Addition–Elimination Reactions of β-Oxygenated Vinyl Sulphones

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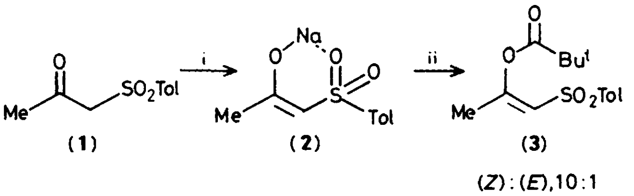
Stereoselective reaction of enol pivalate (**3**) with a variety of higher order organocuprate reagents gives vinyl sulphones in excellent yield.

Vinyl sulphones have recently attracted attention as useful synthetic intermediates,[1] consequently methods for their preparation are valuable.[2] We report here a new stereoselective synthesis of vinyl sulphones based on an addition–elimination reaction of β-oxygenated vinyl sulphones.[3]

Reaction of the β-ketosulphone (**1**) with sodium hydride in tetrahydrofuran (THF) followed by addition of pivaloyl chloride gave the enol derivative (**3**) in 97% yield as a 10:1 (*Z*):(*E*) mixture of isomers,† Scheme 1. The (*Z*) isomer of enol pivalate (**3**) was easily obtained in stereochemically pure form by chromatography, m.p. 55—57 °C. The preference for formation of the (*Z*) enol derivative is presumably the consequence of an internally chelated enolate (**2**).[4]

The enol pivalate (**3**) can be regarded as a β-oxygenated vinyl sulphone. We anticipated employing the known reactivity of vinyl sulphones toward organometallics in a stereoselective addition–elimination sequence, Scheme 2.[5] We envisaged that successful formation of (**5**) in stereoselective fashion would require both formation of the intermediate carbanion (**4**) *and* subsequent expulsion of the carboxylate anion to be stereoelectronically controlled.[6] In addition the reactivity of (**3**) towards the organometallic reagent would need to be greater than the reactivity of (**5**) to avoid over-reaction. A promising result was obtained when enol pivalate (**3**) was treated with $Bu^{n}_{2}CuLi$ in diethyl ether at −50 °C, affording (**5**; R = Bu^n) in 47% yield as a 1:10 (*Z*):(*E*) mixture of isomers. That the sulphone product was predominantly the (*E*) isomer was shown by the characteristic deshielding of the *syn* methyl by the sulphone group leading to a downfield shift of the methyl resonance in the ^1H n.m.r. spectrum.‡[7]

Disappointing results with other dialkyl cuprates led us to examine the use of higher order species $R_2Cu(CN)Li_2$.[8] We were pleased to find that the enol pivalate (**3**) reacted smoothly with a variety of higher order cuprates, Table 1, entries 1—6.§ Immediately apparent is the contrasting (*Z*):(*E*) ratio obtained on using $Bu^{n}_{2}Cu(CN)Li_2$ (58:1, Table 1, entry 2) as opposed to $Bu^{n}_{2}CuLi$ (1:10, *vide supra*). A similarly dramatic change in product stereochemistry is evident in Table 1 (*cf.* entries 2 and 3 with 4—6).



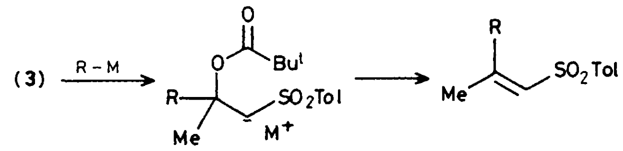
(**1**) (**2**) (**3**)

(*Z*):(*E*),10:1

Tol = tolyl

Scheme 1. *Reagents:* i, NaH, THF, 0 °C; ii, Bu^tCOCl.

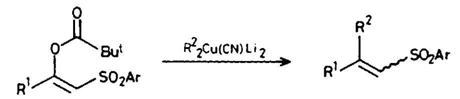
In the hope of obtaining information concerning the origin of these effects we conducted reactions of the enol pivalate (**3**) with $Bu^{n}_{2}Cu(CN)Li_2$ at several temperatures, Table 2. These results suggest that elimination from the kinetically formed α-sulphonyl carbanion (**4**) occurs at low temperature, but at higher temperatures carbanion epimerisation can take place allowing elimination to the more thermodynamically stable (*E*) isomer. Carbanion epimerisation may also explain the predominance of the (*E*) isomer in entries 4—7, Table 1, although alternative explanations are possible.¶[9]



(**4**) (**5**) (or isomer)

Scheme 2. Tol = tolyl.

Table 1.[a]



Entry	R^1	R^2	Ar	% Yield	Ratio (*Z*):(*E*)
1	Me	Me	Tol	82	—
2	Me	Bu^n	Tol	100	58:1
3	Me	Isopentyl	Tol	85	30:1
4	Me	2-Furyl	Tol	62	1:40
5	Me	Bu^t	Tol	81	1:20
6	Me	Isopropenyl	Tol	84	1:40
7	Et	Me	Ph	83	1:50
8	Et	Bu^t	Ph	94	No (*Z*) detected

[a] *Reagents and conditions:* 2 equiv. of $R^2{}_2Cu(CN)Li_2$ in THF, −78 °C, 10—30 min.

Table 2. Reaction of (3) with $Bu^{n}_{2}Cu(CN)Li_2$ at various temperatures to give (5; R = Bu^n) as a mixture of isomers.

Temp./°C	Ratio (*Z*):(*E*)
−78	58:1
−30	2.7:1
0	1:2.5
25	1:2.5

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† All (*Z*):(*E*) ratios were derived by integration of high field ^1H n.m.r. spectra of crude products. Our stereochemical assignments of enol pivalate (3) and the vinyl sulphone products are in full accord with existing ^1H n.m.r. data and are further supported by a number of nuclear Overhauser effect experiments.

‡ The characteristic deshielding of *syn* allylic protons in the vinyl products proved a valuable tool in assignment of double bond stereochemistry.

§ All yields refer to chromatographically homogeneous materials. All new compounds gave satisfactory spectral and analytical (accurate mass and/or combustion analysis) data.

¶ Similar results have been explained by postulating that an antiperiplanar elimination gives rise to one stereochemical outcome whereas a *syn* elimination operates when, owing to the presence of sterically large groups, the former mechanism is disfavoured.

At present it appears that in the reactions of enol pivalate (**3**) with cuprate reagents having primary alkyl groups, (*Z*) vinyl sulphone products result, whereas more sterically demanding groups give the (*E*) isomer. From entries 7 and 8, Table 1, it can be seen that results with a homologue of enol pivalate (**3**) parallel the other results and indicate some generality of this process. The high yields and good stereoselectivity exhibited by this reaction make it an attractive method for preparation of vinyl sulphones and their derivatives.

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