

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

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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.¹ 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,² with benzoyl acetate in 10% yield,³ and with ethanolic sodium hydrosulfide in 32% yield.³

In the previous paper,⁴ we reported that the reaction of 2-alkyl-3-(carbethoxyacetylmethylthio)-5-phenylisothiazolium chlorides (**2**, $R' = \text{MeCOCHCO}_2\text{Et}$, $X = \text{Cl}$) with 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 NaBH_4 or LiAlH_4 at -78°C .⁵

We have found that the reactions of 2-alkyl-5-phenylisothiazolium halides (**2**, $X = \text{Br}$, I) having simple alkylthio group at C-3 with 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**)

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

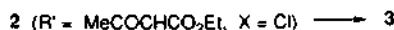
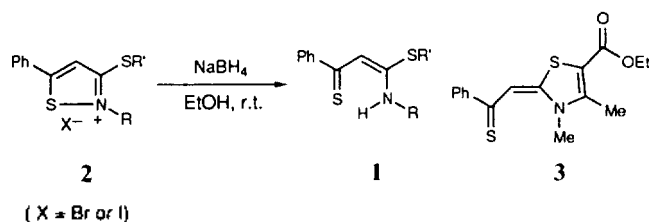
^aIsolated yields. ^bAll melting points are uncorrected.

(0.490 mmol) in 95% ethanol (2 ml) was added portionwise NaBH_4 (0.490 mmol). Upon addition of 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 CH_2Cl_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.