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ASYMMETRIC ALKYLATION AND SULPHENYLATION OF CHIRAL *O*-SILYLATED IMIDE ENOLATES.

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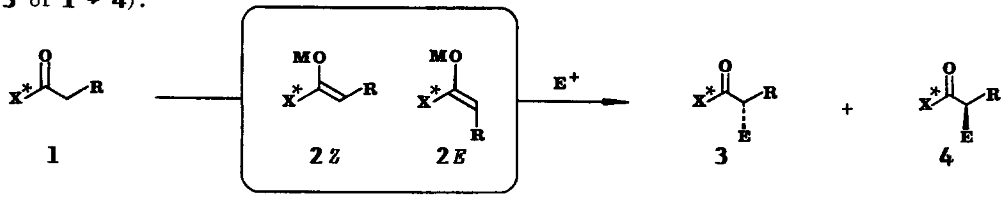
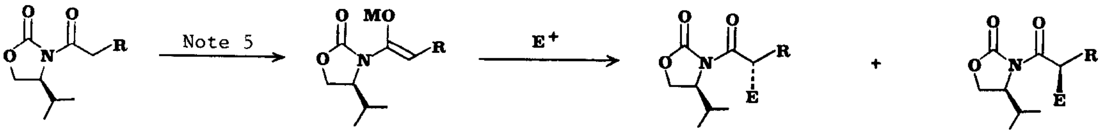
Summary: The chiral *O*-silylated enolates (**5**) can be alkylated or sulphenylated with high diastereoselectivity ($\sim$20:1) by 1,3-dithienium fluoroborate or PhSCl. Phenylthioalkylation, in contrast, proceeds with low diastereoselectivity.

The asymmetric reactions of chiral carbonyl compounds of type (**1**) have recently been extensively developed, although emphasis has generally been on the use of the derived lithium and sodium enolates for alkylation with S_N2-reactive alkyl halides[1a] and boron enolates[1b] for aldol addition to aldehydes. Use of the analogous stereodefined *O*-silylated enolates (**2***E* or **2***Z*, $M=SiR_3$) would be expected to lead to a much expanded range of electrophilic types[2] being available, under appropriate Lewis acid activation, for the asymmetric α-substitution reactions (**1** → **3** or **1** → **4**).[3]

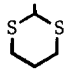


We now report that the chiral *O*-silylated imide enolates (**5**), based on the versatile *L*-valinol derived oxazolidone auxiliary of Evans,[4] can be easily prepared[5] and react directly with 1,3-dithienium fluoroborate[6] (Table, entries 1-5) and phenylsulphenyl chloride (entries 6 and 7) to give the corresponding α-substituted imides with useful diastereoselectivity.[7] Moreover, electrophilic attack occurs preferentially in the same stereochemical sense, i.e. **5** → **6**, as that previously recorded[4] for the analogous lithium and sodium enolates. This was confirmed[7] by reductive desulphurisation (W-2 RaNi, Me_2CO; 80%) of the major 1,3-dithiane produced from **5** for R=Et, which gave the same diastereomer as that obtained selectively[4] by the corresponding lithium enolate methylation (i.e. **6**, E=Me). Furthermore, the major sulphenylation isomer (entries 6 and 7) was identical to that obtained from reaction of the analogous lithium enolate (**5**, M=Li, R=Me) with PhSCl (THF, -78°; 48%). In each of these *O*-silylated enolate reactions, the diastereoselectivity increases with the steric bulk of the alkyl substituents on silicon, where optimum results are obtained for $M=SiMe_2Bu^t$ (entries 3, 5, and 7). The high diastereoselectivity here cannot be simply attributed to a rigid metal-chelated conformation of the enolate, as with M=Li and Na,[4] but must now be due to π-face discrimination in a conformationally mobile system. Similar stereochemical results are anticipated for the reaction of other reactive carbon and heteroatom electrophiles (not requiring Lewis acids) with these chiral *O*-silylated imide enolates.



