Diastereoselective Conjugate Additions Reactions of a Lithiated Allylic Sulfoximine to Acyclic Enones

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The conjugate addition reactions of lithiated *N*-*p*-tosyl *S*-phenyl *S*-prop-2-enyl sulfoximine **4** with cyclic and acyclic enones gives exclusively 1,4-α adducts, the reactions with acyclic enones are highly diastereoselective.

In contrast to the chemistry of allylic sulfoxides[1–4] and sulfones,[5,6] relatively little is known about the chemistry of allylic sulfoximines.[7] In 1979, Johnson[8] disclosed the synthesis of the first reported allylic sulfoximine. The synthesis of enantiomerically pure allylic sulfoximines has been recently reported,[9,10] and Gais has demonstrated they undergo S_N2 or S_N2' like displacement reactions with homocuprates.[9] Harmata[11] reported that the reaction of lithiated **1** with either 2-cyclopentenone or 2-cyclohexenone gave mixtures in which the 1,4-α adducts were slightly favoured over the 1,4-γ adducts. More recently we have reported that the conjugate addition reactions of lithiated **3** with cyclic and acyclic Michael acceptors give mainly 1,4-γ and 1,4-α adducts respectively in THF and 1,4-α and 1,4-γ adducts respectively in HMPA–THF.[12] Although the 1,4-γ adducts from cyclic enones could be isolated in high diastereomeric purity, these reactions proceeded with modest regioselectivity with respect to α verses γ attack on the lithiated sulfoximine. Furthermore acyclic enones gave products from 1,2 and 1,4 addition of lithiated **3**. Here we report the conjugate addition reactions of lithiated *N*-*p*-tolyl *S*-phenyl *S*-prop-2-enyl sulfoximine **4** with cyclic and acyclic enones. In contrast to lithiated **1** and **3**, the conjugate addition reactions of lithiated **4** are highly regioselective with respect to α attack on the allylic anion and are highly diastereoselective for acyclic enones. Furthermore, we report the first stereochemical study of this type of reaction

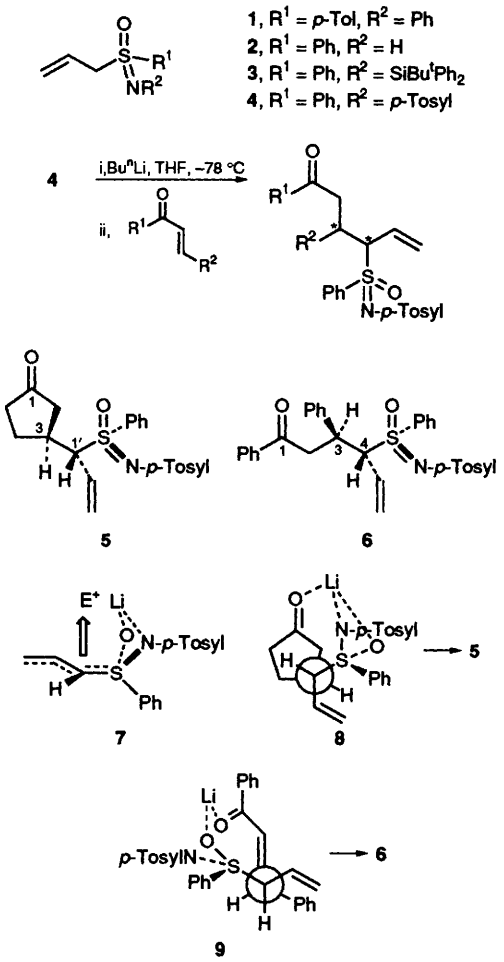

Table 1 Conjugate addition reactions of lithiated **4** with enones

Enone			
R^1	R^2	Diastereoisomeric ratio	Yield (%)
$-(CH_2)_2-$		49 : 33 : 10 : 8	87
$-(CH_2)_3-$		47 : 25 : 14 : 14	92
Ph	Ph	93 : 7	90
Me	Ph	90 : 10	45
Ph	Me	94 : 6	61

