

Acyl Anion Equivalents: Two Simple and Versatile Ketone Syntheses

By PHILIP BLATCHER, J. IAN GRAYSON, and STUART WARREN*

(University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW)

Summary Ketones can be synthesised from alkyl halides and carbonyl compounds *via* two acyl anions equivalents PhS.CLi(R)Z , where Z is either PhS or Ph_2PO .

THE bis(phenylthio) carbanion from (1) (Scheme 1) has been used by Corey and Seebach¹ and others² as an acyl anion equivalent,³ but has never rivalled dithian³⁻⁵ largely because the alkylated derivatives (2) are reluctant to form anions and react with a second alkyl halide.^{1,5} We report

that bis(phenylthio) compounds can in fact be used as acyl anion equivalents with some advantages over dithians.

The crystalline starting material (1) is easy to make^{1,6} and can be alkylated once in high yield (Table 1). It is not necessary to use a second alkyl halide to make a ketone; instead the anion from (2), made with butyl-lithium in the presence of tetramethylethylenediamine (TMEDA), is combined with an aldehyde or ketone to give an alcohol (3). When one of these alcohols is simply dissolved in trifluoro-

TABLE 1. Synthesis of ketones *via* bis(phenylthio) carbanions (from 2)

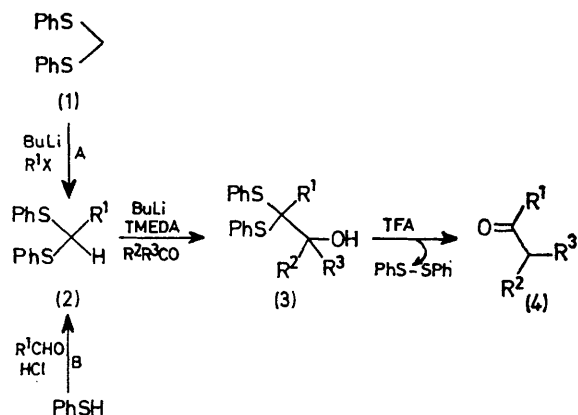
Entry	First alkylation			Second alkylation			Ketone ^b (4)/%
	R ¹	Method ^a	Yield ^b of (2)/%	R ²	R ³	Yield ^b of (3)/%	
1	Me	A	99	Ph	H	57	87 (100)
2	Et	A	75	Ph	H	89	74 (100) ^c
3				Me	H	55	(90)
4				n-hexyl	H	59	31
5				Ph	-[CH ₂] ₆ -	68	64 (100)
6	Pr ¹	B	(100)	Ph	H	42	92

^a See Scheme 1. ^b Yield of isolated compound; figures in parentheses are yields estimated by n.m.r. spectroscopy. ^c Same product as entry 1, Table 2.

TABLE 2. Ketone synthesis from the acyl anion equivalent (7)

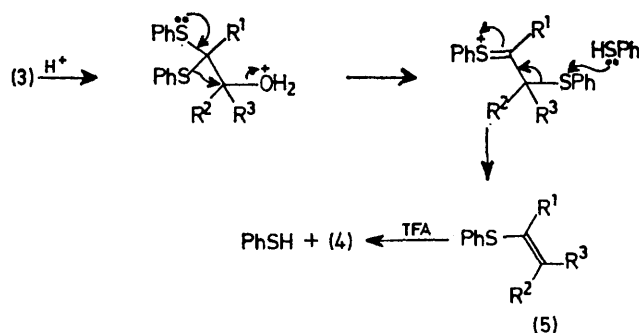
Entry	Formation of (7)		Vinyl sulphide		Ketone (9)		Overall yield from (6)/%
	R ¹	Yield ^{a,b} /%	R ²	Yield ^b /%	Time in TFA/h	Yield ^b /%	
1	Et	73	Ph	93	0.3	78 ^c	53
2	PhCH ₂	79	Ph	90	0.5	97	69
3			n-hexyl	93	0.3	93	69
4	Pr ¹	81	<i>p</i> -MeOC ₆ H ₄	94	1.5	86	66
5			PhCH=CH	93	—	d	—

^a Yield for the introduction of the phenylthio group to the phosphine oxide (6). ^b All yields are those of isolated compounds. ^c Same product as entry 2, Table 1. ^d This compound does not give the enone with TFA.



