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 Seebach[1] and others[2] as an acyl anion equivalent,[3] but has never rivalled dithian[3–5] 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**)

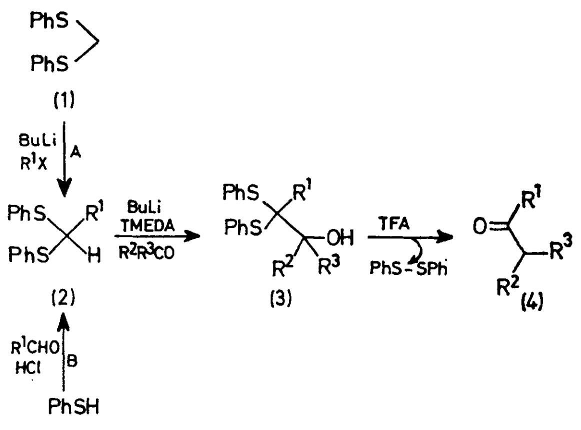
	First alkylation			Second alkylation			Ketone[b](**4**)/%
Entry	R^1	Method[a]	Yield[b] of (**2**)/%	R^2	R^3	Yield[b] of (**3**)/%	
1	Me	A	99	Ph	H	57	87 (100)
2	Et	A	75	Ph	H	89	74 (100)[c]
3				Me	H	55	(90)
4				n-hexyl	H	59	31
5				$-[CH_2]_5-$		68	64 (100)
6	Pr^i	B	(100)	Ph	H	42	92

[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**)

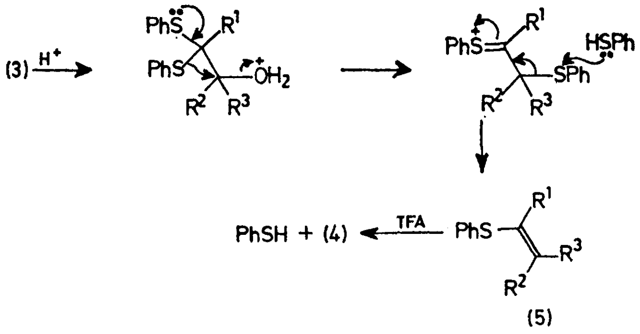
	Formation of (**7**)		Vinyl sulphide		Ketone (**9**)		Overall yeld from (**6**)/%
Entry	R^1	Yield[a,b]/%	R^2	Yield [b]/%	Time in TFA/h	Yield[b]/%	
1	Et	73	Ph	93	0·3	78[c]	53
2	$PhCH_2$	79	Ph	90	0·5	97	69
3			n-hexyl	93	0·3	93	69
4	Pr^i	81	*p*-$MeOC_6H_4$	94	1·5	86	66
5			PhCH=CH	93	—	d	—

[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.



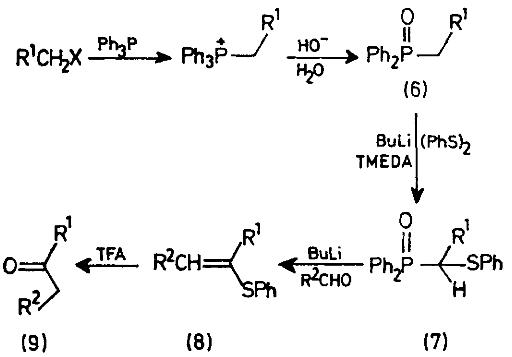
SCHEME 1. X = Halogen

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.

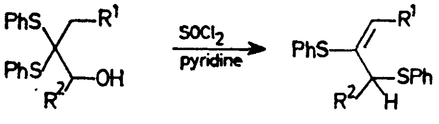


SCHEME 2.

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 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).



SCHEME 3. X = Halogen



(**10**) (**11**)

Where the first alkyl group is branched, it is better to make the starting material (*e.g.*, **2**, $R^1 = Pr^i$) 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

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† 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. Grzejsczak, 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.

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 procedures [9–11] for this last step, most of which work well for $R^1 \neq H$, 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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