

ACYLATION OF EXTENDED ENOLATE IONS FROM  $\alpha$ -PHENYLTHIO(PhS-)CROTONATE ESTERS

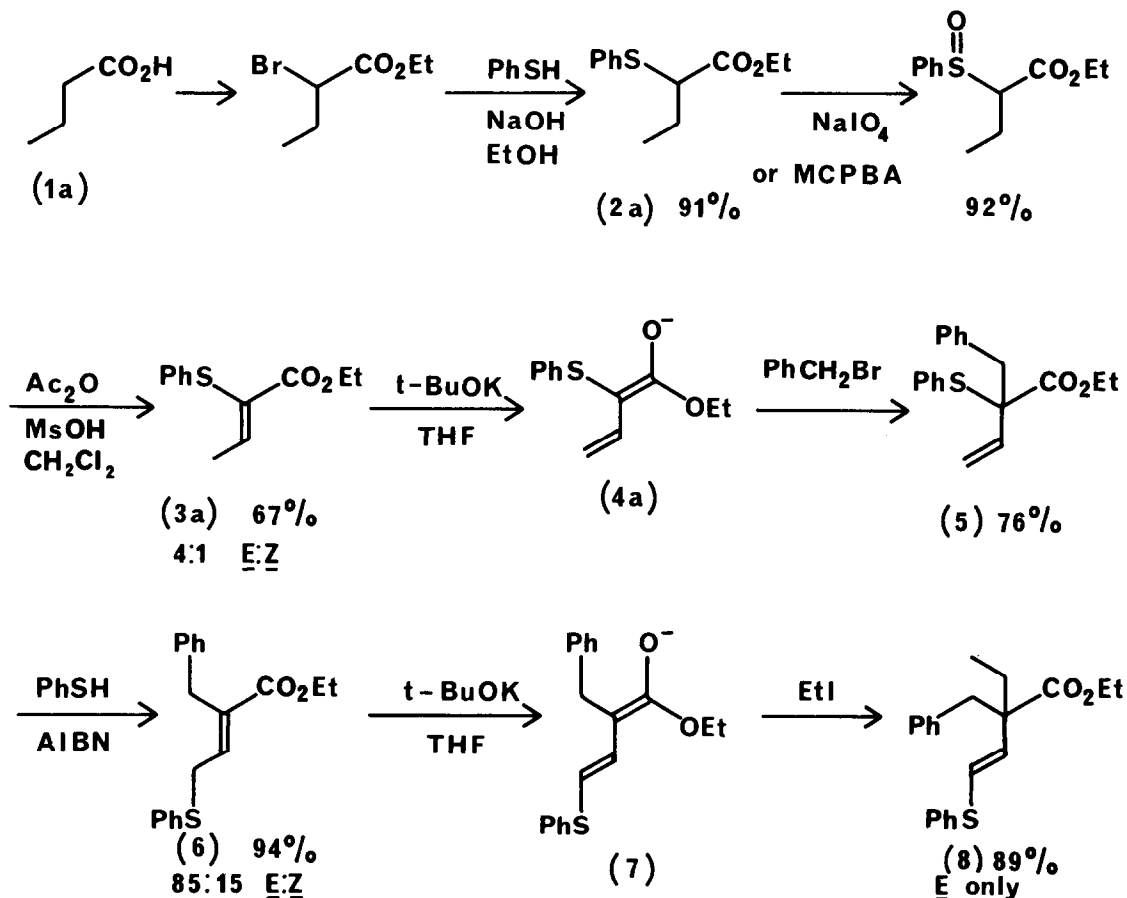
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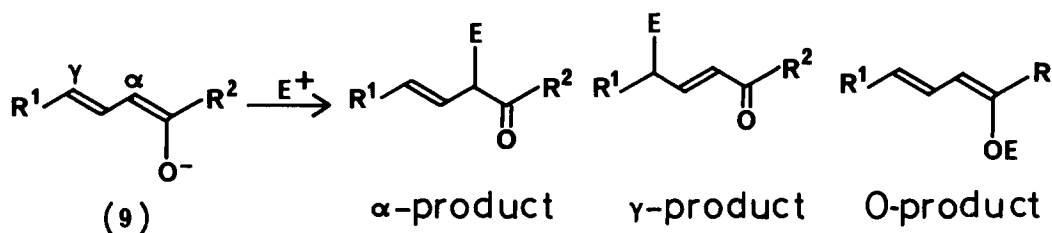
C-Acylation, like alkylation, occurs at the  $\alpha$ -position of the title compounds to give unsaturated keto-esters from which the PhS group may be removed

Alkylation of extended enolates normally occurs at the  $\alpha$ -carbon atom<sup>1</sup> and this behaviour is unaltered by  $\alpha$ -phenylthio (PhS) or  $\gamma$ -PhS substitution. Scheme 1 shows the  $\alpha$ -alkylation<sup>2</sup> of the  $\alpha$ -PhS extended enolate (4a), the transformation of the product (5) by [1,3]PhS shift into the  $\gamma$ -PhS crotonate (6), and the  $\alpha$ -alkylation<sup>3</sup> of the resulting  $\gamma$ -PhS extended enolate (7).

