Phenylthionitromethane: a Versatile Reagent for the Conversion of Aldehydes into α-Substituted *S*-Phenyl Thioesters

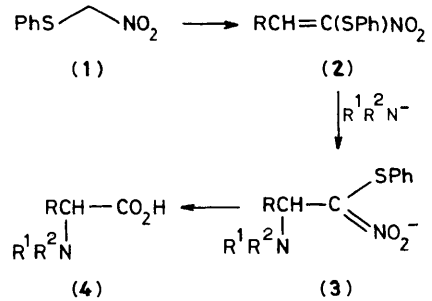
Bernard J. Banks,[a] Anthony G. M. Barrett,*[b] and Mark A. Russell[b]

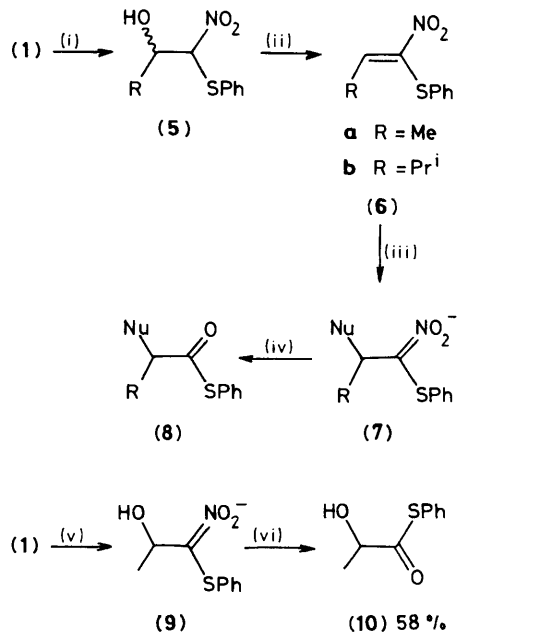
[a] *Pfizer Central Research, Sandwich, Kent CT13 9NJ, U.K.*
[b] *Department of Chemistry, Northwestern University, Evanston, Illinois 60201, U.S.A.*

Acetaldehyde and isobutyraldehyde, RCHO, reacted with phenylthionitromethane (KOH, MeOH) followed by methanesulphonyl chloride (Et_3N, CH_2Cl_2) to give the alkenes, $RCH{=}C(SPh)NO_2$; these reacted with the nucleophiles [Nu = NaOMe, NaOPr^i, potassium phthalimide, $CH_2FCONHK$, *p*-$MeC_6H_4SO_2Na.2H_2O$, or $KCH(CO_2Me)_2$] in *N*,*N*-dimethylformamide (DMF), MeOH, or Pr^{i}OH at −30 °C to give, on subsequent ozonolysis (MeOH–DMF; −78 °C) the title thioesters, [RCH(Nu)COSPh] (46—79%).

Recently we required a method to homologate an aldehyde into an α-amino-acid derivative that circumvented the drastic reaction conditions associated with Strecker protocol.[1] We considered that 1-nitro-1-phenylthioalkenes (**2**), available from phenylthionitromethane (**1**) and aldehydes,[2] should be converted into α-amino-acid derivatives (**4**) by the addition of a nitrogen-centred nucleophile and subsequent oxidation of the nitronate (**3**). Herein we report that the alkenes (**2**) react smoothly with diverse types of nucleophiles. This provides a concise, mild, and convenient method for the synthesis of α-substituted *S*-phenyl thioesters.

Phenylthionitromethane (**1**)[2,3] condensed smoothly with acetaldehyde and isobutyraldehyde in the presence of potassium hydroxide at 0 °C in methanol solution to produce both isomers of the alcohol (**5**). These were dehydrated using methanesulphonyl chloride, MsCl, and triethylamine in dichloromethane solution at −78 °C to 0 °C according to the procedure described by Miyashita *et al.*[2] Chromatography on silica gave the *Z* nitro-alkenes (**6a,b**)[2] in 60% and 31% yields, respectively. In *N*,*N*-dimethylformamide (DMF) solution, both isomers of (**6**) reacted smoothly with several nucleophiles at −30 °C to give the nitronate salts (**7**). These were not isolated but were directly ozonolysed[4] at −78 °C in methanol–





Scheme 1. *Reagents and conditions.* (i) KOH, MeOH, RCHO, 0 °C; HOAc; (ii) MsCl, Et_3N, CH_2Cl_2, −78—0 °C; (iii) Nu^-, DMF, −30 °C; (iv) O_3, MeOH, DMF, −78 °C; (v) MeCHO, KOH, MeOH; (vi) O_3, MeOH, −78 °C.

Table 1.[a] Preparation of α-substituted *S*-phenyl thioesters.

Starting material	Product (**8**) Nu	R	Yield %
(**6a**)	OMe	Me	79
(**6a**)	OPr^i	Me	61
(**6a**)	Phth[b]	Me	68
(**6a**)	CH_2FCONH[c]	Me	62
(**6a**)	p-$MeC_6H_4SO_2$[c]	Me	56
(**6a**)	$CH(CO_2Me)_2$[c]	Me	60
(**6b**)	Phth[b]	Pr^i	46

[a] All new compounds were fully authenticated by microanalyses and spectral data. [b] PhthK = potassium phthalimide. [c] Reactions of these ambident nucleophiles gave only the amide, sulphone, or *C*-alkylated material, respectively.

DMF to produce the α-substituted *S*-phenyl thioesters (**8**) in good, yet unoptimised, yields (Scheme 1 and Table 1). In a typical procedure the nucleophile (1.2 mmol) was added to the nitroalkene (**6**) (1 mmol) in DMF (12 ml) at −30 °C. After 0.5 h the solution was diluted with methanol (30 ml), ozonolysed at −78 °C until blue in colour, and purged with nitrogen. Evaporation and chromatography on silica gave the α-substituted thioester. Wade has reported that 1-phenylsulphonyl-1-nitroalkane anions are oxidised to carboxylic acids by potassium permanganate.[5] We have found this oxidant less satisfactory than ozone for the oxidation of (**7**). Phenylthionitromethane (**1**) may also be used for the synthesis of *S*-phenyl α-hydroxythioesters. Thus (**1**) condensed with acetaldehyde at 0 °C in the presence of methanolic potassium hydroxide. Direct ozonolysis of the nitronate (**9**) at −78 °C gave the thioester (**10**), (Scheme 1).

This versatile reaction demonstrates that aldehydes may easily be converted into α-substituted *S*-phenyl thioesters *via* the intermediacy of 1-nitro-1-phenylthioalkenes with a diverse range of nucleophiles.

We thank the S.E.R.C. and Pfizer Central Research for generous support at Imperial College, London. In addition, we are grateful for the transference of this support to Northwestern University.

Received, 27th February 1984; Com. 257

References

1 S. Harusawa, Y. Hamada, and T. Shioiri, *Tetrahedron Lett.*, 1979, 4663 and references therein.
2 M. Miyashita, T. Kumazawa, and A. Yoshikoshi, *J. Chem. Soc., Chem. Commun.*, 1978, 362.
3 F. G. Bordwell and J. E. Bartmess, *J. Org. Chem.*, 1978, **43**, 3101.
4 J. E. McMurry, J. Melton, and H. Padgett, *J. Org. Chem.*, 1974, **39**, 259.
5 P. A. Wade, H. R. Hinney, N. V. Amin, P. D. Vail, S. D. Morrow, S. A. Hardinger, and M. S. Saft, *J. Org. Chem.*, 1981, **46**, 765.