A Synthetic Approach to Azepin-4-ones exploiting Azide Photolysis in Low-temperature Matrices

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Photolysis of 2,6-dichloro-4-azidophenol and 2,6-dibromo-4-azidophenol in N_2 or Ar matrices at 12–14 K results in ring expansion, yielding in each case either the corresponding hydroxydidehydroazepine or, in more concentrated matrices, the tautomeric azepin-4-one.

Attempts to synthesize derivatives of azepin-4-ones (4-azatropones) **1** have a long history.[1–3] The only efficient route to azepin-4-ones reported so far involves the azepinediones **2**, accessible by the Schmidt reaction of the corresponding quinones. Azepinones of type **3** were prepared from the diones by *O*-alkylation with triethyloxonium fluoroborate.[2,3] 2-Diethylaminoazepin-5-ones (**4**, R = Et, Pr^i) have been isolated in low yields from the photolysis of substituted azidobenzenes in diethylamine,[4] but this is not a viable synthetic route. There appears to be no general method of preparing azepin-4-ones.

Our previous research on the photochemistry of aryl azides isolated in low-temperature matrices[5–8] has suggested a new approach to the synthesis of azepin-4-ones. Provided the positions *ortho* to the azide group are unsubstituted, the photolysis of azidobenzenes in inert, *e.g.* Ar or N_2, matrices results in a ring-expansion reaction, yielding didehydroazepines (*cf.* **9** in Scheme 1). There is good evidence that the reaction proceeds *via* singlet nitrenes **6** and benzazirines **7**, and that any unproductive triplet nitrenes formed in the initial photolysis of the azides can absorb further photons and thus still be transformed into didehydroazepines.[5,9,10] We concluded, therefore, that the matrix photolysis of 4-azidophenols **5** should provide a convenient route to azepin-4-ones, at least in very small quantities, and that the target molecules **8** would be obtained either in the matrices directly, or by intermolecular proton exchange between molecules of **9** upon warming. We now report a study of the photolysis of two halogenated 4-azidophenols (**5**, X = Cl and X = Br) in low-temperature matrices.

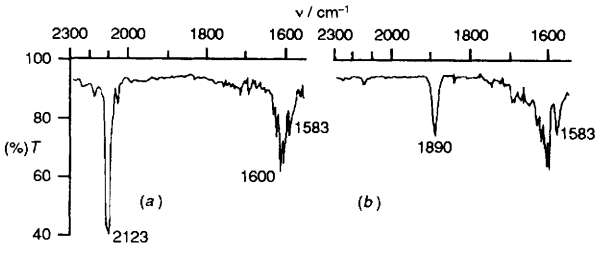


Fig. 1 IR spectra in the range 2300–1550 cm^{-1} of a relatively dilute matrix of (**5**, X = Cl) in N_2 at 14 K: (*a*) before photolysis, (*b*) after 1 h photolysis with λ = 280 ± 10 nm

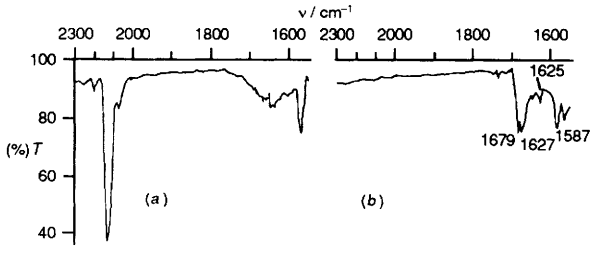


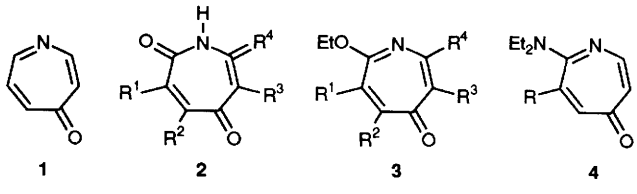
Fig. 2 IR spectra in the range 2300–1550 cm^{-1} of a relatively concentrated matrix of (**5**, X = Cl) in N_2 at 14 K: (*a*) before photolysis, (*b*) after 1 h photolysis with λ = 280 ± 10 nm and a further 1 h with λ > 200 nm

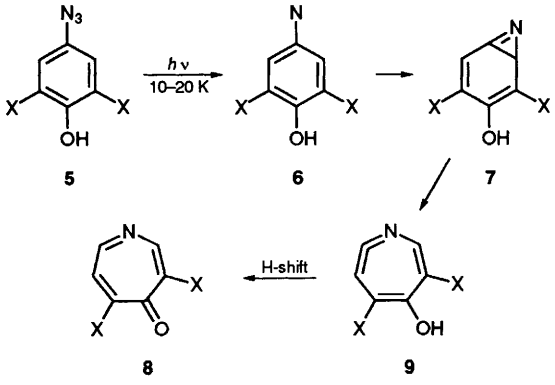
4-Azido-2,6-dichlorophenol (**5**, X = Cl) was prepared from the commercially available 4-amino-2,6-dichlorophenol (Aldrich) by diazotization in aqueous acetic acid containing HCl, followed by treatment with aqueous NaN_3. The azide was obtained in 80% yield as whitish needles, mp 71–72 °C (decomp.), and was purified by recrystallization from redistilled petroleum ether (bp 30–40 °C) followed by vacuum sublimation at approximately 0.1 mbar.† 4-Azido-2,6-dibromophenol (**5**, X = Br), obtained as light-brown crystals with mp 76–78 °C (decomp.), was similarly prepared in 40% yield from 4-amino-2,6-dibromophenol (Aldrich).

