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[HYDROXY(TOSYLOXY)IODO]BENZENE: A TOSYLOXYLATING AGENT WITH SELECTIVITY FOR KETONES IN THE REACTIONS WITH BENZALACETONES

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The treatment of enolizable ketones containing a conjugated double bond, namely benzalacetones with [hydroxy(tosyloxy)iodo]benzene, leads to regioselective tosyloxylation, thereby giving new compounds (α-tosyloxybenzalacetones).

Keywords: Benzalacetones; 1,3-diarylprop-2-en-1-ones (chalcones); [hydroxy(tosyloxy)iodo]benzene; α-tosyloxybenzalacetones

INTRODUCTION

A great deal of work on the synthetic application of [hydroxy(tosyloxy)iodo]-benzene (HTIB, Koser's reagent) has been published in recent years.[1–4] The functionalization of carbonyl compounds at α-carbon represents the most typical reaction of HTIB, that is, to introduce the tosyloxenium ion directly onto carbon.[5–13] Another important reaction of HTIB is the stereospecific ditosyloxylation of olefinic compounds, including chalcones.[14] For several years, we have been carrying out research on the use of HTIB in functionalization of carbonyl compounds.[12,15–17] In a previous communication from our laboratory, we have reported the synthesis and chemistry of α,β-ditosyloxyketones **4**, obtained from the reaction of α,β-unsaturated ketones (1,3-diarylprop-2-en-1-ones (**3**), chalcones) with HTIB in dichloromethane (Scheme 1).[17]

In continuation the research on synthetic applications of HTIB, we have examined the reaction of α,β-unsaturated ketones having enolizable moieties (i.e., benzalacetones) with HTIB. The aims were to ascertain the selectivity of the reaction and achieve α-tosyloxylation of ketones. As a consequence of this effort, we report selective α-tosyloxylation of ketones in the presence of a double bond by using HTIB.

The reaction was conducted following the procedure outlined here: 1.1 eq. of HTIB was added to dichloromethane solution of benzalacetone **1a**. After being stirred at room temperature for about 3 h followed by workup, the reaction afforded a single solid product, α-tosyloxybenzalacetone (**2a**) (Scheme 2) in 75% yield. The

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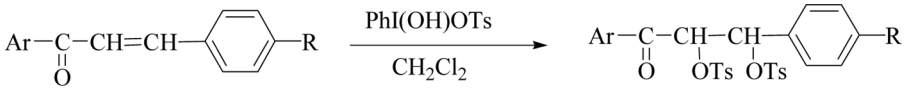

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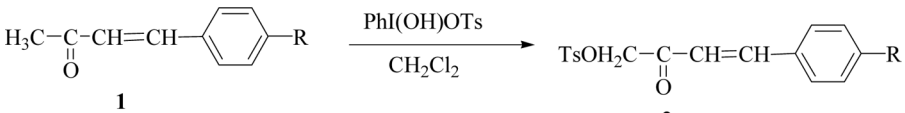
Scheme 1. Tosyloxylation of α,β-unsaturated ketones.



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Scheme 2. R=H, CH_3, OCH_3, Br, Cl, F, NO_2.

structure of the product was confirmed on the basis of elemental analysis and spectral data. The infrared (IR) spectrum displayed a carbonyl stretch at 1695 cm^{-1}. The ^1H NMR spectrum of **2a** showed a characteristic singlet at 4.74 due to the methylene group, which was further confirmed by DEPT-135 because of a negative peak.

Encouraged by the successful results, we studied the scope of new method for the synthesis of various aryltosyloxybenzalacetones (**2b–g**). The reaction of various benzalacetone derivatives (**1b–g**) with HTIB afforded the corresponding tosyloxybenzalacetones (**2b–g**) in good yields (Scheme 2; Table 1).

The physical data of products 4-aryl-1-tosyl-but-3-en-2-ones (**2a–g**) is given in Table 1.

