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A PRACTICAL ACCESS TO ALLYLIC SULPHONES AND LACTONES FROM ALLYLIC NITRO COMPOUNDS

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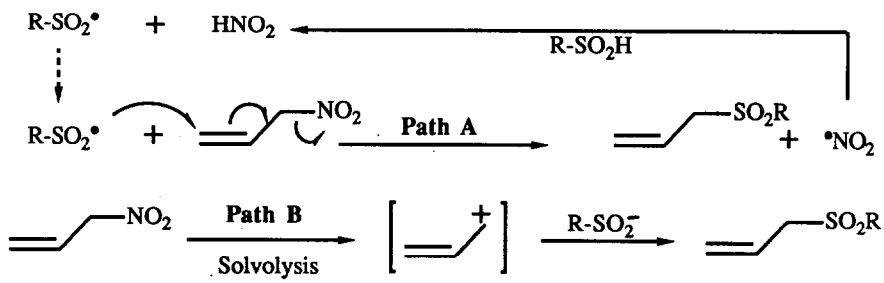
Summary. Allylic nitro derivatives can be readily solvolysed in aqueous acetic acid to give allylic sulphones in the presence of a sulphinate salt or allylic lactones if the substrate contains a suitably located ester group.

A few years ago we reported that ethylenediamine and some of its congeners were efficient catalysts for the Knoevenagel type condensation of ketones with nitroalkanes, and especially nitromethane[1]. The resulting nitro alkylidene derivatives are easily converted into the corresponding allylic isomers or further elaborated into a variety of synthetically useful intermediates containing an allylic nitro group.

As part of a project concerned with novel aspects and applications of the chemistry of aliphatic nitro compounds, we required a convenient method for replacing an allylic nitro group with a sulphone unit. Such a transformation had hitherto been described[2] which involved displacement of the nitro moiety with a sulphinate anion under catalysis by palladium complexes. It seemed possible, however, to achieve a similar conversion by adding a sulphonyl radical onto the olefinic linkage followed by expulsion of nitrogen dioxide, as pictured by the reaction sequence in scheme 1 below (path A).

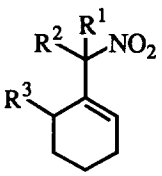


Scheme 1

Allylic sulphones have been shown to undergo a conceptually analogous radical reaction whereby one sulphone group is replaced by another[3,4]. Whitham and co-workers[3a-c], who have studied this reaction most extensively, have found that this transformation could be accomplished either by using the appropriate sulphinic acid and a small amount of dibenzoyl peroxide as initiator or by simply heating the allylic sulphone along with the sulphinate salt in aqueous acetic acid. Under the latter conditions, an

isomerisation of the initial sulphone was sometimes observed which they explained in terms of a "fairly intimate" ion pair in concert with a dissociation recombination mechanism, in addition to the radical process.

When 1-nitromethyl cyclohexene **1a** was heated in aqueous acetic acid containing sodium phenylsulphinate under similar conditions to those reported by Whitham et al.[3b] the corresponding sulphone **2a** was indeed produced, albeit in 31% yield (40% by NMR). In the same way, **1b** gave **2b** in a much better yield (84%). Interestingly, neither **3a** nor **3b** could be observed in the NMR spectra of the crude reaction mixtures following removal of the solvent . This regioselectivity is probably due to the fact that the process is under thermodynamic control; it is thus more a reflection of the relative stability of the isomeric sulphones than a selectivity in the actual substitution step.



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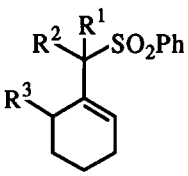

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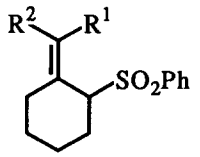

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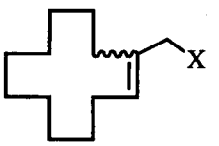
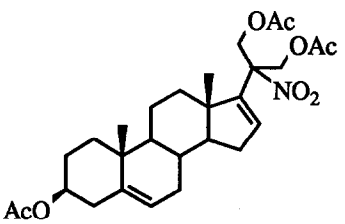


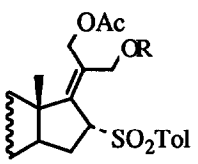
1f, X= -NO_2
2f, X= -SO_2Ph

1, 2, 3

a, $R^1 = R^2 = R^3 = H$
b, $R^1 = R^3 = H$; R^2= Me
c, $R^1 = R^2 = H$; R^3= Me
d, $R^1 = R^2$ = -CH_2CH_2CN ; $R^3 = H$
e, $R^1 = R^2$ = -$CH_2CH_2SO_2Ph$; $R^3 = H$



