

I_2 -INDUCED ENOLETHERIFICATION OF α -ALLYL SUBSTITUTED β -KETO SULFONES;
A ROUTE TO 3-PHENYLSULFONYL-2,5-DISUBSTITUTED FURANS

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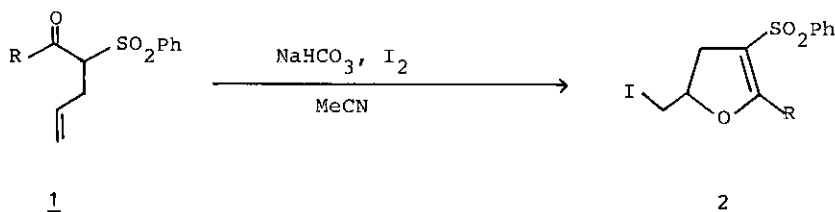
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Abstract - Iodine-induced enoletherification of α -allyl substituted β -keto sulfones leads to 4,5-dihydro-5-iodomethylfurans which are readily converted to 3-phenylsulfonyl-2,5-disubstituted furans.

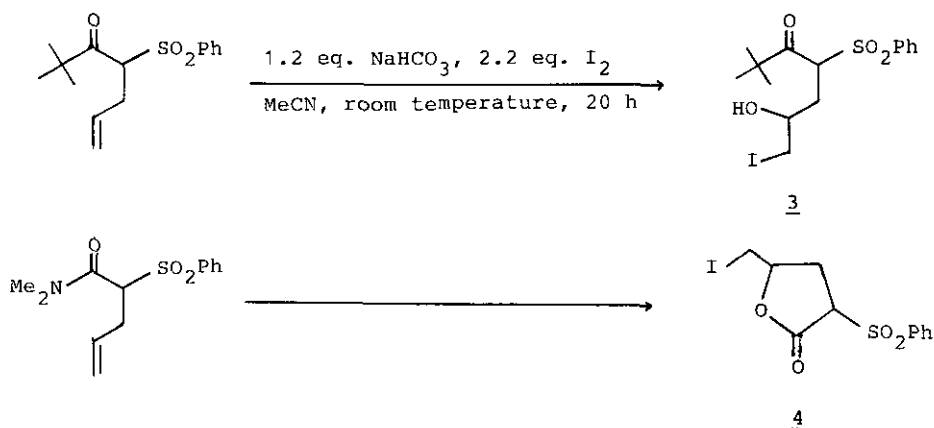
Electrophilic additions to functionalized alkenes leading to heterocyclic skeletons via a cyclization of the remote functional group of alkene are widely used in organic synthesis.¹ Many electrophiles have been studied, but iodocyclization is particularly well developed because of the mild conditions of cyclization and the ease of subsequent elaboration.² Numerous examples of iodolactonization,³ iodoetherification,⁴ and iodolactamization⁵ 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.⁶ In this paper we report the iodine-induced enoletherification of α -allyl substituted β -keto sulfones and subsequent transformation of the iodide products.



In the course of investigation on the reactivity of β -keto sulfone, we have found that a mixture of iodine, anhydrous sodium bicarbonate and α -allyl substituted β -keto sulfones (**1**) in dry acetonitrile provided 4,5-dihydro-5-iodomethylfurans (**2**). The required α -allyl substituted β -keto sulfones were easily prepared from β -keto

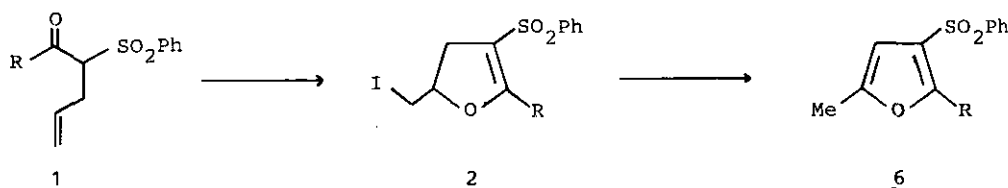
sulfones and allyl bromide in the presence of potassium carbonate in DMF or acetonitrile. In order to find out optimum conditions, we have examined several reaction conditions by using 4-(phenylsulfonyl)-6-hepten-3-one(1, R = Et) as a model compound. The reaction proceeded smoothly under 2.2 equiv. of iodine and 1.2 equiv. of sodium bicarbonate in acetonitrile(0.03 M) at ambient temperature.⁷

