Generation of Thioaldehydes by Base-catalysed Cleavage of *N*-(Alkoxycarbonylmethylthio)phthalimides

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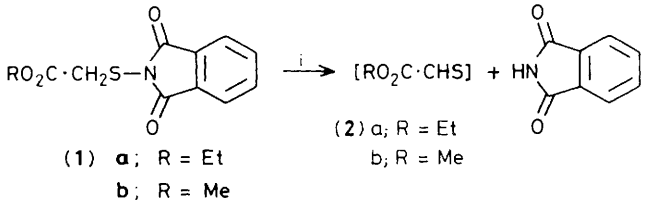
N-(Methoxycarbonylmethylthio)- and *N*-(ethoxycarbonylmethylthio)-phthalimide react at room temperature with triethylamine to generate the corresponding alkyl thioxoacetates, which have been trapped, *in situ*, by cycloaddition to conjugated dienes; the *endo*- and *exo*-adducts of cyclopentadiene and ethyl thioxoacetate dissociate at 111 °C thereby allowing transfer of the thioaldehyde to other conjugated dienes.

We reported[1] that treatment of ethoxycarbonylmethanesulphenyl chloride with triethylamine effects 1,2-elimination of hydrogen chloride to give ethyl thioxoacetate (**2a**). This transient thioaldehyde was trapped *in situ* by various con-



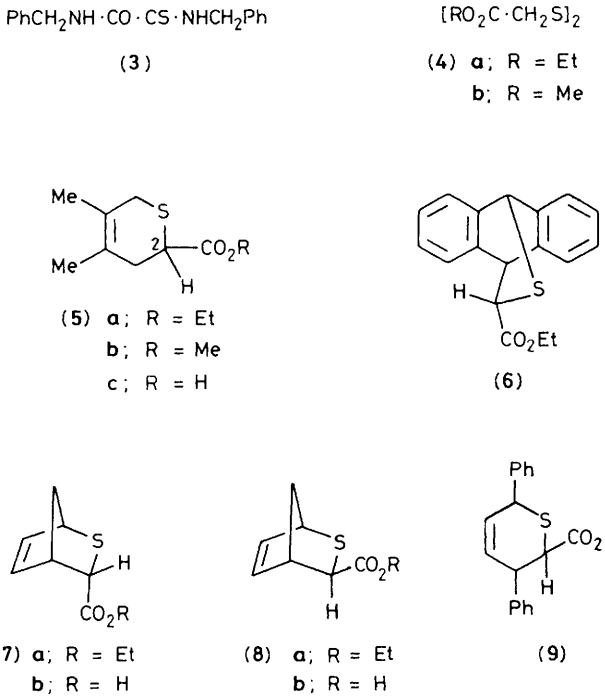
Scheme 1. i, Et_3N at room temperature.

jugated dienes to give Diels–Alder adducts, generally in satisfactory yield. However, we noted that, with cyclohexa-1,3-diene, the corresponding cycloadduct was accompanied by products apparently arising from attack of the sulphenyl chloride on the diene in competition with elimination to give the thioaldehyde. We report here alternative precursors (**1**) for alkyl thioxoacetates which do not react competitively with dienes (Scheme 1).

Harpp and Back[2] studied the reaction of *N*-(methoxycarbonylmethylthio)phthalimide (**1b**) with benzylamine at room temperature and obtained phthalimide (69%), *N*-benzylphthalimide (16%), and the thio-oxamide (**3**) (27%). They suggested that this last product was formed, in a complex manner, from methyl thioxoacetate (**2b**). With this suggestion in mind, we examined the reactions of the derivatives (**1**) with triethylamine in the presence of conjugated dienes.

The disulphide (**4a**) was heated with *N*-bromophthalimide in benzene containing a catalytic amount of dibenzoyl peroxide to give[3] (67%) the ethyl ester (**1a**), m.p. 76—82 °C (decomp.), δ ($CDCl_3$) 3.51 (s, CH_2). The methyl ester (**1b**), m.p. 125—130 °C (decomp.), δ ($CDCl_3$) 3.51 (s, CH_2) was obtained (70%) similarly from the disulphide (**4b**). The ethyl ester (**1a**) (2.26 mmol) was treated with triethylamine (2.71 mmol) at room temperature in benzene (23 ml) containing 2,3-dimethylbuta-1,3-diene (2.26 mmol). After *ca.* 30 min, phthalimide began to crystallise out and, after 3 h, the oily cycloadduct[1] (**5a**) was isolated (78%) from the reaction mixture. Similarly, the methyl ester (**1b**) and 2,3-dimethylbuta-1,3-diene gave the oily cycloadduct (**5b**) (85% after distillation), which was identified by hydrolysis to give the crystalline acid[1] (**5c**). When the foregoing preparation of (**5a**) was conducted in benzene containing CD_3OD (2% by volume), the product contained no detectable (^1H n.m.r. spectroscopy) amount of deuterium. Thus, base-catalysed exchange of the methylene hydrogens of (**1a**) was slow relative to elimination of phthalimide, and the product (**5a**) did not undergo exchange of hydrogen at the chiral centre (C-2). Significantly, dimethylbutadiene and the ester (**1a**) did not react in the absence of triethylamine when kept in benzene for 60 h at room temperature. Further, when anthracene (0.38 mmol) and (**1a**) (0.38 mmol) were heated with triethylamine (0.45 mmol) in benzene (4 ml) under reflux for 4 h, the cycloadduct (**6**) formed in a yield (53% after chromatography) superior to that (37%) obtained[1] using ethoxycarbonylmethanesulphenyl chloride as a source of the thioaldehyde (**2a**).

