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1-Benzyloxy-3-(*p*-tolylsulfonyl)propene as an Acrolein β-Anion Equivalent. Synthesis of 4-Substituted 2-Butenolides

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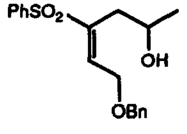
Abstract: **Lithiation of 1-benzyloxy-3-(*p*-tolylsulfonyl)propene 6 and reaction with aldehydes gives alcohols 7. Sequential hydrolysis–cyclization, oxidation and DBU-mediated elimination of the elements of *p*-$TolSO_2H$ gives 4-substituted 2-butenolides 10 in good overall yield.**

During recent studies directed towards tetrahydrofuran synthesis *via* 5-*endo*-trig cyclization reactions of sulfonyl-substituted homoallylic alcohols,[1] we observed the rapid, quantitative isomerization of the allylic ether **1** to the enol ether **2** on exposure to *t*-BuOK–*t*-BuOH in THF. It occurred to us that the analogous transformation of vinylic sulfones **3** would yield the enol ether-containing allylic sulfones **4**. Deprotonation of **4**, and reaction of the resulting anions with electrophiles followed by hydrolysis and elimination of $ArSO_2H$ would give the products of formal reaction with electrophiles of the acrolein β-anion equivalent **5**. In this Letter we report the successful application of this strategy to the synthesis of 4-substituted 2-butenolides, starting from 1-benzyloxy-3-(*p*-tolylsulfonyl)propene **6** and aldehydes.



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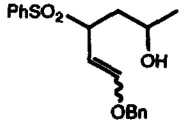

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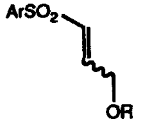

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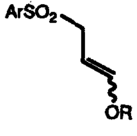

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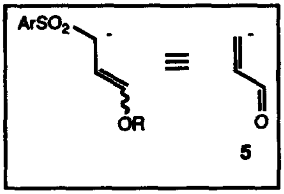
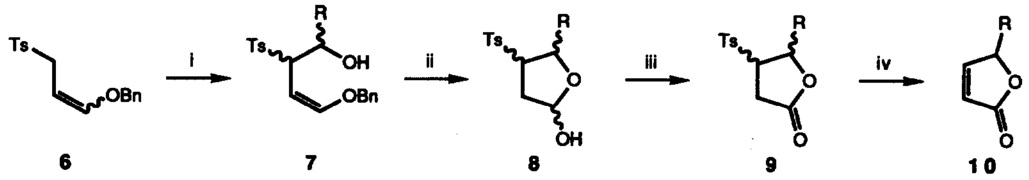


1-Benzyloxy-3-(*p*-tolylsulfonyl)propene **6** was prepared as a *ca.* 3:1 *Z*:*E* mixture by reaction of (diethylphosphonyl)lithio(*p*-tolylsulfonyl)methane[2] with 2-benzyloxyethanal[3] in THF (90%), followed by isomerization using potassium *t*-butoxide (0.1 eq.) in the presence of *t*-BuOH (20 eq.) in THF (0.16M) at r.t. (99%). Stepwise treatment of cold THF solutions of **6** with *n*-BuLi and an aldehyde gave the alcohols **7** as diastereomeric mixtures upon low-temperature proton quench and chromatographic purification. Interestingly, compounds **7** were generally obtained almost exclusively as the Z-isomers. Acidic hydrolysis of **7** in aqueous acetonitrile effected ring-closure to give lactols **8**. PDC-Mediated oxidation to lactones **9** followed by elimination using DBU in CH_2Cl_2[4] gave 4-substituted 2-butenolides **10** in good overall yields for the four-step sequence from **6** (Scheme, Table). Although aryl- and (1-alkenyl)-substituted lactone precursors **9** were all successfully prepared according to the Scheme, attempted DBU-mediated elimination under a variety of conditions gave unacceptably low yields of butenolides **10**. Reaction with DBU of the 4-propenyl-substituted analogue of **9** gave a mixture of the corresponding α,β- and β,γ-unsaturated γ-lactones.[4]



