I$_2$-INDUCED ENOLETHERIFICATION OF $\alpha$-ALLYL SUBSTITUTED $\beta$-KETO SULFONES; A ROUTE TO 3-PHENYL SULFONYL-2,5-DISUBSTITUTED FURANS

Jae Wook Lee and Dong Young Oh*
Department of Chemistry
Korea Advanced Institute of Science and Technology
Seoul 130-650, Korea

Abstract - Iodine-induced enoletherification of $\alpha$-allyl substituted $\beta$-keto sulfones leads to 4,5-dihydro-5-iodomethylfurans which are readily converted to 3-phenylsulfonyl-2,5-disubstituted furans.

Electrophilic additions to functionalized alkenes leading to heterocyclic skeletons via a cyclization of the remote functional group of alkene are widely used in organic synthesis. Many electrophiles have been studied, but iodocyclization is particularly well developed because of the mild conditions of cyclization and the ease of subsequent elaboration. Numerous examples of iodolactonization, iodoetherification, and iodolactamization have been reported, and considerable progress has been made for cyclization. On the other hand, few investigations have been made for halo-cyclization which was introduced simultaneously functional group. In this paper we report the iodine-induced enoletherification of $\alpha$-allyl substituted $\beta$-keto sulfones and subsequent transformation of the iodide products.

In the course of investigation on the reactivity of $\beta$-keto sulfone, we have found that a mixture of iodine, anhydrous sodium bicarbonate and $\alpha$-allyl substituted $\beta$-keto sulfones (1) in dry acetonitrile provided 4,5-dihydro-5-iodomethylfurans (2). The required $\alpha$-allyl substituted $\beta$-keto sulfones were easily prepared from $\beta$-keto...
sulfones and allyl bromide in the presence of potassium carbonate in DMF or acetonitrile. In order to find out optimum conditions, we have examined several reaction conditions by using 4-(phenylsulfonyl)-6-hepten-3-one (\(1_R = \text{Et}\)) as a model compound. The reaction proceeded smoothly under 2.2 equiv. of iodine and 1.2 equiv. of sodium bicarbonate in acetonitrile (0.03 M) at ambient temperature. As shown in Table 1, the present method was successfully applied to various \(\alpha\)-allyl substituted \(\beta\)-keto sulfones. For example, 1-phenyl-2-(phenylsulfonyl)-4-pentenone (\(1_R = \text{Ph}\)) and 3-(phenylsulfonyl)-5-hexen-2-one (\(1_R = \text{Me}\)) were cyclized to the corresponding dihydrofurans (3) in 62% and 85% yield, respectively. However, this method reaches a limit with 2,2-dimethyl-4-(phenylsulfonyl)-6-hepten-3-one (\(1_R = \text{Bu}^t\)) and iodo-hydroxylated product (3) was obtained instead of dihydrofuran under the present conditions. On the other hand, it was found that the halocyclization of \(N, N\)-dimethyl-2-(phenylsulfonyl)-4-pentanamide (\(1_R = \text{NMe}_2\)) under the present conditions gave 4-iodomethyl-2-(phenylsulfonyl)-\(\gamma\)-butyrolactone (4) after aqueous work-up. The stereochemistry of 3 and 4 was not established.

\[
\begin{align*}
&\text{SO}_2\text{Ph} \quad 1.2 \text{ eq. NaHCO}_3, 2.2 \text{ eq. I}_2 \\
&\text{MeCN, room temperature, 20 h} \\
\end{align*}
\]

\[
\begin{align*}
&\text{SO}_2\text{Ph} \\
&\text{Me}_2\text{N} \quad \text{I} \\
\end{align*}
\]

It was expected that dehydroiodination and subsequent isomerization of 4,5-dihydro-5-iodomethylfurans would lead to furan derivatives. Therefore we have investigated reaction conditions by using 2-ethyl-5-(iodomethyl)-3-(phenylsulfonyl)-4,5-dihydrofuran (2, \(R = \text{Et}\)) as a model compound to convert 4,5-dihydro-5-iodomethylfurans into furan derivatives. It was found that the dehydroiodination of 2 (\(R = \text{Et}\)) by 1.2 equiv. of \(\text{DMU}\) in benzene at room temperature gave 4,5-dihydro-5-methylenefuran (5) in quantitative yield. With this result in hand, we next turned our attention to examining the isomerization of eliminated product in situ. When 5 equiv. of \(\text{DMU}\) are used at room temperature, after 24 h dehydroiodination reaction led directly to furans which is attributed to basic isomerization of 4,5-dihydro-5-methylenefuran.
Table 1. Synthesis of Furan Derivatives (6) from \(\alpha\)-Allyl Substituted \(\beta\)-Keto Sulfones (1) via Iodine-Induced Enoletherification.

<table>
<thead>
<tr>
<th>Entry</th>
<th>(R)</th>
<th>Yield(%)(^a) of 2</th>
<th>Yield(%)(^a) of 6</th>
<th>m.p.((^\circ)C) of 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Me</td>
<td>85</td>
<td>95</td>
<td>65 - 66</td>
</tr>
<tr>
<td>b</td>
<td>Et</td>
<td>81</td>
<td>93</td>
<td>oil</td>
</tr>
<tr>
<td>c</td>
<td>n-Pr</td>
<td>78</td>
<td>92</td>
<td>58 - 59</td>
</tr>
<tr>
<td>d</td>
<td>i-Pr</td>
<td>70(^b)</td>
<td>75</td>
<td>oil</td>
</tr>
<tr>
<td>e</td>
<td>Ph</td>
<td>62</td>
<td>94</td>
<td>106 - 107</td>
</tr>
</tbody>
</table>

\(^a\) Isolated yield of pure product. \(^b\) Involving small amount of impurity.

