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

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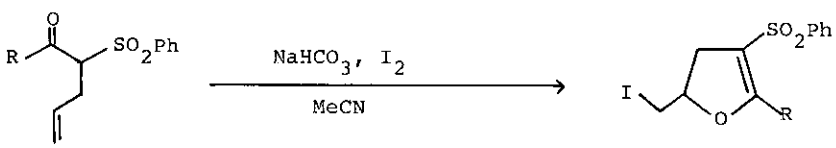
Abstract - Iodine-induced enoletherification of α-allyl substituted β-keto sulfones leads to 4,5-dihydro-5-iodomethylfurans which are readily converted to 3-phenylsulfonyl-2,5-disubstituted furans.

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 iodolactamization[5] 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.



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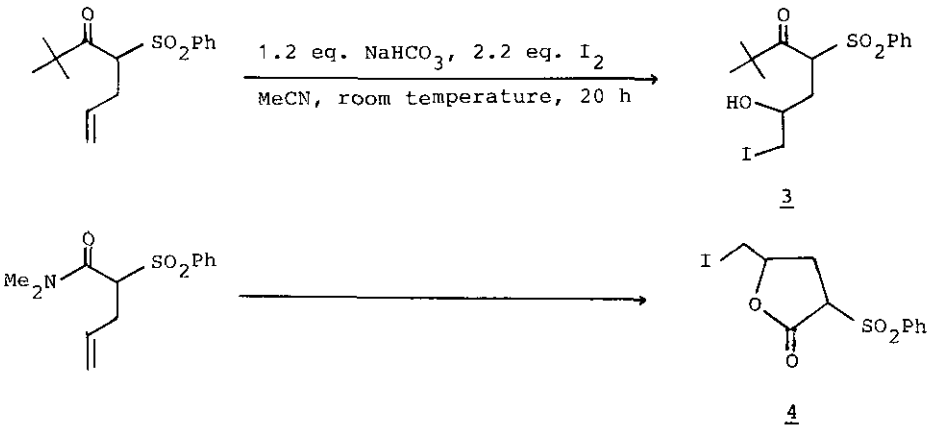
In the course of investigation on the reactivity of β-keto sulfone, we have found that a mixture of iodine, anhydrous sodium bicarbonate and α-allyl substituted β-keto sulfones (1) in dry acetonitrile provided 4,5-dihydro-5-iodomethylfurans(2). The required α-allyl substituted β-keto sulfones were easily 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=NMe_2) 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.*



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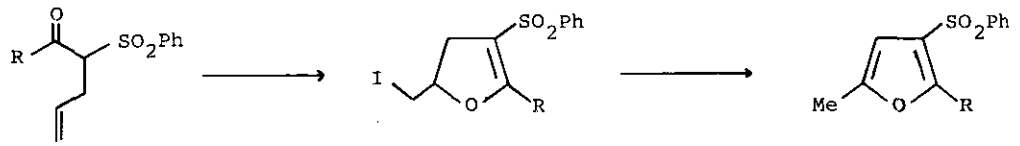
It was expected that dehydroiodination and subsequent isomerization of 4,5-dihydro-5-iodomethylfurans would lead to furan derivatives. Therefore we have investigated reaction conditions by using 2-ethyl-5-(iodomethyl)-3-(phenylsulfonyl)-4,5-dihydrofuran(2,R=Et) as a model compound to convert 4,5-dihydro-5-iodomethylfurans 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.



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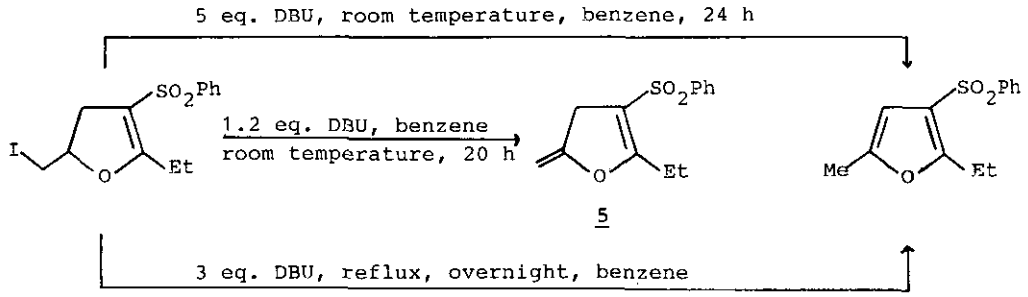
Entry	R	Yield(%)[a] of 2	Yield(%)[a] of 6	m.p.(°C) of 6
a	Me	85	95	65 - 66
b	Et	81	93	oil
c	n-Pr	78	92	58 - 59
d	i-Pr	70[b]	75	oil
e	Ph	62	94	106 - 107

[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-iodomethylfuran.[3]



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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 × 5 ml), brine(2 × 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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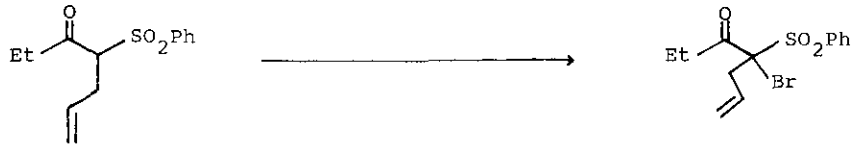
7. cf. We have found that the reaction of 4-(phenylsulfonyl)-6-hepten-3-one with 1.2 equiv. of NBS in the presence of 1.2 equiv. of $NaHCO_3$ in acetonitrile gave α-brominated product.



8. All the compounds described in this communication have been characterized by spectroscopic data. Representative spectral data; 2a: ^{1}H-Nmr($CDCl_3$) 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: ^{1}H-Nmr($CDCl_3$) 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, 1091cm^{-1}. Mass(70 eV), m/z(%) 77(100), 125(86.7), 169(92.3), 195(51.7), 367(21.2, M^+- Bu^t).

4: ^{1}H-Nmr($CDCl_3$) δ=2.1-3.2(m,1H), 3.38(d,J=5Hz,2H), 4.2(dd,J=10Hz,4Hz,1H), 4.4-4.87(m,1H), 7.5-8.03(m,5H). Ir(KBr) 3060, 1774, 1320, 1184, 1157cm^{-1}. Mass(70 eV), m/z(%) 77(100), 97(32.5), 141(37.8), 239(25.8), 366(M^+, 0.2).

5: ^{1}H-Nmr($CDCl_3$) 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, 1161cm^{-1}.

6a: ^{1}H-Nmr($CDCl_3$) 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}H-Nmr($CDCl_3$) 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, 1155cm^{-1}. Mass(70 eV), m/z(%) 77(93.9), 108(40.3), 125(91.1), 250(M^+,100).

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