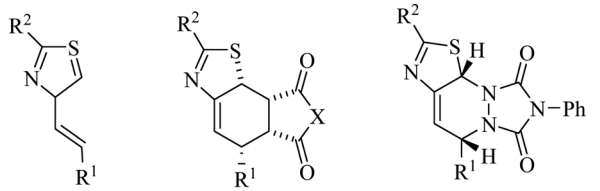
The α-tosyloxyketones (**2a–g**) obtained from this study are new compounds and are potential precursors for the synthesis of various α-functionalized ketones and heterocyclic compounds such as styrylthiazoles **5**, which find utility in the synthesis of compounds **6** and **7**[18,19] (Scheme 3) and other thiazole derivatives.

In summary, this study demonstrates that HTIB, a tosyloxylating agent, possesses selectivity for ketones in the presence of an α,β-unsaturated conjugated double bond. The reaction involves mild conditions and is a simple and high-yielding procedure. All the products, α-tosyloxybenzalacetones, synthesized in this study are new compounds that are potential precursors for further chemical modification to

Table 1. Physical data of 4-aryl-1-tosyl-but-3-en-2-ones (**2a–g**)

Compound	R	Mp (°C)	Yield (%)[a]
2a	H	60–61	75
2b	CH_3	132–134	74
2c	OCH_3	94–95	73
2d	Br	65–66	73
2e	Cl	67–68	74
2f	F	68–70	75
2g	NO_2	130–131	72

[a]Yields (%) of the products were calculated with respect to the corresponding benzalacetones **1**.



Scheme 3. Heterocyclic compounds.

synthesize the biologically active heterocyclic compounds. It is hoped that further studies will provide useful results in the synthesis of various α-functionalized α,β-unsaturated ketones and heterocyclic compounds.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer IR spectrophotometer. The ^{1}H NMR spectra were recorded on a Brucker 300-MHz instrument. The chemical shifts are expressed in parts per million downfield from an internal tetramethylsilane (TMS) standard. Benzalacetones were prepared according to literature procedures by condensation of acetone with substituted aldehydes in 10% aq. NaOH.[20]

General Procedure for Tosyloxylation of Benzalacetones (2a–g)

HTIB (11 mmol, 4.31 g) was added to a solution of benzalacetone **1a** (10 mmol, 1.46 g) in dichloromethane. The resulting mixture was allowed to stir at room temperature for 3–4 h. The solvent was evaporated in vaccuo. The gummy mass so obtained was triturated with petroleum ether (60–80 °C) to remove iodobenzene. The colorless solid obtained was thoroughly washed with water to remove the *p*-toluenesulphonic acid that formed as by-product. The solid was recrystallized from acetonitrile to give the pure product **2a**. Other derivatives **2b–g** were prepared in a similar manner.

Selected Data

4-Phenyl-1-tosyl-but-3-en-2-one (2a). IR (ν_{max}, in KBr): 1695 cm^{-1} (C=O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ): 2.43 (s, 3H, CH_3), 4.74 (s, 2H, CH_2), 6.91 (d, 1H, CH, $J = 16.04$ Hz), 7.38–7.56 (m, 5H, Ar-H), 7.36 (d, 2H, Ar-H, $J = 8.1$ Hz), 7.66 (d, 1H, CH, $J = 16.04$ Hz), 7.85 (d, 2H, Ar-H, $J = 8.1$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, δ): 21.70, 71.60, 120.10, 128.15, 128.79, 129.05, 130.06, 131.34, 132.41, 145.45, 191.40. Anal. calcd. for $C_{17}H_{16}O_4S$: C, 64.56; H, 5.06. Found: C, 64.35; H, 4.99. Mass, m/z: 316.

4-(4-Methylphenyl)-1-tosyl-but-3-en-2-one (2b). IR (ν_{max}, in KBr): 1695 cm^{-1} (C=O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ): 2.44 (s, 3H, CH_3), 2.35

(s, 3H, CH_3), 4.73 (s, 2H, CH_2), 6.92 (d, 1H, CH, $J = 16.04$ Hz), 7.34–7.51 (m, 4H, Ar-H), 7.41 (d, 2H, Ar-H, $J = 8.3$), 7.65 (d, 1H, CH, $J = 16.04$ Hz), 7.84 (d, 2H, Ar-H, $J = 8.3$). Anal. calcd. for $C_{18}H_{18}O_4S$: C, 65.45; H, 5.45. Found: C, 65.30; H, 5.29.

