Rationale for the Direction of Regioselectivity in the Photocycloaddition of Arylazirines

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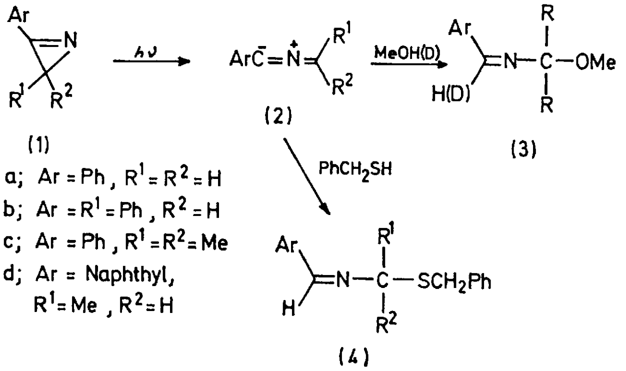
Summary The photoconversion of substituted arylazirines (**1**) into methoxyimines (**3**) proceeds *via* a nitrile ylide intermediate (**2**); deuterium labelling results indicate that the electron density is highest on the disubstituted carbon atom of the nitrile ylide.

WE recently reported on the structural details of the photocycloaddition of arylazirines with electron deficient olefins and related dipolarophiles.[1] The formation of the adducts was interpreted as proceeding by way of irreversible ring opening of the azirine ring to form a nitrile ylide intermediate which is subsequently trapped by a suitable π-system. The origin of the orientation or regioselectivity in this and related 1,3-dipolar cycloadditions has been one of the major unsolved problems in this area of chemistry.[2,3] Houk has successfully used the frontier orbital method for rationalizing the effect of substituents on rates and regioselectivity of 1,3-dipolar cycloadditions.[4] We provide here additional information on the photochemistry of arylazirines, which further supports the perturbation model[4] for the rationalization of regioselectivity in nitrile ylide cycloadditions.[5]

According to the perturbation model,[4] the relative reactivity of a given 1,3-dipole toward a series of dipolarophiles will be determined primarily by the extent of stabilization afforded the transition state by interaction of the frontier orbitals of the two reactants. When nitrile ylides are used as 1,3-dipoles, the dipole highest occupied (HO) and dipolarophile lowest unoccupied (LU) interaction will be of greatest importance in stabilizing the transition state. The favoured cycloadduct will be that formed by union of the atoms with the largest coefficient in the dipole

HO and the dipolarophile LU. An electron deficient olefin has the largest coefficient on the unsubstituted carbon in the LU orbital. In order to predict regioselectivity in the photoaddition process, it becomes necessary to determine the relative magnitudes of the coefficients in the highest occupied orbital of the nitrile ylide. We have solved this problem by carrying out the irradiation of a number of arylazirines in protic solvents.



When a solution of 2-phenylazirine (**1a**) in methanol was irradiated through a Pyrex filter, the only product formed (98%) was identified as (**3a**). Similar irradiation of (**1b**), (**1c**), and (**1d**) in methanol afforded the analogous photoproducts (**3b**—**d**) in essentially quantitative yield.†

Chemical confirmation of structure (**3c**) was obtained by acid hydrolysis to benzaldehyde and acetone. Structure (**3c**) was further confirmed by lithium aluminium hydride reduction to *N*-isopropylbenzylamine. Irradiation of (**1b**) in $PhCH_2SH$ proceeded similarly and gave the adduct (**4**) in high yield (65%).

The photoconversion of arylazirines (**1**) into the methoxyimines (**3**) and the thioimine (**4**) may be formulated as proceeding *via* a nitrile ylide intermediate (**2**) which undergoes subsequent addition of MeOH (or $PhCH_2SH$). Support for the suggested intermediate is provided by the deuterium incorporation observed in the course of the photolysis. Irradiation of arylazirines (**1**) in MeOD gave the deuteriated methoxyimines (**3a**—**d**). The extent of deuterium incorporation was determined by mass spectrometry, and the position of deuteriation was determined by n.m.r. analysis. The incorporation of a single deuterium atom at the imine carbon is expected for an intermediate corresponding to (**2**) in this reaction.

These results indicate that the coefficient at the disubstituted carbon atom of the nitrile ylide is larger than the coefficient at the trisubstituted carbon atom. With this conclusion, all of the regiochemical data found in the photoaddition of arylazirines[1,5] with dipolarophiles are in accord with the expectations of the frontier orbital method.

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† All compounds gave satisfactory analyses. Complete spectroscopic and degradative details will be given in the full report.

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[4] K. N. Houk, *J. Amer. Chem. Soc.*, 1972, **94**, 8953.

[5] See R. Huisgen, H. Stangl, H. J. Sturm, and H. Wagenhofer, *Chem. Ber.*, 1972, **105**, 1258 and B. Jackson, M. Marky, H. J. Hansen, and H. Schmid, *Helv. Chim. Acta*, 1972, **55**, 919, for further examples of regioselectivity in nitrile ylide cycloadditions.