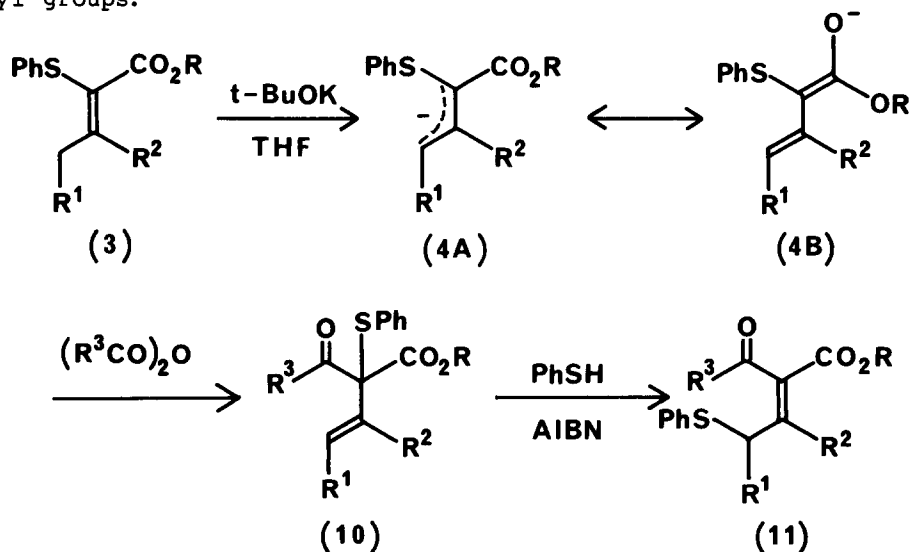
Scheme 1: Alkylation of  $\alpha$ -PhS and  $\gamma$ -PhS Extended Enolates



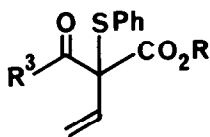
In other systems reactions of carbonyl compounds (aldehydes and ketones) often show a different regioselectivity from alkylation, and acylation may be different again. Thus O-acylation is common with enolate ions which react at carbon with aldehydes and ketones. Kende<sup>1</sup> has shown that aldehydes and ketones react with extended enolates (9) at the  $\alpha$ -carbon atom and others have shown that hard electrophiles such as  $\text{Me}_3\text{SiCl}$ <sup>4</sup> or  $\text{Me}_2\text{SO}_4$ <sup>5</sup> react at oxygen. We now describe the acylation of  $\alpha$ -PhS extended enolates (4).



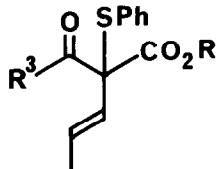
The starting materials (3) were prepared from unfunctionalised carboxylic acids (1) via  $\alpha$ -PhS esters (2) by Pummerer elimination on the sulfoxides.<sup>2</sup> The anions (4) formed cleanly with *t*-BuOK: these are allyl anions<sup>6</sup> (4A) stabilised by PhS and  $\text{CO}_2\text{R}$  as well as extended enolates (4B). Acylation occurred cleanly at the  $\alpha$ -carbon atom to give unsaturated keto esters (10) with a branched chain and with multiple functionality extending back to C-4 along the original chain. The PhS group prevents the double bond from moving into conjugation with the carbonyl groups.



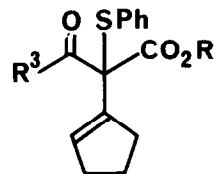
Acid chlorides gave poor yields even at  $-78^\circ\text{C}$  but anhydrides gave better yields (table). No products of O- or  $\gamma$ -acylation were observed, the only by-products being high molecular weight compounds. Yields were consistently higher with benzoic than with acetic anhydride. The double bond in the product may be open chain or in a ring, and can have one (10a, b), two (10c, d), or three (10e, f) substituents. Products (10c) and (10d) from (4,  $\text{R}^1=\text{Me}$ ,  $\text{R}^2=\text{H}$ ) were formed exclusively with a trans double bond, as is the case with alkylation.



