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## Phenylthionitromethane: a Versatile Reagent for the Conversion of Aldehydes into $\alpha$ -Substituted S-Phenyl Thioesters

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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<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Na.2H<sub>2</sub>O, or KCH(CO<sub>2</sub>Me)<sub>2</sub>] in *N*,*N*-dimethylformamide (DMF), MeOH, or PriOH 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  $\alpha$ -amino-acid derivative that circumvented the drastic reaction conditions associated with Strecker protocol.<sup>1</sup> We considered that 1-nitro-1-phenylthioalkenes (2), available from phenylthionitromethane (1) and aldehydes,<sup>2</sup> should be converted into  $\alpha$ -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  $\alpha$ -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.*<sup>2</sup> Chromatography on silica gave the Z nitro-alkenes (**6a,b**)<sup>2</sup> 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<sup>4</sup> at -78 °C in methanol-



Scheme 1. Reagents and conditions. (i) KOH, MeOH, RCHO, 0 °C; HOAc; (ii) MsCl, Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, -78-0 °C; (iii) Nu<sup>-</sup>, DMF, -30 °C; (iv) O<sub>3</sub>, MeOH, DMF, -78 °C; (v) MeCHO, KOH, MeOH; (vi) O<sub>3</sub>, MeOH, -78 °C.

Table 1.<sup>a</sup> Preparation of  $\alpha$ -substituted S-phenyl thioesters.

Stanting	Product (8)		
material	Nu	R	Yield %
( <b>6a</b> )	OMe	Me	79
(6a)	OPr <sup>i</sup>	Me	61
(6a)	Phth <sup>b</sup>	Me	68
(6a)	CH <sub>2</sub> FCONH <sup>c</sup>	Me	62
(6a)	p-MeC <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> <sup>c</sup>	Me	56
(6a)	CH(CO <sub>2</sub> Me) <sub>2</sub> <sup>c</sup>	Me	60
(6b)	Phthb	$\mathbf{Pr^{i}}$	46

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

DMF to produce the  $\alpha$ -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  $\alpha$ -substituted thioester. Wade has reported that 1-phenylsulphonyl-1-nitroalkane anions are oxidised to carboxylic acids by potassium permanganate.<sup>5</sup> 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  $\alpha$ -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  $\alpha$ -substituted S-phenyl thioesters via the intermediacy of 1-nitro-1-phenylthioalkenes with a diverse range of nucleophiles.

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