(i) *n*-BuLi (1.1 eq.), THF (0.12-0.15M), -78°C, 5 min; add RCHO–THF (1 eq.), -78°C, 5 min; add AcOH–THF (1.1 eq.), -78°C to r.t.; (ii) conc. H_2SO_4 (100 μl/ml), 15% aq. MeCN (0.05M), 65°C, 2-7 h; (iii) PDC (1.5 eq.), 4Å sieves (1 mg/mmol), CH_2Cl_2 (0.05-0.1M), r.t., 1.5-4 h; (iv) DBU (0.6 eq.), CH_2Cl_2 (0.1M), -78°C, 0.5-4 h; add AcOH–THF (0.6 eq.), -78°C to r.t.

Scheme

Entry	R	Yield of 7[5]	Yield of 8	Yield of 9	Yield of 10
a	n-$C_{11}H_{23}$	99	85	83	91
b	*i*-Pr	90	95	87	87
c	c-C_6H_{11}	85	95	86	95
d	*t*-Bu	95	59[6]	85	93
e	(*E*,*E*)-MeCH:CHCH:CH$(CH_2)_4$	98	89	82	91
f	$BnOCH_2$	98	99	81	93
g	$BnO(CH_2)_2$	96	87	47[7]	90
h	$TBDMSO(CH_2)_5$	78[8]	80[9]	86	94

Table

In summary, the present method enables the synthesis of a variety of 4-substituted 2-butenolides in good overall yield from readily available 1-benzyloxy-3-(*p*-tolylsulfonyl)propene and aldehydes.[10] We are currently looking at the synthesis of furans using related methodology involving the elimination of the elements of H_2O and *p*-$TolSO_2H$ from **8**. The results of these and related studies will be reported in due course.

Acknowledgements

We thank the SERC (Quota studentships to C. J. E. and A. M. S.), ICI plc and Pfizer Central Research for financial support of this research.

References and notes

1. Craig, D.; Smith, A. M. *Tetrahedron Lett.* **1992**, *33*, 695.
2. (Diethylphosphonyl)(*p*-tolylsulfonyl)methane was prepared in 91% recrystallized yield by sequential addition to LDA–THF (2.2 eq.) at -78°C of (*p*-tolylsulfonyl)methane (1 eq.) and $(EtO)_2P(O)Cl$ (1.1 eq.), followed by warming to r.t. and quenching with AcOH–THF.
3. Prepared in 87% yield by ozonolysis (MeOH, -78°C; 0.5 eq. thiourea work-up) of 3-benzyloxypropene.
4. Carretero, J. C.; De Lombaert, S.; Ghosez, L. *Tetrahedron Lett.* **1987**, *28*, 2135.
5. All % yields cited herein are for pure materials isolated by flash chromatography on silica gel. All new compounds gave nmr and ir data, and elemental combustion analyses in accord with the proposed structures.
6. (*E*)-4-Hydroxy-5,5-dimethyl-2-hexenal was formed as a by-product (26%) in this reaction.
7. Butenolide **10g** (35%) was formed as a by-product in this reaction.
8. R = $AcO(CH_2)_5$.
9. R = $HO(CH_2)_5$. This hydroxylactol was converted into **8h** in 85% yield using TBDMSCl–Et_3N–DMAP in CH_2Cl_2.
10. For another acrolein β-anion equivalent, see: Meyers, A. I.; Spohn, R. F. *J. Org. Chem.* **1985**, *50*, 4872. For acrylate β-anion equivalents, see *inter alia*: (i) ref.4, and references therein; (ii) Tanaka, K.; Wakita, H.; Ioda, H.; Kuji, A. *Chem. Lett.* **1984**, 1359; (iii) Dziadulewicz, E.; Hodgson, D.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3367.

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