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# SILVER TETRAFLUOROBORATE INDUCED REACTION OF TRIMETHYLSILYL ENOL ETHERS WITH 2,3-DIIODO-1-(PHENYLSULFONYL)-1-PROPENE AS A METHOD FOR PREPARING SUBSTITUTED FURANS

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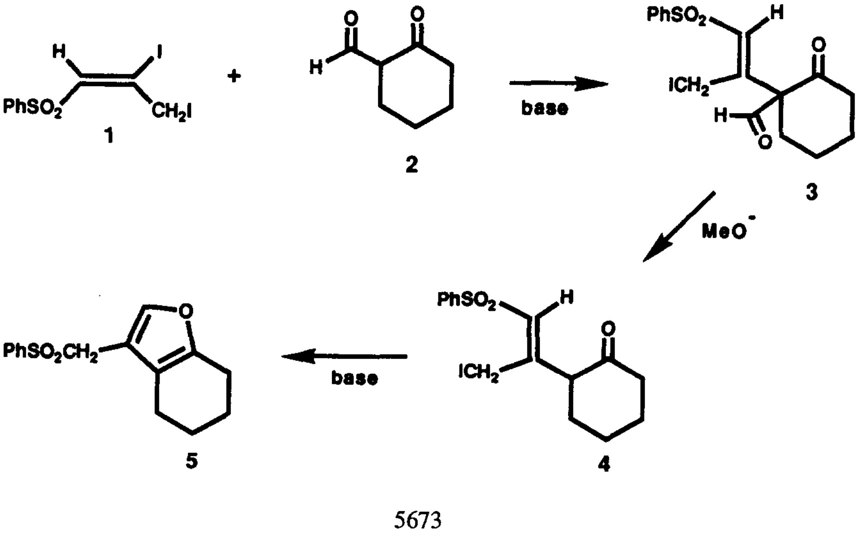
**Abstract:** *Treatment of 2,3-diiodo-1-(phenylsulfonyl)-1-propene (DIP) with various trimethylsilyl enol ethers in the presence of silver tetrafluoroborate gives alkylation products derived from $S_N2$ displacement of the terminal halide. These compounds readily cyclize with base to produce substituted furans.*

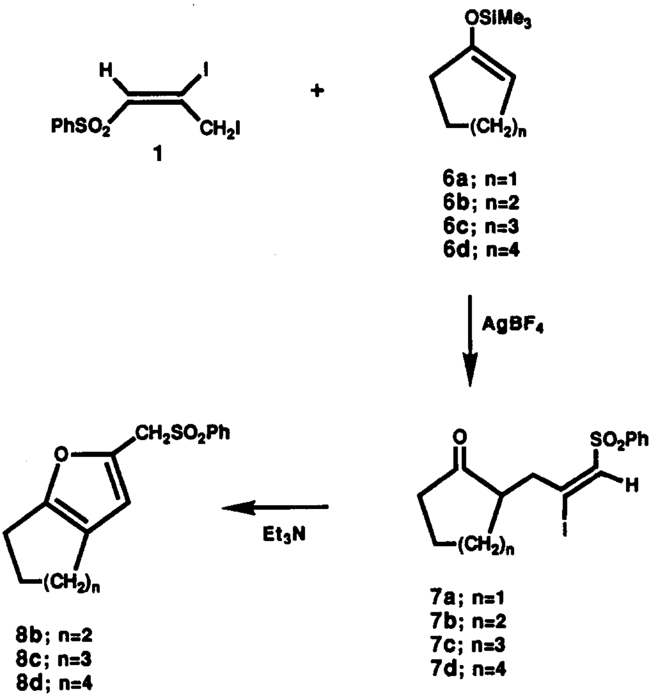
Fused multicyclic furans have continued to hold a fascination for synthetic organic chemists.[1-7] The furan nucleus occurs in a variety of natural products from both land and marine sources[8], with 2,3- and 3,4-substitution being most commonly found in nature. Furans are also useful synthetic intermediates as they participate in inter- and intramolecular Diels-Alder reactions and may be converted by oxidation to a variety of products.[9] A well-studied class of compounds, the annulated furans can boast a daunting number of biologically significant members, some known since antiquity.[10] Various types of sesqui- and diterpenes contain an annulated furan ring as a common structural feature. Some prominent members of this class of compounds are the paniculides[11], the cytotoxic furanonaphthoquinones[12], as well as furodysin and furodysinin.[13]

In a recent paper we reported on the use of 2,3-dibromo-1-phenylsulfonyl-1-propene (DBP) as an effective reagent for the synthesis of substituted furans.[14] An analogous reaction also occurs with the related iodo reagent DIP.[15] As indicated in the illustration, the first step involves an

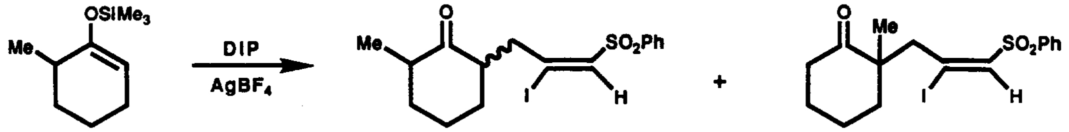


addition-elimination reaction of the β-dicarbonyl enolate onto the activated π-bond of DIP.[16] The initially formed ketoaldehyde **3** was readily deformylated upon exposure to sodium methoxide. The resulting halo sulfone **4** affords furan **5** by intramolecular displacement of the halide by the resulting enolate anion. If reaction of the enolate with DIP could be induced to occur on the allylic rather than the vinylic carbon atom, the expansion of this methodology into the synthesis of a series of isomeric furans could be realized. In this communication we report that the reaction of trimethylsilyl enol ethers with DIP in the presence of silver tetrafluoroborate induces a complete reversal in the regioselectivity of furan formation.

