Preparation and Synthetic Utility of 1-Phenylthio-1-nitro Epoxides. Facile Preparation of α-Substituted *S*-Phenyl Thio esters

Mark Ashwell and Richard F. W. Jackson*

Department of Organic Chemistry, Bedson Building, The University, Newcastle-upon-Tyne NE1 7RU, U.K.

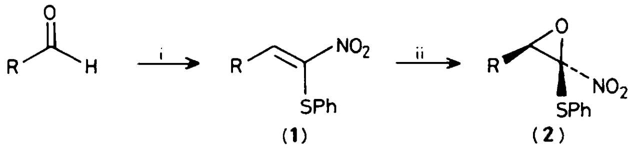
Novel 1-Phenylthio-1-nitro epoxides (**2**), readily prepared by epoxidation of the corresponding 1-phenylthio-1-nitroalkenes (**1**), react efficiently under mild conditions with a variety of hetero nucleophiles to give α-substituted *S*-phenyl thioesters (**4**).

Recently, the preparation of α-substituted *S*-phenyl thioesters by nucleophilic addition to phenylthio-nitro-alkenes (**1**), followed by ozonolysis of the derived nitronates, has been reported.[1] We now report our preliminary results, in which epoxidation of 1-phenylthio-1-nitroalkenes (**1**) to give 1-phenylthio-1-nitro epoxides (**2**) is followed by nucleophilic attack on these epoxides leading to α-substituted *S*-phenyl thioesters. The best precedent for nucleophilic attack on epoxides (**2**) is provided by the reaction of the dicyano epoxides (**3**) with hydrogen halides in alcoholic solvents at reflux.[2] We hoped that the presence of a good leaving group (nitro) would increase the scope of this type of epoxide ring-opening, by allowing it to occur under milder conditions.

In order to investigate this idea, we have developed a one-step procedure for the preparation of 1-phenylthio-1-nitroalkenes (**1**) by piperidinium acetate catalysed condensation of phenylthionitromethane (2 equiv.) with the corresponding aldehydes, in either dichloromethane or toluene as solvent.† The procedure is milder than that previously used,[1] and is therefore likely to be of wider applicability. Nucleophilic epoxidation of these 1-phenylthio-1-nitroalkenes (**1a**—**g**), using t-butyl hydroperoxide and n-butyl-lithium,[3] proceeds exceptionally smoothly at −78 °C within one hour, to give high yields of the corresponding 1-phenylthio-1-nitro epoxides (**2a**—**g**).‡ Our results for the preparation of the alkenes (**1**) and their oxidation are presented in Table 1. No oxidation at sulphur has been observed during the epoxidation reaction.

The 1-phenylthio-1-nitro epoxides which we have prepared are best stored at −20 °C, although all except the epoxide (**2g**) are stable at higher temperatures. Epoxides (**2b**—**f**) are stable to column chromatography, whilst (**2g**) can be purified by recrystallisation. As yet, we have found no satisfactory method for the purification of (**2a**), although the crude product is obtained in a satisfactory state of purity for further reaction. Our initial investigations into the nucleophilic opening of 1-phenylthio-1-nitro epoxides[4] have concentrated on compound (**2c**), derived originally from 2-methylpropanal, since it is crystalline and especially easy to prepare. Our results are described in Table 2, and demonstrate remarkable reactivity of the 1-phenylthio-1-nitro epoxide functional group towards nucleophilic attack, generating α-substituted *S*-phenyl thioesters (**4a**—**f**) in high yield under mild conditions.

The efficient reactions with both trifluoroacetic acid, to give the trifluoroacetate (**4d**), and methanesulphonic acid, to give the methanesulphonate (**4e**) are particularly noteworthy. We have made an extensive study of the reaction with metal halides, and noted that use of co-ordinating cations is important for clean reaction. For example, treatment of the epoxide (**2c**) with potassium iodide in toluene, in the presence of 18-crown-6, leads to a complex mixture of products. Clearly co-ordination of the epoxide oxygen (either by metal cation,



Scheme 1. *Reagents*: i, $PhSCH_2NO_2$ (2 equiv.), piperidinium acetate (5 mole %); ii, Bu^tOOH (1.5 equiv.), Bu^nLi (1.1 equiv.).

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† All 1-phenylthio-1-nitroalkenes are single geometrical isomers, and are assigned the *Z* configuration on the basis of the chemical shift of the vinyl proton.[1]

‡ All 1-phenylthio-1-nitro epoxides are single diastereoisomers. They are drawn on the assumption that epoxidation is a stereospecific *cis* process, which is the case for epoxidations of other systems with t-butyl hydroperoxide/n-butyl-lithium.[3]

Table 1. Preparation of 1-phenylthio-1-nitro epoxides (**2**) (Scheme 1).

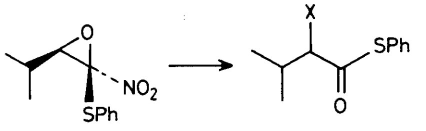
	Condensation					Epoxidation	
R	Solvent	Time/h	Temp./°C	Product	% Yield[a]	Product	% Yield
Me	CH_2Cl_2	2	0	(**1a**)	59	(**2a**)	90[b]
Pr^n	CH_2Cl_2	2.5	0	(**1b**)	76	(**2b**)	80
Pr^i	CH_2Cl_2	7.5	Reflux	(**1c**)	78	(**2c**)	91
Bu	CH_2Cl_2	2.5	0	(**1d**)	75	(**2d**)	78
Pentyl	CH_2Cl_2	2.5	0	(**1e**)	71	(**2e**)	77
Hexyl	CH_2Cl_2	1.5	0	(**1f**)	56	(**2f**)	80
Ph	Toluene	5	Reflux	(**1g**)	79	(**2g**)	66

[a] Yields of 1-phenylthio-1-nitroalkenes are based on phenylthionitromethane consumed. [b] Crude yield, pure by ^1H n.m.r.

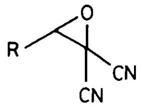
Table 2. Reactions of 1-phenylthio-1-nitro epoxide (**2c**).

Reagent[a]	Solvent	Time/h	Temp./°C	Product	(4), X	% Yield
LiCl	Acetone	1.5	20	(**4a**)	Cl	78
$MgBr_2 \cdot Et_2O$	Et_2O	2.5	20	(**4b**)	Br	85
MgI_2	Et_2O	0.5	0	(**4c**)	I	91
CF_3CO_2H	Toluene	6	Reflux	(**4d**)	CF_3CO_2	70
CH_3SO_3H	Toluene	0.5	Reflux	(**4e**)	CH_3SO_3	76
$BF_3 \cdot Et_2O$	Toluene	12	20	(**4f**)	F	96

[a] All reactions were performed using 1.2—1.5 mol equiv. of reagent and 0.1—0.2 M expoxide.



(**2c**) (**4**)



(**3**)

or a proton) is an essential first step in promoting efficient ring-opening. The most interesting observation is the mild and efficient introduction of fluorine, using boron trifluoride–diethyl ether, to give the α-fluoro thioester (**4f**). Use of either potassium fluoride in toluene, in the presence of 18-crown-6, or tetra-n-butylammonium fluoride in tetrahydrofuran, gave poorer conversions and mixtures of products. Here, again, initial co-ordination of the reagent is clearly important.§

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§ The possibility that hydrogen fluoride is the actual reagent in this process has not been ruled out. However, the reaction works as well with freshly opened bottles of boron trifluoride–diethyl ether as it does with older bottles, which would be expected to contain more hydrogen fluoride.