Sulfur-Stabilized Carbanions: Electrophilic Reactions of an Allylic Anion Containing Propanedithio and Phenylthio Substituents

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Abstract: In contrast to the γ -regioselective reactions of 1,1,3-tris(phenylthio)propene, the anion of 2-(2-phenylthioethylidene)-1,3-dithiane reacts with halides and aldehydes preferentially at the propanedithio-substituted carbon (α -regioselective reaction), but at the phenylthio-substituted carbon with open-chain aliphatic ketones. This umpolung reagent is utilized to prepare α,β -unsaturated ketones and oxygen-containing heterocyclic compounds.

α -Hetero-substituted carbanions have been widely employed in the carbon-carbon bond formation. The sulfur-stabilized carbanions are especially useful synthons because they are easily accessible and the reaction products can be further elaborated to other functional compounds. For example, 1,3-bis(methylthio)propene and 1,3-bis(phenylthio)propene has been used as umpolung reagent via a sequence of deprotonation, alkylation and hydrolysis to give α,β -unsaturated aldehydes.¹ Although an unsymmetric allylic anion may have two reactive sites, the anion of allyl phenyl sulfide (1 or 2) reacts with alkyl halides selectively at the phenylthio-substituted carbon (the α -site).² However, the regiochemistry for the electrophilic reaction of sulfur-stabilized allylic anions can be affected by several factors³ including the substituents of the allylic anion, the attacking electrophile, the counter cation, the solvent, the Lewis acid, and the reaction temperature. We and others have studied a series of 2-vinyl-1,3-dithianes to find that the regioselectivity for these ambident anions is greatly influenced by γ -substituents,⁴ such as the cyano, the methyl, the phenyl, and the *o*-methoxyphenyl groups. The present study of the electrophilic reactions of an analog **3** having the γ -substituent of phenylthio group is designed to test the power of the propanedithio-substituent verse the phenylthio-substituent in control of the regiochemistry. It is also interesting to compare the reactivity of **3** with that of 1,1,3-tris(phenylthio)propene (**4**).⁵

- 1 R = H
2 R = Me
3 R,R = S(CH₂)₃S
4 R = SPh

The substrate 2-(2-phenylthio-ethylidene)-1,3-dithiane **3** was prepared according to Scheme 1 by (i) consecutive treatment of α -bromoacrolein with thiophenol (1 equiv) and 1,3-propanedithiol (1 equiv) in the presence of borontrifluoride and (ii) subsequent dehydrobromination with 1,8-diazabicyclo[5.4.0]undec-7-ene. Deprotonation of **3** with *n*-BuLi in THF gave an unsymmetric allylic anion, which underwent electrophilic reactions at -78°C with alkyl halides, aldehydes and ketones as shown in Table I.⁶ Unlike the exclusive γ -regioselective reactions of 1,1,3-tris(phenylthio)propene,⁵ the preliminary result for **3** indicated variable selectivities depending on the respective attacking

electrophile. The reaction with methyl iodide or benzyl bromide occurred predominantly at the propanedithio-substituted carbon to give the α -substitution product **5a** or **6a**. Over 80% of α -addition was also observed with the electrophiles of most aldehydes and benzophenone. On the contrary, the addition of open-chain aliphatic ketones favored at the phenylthio-substituted carbon. The reason for such non-unified regiochemical outcome is not obvious. Neither the steric effect nor the electronic effect, e.g. the HSAB principle,^{4,5} can be satisfactorily applied to explain the difference in regiochemistry.

Scheme 1

Table I. Electrophilic Reactions of the Anion of **3**.

Electrophile	R =	product (yield, %)
iodomethane	Me	5a (52) ^a + 5b (30)
benzyl bromide	CH ₂ Ph	6a (63) + 6b (27)
propanal	CH(OH)CH ₂ Me	7a (86)
isobutanal	CH(OH)CHMe ₂	8a (62) + 8b (16) ^b
acrolein	CH(OH)CH=CH ₂	9a (58)
benzaldehyde	CH(OH)Ph	10a (68)
cinnamaldehyde	CH(OH)CH=CHPh	11a (23) + 11b (47) ^b
2-butanone	MeC(OH)CH ₂ Me	12a (20) + 12b (65) ^b
3-pentanone	MeCH ₂ C(OH)CH ₂ Me	13b (87)
2-heptanone	Me(CH ₂) ₄ C(OH)Me	14b (90) ^b
cyclopentanone	(CH ₂) ₄ C(OH)	15a (41) + 15b (41)
benzophenone	PhC(OH)Ph	16a (83)

(a) All α -addition products (**5a-16a**) have the *E*-double bonds as inferred from large coupling constants (*ca.* 16 Hz) of the vinyl protons. (b) The γ -addition product **12b** or **14b** consists of two diastereomers in nearly equal amounts, whereas **8b** or **11b** is homogeneous presumably to have the threo-configuration.

The present method serves an entry to syntheses of α,β -unsaturated ketones and oxygen-containing heterocyclic compounds (Eq 1-4). For instance, hydrolysis of the α -addition product 16a, obtained from the reaction with benzophenone, with HgCl_2 yielded an α' -hydroxy- α,β -unsaturated ketone 17. The α -addition product 8a cyclized in similar conditions to give a tetrahydrofuran 18 without hydrolysis of the dithioacetal, while 10a ended up with a furan 19 by further elimination of PhSH and opening of the dithiane ring. The γ -addition products 8b, 12b and 14b were successfully transformed into the butenolides 20-22.

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- (6) Compounds 3 and 5-22 are fully characterized by spectral methods (IR, MS and NMR) and by elemental analyses or exact mass measurements.