The viability of the desired $S_N2$ displacement would depend on our ability to activate the allylic iodide as a leaving group. The potential reactivity of the vinyl iodide and sulfone in the presence of Lewis acids was a concern. However, the reaction of **1** and the TMS enol ether **6b** with $TiCl_4$ or $ZnCl_2$ led only to the destruction of the enol silyl ether, and DIP was recovered unchanged. We found that treating **1** and **6a** at 25°C in methylene chloride (0.05 M) with 2.0 equiv. of silver tetrafluoroborate produced **7a** in 82% yield after chromatographic purification[17]. A related set of reactions took place with the silyl enol ethers derived from cyclohexanone (**7b**, 71%), cycloheptanone (**7c**, 88%) and cyclooctanone (**7d**, 81%). Treatment of iodo-(phenylsulfonyl) ketones 7b-7d with triethylamine in THF at 25°C proceeded smoothly to give the 2-phenylsulfonylmethyl substituted furans **8b-8d** in 65%, 76% and 86% yield, respectively[18].



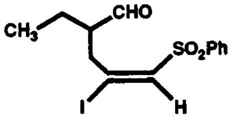
Further investigation of this reaction with the silyl enol ether derived from 2-methylcyclohexanone revealed that the alkylation occurred from the kinetically produced enolate. Thus, the major product obtained was a 71:23 mixture of diastereomers **9a** and **9b** with only a trace of the 2,2-dialkylated ketone **10** (<5%).



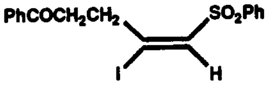
**9a**; *trans* (71%)
**9b**; *cis* (23%)

**10** (5%)

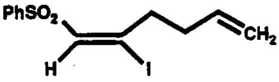
In addition to the cyclic ketones, silyl enol ethers derived from butyraldehyde and acetophenone were also successfully employed in this reaction sequence to give **11** and **12**, although in a somewhat diminished yield (50%). Allyl silane was also found to act as a nucleophile producing **13** in good yield when treated with DIP and silver tetrafluoroborate.



**11**



**12**



**13**

It is important to note that $AgBF_4$ was critical to the success of the alkylation[19]. Without it, the reaction did not proceed. We believe that $AgBF_4$ serves not only to induce charge buildup on the allylic position but also to assist in the desilylation step. This presumably occurs by attack of some fluoride ion on the silicon atom and the resulting enolate then reacts to give products formally derived from $S_N2$ displacement of the terminal halide. The regioselectivity of alkylation using these conditions nicely complements that encountered with β-dicarbonyl anions which gives products derived from vinylic displacement.[14] Thus, by altering the experimental conditions, it is possible to prepare either 2,3,4- (**5**) or 2,3,5- (**8**) substituted furans. In addition to its ease of removal, the pendant sulfone also offers a convenient and versatile site for further elaboration (via alkylation[20] or Julia coupling[21]). This strategy toward furans clearly could be applied to more complex targets. We are currently investigating the scope of this protocol and additional findings will be reported at a later time.

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### References and Notes

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15. DIP is prepared by the addition of iodine in benzene to (phenylsulfonyl)allene using a 250 W sunlamp. It is a stable, crystalline solid, mp 91-92°C; NMR ($CDCl_3$, 90 MHz) $\delta$ 5.16 (s, 2H), 6.91 (s, 1H), 7.60-7.79 (m, 3H), and 7.94-8.12 (m, 2H). The stereochemistry about the pi-bond was established as *E*, on the basis of an X-ray single crystal structure analysis.
16. Alkylation of simple aldehydes or ketones with DIP using various bases gave complex reaction mixtures.
17. Compound **7a**: mp 98-99°C; NMR ($CDCl_3$, 300 MHz) $\delta$ 1.60-1.90 (m, 2H), 2.00-2.30 (m, 3H), 2.30-2.52 (m, 2H), 3.05 (dd, 1H, J=14.4 and 4.2 Hz), 3.46 (dd, 1H, J=14.4 and 9.9 Hz), 7.05 (s, 1H), 7.50-7.70 (m, 3H), and 7.80-8.00 (m, 2H).
18. Compound **8b**: mp 100-101°C; NMR ($CDCl_3$, 300 MHz) $\delta$ 1.60-1.70 (m, 2H), 1.70-1.80 (m, 2H), 2.34 (t, 2H, J=5.9 Hz), 2.41 (t, 2H, J=6.0 Hz), 4.33 (s, 2H), 6.09 (s, 1H), 7.45-7.55 (m, 2H), 7.60-7.67 (m, 1H), and 7.73-7.80 (m, 2H).

    Compound **8c**: mp 92-93°C; NMR ($CDCl_3$, 300 MHz) $\delta$ 1.53-1.80 (m, 6H), 2.38 (t, 2H, J=5.4 Hz), 2.54 (t, 2H, J=5.9 Hz), 4.29 (s, 2H), 6.06 (s, 1H), 7.45-7.55 (m, 2H), 7.60-7.70 (m, 1H), and 7.70-7.80 (m, 2H).

    Compound **8d**: mp 64-65°C; NMR ($CDCl_3$, 300 MHz) $\delta$ 1.35-1.47 (m, 4H), 1.50-1.65 (m, 4H), 2.43 (t, 2H, J=6.3 Hz), 2.54 (t, 2H, J=6.3 Hz), 4.32 (s, 2H), 6.04 (s, 1H), 7.43-7.50 (m, 2H), 7.55-7.65 (m, 1H), and 7.67-7.75 (m, 2H).
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