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REGIOSELECTIVE GENERATION AND TRAPPING OF MONO- AND DIANIONS OF 3-ARYLSULFONYL FURANS. BIDENTATE CARBANION STABILIZATION VIA SULFONES

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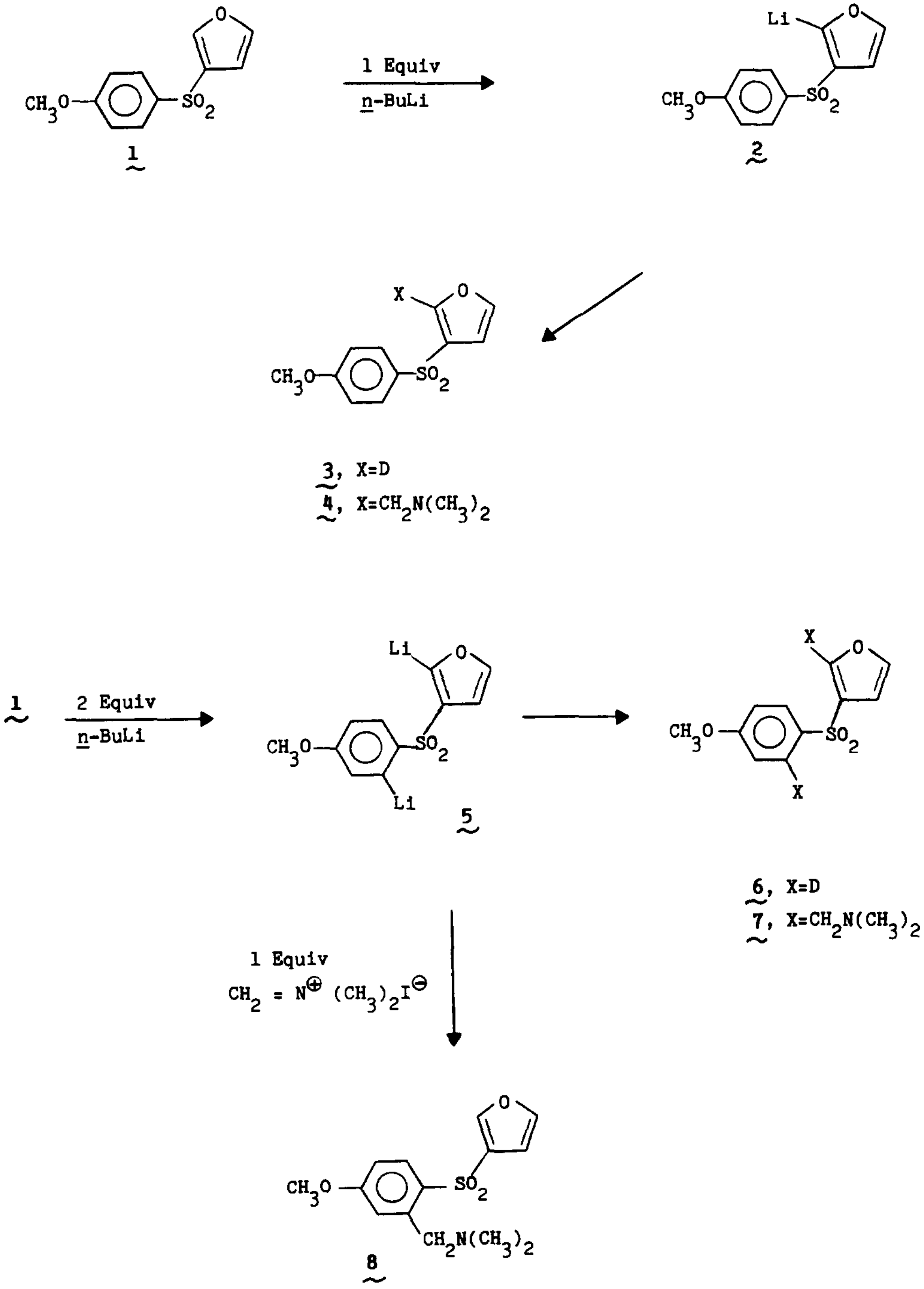
SUMMARY: Mono- and dianions of 3-(4-methoxyphenylsulfonyl) furan are regioselectively generated and trapped illustrating the unique carbanion stabilizing abilitv of the sulfone.

The occurrence of the furan nucleus in an intriguing array of natural products[1] has fostered much interest in new synthetic methods.[2] Of singular importance toward the goal of regioselective functionalization of the furan nucleus is progress in heteroatom-assisted generation of mono- and dianions.[3-5] Since only a few substituents are known which effectively direct deprotonations at the ring carbons of furan, new alternatives demonstrating orientational control are of interest. In this letter we report that the 3-(4-methoxyphenylsulfonyl) group exerts dramatic orientational control over both mono- and dianion formation, making use in the latter case of its unique bidentate carbanion stabilizing potential, thus allowing the efficient synthesis of regioselectively functionalized furans.

