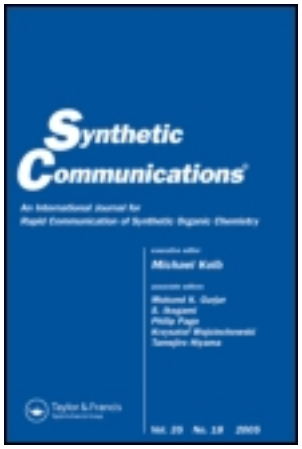

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
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Accepted author version posted online: 13 Feb 2012.Version of record first published: 08 Nov 2012.

To cite this article: Om Prakash , Nitya Sharma & Pooja Ranjan (2013): HTIB-Mediated One-Pot Synthesis of Some 2-Substituted 4-Styrylthiazoles from (E)-4-Arylbut-3-en-2-ones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 43:4, 582-586

To link to this article: http://dx.doi.org/10.1080/00397911.2011.604815

Synthetic Communications®, 43: 582–586, 2013

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2011.604815

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HTIB-MEDIATED ONE-POT SYNTHESIS OF SOME 2-SUBSTITUTED 4-STYRYLTHIAZOLES FROM (*E*)-4-ARYLBUT-3-EN-2-ONES

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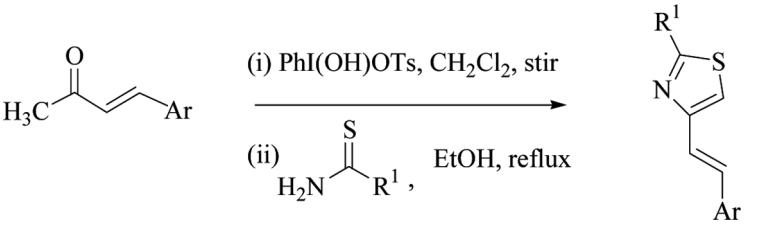
GRAPHICAL ABSTRACT



Abstract *The reaction of (*E*)-4-arylbut-3-en-2-ones with [(hydroxy(tosyloxy)iodo]benzene (HTIB) followed by treatment with thioureas, thioamide, and thiobenzamide has offered a one-pot synthesis of 2-substituted 4-styrylthiazoles.*

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Keywords (*E*)-4-Arylbut-3-en-2-ones; (*E*)-4-aryl-1-tosyloxy-but-3-en-2-ones; α-haloketones; [hydroxy(tosyloxy)iodo]benzene; 4-styrylthiazoles; α-tosyloxyketones

INTRODUCTION

4-Styrylthiazoles **4** are associated with some biological activitities.[1] Recent studies by Alajarin et al.[2,3] have demonstrated that 4-styrylthiazoles **4** behave as all-carbon dienes in Diels–Alder reactions with the participation of the formal C-C double bond of the thiazole ring and the side-chain double bond. The reactions with N-substituted maleimides, maleic anhydride, and naphthaquinone take place with a high level of stereocontrol to give the corresponding *endo*-cycloadducts in good to excellent yields. These studies have opened new synthetic perspectives for the functionalization of the thiazole ring. It is also known that 4-styrylthiazoles **4** are important precursors in the synthesis of chiral 2-substituted thiazolecarboxylic

Received March 7, 2011.

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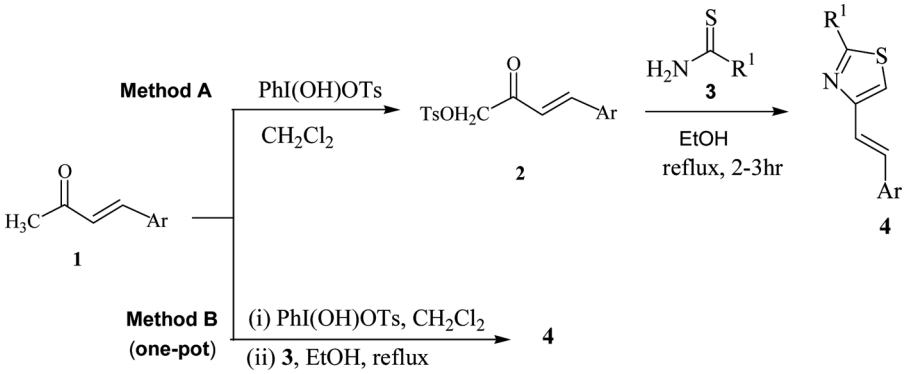
acids, which are building blocks for a number of thiazole-containing natural products.[4,5]

Synthetic access to these 4-styrylthiazoles **4** was facilitated by Hantzsch thiazole synthesis involving the reaction between α-halobenzalacetones and thioamides **3**. While initial studies employed α-iodo and α-bromobenzalacetones,[6] the most recent reports replaced them with α-chlorobenzalacetones.[2,3]

In view of the problems associated with the preparation and handling of α-haloketones, the development of alternative methodology avoiding the use of α-haloketones is always desirable. A great deal of research work from our laboratory and other research groups has emphasized the advantageous use of α-tosyloxyketones, thereby offering a superior alternative to conventional approach involving α-haloketones.[7–13] In continuation of our interest in developing simple and efficient procedures for the synthesis of various heterocycles, we report herein a facile synthesis of 4-styrylthiazoles **4** from (*E*)-4-arylbut-3-en-2-ones **(1)** via (*E*)-4-aryl-1-tosyloxy-but-3-en-2-ones **(2)**.