As shown in Table 1, the present method was successfully applied to various α -allyl substituted β -keto sulfones. For example, 1-phenyl-2-(phenylsulfonyl)-4-pentenone(1, R=Ph) and 3-(phenylsulfonyl)-5-hexen-2-one(1, R=Me) were cyclized to the corresponding dihydrofurans(2)⁸ in 62% and 85% yield, respectively. However, this method reaches a limit with 2,2-dimethyl-4-(phenylsulfonyl)-6-hepten-3-one(1, R=Bu^t) and iodo-hydroxylated product(3)⁸ 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-pentenamide(1, R=NMe₂) under the present conditions gave 4-iodomethyl-2-(phenylsulfonyl)- γ -butyrolactone(4)⁸ after aqueous work-up.⁹ The stereochemistry of 3 and 4 was not established.



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=Et) as a model compound to convert 4,5-dihydro-5-iodomethylfurans into furan derivatives. It was found that the dehydroiodination of 2 (R=Et) by 1.2 equiv. of DBU 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 DBU 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

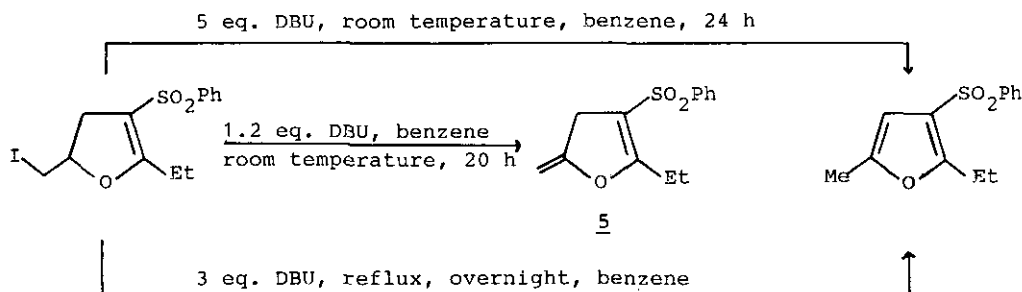
Table 1. Synthesis of Furan Derivatives (6) from α -Allyl Substituted β -Keto Sulfones(1) via Iodine-Induced Enoletherification.



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

^aIsolated yield of pure product. ^bInvolving 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-iodomethylfuran.³



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 $NaHCO_3$ (1.2 mmol) and α -allyl substituted β -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 DBU(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

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7. cf. We have found that the reaction of 4-(phenylsulfonyl)-6-hepten-3-one with 1.2 equiv. of NBS 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=1Hz, 3H), 2.49-3.09(m, 2H), 3.23(d, J=6Hz, 2H), 4.37-4.84(m, 1H), 7.39-7.91(m, 5H). Mass(70 eV), m/z(%) 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=5Hz, 2H), 4.18(s, 1H),

3.78-4.48(m,1H), 3.78-4.48(m,1H), 4.98(dd,J=9Hz,5Hz,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, $\text{M}^+ - \text{Bu}^t$).

4: $^1\text{H-Nmr}(\text{CDCl}_3)$ δ =2.1-3.2(m,1H), 3.38(d,J=5Hz,2H), 4.2(dd,J=10Hz,4Hz,1H), 4.4-4.37(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: $^1\text{H-Nmr}(\text{CDCl}_3)$ δ =1.2(t,J=7Hz,3H), 2.78(q,J=7Hz,2H), 3.52(m,2H), 4.24(m,1H), 4.62(m,1H), 7.4-7.63(m,3H), 7.73-7.93(m,2H), Ir(NaCl)1673, 1635, 1311, 1161 cm^{-1} .

6a: $^1\text{H-Nmr}(\text{CDCl}_3)$ 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: $^1\text{H-Nmr}(\text{CDCl}_3)$ δ =1.2(t,J=7Hz,3H), 2.22(s,3H), 2.92(d,J=7Hz,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).

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