, 230-400 mesh) using  $\text{CH}_2\text{Cl}_2$  as an eluent. The yield of **1b** was 98%. Yields and physical properties of **1** are summarized in Table 1.

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**Scheme 1.**