SCHEME 1. X = Halogen

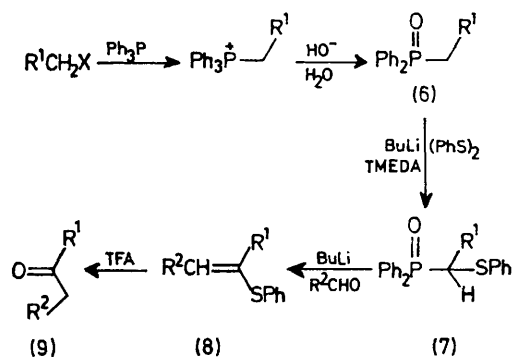
acetic acid (TFA) at room temperature, a precipitate of diphenyl disulphide appears at once; filtration and chromatography gives the pure ketone (4). We have some evidence that the mechanism of this reaction is that shown in Scheme 2.



SCHEME 2.

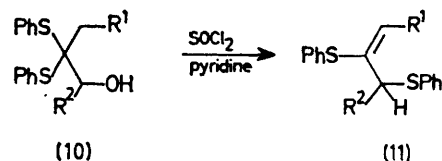
† Both the corresponding phosphonium salts (T. Mukaiyama, S. Fukuyama, and T. Kumamoto, *Tetrahedron Letters*, 1968, 3787) and phosphonate esters (reference 9, and H. M. McGuire, H. C. Odom, and A. R. Pinder, *J.C.S. Perkin I*, 1974, 1879; M. Mikolajczyk, S. Grzejszczak, and A. Zatorski, *J. Org. Chem.*, 1975, 40, 1979; P. Coutrot, C. Laurence, J. Petrova, and P. Savignac, *Synthesis*, 1976, 107; M. Mikolajczyk, S. Grzejszczak, W. Midura, and A. Zatorski, *ibid.*, 1975, 278; I. Shahak and J. Almog, *ibid.*, 1969, 170; 1970, 145) have been used to make vinyl sulphides.

The advantages over the dithian route are that the product (4) is more easily released from (3) than in the sometimes troublesome hydrolyses of dithians,^{4,5,7} and



SCHEME 3. X = Halogen

that the relatively reactive carbonyl compounds are used instead of alkyl halides. The method is satisfactory for alkyl and aryl aldehydes, and for cyclic ketones (Table 1).



Where the first alkyl group is branched, it is better to make the starting material (*e.g.*, 2, R¹ = Pr¹) from the aldehyde and benzenethiol (route B, Scheme 1),² so that in these cases the product is made from two carbonyl compounds.

Our second acyl anion equivalent has a diphenylphosphinoyl group instead of one phenylthio group† (7) and is

easily made in three steps (Scheme 3) from triphenylphosphine and the alkyl halide.⁸ Reaction of the anion of (7) with aldehydes gives the vinyl sulphides (8) which can be hydrolysed to the ketone (9) without purification. There are many published procedures⁹⁻¹¹ for this last step, most of which work well for R¹ ≠ H, but we have found that the vinyl sulphides (8) are rapidly hydrolysed when dissolved in TFA at room temperature[‡] (see Table 2).

This sequence is perhaps easier to carry out as the phosphorus-containing products are all crystalline, and yields are very high (Table 2), but only one side of the ketone may be branched as the anion from (7) does not react satisfactorily with ketones. It does however react with alkyl,

aryl, and $\alpha\beta$ -unsaturated aldehydes (Table 2), and a branched chain may be introduced as the first alkyl group (*e.g.*, entries 4 and 5, Table 2).

We have described these reactions as those of the nucleophilic acyl anion equivalents [from (2) and (7)]; they may equally well be regarded during synthetic planning as '1,2-alkylative carbonyl transpositions'^{11,12} on the electrophile. The intermediate (10) has potentially greater versatility; under different conditions it rearranges to the specific enolate equivalent (11).

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‡ As also must be the vinyl sulphide (5) if it is an intermediate in the formation of (4) from (3). The ketones (9) may be freed from PhSH by washing with aqueous mercuric chloride or sodium carbonate solutions.

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⁷ See for example, T. Oishi, K. Kamemoto, and Y. Ban, *Tetrahedron Letters*, 1972, 1085; M. Fetizon and M. Jurion, *J.C.S. Chem. Comm.*, 1972, 382.

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