5 6 7

TABLE: Reaction of *O*-silylated enolates (**5**) with (a) 1,3-dithienium fluoroborate (3:1 CH_2Cl_2 /CH_3NO_2, -78°C, 0.5h); (b) PhSCl (CH_2Cl_2, -78°C, 10 min); (c) PhSCHClMe/$TiCl_4$ (CH_2Cl_2, -23°C, 2h).

Entry	Reagent	M	R	E	**6**:**7**[7]	Yield (%)
1	(a)	$SiMe_3$	Et		89:11	80
2	(a)	$SiEt_3$	Et		90:10	88
3	(a)	$SiMe_2Bu^t$	Et		95: 5	82
4	(a)	$SiMe_3$	Me		87:13	66
5	(a)	$SiMe_2Bu^t$	Me		96: 4	73
6	(b)	$SiMe_3$	Me	PhS	83:17	90
7	(b)*	$SiMe_2Bu^t$	Me		92: 8	83
8	(c)	$SiMe_3$	Me	PhSCHMe	60:40	68
9	(c)	$SiEt_3$	Me		60:40	37

*reaction at -100°C.

Finally, as a model for the Lewis acid-promoted alkylation reactions of this new class of *O*-silylated enolates, the phenylthioethylation[8] of **5** (R=Me) was examined. Disappointingly, little or no alkylation was obtained under a wide range of conditions and Lewis acids with M=Bu^tMe_2Si, while the Me_3Si and Et_3Si derivatives of **5** each gave with $TiCl_4$ a complex mixture of four diastereomers (entries 8 and 9), which simplified to a 60:40 ratio of isomers (**6**[9] and **7**, E=Et) after desulphurisation (W-2 RaNi, Me_2CO; 76%). The Lewis acid, which is required to promote alkylation, may well be here impairing the facial bias of the enolate by competing complexation to **5** and/or titanium enolate formation.[10]

Notes and References:

1. (a) D. A. Evans, *Asymmetric Synthesis*, **3**, Ed. J. D. Morrison, Ch.1, Academic Press, New York, (1984); (b) C.H. Heathcock , *ibid*, Ch.2; D. A. Evans, J. V. Nelson, and T. R. Taber, *Topics in Stereochemistry*, **13**, 1 (1982).
2. P. Brownbridge, *Synthesis*, 1 (1983); M. T. Reetz, *Angew. Chem. Int. Ed.*, **21**. 96 (1982).
3. For the asymmetric acetoxylation of chiral *O*-silylated ester enolates, see: W. Oppolzer and O. Dudfield, *Helv. Chim. Acta*, **68**, 216 (1985).
4. D. A. Evans, M. D. Ennis, and D. J. Mathre, *J. Am. Chem. Soc.*, **104**, 1737 (1982).
5. *O*-Silylated enolates (**5**, R=Me and Et) were prepared from the intermediate lithium enolates[4] (LDA) by reaction with the appropriate silyl chloride (THF or THF-HMPA, -78°C - r.t.; >95%), followed by non-aqueous workup and distillation (10^{-3} mmHg) or chromatography (SiO_2) for the more hydrolytically stable Bu^tMe_2Si derivatives. The *Z* double bond geometry (>97% isomeric purity by ^{13}C-NMR) is assumed from previous work.[4] Experimental conditions for their reactions with electrophiles are as previously reported.[6,8]
6. I. Paterson and L. G. Price, *Tetrahedron Lett.*, **22**, 2829 (1981).
7. Isomeric purity was determined by ^{13}C- and ^1H-NMR (250 MHz) and HPLC or capillary GC. Isomer ratios were measured by ^1H-NMR of the crude product mixtures and confirmed by weighing the chromatographically separated components.
8. I. Paterson and I. Fleming, *Tetrahedron Lett.*, 2179 (1979).
9. Identical to the major isomer[4] obtained by ethylation of **5** (M=Li, R=Me).
10. E. Nakamura, J. Shimada, Y. Horiguchi, and I. Kuwajima, *Tetrahedron Lett.*,**24**, 3341 (1983).

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