We started our work with the preparation of (*E*)-4-aryl-1-tosyloxy-but-3-en-2-ones **(2)** according to the procedure described in our previous study.[14] The resulting **2** was refluxed with equimolar quantities of **3** in EtOH for 2–3 h to give 4-styrylthiazoles **4** (method A) (Scheme 1). Encouraged by the result of stepwise procedure, it was considered worthwhile to attempt the synthesis of **4** through direct procedure without isolating (*E*)-4-aryl-1-tosyloxy-but-3-en-2-ones **(2)** (Method B) (Scheme 1); thus (*E*)-4-arylbut-3-en-2-one **1a** was oxidized with [hydroxy(tosyloxy)iodo]benzene (HTIB) in dichloromethane. Subsequently the residual mass obtained after removal of dichloromethane was treated with thiourea to afford 4-styrylthiazole **4a** in 86% yield. Other derivatives **(4b–4n)** were prepared in a similar manner in 80–89% yield. The formation of the known 4-styrylthiazoles **4a, 4g**, and **4k** was confirmed by comparing the melting points with those reported in the literature.[6,15] The new 4-styrylthiazoles **4b–4f** and **4h–j** were confirmed on the basis of elemental analysis and spectral data. These results along with physical data of **4** are summarized in Table 1.

A new facile HTIB method for the synthesis of 4-styrylthiazoles **4** has been developed. Compared to the previously reported methods, the new one-pot synthesis



Scheme 1.

Table 1. Physical data of 2-substituted 4-styrylthiazoles **4**

Compound	Ar	R^1	Mp (°C)	Yield (%)	
				Method A[a]	Method B[b]
4a	C_6H_5	NH_2	157–159[c]	71	86
4b	4-$CH_3C_6H_4$	NH_2	113–115	67	85
4c	4-$OCH_3C_6H_4$	NH_2	97–99	65	82
4d	4-BrC_6H_4	NH_2	132–134	75	89
4e	4-ClC_6H_4	NH_2	119–121	74	87
4f	4-FC_6H_4	NH_2	189–190	72	83
4g	C_6H_5	C_6H_5 NH	79–81[c]	77	89
4h	4-$CH_3C_6H_4$	C_6H_5 NH	163–165	75	88
4i	4-BrC_6H_4	C_6H_5 NH	135–137	73	87
4j	4-ClC_6H_4	C_6H_5 NH	82–84	76	88
4k	C_6H_5	CH_3	175–178[d] (picrates)	68	80
4l	4-$CH_3C_6H_4$	CH_3	79–81	67	83
4m	C_6H_5	C_6H_5	93–95	69	81
4n	4-$CH_3C_6H_4$	C_6H_5	110–112	65	80

[a]Yields of products **4** with regard to **2**.
[b]Yields of products **4** with regard to **1**.
[c]Lit mp°C (**4a** 160–162, **4g** 83, and **4k** 177–180).
[d]Yield of product **(4a** 49%, **4g** 64%, and **4k** 19%) with regard to iodomethylstyrylketone. To compare the results of present study with literature procedure, we carried out the synthesis of *p*-methylliodobenzalacetone according to Ref. 6, which on treatment with thioacetamide resulted in the formation of **4l.** However, overall yield of the product **4l** was only 10% against 83% obtained from the present study.

is not only manipulatively simpler but also affords much better overall yields than literature procedure.[6] Finally, the results of the present study further establish the advantage of HTIB-mediated syntheses of heterocyclic compounds.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer IR spectrophotometer. The ^1H NMR spectra were recorded on a Brucker 300-MHz instrument. The chemical shifts were expressed in parts per million (ppm) units downfield from an internal tetramethylsilane (TMS) standard.

Method B: One-Pot Synthesis of 2-Amino-4-(2-phenylethenyl)thiazole (4a)

HTIB (11 mmol) was added to a solution of (*E*)-4-phenylbut-3-en-2-one **1a** (10 mmol) in dichloromethane and the reaction mixture was stirred for 3–4 h. Most of the dichloromethane was removed by distillation and ethanol was added to it. Thiourea (10 mmol) was added to the resulting solution and the solution was refluxed for 2–3 h. Most of the solvent was concentrated in vacuo, and the resulting residue was basified with a saturated solution of $NaHCO_3$. The solid product thus

obtained was filtered, washed with water, and recrystallized from ethanol to afford the pure thiazole **4a**.

The same experimental procedure was adopted for the synthesis of other 4-styrylthiazole derivatives **4b–4n** (Table 1).

ACKNOWLEDGMENT

We are thankful to Kurukshetra University, Kurukshetra, India, for the award of a university research scholarship to Nitya Sharma and to the Council of Scientific and Industrial Research, New Delhi, India, for the award of a senior research fellowship to Pooja Ranjan for carrying out this work. The authors are also thankful to the Council of Scientific and Industrial Research (CSIR 01(2186)/07/EMR-II) for financial support.

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