In situ by excess DBU. Thus we have obtained furan derivatives (6) from 4,5-dihydro-5-iodomethylfurans (2) under refluxing benzene overnight in the presence of 3 equiv. of DBU. The results of elimination and subsequent isomerization of 4,5-dihydro-5-iodomethylfuran in one-flask are shown in Table 1. This method was successfully applied to all 4,5-dihydro-5-iodomethylfurans.\(^3\)

5 eq. DBU, room temperature, benzene, 24 h

\[ \begin{array}{c}
\text{SO}_2\text{Ph} \\
\text{Et}
\end{array} \]

1.2 eq. DBU, benzene

room temperature, 20 h

In conclusion, the proposed sequence, involving both readily available reagents and simple and mild conditions, may be considered as an effective and versatile approach to dihydrofuran and furan derivatives.

General procedure: A mixture of \(I_2\) (2.2 mmol), anhydrous \(\text{Na}_2\text{CO}_3\) (1.2 mmol) and \(\alpha\)-allyl substituted \(\beta\)-keto sulfone (1 mmol) in dry acetonitrile (30 ml) was stirred at
room temperature for 24 h. Then ether (70 ml) was added and the organic phase was washed with 0.1 N sodium thiosulfate (2 x 5 ml), brine (2 x 5 ml) and dried over anhydrous magnesium sulfate. Removal of the solvent under a reduced pressure afforded 4,5-dihydro-5-iodomethylfuran. Then DRU (3 equiv.) was added to a solution of 4,5-dihydro-5-iodomethylfuran in benzene (7 ml) and the mixture was refluxed overnight. After the usual work-up was performed, isolation of furan derivatives was readily accomplished by flash column chromatography on silica gel.

REFERENCES AND NOTES

7. cf. We have found that the reaction of 4-(phenylsulfonyl)-6-hepten-3-one with 1.2 equiv. of HBS in the presence of 1.2 equiv. of NaHCO₃ in acetonitrile gave α-brominated product.

8. All the compounds described in this communication have been characterized by spectroscopic data. Representative spectral data: 2a: ¹H-Nmr(CDCl₃) δ = 2.24 (t, J = 1 Hz, 3H), 2.49-3.09 (m, 2H), 3.23 (d, J = 6 Hz, 2H), 4.37-4.84 (m, 1H), 7.39-7.91 (m, 5H). Mass (70 eV), m/z (5) 77 (100), 125 (95.4), 364 (M⁺, 46.9).
   3: ¹H-Nmr(CDCl₃) δ = 1.25 (s, 9H), 1.88-2.22 (m, 2H), 3.26 (d, J = 5 Hz, 2H), 4.18 (s, 1H),

— 1420 —
3.78-4.48 (m, 1H), 3.78-4.48 (m, 1H), 4.98 (dd, J=9 Hz, 5 Hz, 1H), 7.42-7.95 (m, 5H). IR (KBr) 3449, 1703, 1400, 1369, 1307, 1143, 1091 cm⁻¹. Mass (70 eV), m/z (%) 77(100), 125(86.7), 169(92.3), 195(51.7), 367(21.2, M⁺, Br⁻).

4: ¹H-NMR (CDCl₃) δ=2.1-3.2 (m, 1H), 3.38 (d, J=5 Hz, 2H), 4.2 (d, J=10 Hz, 4H, 1H), 4.4-4.97 (m, 1H), 7.5-8.03 (m, 5H). IR (KBr) 3060, 1774, 1320, 1184, 1157 cm⁻¹. Mass (70 eV), m/z (%) 77(100), 97(32.5), 141(37.8), 239(25.8), 366(M⁺, 0.2).

5: ¹H-NMR (CDCl₃) δ=1.2 (t, J=7 Hz, 3H), 2.78 (q, J=7 Hz, 2H), 3.52 (m, 2H), 4.24 (m, 1H), 4.62 (m, 1H), 6.4-7.63 (m, 3H), 7.7-7.93 (m, 3H). IR (NaCl) 1673, 1635, 1311, 1161 cm⁻¹.

6a: ¹H-NMR (CDCl₃) δ=2.21 (s, 3H), 2.54 (s, 3H), 6.13 (s, 1H), 7.35-7.62 (m, 3H), 7.72-8.02 (m, 2H). IR (KBr) 1616, 1573, 1311, 1155 cm⁻¹. Mass (70 eV), m/z (%) 77(77.9), 111(56.5), 126(43), 236(M⁺, 100).

6b: ¹H-NMR (CDCl₃) δ=1.42 (t, J=7 Hz, 3H), 2.22 (s, 3H), 2.92 (d, J=7 Hz, 2H), 6.13 (s, 1H), 7.38-7.62 (m, 3H), 7.77-7.98 (m, 2H). IR (NaCl) 1608, 1567, 1313, 1155 cm⁻¹. Mass (70 eV), m/z (%) 77(93.9), 108(40.3), 125(91.1), 250(M⁺, 100).


Received, 7th May, 1990