

Nitroacetylene Equivalents. Preparation and Cycloadditions of 2-Phenylsulphinyl-1-nitroalkenes¹

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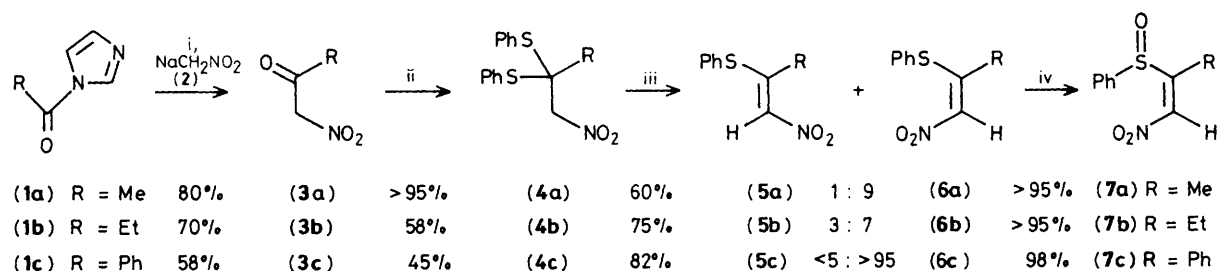
β -Phenylsulphinyl-nitro-alkenes (**7**) are readily prepared from acyl imidazoles and react as nitroacetylene equivalents in Diels–Alder reactions to give good yields of cycloadducts and their further products.

Nitroacetylenes, potentially useful electron-deficient compounds for cycloadditions and Michael additions, are too unstable towards polymerization to be generally useful.^{2,3} The only nitroacetylene that has been isolated² bears the very bulky *t*-butyl group on the acetylene which presumably blocks facile polymerization. Viehe reported² that this compound undergoes fast cycloaddition with cyclopentadiene implying that the activating effect of the nitro group outweighs the steric hindrance of the *t*-butyl group. Since nitroacetylenes with simple alkyl groups on the acetylene β -carbon would be predicted to be so unstable towards polymerization as to preclude isolation, we decided to investigate the use of β -phenylsulphinyl-nitro-alkenes as isolable equivalents of nitroacetylenes. Herein we report their easy preparation and reactions with electron-rich dienes.⁴

Of the several possible synthetic routes to β -phenylsulphinyl-nitro-alkenes, we settled on the following as the

most general and efficient. The acyl imidazole (**1**; R = Me, Et, or Ph) was treated with the preformed sodium salt of nitromethane (**2**) in tetrahydrofuran (THF) to give good yields (60–80%) of the α -nitroketones (**3**).[†] Formation of the dithioacetals (**4**) occurred in excellent crude yields (isolated

[†] These compounds have been prepared before from various activated acyl derivatives by reaction with nitrocarbanions: G. B. Bachman and T. Hokama, *J. Am. Chem. Soc.*, 1959, **81** 4882; D. C. Baker and S. R. Pott, *Synthesis*, 1978, 478; G. F. Field and W. J. Zally, *ibid.*, 1979, 295. **Caution:** After several successful deprotections of the excess of the powdery sodium salt of nitromethane by pouring water on it, one such attempt resulted in a violent explosion and this procedure is therefore not recommended. All new compounds exhibited spectroscopic data (500 MHz ¹H and 125 MHz ¹³C n.m.r.; i.r., high resolution mass, and/or elemental analysis) in full accord with their assigned structures.



Scheme 1. Reagents and conditions: i, THF, heat; ii, PhSH, $\text{BF}_3 \cdot \text{OEt}_2$; iii, $\text{Hg}(\text{O}_2\text{CCF}_3)_2$, Li_2CO_3 (6 equiv.), MeCN, -23 or 25°C ; iv, MCPBA, CH_2Cl_2 , 25°C .

Table 1. Cycloaddition of β -phenylsulphanyl-nitro-alkenes (7) with dienes.