(10a,b)



(10c,d)



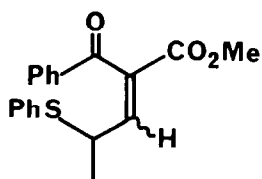
(10e,f)

Table: Acylation of  $\alpha$ -PhS Extended Enolates (4)

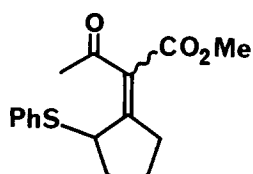
Starting Material	R	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	T °C	Product	Yield(%)
(3a)	Et	H	H	Me	-78	10a	58 (37) <sup>a</sup>
(3a)	Et	H	H	Ph	-78	10b	76 (52) <sup>a</sup>
(3b)	Me	Me	H	Me	-20	<u>E</u> -10c	61
(3b)	Me	Me	H	Ph	-20	<u>E</u> -10d	74
(3c)	Me	(CH <sub>2</sub> ) <sub>3</sub>		Me	-78	10e	55
(3c)	Me	(CH <sub>2</sub> ) <sub>3</sub>		Ph	-78	10f	74

a. with acid chloride

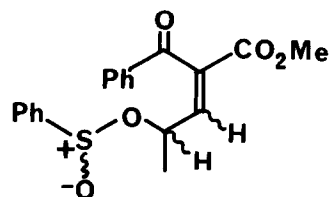
The products (10) were remarkably resistant to the [1,3]PhS shift.<sup>3,7</sup> Four weeks in sunlight gave only 24% of (11b) from (10b), but reasonable yields (57% of 11d and 53% of 11e, both as 1:1 mixtures of E:Z isomers) were obtained with 0.5 equivalents of AIBN and two equivalents of PhSH in CCl<sub>4</sub> under reflux. We have already reported<sup>3</sup> anion formation from the related compounds (7). By contrast, the [2,3] sigmatropic shift in the Evans-Mislow rearrangement<sup>8</sup> was so rapid that oxidation (MCPBA) of (10d) gave the rearranged sulphinate ester (12) (100%, 1:1:1:1 diastereoisomers) directly.



(11d)

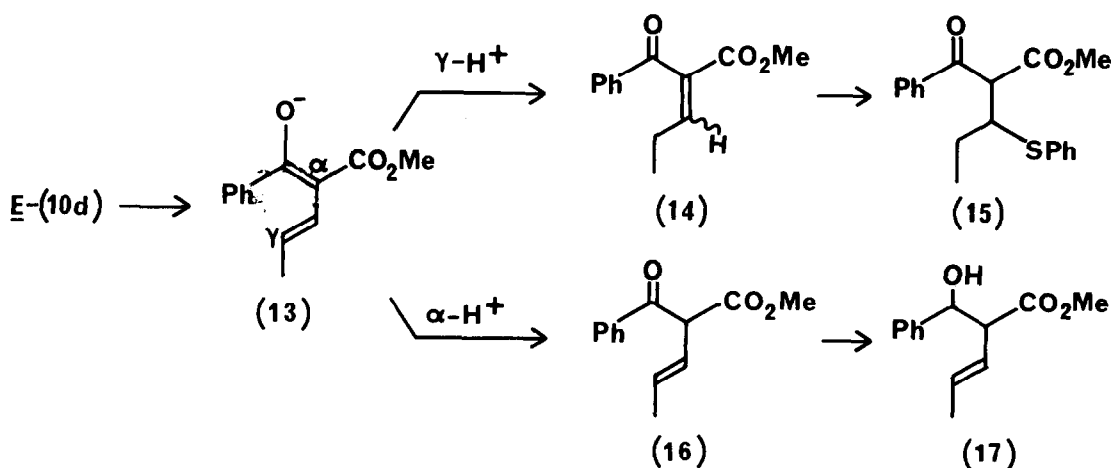


(11e)



(12)

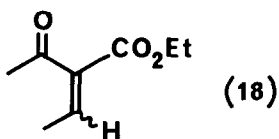
Removal of the PhS group from adducts (10) can be achieved by thiophilic attack with PhS<sup>-</sup> or by reduction. Treatment with NaOH gave starting material (3) by deacylation but excess PhS<sup>-</sup> (3PhSH + 2NaOH) gave the unsaturated keto-ester<sup>9</sup> (14) in 81% yield from E-(4d) presumably by  $\gamma$ -protonation of the extended enolate (13). A larger excess of PhSH (4PhSH + 3NaOH) gave the  $\beta$ -PhS-ketoester (15, 57%), presumably by Michael addition to (14). Reduction (Al/Hg) gave the deconjugated ketoester (16) (39%) after 10 minutes, by  $\alpha$ -protonation of (13), or the corresponding alcohol (17) (44%) after five hours. These products are formally derived<sup>10</sup> from the extended enolate (9, R<sup>2</sup>=OR) by  $\alpha$ -acylation or addition of PhCHO.



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#### References

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9. Attempted hydrolysis of the ester in (10a) with  $\text{NaI}/\text{Me}_3\text{SiCl}$  in MeCN gave 38% and 24% of the two geometrical isomers of (18) after chromatography. This compound has previously been made as an *E:Z* mixture by J. Bruhn, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, 1979, 62, 2630.



10. Kende (ref. 1) has made unsaturated hydroxy esters similar to (17) by addition of aldehydes to extended enolates derived from unsaturated esters.

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