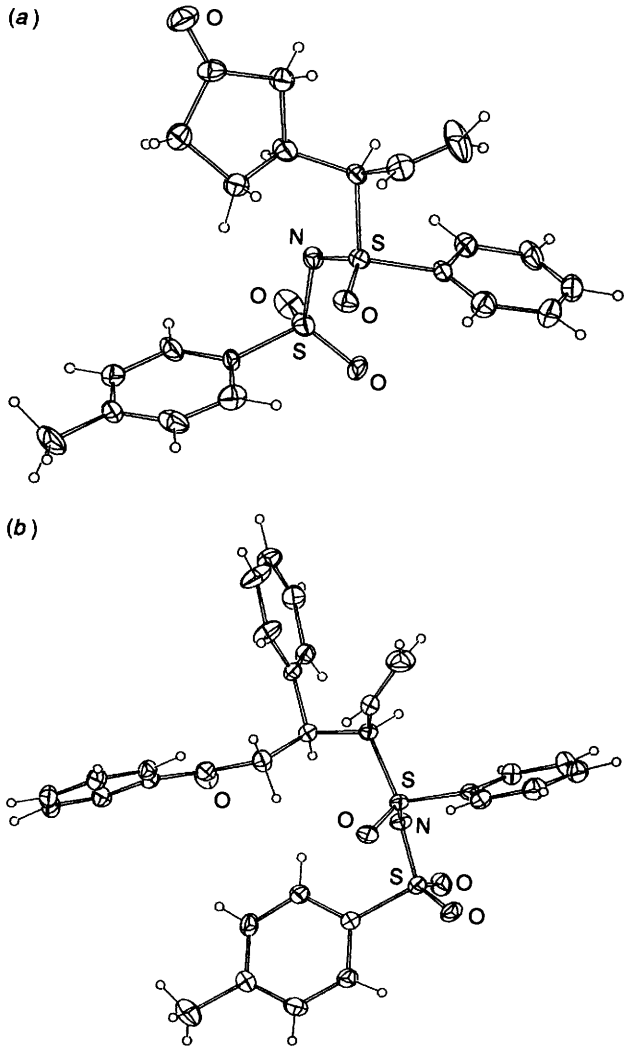

Fig. 1 Molecular projections of (*a*) **5** and (*b*) **6**; 20% thermal ellipsoids are shown for the non-hydrogen atoms, hydrogen atoms having arbitrary radii of 0.1 Å

from single crystal X-ray structural analyses of two of the reaction products.

Racemic allyl sulfoximine **4** (mp 82–83 °C) was prepared in 81% yield from sulfoximine **2**[12] by treatment with *p*-toluenesulfonyl chloride (1.2 equiv.) and pyridine (1.2 equiv.) in dichloromethane at 22 °C for 1 h. Addition of *n*-butyllithium (Bu^{n}Li, 1.1 equiv.) to a solution of **4** in THF at −78 °C gave an immediate yellow-orange solution of lithiated **4**. After 15 min, the solution was treated with the enone (1.2 equiv.). After 3 min at −78 °C the almost colourless reaction mixture was quenched with acetic acid (1 equiv.) and then an aqueous solution of saturated ammonium chloride. The diastereoselectivities of these reactions were determined by ^{1}H NMR analysis of the crude reaction mixtures. The reaction products were purified by column chromatography on silica gel with ethyl acetate-hexanes as eluent and the chemical yields were determined on purified samples. The results of these investigations are summarized in Table 1.

In contrast to the chemistry reported for lithiated **1** and **3**, lithiated **4** gave exclusively 1,4-α adducts with both cyclic and acyclic enones. Interestingly the regiochemistry of the reaction of lithiated **4** with enones is also different to that of lithiated allyl phenyl sulfone which gives exclusive 1,4-γ adducts with cyclic enones and 1,4-α adducts with acyclic enones.[5]

When 2-cyclopentenone and 2-cyclohexenone were treated with lithiated **4**, the 1,4-α adducts were obtained but as a mixture of the four possible diastereoisomers (Table 1). The relative (3*S**, 1′*R**, *SS**) stereochemistry of the major diastereomeric adduct **5** from the former reaction was secured by a single crystal X-ray structural analysis as shown in Fig. 1*a*. The relative stereochemistry of the major adduct from the reaction of lithiated **4** and 2-cyclohexanone is assumed to be the same as that in **5** on the basis of its similar ^{1}H NMR spectrum.

In contrast, the reaction of lithiated **4** and the acyclic enones, benzylideneacetophenone, benzalacetone and (*E*)-1-phenylbut-2-en-1-one were highly diastereoselective (Table 1). The relative (3*R**, 4*R**, *SS**) stereochemistry of the major diastereomeric adduct **6** from the reaction of lithiated **4** and benzylideneacetophenone was determined by a single crystal X-ray structural analysis (Fig. 1*b*). The relative stereochemistry of the major adducts from the reaction of lithiated **4** and benzalacetone and (*E*)-1-phenylbut-2-en-1-one is assumed to be the same as that in **6** on the basis of their similar ^{1}H NMR spectra.

The stereochemical outcome of these reactions with respect to the stereogenic centre α to the sulfoximine group can be rationalised as arising from attack on the carbanion whose structure is as shown in **7** (only the monomeric species is considered) that may be similar to that of an α-lithiated benzyl sulfone or sulfoximine.[13,14] The α-substituent (CH···CH$_2$) of the sulfoximine would be expected to be *anti* to the bulky *N*-*p*-tosyl group. Electrophilic attack on **7** should occur *anti* to the *S*-phenyl group and *syn* to lithium. The overall stereochemical outcome of these reactions can be rationalised as arising from the chelated transition states **8** and **9** in which the two bulky groups of each reaction partner, the sulfoximidoyl group and the β-enone substituent, are *anti* to minimise steric interactions.

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Footnote

† *Crystal data* for **5**: $C_{21}H_{23}NO_4S_2$, a = 21.534(5), b = 5.867(3), c = 18.288(5) Å, β = 116.17(2)°, V = 2074 Å^3. $2\theta_{max}$ = 47.5°; N = 2671, N_o = 1177; R = 0.055, R_w = 0.050. (x, y, z, $U_{iso})_H$ included constrained at estimated values.

6: $C_{31}H_{29}NS_2O_4$, a = 12.205(4), b = 12.566(6), c = 19.669(6) Å, β = 112.71(2)°, V = 2783 Å^3. $2\theta_{max}$ = 60°; N = 4804, N_o = 2825; R = 0.052, R_w = 0.053. (x, y, z, $U_{iso})_H$ all refined.

Unique, room temp. diffractometer data sets (T *ca.* 295 K, 2θ/θ scan mode, monochromatic Mo–Kα radiation, λ = 0.71073 Å) yielding N independent, gaussian-absorption-corrected data, N_o with $I > 3\sigma(I)$ used in the full-matrix least-squares refinement (anisotropic non-hydrogen thermal parameter form, statistical reflection weights). Both structures monoclinic, $P2_1/c$.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1, 1994.

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