An attempt to prepare the adducts (**7a**) and (**8a**) of cyclopentadiene and ethyl thioxoacetate (**2a**), using ethoxycarbonylmethanesulphenyl chloride and triethylamine in the usual way,[1] led to a complex mixture containing only *ca.* 19% of the desired products. It appeared that attack of the sulphenyl chloride on cyclopentadiene occurred more rapidly than elimination of hydrogen chloride. In contrast, when (**1a**) (0.75 mmol) was treated with triethylamine (0.9 mmol) at room temperature for 3 h in benzene (8 ml) containing cyclopentadiene (0.75 mmol), the cycloadducts (**7a**) and (**8a**) were obtained essentially quantitatively. The oily *endo*-(**7a**) [δ($CDCl_3$) 4.42 (d, *J* 4.2 Hz, 3-H)] and *exo*-adduct (**8a**) [δ($CDCl_3$) 3.30 (br. s, 3-H)] were separated (*endo: exo* ratio, 7:3) on silica plates and further characterised by hydrolysis to the corresponding acids (**7b**), m.p. 102—104 °C, and (**8b**), m.p. 102—104 °C. Repetition of this experiment in benzene containing CD_3OD (2% by volume) gave the adducts (**7a**) and (**8a**), in the same ratio, without incorporation of deuterium. The preparation of (**7a**) and (**8a**) was also accomplished in high yield using a catalytic amount (0.1 mol equiv.) of triethylamine but a longer reaction time (*ca.* 24 h) was then required.



Heating the kinetically determined mixture of (**7a**) (70%) and (**8a**) (30%), or each isomer separately, in toluene under reflux for 7 h gave, cleanly, the same equilibrium mixture of (**7a**) (30%) and (**8a**) (70%). This suggested that the mixture of cyclopentadiene adducts might, by thermal dissociation, be used preparatively as a 'clean' source of ethyl thioxoacetate since the only by-product, cyclopentadiene, would be readily removed by evaporation. Thus, the 'kinetic mixture' of (**7a**) and (**8a**) (1.4 mmol) was heated with 2,3-dimethylbuta-1,3-diene (1.54 mmol) in toluene (6 ml) under nitrogen at 120 °C (sealed tube) for 21 h. Evaporation of the toluene gave the adduct (**5a**) contaminated with a small amount of cyclopentadiene dimer. Distillation (Kugelrohr) gave the pure adduct (**5a**) (82%). The value of this method was demonstrated further using *trans,trans*-1,4-diphenylbuta-1,3-diene, which is known[4] to react with maleic anhydride 114 times more slowly than does 2,3-dimethylbuta-1,3-diene. The 'kinetic mixture' of (**7a**) and (**8a**), prepared from (**1a**) (1.13 mmol) and used without purification, was heated under reflux in xylene (15 ml) containing 1,4-diphenylbuta-1,3-diene (1.13 mmol) for 24 h under a slow stream of argon to remove cyclopentadiene. Evaporation of the solvent gave a residue consisting largely of the adduct (**9**) as a mixture of stereoisomers. The major isomer (the stereochemistry has not been determined) was separated chromatographically as an oil (48%) which was characterised spectroscopically and by accurate mass measurement. In contrast, treatment of 1,4-diphenylbuta-1,3-diene with (**1a**) and triethylamine under the

usual conditions gave only a low yield (*ca.* 9%) of the mixture of stereoisomers (**9**) together with diphenylbutadiene and decomposition products of (**2a**).

In summary, derivatives of the type (**1**) are excellent precursors for the generation of thioxoacetates (**2**) and, thereby, dihydrothiincarboxylates well suited for further synthetic manipulation. In principle, this approach should be applicable to the synthesis of other thioaldehydes[5] of the type, XCHS, where X is a group able to stabilise an adjacent negative charge.

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