On the Control of Sulphenylations at Carbon

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Controlled monosulphenylation at carbon adjacent to electron-withdrawing groups can be achieved by the controlled reduction of readily available bis-sulphenylated products.

In recent years, α-sulphenylated carbonyl compounds have become intermediates of significant importance in synthetic organic chemistry.[1,2] Although numerous sulphenylations using different reagents have been reported,[3–6] controlled monosulphenylation is often difficult.

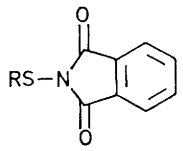
Our reagents of choice for sulphenylation of (**1**) were *N*-alkylthio- or arylthio-phthalimides (**2**) which have been extensively used as sulphenyl transfer reagents for hetero-atoms.[7] We have simply treated the appropriate substances (**1**) with (**2**) as outlined in Table 1. It should be noted that the degree of sulphenylation in the cases of some β-ketosulphides and β-ketosulphones could be controlled simply by stoicheiometry; in all other cases mixtures were obtained unless two equiv. of thiophthalimide were used. Then, only clean bis-sulphenylated compounds were obtained.

Of significance, however, is our observation that *all bis-sulphenylated products can be cleanly reduced to monosulphenylated compounds by the following procedure*. Thus, as outlined in Table 2, reaction of a bis-sulphenylated compound with sodium ethanethiolate in the presence of an excess of base proceeded only to the anion of the monosulphenylated compound, which was not further reduced by thiolate. If this reaction was carried out in the presence of a proton source (for example, an excess of ethanethiol), complete reduction occurred.† These reductions evidently take place by nucleophilic attack of thiolate at the sulphenyl sulphur atom, since we could at all times isolate an appropriate range of sulphur compounds.‡

We believe that these results delineate an experimentally facile and reliable method for controlled sulphenylation at carbon in a useful range of structure types.§ Alternatively, the reactions may have potential as a blocking–deblocking sequence in certain situations.

$$Y-CH_2-Z$$

(1) a; Y, Z = -COR, $-CO_2R'$, or $-SO_2R''$
b; Y = PhCO, Z = H



(2) a; R = Me
b; R = Et
c; R = Ph

Table 1. Products from sulphenylations at carbon.[a]

Substrate (**1**)	Reagent[b]	Product[c]	%Yield[d]
$PhCOCH_2SO_2Me$	(**2a**) (1 : 1)	$PhCOCH(SMe)SO_2Me$[e]	88
$PhCOCH_2SO_2Me$	(**2b**) (2 : 1)	$PhCOC(SEt)_2SO_2Me$	87
$PhCOCH_2SO_2Ph$	(**2a**) (1 : 1)	$PhCOCH(SMe)SO_2Ph$	90
$(EtSO_2)_2CH_2$	(**2a**) (2 : 1)	$(EtSO_2)_2C(SMe)_2$	89
$(EtO_2C)_2CH_2$	(**2c**) (2 : 1)	$(EtO_2C)_2C(SPh)_2$	94
$MeCOCH_2CO_2Et$	(**2c**) (2 : 1)	$MeCOC(SPh)_2CO_2Et$	93
PhCOMe	(**2b**) (2 : 1)	$PhCOCH(SEt)_2$	76
PhCOMe	(**2b**) (3 : 1)	$PhCOC(SEt)_3$	82
$PhCOCH_2SEt$	(**2b**) (1 : 1)	$PhCOCH(SEt)_2$	81

[a] Reactions were carried out by stirring the substrate (2—20 mmol) at room temperature in dichloromethane containing 2 mol. equiv. of triethylamine, except in the case of acetophenone and its derivatives which required potassium t-butoxide and dimethyl sulphoxide (DMSO) as base and solvent respectively. [b] The numbers in parentheses give the molar ratio of (**2**) : (**1**). [c] Work-up of reactions carried out in dichloromethane was by evaporation of solvent; for reactions in DMSO, the mixture was poured into water, acidified (HCl), and extracted with ether. Crude products were free of starting materials (confirmed by ^1H n.m.r. and t.l.c. analyses) and phthalimide could be removed by making use of its very low solubility in dichloromethane. All compounds were characterized by t.l.c., ^1H and ^{13}C n.m.r., and i.r. spectroscopy. Solids were recrystallized and their m.p.s determined. Most compounds did not give molecular ions with e.i. mass spectroscopy. [d] Yields are for isolated, clean products. [e] m.p. 117—117.5 °C; lit. (G. A. Russell and E. T. Sabourin, *J. Org. Chem.*, 1969, **34**, 2336) 115—117 °C.

Table 2. Reduction of polysulphenylated compounds.[a]

Substrate	Reagent	Product	% Yield
$PhCOC(SMe)_2SO_2Me$	[b]	$PhCOCH(SMe)SO_2Me$	90[c]
$PhCOC(SEt)_2SO_2Me$	[b]	$PhCOCH(SEt)SO_2Me$	80[c]
$PhCOC(SEt)_2SO_2Me$	[d]	$PhCOCH(SEt)SO_2Me$	85[c]
$PhCOC(SEt)_2SO_2Me$	[e]	$PhCOCH_2SO_2Me$	80[c]
$(EtSO_2)_2C(SMe)_2$	[b]	$(EtSO_2)_2CH{\cdot}SMe$	94[c]
$(EtCO_2)_2C(SPh)_2$	[b]	$(EtCO_2)_2CH{\cdot}SPh$	72[f]
$(EtCO_2)_2C(SPh)_2$	[d]	$(EtCO_2)_2CH{\cdot}SPh$	89[f]
$MeCOC(SPh)_2CO_2Et$	[d]	$MeCOCH(SPh)CO_2Et$	83[f]
$PhCOC(SEt)_3$	[d]	$PhCOCH_2SEt$	83[g]
$PhCOCH(SEt)_2$	[d]	$PhCOCH_2SEt$	62[g]

[a] All reductions were carried out for 2 h at 25 °C. [b] NaSEt/excess of NaH in tetrahydrofuran solvent. [c] Yields are for isolated products, obtained by washing the crude reaction products with light petroleum (b.p. 30—60 °C) to free them from minor amounts of EtSSEt. [d] NaSEt/excess of NaOEt in EtOH solvent. [e] NaSEt/excess of EtSH in EtOH solvent. [f] Yields are based on ^1H n.m.r. analysis of a mixture containing the product, EtSSEt and PhSH. [g] Yields are based on ^1H n.m.r. analysis of a mixture containing the product and EtSSEt; clean product was obtained by pumping off the EtSSEt.

† α-Ethylthioacetophenone was not reduced further under our reaction conditions, although its reduction has been reported under more vigorous conditions: M. Ōki, W. Funakoshi, and A. Nakamura, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 828.

‡ These are mostly disulphides, details of which will be provided in the full paper. Apparently, the reaction does not involve radical anions since it proceeds in the same manner in the presence of either *m*-dinitrobenzene or nitrobenzene: N. Kornblum, S. C. Carlson, and R. G. Smith, *J. Am. Chem. Soc.*, 1979, **101**, 647.

§ It has been claimed[5] that active methylene compounds such as diethyl malonate may be selectively monosulphenylated with *N*,*N*-disubstituted benzenesulphenamides. In our hands *pure* sulphenamides were totally unreactive towards diethyl malonate or ethyl acetoacetate either in neutral or in mildly basic (triethylamine) dichloromethane, but in the presence of added triethylammonium chloride gave a mixture of bis-sulphenylated product and unchanged ester only.

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