Tetrahedron Letters,Vol.24,No.20,pp 2113-2116,1983 0040-4039/83/202113-04$03.00/0
Printed in Great Britain ©1983 Pergamon Press Ltd.

ALKYLATION OF EXTENDED ENOLATES FROM α-PHENYLTHIO CROTONATE ESTERS

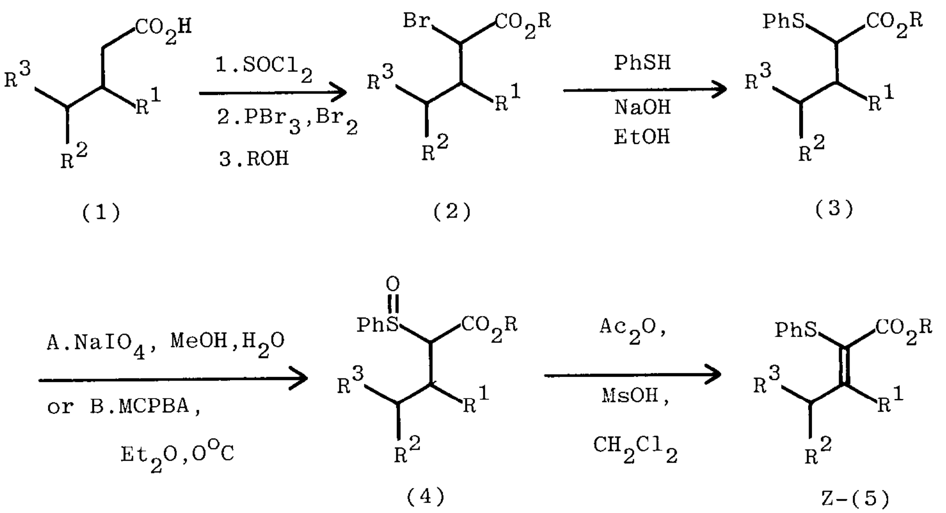
John Durman, Paul G Hunt, and Stuart Warren*
University Chemical Laboratories, Lensfield Road, Cambridge CB2 1EW.

Conditions are described for the formation of enolate anions from substituted α-phenylthio-crotonate esters and their alkylation at the α-carbon atom.

Alkenes with sulphide and carbonyl substituents at the same end, e.g. (5), have been used in synthesis as Michael acceptors and in Diels-Alder reactions.[1] We report that esters (5) can be converted into extended enolate ions (6) which react cleanly at the α-carbon atom with alkyl halides.

Esters of type (5) have been synthesised by two main routes, condensation of α-phenylthio (PhS) acetate carbanions with aldehydes and ketones,[2] or Pummerer-style dehydration of sulphoxides[3] (4). We find the conversion of acids (1) into α-PhS esters (3) via bromination and displacement convenient and efficient (Scheme, Table 1). Oxidation of (3) to sulphoxides (4) with MCPBA[4] is rapid, but requires careful monitoring to prevent over-oxidation. The alternative[5] $NaIO_4$ is slow but gives good yields of (4) with no trace of sulphone.

SCHEME



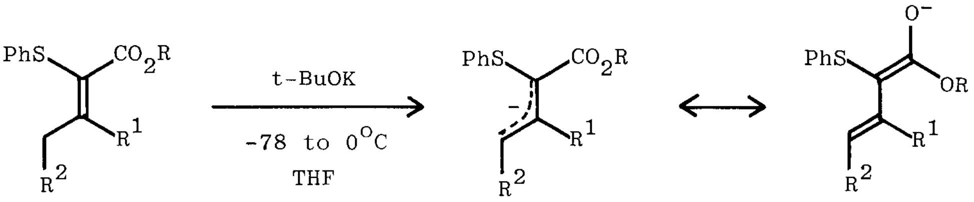
Pummerer elimination[6] gives esters (5) as mixtures of E and Z isomers becoming almost entirely the more stable Z-isomer on standing (Table 1). These compounds are stable indefinitely if kept cool and dark.

Most bases add Michael fashion to esters (5) with no sign of anion formation. We finally discovered that inverse addition of (5, R^3=H) to t-BuOK in THF at -78° to 0°C gave clean deprotonation to anion (6).

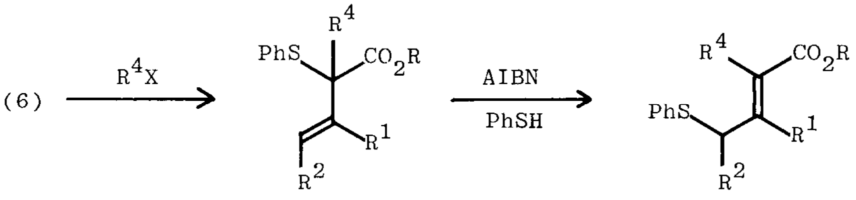
TABLE 1

Synthesis of α-Phenylthio-Crotonate Esters (5)