Treatment of 3-(4-methoxyphenylsulfonyl)furan (1), prepared from MCPBA oxidation of the coupling product of 3-furyllithium and 4-methoxyphenvldisulfide,[6] with 1 equivalent of n-BuLi at -78° in tetrahydrofuran gave the anion 2 as a clear yellow solution. This anion was trapped[7] with D_2O and N,N-dimethylmethyleneammonium iodide (Eschenmoser's salt) to provide 3 and 4,[8] respectively. Analysis of the 300 MHz H^1 NMR spectrum of the crude reaction mixtures showed no evidence for significant amounts of isomeric products. Thus, the 3-phenylsulfonyl group, as was found for the carboxv[9] and acetal[10] functions, directs metallation cleanly to the adjacent 2-position.

Treatment of 1 with 2 equivalents of n-BuLi afforded a clear yellow solution of dianion 5, as shown by trapping with excess D_2O or Eschenmoser's salt to give 6 and 7, respectively. Generation of 5 at -78° and trapping with D_2O at 15 minutes, 1 hour and 2 hours gave only 6, illustrating

SCHEME


1
1 Equiv
n-BuLi
Li
2
3, X=D
4, X=CH2N(CH3)2
1
2 Equiv
n-BuLi
Li
Li
5
X
X
6, X=D
7, X=CH2N(CH3)2
1 Equiv
CH2 = N⊕ (CH3)2I⊖
CH2N(CH3)2
8
CH3O
SO2
O

the stability of this dianion at low temperature. Treatment of the tetrahydrofuran solution of 5 with 1 equivalent of Eschenmoser's salt gave 8 as the sole major product, as expected from alkylation at the more reactive phenyl carbanion site. In preparative scale runs, the yields of amines 7[8] and 8[8] were 82% and 88%, respectively, demonstrating the synthetic utility of the present method.[11]

The regioselective generation of 5 from 2 is remarkable since ample precedent exists for deprotonation at C-5 of the furan to give the furan dianion,[12] as well as at C-3' of the phenyl ring, utilizing the well-documented ortho directing effect of the methoxy function.[3,13] We feel that the dramatic orientational control of the sulfone function is a consequence of its unique bidentate carbanion stabilizing ability in which (Figure 1) the sulfone oxygens simultaneously stabilize the dilithio intermediate. This effect, although previously noted,[14,15] has been largely neglected by synthetic chemists.

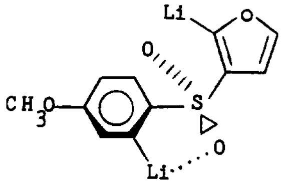


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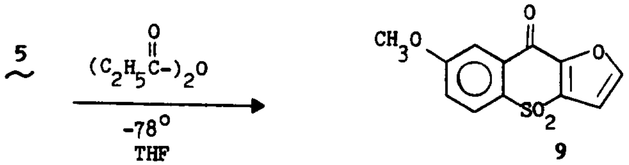
Figure 1

We have also found that the dilithio species 5 is a viable precursor to more complex polycyclic compounds. For example, treatment of 5 at -78° with the conjunctive reagent diethylcarbonate



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affords the tricyclic ketone 9, which is not readily accessible by other means.

In summary, we have demonstrated the unique potential of the sulfone function for regioselective generation of mono- and dianions of an arylsulfonyl furan. Trapping of these stabilized carbanions with electrophiles gives, in high yield, specific regioisomers which are not readily accessible by other methods. We anticipate broad applicability of these concepts to other heterocycles as well.

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7. In this and all other experiments the electrophile in THF solution was added dropwise to the THF solution of the anion.
8. The NMR spectra were as follows: **4**; (300 MHz, $CDCl_3$) δ 2.29 (6H, s), 3.85 (2H, s), 3.87 (3H, s), 6.60 (1H, d, J = 2 Hz), 6.99 (2H, dd, J = 8 Hz, 2 Hz), 7.38 (1H, d, J = 2 Hz), 7.90 (2H, d, J = 8 Hz). **7** (300 MHz, $CDCl_3$) δ 2.19 (6H, s), 2.25 (6H, s), 3.71 (2H, s), 3.77 (2H, s), 3.90 (3H, s), 6.56 (1H, d, J = 2 Hz), 6.90 (1H, dd, J = 2, 8 Hz), 7.38 (2H, m), 8.11 (1H, d, J = 8 Hz). **8** (300 MHz, $CDCl_3$) δ 2.25 (6H, s), 3.75 (2H, s), 3.80 (3H, s), 6.58 (1H, d, J = 2 Hz), 6.90 (1H, dd, J = 2, 8 Hz), 7.38 (2H, m), 7.95 (1H, s), 8.05 (1H, d, J = 8 Hz).
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