1 g



3g, R = Ac
4 , R = H

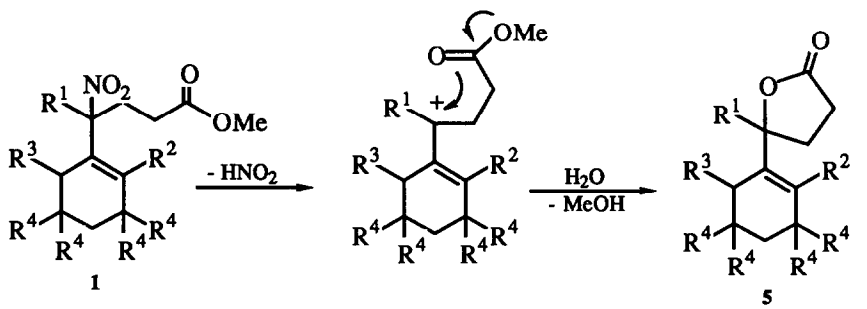
Table: Solvolysis of allylic nitro derivatives in refluxing aqueous acetic acid.

Entry	Nitro compound	Sulphinate salt (3 eq.)	Reaction time (hrs)	Product	yield (%)
1	**1a**	$PhSO_2Na$	1	**2a**	31
2	**1b**	$PhSO_2Na$	1	**2b**	84
3	**1c**	$PhSO_2Na$	1.5	**2c**	59
4	**1d**	$PhSO_2Na$	1	**3d**	59
5	**1e**	$PhSO_2Na$	1.5	**3e**	61
6	**1f**	$PhSO_2Na$	2	**2f**	63
7	**1g**	p-$TolSO_2Na$	2.5	**3g**	78[a)]
8	**1h**	none	1.25	**5h**	75
9	**1i**	none	1.5	**5i**	62
10	**1j**	none	1	**5j**	71
11	**1k**	none	19	**5k**	64

a) Combined yield after acetylation of **4** back to **3g**.

This transformation was successfully extended to a number of other compounds bearing an allylic nitro group. As shown by the results collected in the Table, yields are moderate to good, and essentially one regioisomer was formed in most of the cases studied (of type **2** or **3** depending on the starting nitro derivative).

Although the above results could be rationalised in terms of a radical chain process, evidence soon emerged pointing more and more persistently towards a solvolytic mechanism (Scheme 1, path B). For example, in a blank experiment, simply heating **1b** or **1d** in aqueous acetic acid caused its decomposition; however, a complex mixture was obtained apparently due to uncontrolled reactions involving the co-produced nitrous acid. Moreover, the partial, yet selective, hydrolysis of one of the side chain acetates in the steroid example **1g** to give **3g** and **4** (ratio 3:2) was surprising under the relatively mild experimental conditions but could be accounted for by invoking an allylic cation and a neighbouring group participation which triggers the hydrolysis of one of the side chain acetates (cf scheme 2 for analogy). Finally, when nitro ester **1h** was exposed to the reaction conditions, no sulphone was produced. Instead lactone **5h** was isolated in good yield. The same lactone was produced in the absence of the sulphinate salt as would be expected from a solvolytic mechanism where the incipient allylic cation is captured by the carbonyl oxygen of the ester group (scheme 2). Hydrolysis of the intermediate with loss of methanol finally gives the lactone. This constitutes an interesting and apparently general approach to the synthesis of allylic lactones as illustrated by examples **5h-k** (table 1, entries 8-11). The precursors are very easily accessible through a Michael addition of allylic nitronates onto methyl acrylate.



1 5

5

1, 5
h, R^1 = -$CH_2CH_2CO_2Me$; R^2= R^3= H ; R^4= Me
i, R^1 = -$CH_2CH_2CO_2Me$; R^2= Me ; R^3= H ; R^4= H
j, R^1 = -$CH_2CH_2CO_2Me$; R^2= H ; R^3= Me ; R^4= H
k, R^1 = H ; R^2= H ; R^3= Me ; R^4= H

Scheme 2

Heterolytic cleavage of the carbon nitrogen bond in nitroalkanes has been postulated in a few instances for reactions employing a powerful mineral or Lewis acid[5]. By comparison with the allylic sulphone case reported by Whitham's group[3a-b], the ease of replacement of the nitro group with the sulphinate indicates perhaps a 'looser' ion pair arising through solvolysis; however, the fact that the nitrite anion is unstable in the acetic acid medium (in contrast to the sulphinate) is a factor that must be taken into account. Indeed, the irreversible decomposition of the nitrite anion can, at least in principle, force the

dissociation process towards formation of the allylic cation which is then quenched either directly by the sulphinate or by acetic acid (or water) to give first an allylic acetate (or alcohol) which can in turn solvolyse back to the cation[6]. A possible contribution of the radical chain displayed in scheme 1 (path A) towards the formation of the allylic sulphone cannot however be ruled out at this stage.

The possibility of solvolysing an allylic nitro group under such mild conditions is of considerable synthetic interest. In addition to the formation of sulphones and lactones, other nucleophiles could in principle be used leading to a variety of synthetically useful transformations. Preliminary explorations in this direction are very encouraging.

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