				INTERMEDIATES Yield (%)				PRODUCT Yield	Stereo
R	R^1	R^2	R^3	(2)	(3)	(4)	(5)	(%)	(Z:E)
Et	H	H	H	-	91	92	(5a)	67	4:1
Me	Me	H	H	-	89	83	(5b)	90	-
Me	H	Me	H	52	89	100	(5c)	82	3:1
Me	H	Et	H	-	95	92	(5d)	93	2:1
Me	$(CH_2)_3$		H	83	93	100	(5e)	68	-
Me	H	Me	Me	54	95	69	(5f)	88	1:1



(5, R^3=H) (6a) (6b)



(6) (7) (8)

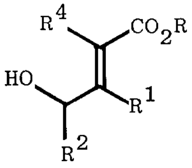
The new anion (6) is both an allyl sulphide anion[7] (6a) and an extended enolate[8] (6b). On separate molecules these two features each promote α-alkylation and here in combination they give (7) with no trace of γ-product (Table 2). Reaction has occurred at the carbon atom having both CO_2Et and PhS substituents : it appears that each reinforces the α-directing effect of the other. When R^1=H, the new β,γ-double bond in (7) is E regardless of the geometry of (5) (cf. ref. 8).

TABLE 2

Alkylation of Extended Enolate (6)

	Starting Material			Alkyl Halide	Product (7)		Product (8)	
	R	R^1	R^2	R^4X	Yield (%)	Stereo	Yield (%)	Stereo (E:Z)
(5a)	Et	H	H	MeI	87	-	100	100:0
				$PhCH_2Br$	76	-	94	85:15
(5b)	Me	Me	H	MeI	96	-	96	57:43
				EtI	94	-	-	-
				$PhCH_2Br$	98	-	100	67:33
				allyl Br	78	-	-	-
(5c)	Me	H	Me	MeI	73	E	-	-
(5d)	Me	H	Et	EtI	87	E	92	82:18
(5e)	Me	$(CH_2)_3$		MeI	73	-	-	-

Products (7) promise to be useful synthetic intermediates. Their conversion into (9), via the sulphoxide of (8) and the sulphenate rearrangement (including one version of (3) to (7) on a lactone[9]), has already been reported.[3,10] We find that the [1,3] PhS shift[11] to γ-PhS crotonate esters (8) (Table 2) is caused by radical initiation with AIBN. The anions of (8) also react with alkyl halides and provide another example of the use of extended enolates in synthesis.[12]



(9)

References

1. S. Warren, Chem. Ind. (London), 1980, 824 and references therein; S. Knapp, R. Lis, and P. Michna, J. Org. Chem., 1981, 46, 624.
2. L. Horner and E.-O. Renth, Liebigs Ann. Chem., 1967, 703, 37; K. Takaki, A. Okamura, Y. Ohshiro, and T. Agawa, J. Org. Chem., 1978, 43, 402; S. Yamagiwa, N. Hoshi, H. Sato, H. Kosugi, and H. Uda, J. Chem. Soc., Perkin Trans. 1, 1978, 214; S. Yamagiwa, H. Sato, N. Hoshi, H. Kosugi, and H. Uda, Ibid., 1979, 570.
3. H. Hagiwara, K. Nakayama, and H. Uda, Bull. Chem. Soc. Jpn., 1975, 48, 3769; K. Iwai, H. Kosugi, H. Uda, and M. Kawai, Bull. Chem. Soc. Jpn., 1977, 50, 242; J. Nokami, K. Nishiuchi, S. Wakabayashi, and R. Okawara, Tetrahedron Lett., 1980, 4455; L. Leyendecker and M. T. Comte, Ibid., 1982, 23, 5031.
4. C. R. Johnson, D. Diefenbach, J. E. Kaiser, and J. C. Sharp, Tetrahedron, 1969, 25, 5649.
5. C. R. Johnson and J. E. Kaiser, Org. Synth., 1966, 46, 78.
6. Method of H. J. Monteiro and A. L. Gemal, Synthesis, 1975, 437.
7. P. Brownbridge and S. Warren, J. Chem. Soc., Perkin Trans. 1, 1977, 1311, 2272 and references therein.
8. A. S. Kende and B. H. Toder, J. Org. Chem., 1982, 47, 163, and references therein.
9. S. Yamagiwa, H. Kosugi, and H. Uda, Bull. Chem. Soc. Jpn., 1978, 51, 3011.
10. H. Kosugi, H. Uda, and S. Yamagiwa, J. Chem. Soc., Chem. Commun., 1975, 192; 1976, 71; P. Ortiz de Montellano and C. K. Hsu, Tetrahedron Lett., 1976, 4215; J. Nokami, T. Mandai, Y. Imakura, K. Nishiuchi, M. Kawada, and S. Wakabayashi, Ibid., 1981, 22, 4489; Q. B. Cass, A. A. Jaxa-Chamiec, and P. G. Sammes, J. Chem. Soc., Chem. Commun., 1981, 1248; F. Kido, Y. Noda, and A. Yoshikoshi, Ibid., 1982, 1209.
11. P. Brownbridge and S. Warren, J. Chem. Soc., Perkin Trans. 1, 1976, 2125.
12. P. Brownbridge, P. G. Hunt, and S. Warren, Tetrahedron Lett., 1983, 24, 000.

(Received in UK 4 March 1983)