4-(4-Methoxyphenyl)-1-tosyl-but-3-en-2-one (2c). IR (ν_{max}, in KBr): 1696 cm^{-1} (C=O str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.34 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.73 (s, 2H, CH_2), 6.92 (d, 1H, CH, $J = 16.04$ Hz), 7.36–7.54 (m, 4H, Ar-H), 7.39 (d, 2H, Ar-H, $J = 8.3$), 7.63 (d, 1H, CH, $J = 16.04$ Hz), 7.84 (d, 2H, Ar-H, $J = 8.3$). Anal. calcd. for $C_{18}H_{18}O_5S$: C, 62.43; H, 5.20. Found: C, 62.40; H, 4.98.

4-(4-Bromophenyl)-1-tosyl-but-3-en-2-one (2d). IR (ν_{max}, in KBr): 1697 cm^{-1} (C=O str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.45 (s, 3H, CH_3), 4.75 (s, 2H, CH_2), 6.93 (d, 1H, CH, $J = 16.02$ Hz), 7.28 (d, 2H, Ar-H, $J = 8.1$), 7.36–7.53 (m, 4H, Ar-H), 7.61 (d, 1H, CH, $J = 16.02$ Hz), 7.86 (d, 2H, Ar-H, $J = 8.1$). Anal. calcd. $C_{17}H_{15}BrO_4S$: C, 51.65; H, 3.79. Found: C, 51.60; H, 3.79. Mass, m/z: 394.

4-(4-Chlorophenyl)-1-tosyl-but-3-en-2-one (2e). IR (ν_{max}, in KBr): 1697 cm^{-1} (C=O str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.45 (s, 3H, CH_3), 4.73 (s, 2H, CH_2), 6.91 (d, 1H, CH, $J = 15.9$ Hz), 7.34–7.51 (m, 4H, Ar-H), 7.41 (d, 2H, Ar-H, $J = 8.4$), 7.63 (d, 1H, CH, $J = 15.9$ Hz), 7.86 (d, 2H, Ar-H, $J = 8.4$); ^{13}C NMR ($CDCl_3$, 100 MHz, δ): 21.65, 72.20, 126.3, 127.8, 128.80, 129.00, 129.60, 130.60, 133.3, 133.50, 142.29, 199.50. Anal. calcd. $C_{17}H_{15}ClO_4S$: C, 58.20; H, 4.27. Found: C, 58.06; H, 4.16. Mass, m/z: 350.

4-(4-Fluorophenyl)-1-tosyl-but-3-en-2-one (2f). IR (ν_{max}, in KBr): 1698 cm^{-1} (C=O str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.45 (s, 3H, CH_3), 4.74 (s, 2H, CH_2), 6.93 (d, 1H, CH, $J = 16.00$ Hz), 7.36–7.55 (m, 4H, Ar-H), 7.39 (d, 2H, Ar-H, $J = 8.3$), 7.61 (d, 1H, CH, $J = 16.00$ Hz), 7.84 (d, 2H, Ar-H, $J = 8.3$). Anal. calcd. $C_{17}H_{15}FO_4S$: C, 61.08; H, 4.49. Found: C, 61.05; H, 4.31.

4-(4-Nitrophenyl)-1-tosyl-but-3-en-2-one (2g). IR (ν_{max}, in KBr): 1700 cm^{-1} (C=O str.); ^1H NMR ($CDCl_3$, 300 MHz, δ): 2.45 (s, 3H, CH_3), 4.74 (s, 2H, CH_2), 6.93 (d, 1H, CH, $J = 16.00$ Hz), 7.39 (d, 2H, Ar-H, $J = 8.3$), 7.61 (d, 1H, CH, $J = 16.00$ Hz), 7.84 (d, 2H, Ar-H, $J = 8.3$), 8.21–8.45 (m, 4H, Ar-H).

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