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## Swern Oxidation of Diaziridines to Diazirines

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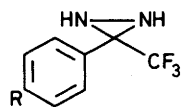
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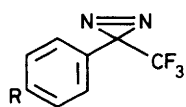
The trifluoromethyldiaziridines (**1**)—(**6**) have been converted into the photolabile diazirines (**7**)—(**12**) using dimethyl sulphoxide–oxalyl chloride; several of these diazirines have previously been used as intermediates in the preparation of photoaffinity labels.

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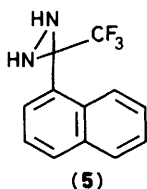
The introduction of a photolabile group into a biologically active molecule forms the basis for the technique of photoaffinity labelling, which has been widely used to study biological systems.<sup>1</sup> Among the photoactive groups available, recent attention has been focussed on the aryltrifluoromethyldiazirines, for example (7),<sup>2</sup> which has been used in the preparation of a



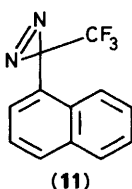
- (1) R = Me  
 (2) R = Bu<sup>t</sup>Me<sub>2</sub>SiOCH<sub>2</sub>  
 (3) R = Bu<sup>t</sup>OCH<sub>2</sub>  
 (4) R = Ph



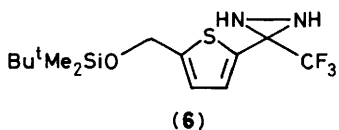
- (7) R = Me  
 (8) R = Bu<sup>t</sup>Me<sub>2</sub>SiOCH<sub>2</sub>  
 (9) R = Bu<sup>t</sup>OCH<sub>2</sub>  
 (10) R = Ph



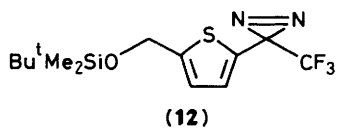
(5)



(11)



(6)



(12)

photoactivatable analogue of phenylalanine.<sup>3</sup> Increased interest in these species can be largely attributed to their ability to photolyse to a highly reactive carbene having the potential for greater active site selectivity than the more widely used aryl nitrenes,<sup>4</sup> and a reduced propensity for rearrangement to less reactive intermediates.<sup>2-4</sup>

The usual synthetic route to diazirines involves oxidation of the corresponding diaziridines. In connection with an ongoing project on photoaffinity labelling we recently found that application of the generally recommended procedures for this transformation were unsuccessful for our compounds. Neither silver oxide<sup>2</sup> nor positive halogens<sup>5</sup> gave the desired product and other published procedures involving the use of heavy metals<sup>6</sup> were deemed incompatible with our substrates. These observations, together with the potential disadvantages associated with the published procedures including chemoselectivity and, in the case of silver oxide, cost and the need for freshly prepared reagent, led us to investigate alternative conditions for this oxidation.

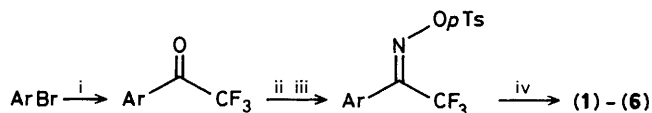
The use of activated dimethyl sulphoxide (DMSO) for the oxidation of amines and their derivatives appears to have received little attention, although a recent report on the oxidation of indolines to indoles has appeared.<sup>7</sup> We report here our results on the use of the Swern oxidation for the preparation of diazirines.

A series of model diaziridines, (1)–(6), were used in order to test the applicability of the method. These were prepared from the corresponding aryl bromides according to the procedure

Table. Oxidation of diaziridines

Diaziridine	Diazirine *	Yield (%)
(2)	(8)	75
(3)	(9)	75
(4)	(10)	86
(5)	(11)	71
(6)	(12)	51

\* Details of the i.r., mass, and <sup>1</sup>H and <sup>13</sup>C n.m.r. spectra and analyses are available as a supplementary publication [Sup. No. 56754 (2 pp.)]. For details of the supplementary publications scheme, see Instructions for Authors (1989), *J. Chem. Soc., Perkin Trans. I*, 1989, Issue 1.



Scheme. Reagents and conditions: i, BuLi, Et<sub>2</sub>O, -78 °C then CF<sub>3</sub>CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>; ii, H<sub>2</sub>NOH-HCl, pyridine; iii, *p*-TsCl, Et<sub>3</sub>N, 4-dimethylaminopyridine, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C to room temperature; iv, liquid NH<sub>3</sub>, THF.

shown in the Scheme. In a preliminary experiment, the oxidation of (1) to (7) was successful using DMSO-oxalyl chloride. The volatility of the diazirine (7), however, precluded accurate quantification of the yields obtained. Oxidation of the diaziridines (2)–(6), proved more reliable. A typical procedure involved treatment of a solution of oxalyl chloride (8.3 mmol) in dichloromethane (20 ml) with DMSO (9.1 mmol) at -78 °C. After 5 min the diaziridine (7.6 mmol) was introduced, followed after a further 15 min by triethylamine (38 mmol). The reaction mixture was allowed to warm to room temperature over 1.5 h, quenched into water, and the organic phase separated and dried (Na<sub>2</sub>SO<sub>4</sub>). The residue was chromatographed on silica gel (Merck grade 7734 eluting with 10% ethyl acetate in light petroleum) to give the pure products. Under these conditions the diazirines (8)–(12) were isolated in the yields shown in the Table.

The previously described diazirines (8) and (9)<sup>2</sup> gave i.r., and <sup>1</sup>H and <sup>13</sup>C n.m.r. spectra identical with compounds prepared by the known route.<sup>2</sup> Compounds (10)–(12) exhibited spectral and analytical data in accordance with their structure. An attempt to repeat the reaction with a recently reported variant on the Swern oxidation using P<sub>2</sub>O<sub>5</sub><sup>8</sup> failed to give more than a trace of product.

We expect that some functional groups which are potentially susceptible to silver oxide or halogens, for example sulphides, will be unaffected by the conditions described here and this should allow access to a wider variety of diazirines. In conclusion we believe that the use of DMSO-oxalyl chloride represents a useful, mild, inexpensive procedure for the synthesis of diazirines and one which should find widespread use in photoaffinity labelling.

## References

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