Dienophile	Diene	Product
(7a) (7c)	(8)	(9a) R = Me ^a (9c) R = Ph ^a
(7a) (7b)	(10)	(11a) R = Me, 73% (11b) R = Et, 52%
(7a) (7b)	(12)	(13a) R = Me, 32% (13b) R = Et, 30%
(7a) (7b)	(14)	(15a) R = Me, 32% (15b) R = Et, 32%

^aQuantitative yield.

yields ~60%) by treatment of (3) with benzenethiol and boron trifluoride-diethyl ether. Elimination of one of the phenylthio groups β to the nitro group was attempted with mixed success under a variety of acidic and basic conditions (including adsorption on silica gel for several days). We found that the following two methods were generally useful for the clean preparation of (5) and (6). Oxidation of (4a) with 1 equiv. of *m*-chloroperoxybenzoic acid (MCPBA) in dichloromethane at 0°C produced a 38 : 62 mixture of (5a) and (6a) in 60% yield.

However a more consistently useful preparation involved treatment of the dithioacetal (4) with 1 equiv. of mercury(II) trifluoroacetate and 6 equiv. of lithium carbonate in acetonitrile at 25°C (4a, 4c) or -23°C (4b)† to give in excellent yields a mixture of isomers in which the *Z*-isomer (6) predominated over the *E*-isomer (5). The isomers could be separated by fractional crystallization or careful column chromatography. Finally the *Z*-isomer (6) was oxidized to the desired phenylsulphanyl-alkene (7) by simple oxidation with MCPBA in dichloromethane at room temperature in essentially quantitative yield. The stereochemistry of the isomers was determined by a difference nuclear Overhauser enhancement (n.O.e.) experiment on (7b). Irradiation of the olefinic proton (with gated decoupling) caused an n.O.e. increase of 10% in the methyl group, thereby indicating their *cis*-arrangement. This is in agreement with similar n.O.e. determinations for analogous compounds.⁵ Thus the β -phenylsulphanyl-nitro-alkenes (7a–c) are available from (1a–c) via a four-step synthesis in good overall yield.

The β -phenylsulphanyl-nitro-alkenes (7) are quite reactive in cycloaddition reactions. Typical cycloadditions with a variety of dienes are listed in Table 1. Thus both (7a) and (7c) react with cyclopentadiene (8) at room temperature in benzene to give quantitative disappearance of starting material and clean conversion into the expected *endo*-nitro adducts (9a,c). The stereochemistry of these adducts was determined by the coupling constant of the proton α to nitro with the adjacent bridgehead proton (J 3.5–3.9 Hz) and the lack of any *W* coupling to the bridge protons. A remarkable substituent effect has been observed in this system. Whereas the methyl derivative (7a) reacts completely with (8) (C_6H_6 , 25°C , 10 h) to give (9a), the corresponding ethyl derivative (7b) does not react at all with (8) under the same conditions or even after 2 days at 25°C .§

One of the best uses of a nitroacetylene equivalent would be as the dienophilic component in a cycloaddition approach to substituted nitro-aromatic compounds which could themselves serve as precursors to substituted indoles. We have now demonstrated that the sulphanyl-nitro-alkenes (7) can be used in just such an approach. For example, reaction of Danishefsky's diene (10) with (7a,b) (C_6H_6 , 25°C , 1 day; 65°C , 1 day; dil. HCl–THF) afforded the 3-alkyl-4-nitrophenols (11a,b) in unoptimized yields of 73 and 52%, respectively. In

† When this elimination of (4b) was carried out at 25°C rather than -23°C , the major product was the β,γ -unsaturated nitro compound, $\text{NO}_2\text{CH}_2\text{C}(\text{SPh})=\text{CHMe}$, as a mixture of *E*- and *Z*-isomers, with (5b) and (6b) being minor products.

§ The reasons for this remarkable substituent effect will be discussed in detail elsewhere.

this case there is no major substituent effect on the reactivity as is the case with (7a,b) and (8). Other 1-alkoxy- or 1-acyloxy-butadienes have also been tested in this process. Reaction of 1-acetoxy-3-methylbutadiene (12)⁶ with (7a,b) (C₆H₆, heat, 1 day; aq. base) furnished directly the nitro-*m*-xylene (13a) and the ethyl analogue (13b) in unoptimized yields of 32 and 30%, respectively. Finally, the methyl trimethylsilyl ketene acetal (14)⁷ reacted with (7a,b) to give 3-alkyl-5-methyl-2-nitrophenol (15a,b) (alkyl = Me or Et) in fair yield. We are now investigating the use of analogues of (7) with more functionalized alkyl groups in a cycloaddition route to substituted indoles.

Thus we have developed a new general method for the preparation of β -phenylsulphinyl-nitro-alkenes and demonstrated their use in cycloadditions, especially for the synthesis of nitro-aromatic compounds.

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