Ar and N_2 matrices containing these halogenated azidophenols were deposited on a CsBr window at 12–14 K, using equipment similar to that previously described in detail.[11] Both azidophenols had low volatility and were therefore sublimed from a side-arm attached to the vacuum chamber enclosing the cold window, while an excess of the host gas was deposited simultaneously. In these conditions it was impossible to determine matrix ratios (host:guest), but control of the rate of host–gas deposition allowed the matrix ratios to be varied so as to give relatively more or less concentrated matrices.

Fig. 1 shows IR spectra recorded when (**5**, X = Cl) was deposited at low concentration in N_2 and photolysed with light of λ = 280 ± 10 nm.‡ After photolysis, the strong ν_{N_3} bands of the azidophenol at 2120–2130 cm^{-1} had virtually disappeared, while a prominent new band arose at 1890 cm^{-1}. The latter is characteristic of didehydroazepines,[7,12] and is therefore assigned as the $\nu_{C=C=N}$ band of the expected intermediate (**9**, X = Cl). Absorptions near 1600 cm^{-1} due to $\nu_{C=C}$ modes and traces of matrix isolated H_2O showed only slight changes in this process, and it is noteworthy that no new band arose in the $\nu_{C=O}$ region (1650–1750 cm^{-1}). Attempts to induce intramolecular proton transfer in (**9**, X = Cl), by (*i*) warming the matrix to about 30 K and (*ii*) further photolysis with light of various wavelengths, were all unsuccessful.

Fig. 2 shows IR spectra recorded in a similar experiment, in which (**5**, X = Cl) was trapped in a more concentrated N_2 matrix. Because of molecular aggregation, the IR absorptions of the azidophenol were less well resolved than those of Fig. 1 and also shifted slightly to lower frequency. The product spectrum, in marked contrast to that of Fig. 1, shows no absorption due to the didehydroazepine (**9**, X = Cl), but instead new bands in the carbonyl region at 1679 and 1672 cm^{-1}, a weaker band at 1625 cm^{-1} $\nu_{C=N}$, and some changes in the $\nu_{C=C}$ region below 1600 cm^{-1}. The bands at 1679 and 1672 cm^{-1} suggest the presence of a highly conjugated carbonyl group. Previously prepared azepin-4-ones[2] and several benzannelated analogues[3] were reported to have $\nu_{C=O}$ bands in the range 1661–1620 cm^{-1}. We thus identify the photoproduct of (**5**, X = Cl) in concentrated N_2 matrices as the azepine-4-





Scheme 1

one (**8**, X = Cl), arising from intermolecular proton transfer between molecules of (**9**, X = Cl). The carbonyl stretching frequency of (**5**, X = Cl) is slightly higher than those reported previously for azepin-4-ones, and this may be due to either a chlorine substituent effect or to the very different conditions under which the various IR spectra were obtained.

Progressive warming of matrices containing (**8**, X = Cl) resulted in volatilization of the host gas, and a marked deterioration of the quality of subsequently recorded IR spectra. Nevertheless, the carbonyl bands of the azepinone persisted up to near room temp., indicating that this compound is stable at well above the extremely low temperature at which it was formed. Matrix isolation experiments are carried out with very small amounts of the guest material (usually <1 mg). A number of attempts have been made to recover a sample of the azepinone, for *e.g.* mass-spectral analysis, but so far these have all failed.

Similar experiments with the dibromo analogue (**5**, X = Br) gave exactly similar results. In dilute N_2 matrices, the didehydroazepine (**9**, X = Br) was formed ($\nu_{C=C=N}$ 1887 cm^{-1}); while in more concentrated matrices the azepinone (**8**, X = Br) ($\nu_{C=O}$ 1669 cm^{-1}, $\nu_{C=N}$ 1625 cm^{-1}) was the observed product.

The photolysis of azidophenols thus provides a potentially attractive route to azepin-4-ones. Turning these preliminary matrix isolation experiments into a synthetically useful method, however, presents formidable problems. Investigations on the room-temperature photolysis of the azidophenols has revealed that yields of tractable products are low or non-existent in these conditions.[13] On the other hand, the photolysis of compounds in low-temperature solids can only be carried out efficiently in thin layers, because otherwise light penetration to the interior of the sample is severely reduced. If the azidophenol route to azepinones is to become a viable synthetic option, a technique for carrying out preparative scale photolysis in Ar matrices must be developed.

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Footnotes

† New compounds (**5**, X = Cl and Br) both gave satisfactory elemental analyses and fully consistent spectroscopic data.
‡ IR spectra were recorded on a Perkin-Elmer Model 684 grating instrument interfaced with a Perkin-Elmer 3600 Data Station; quoted frequencies are accurate to within 2 cm^{-1}.

References

1 R. K. Smalley, in *Comprehensive Heterocyclic Chemistry*, ed. A. R. Katritzky and C. W. Rees, vol. 7, ed. W. Lwowski, Pergamon, Oxford, 1984, p. 502.
2 E. J. Moriconi and I. A. Maniscalco, *J. Org. Chem.*, 1972, **37**, 208.
3 R. G. Cooke and I. M. Russell, *Aust. J. Chem.*, 1972, **25**, 2421.
4 R. J. Sundberg, S. R. Suter and M. Brenner, *J. Am. Chem. Soc.*, 1972, **94**, 513.
5 I. R. Dunkin and P. C. P. Thomson, *J. Chem. Soc., Chem. Commun.*, 1980, 499.
6 I. R. Dunkin and P. C. P. Thomson, *J. Chem. Soc., Chem. Commun.*, 1982, 1192.
7 T. Donnelly, I. R. Dunkin, D. S. D. Norwood, A. Prentice, C. J. Shields and P. C. P. Thomson, *J. Chem. Soc., Perkin Trans. 2*, 1985, 307.
8 I. R. Dunkin, T. Donnelly and T. S. Lockhart, *Tetrahedron Lett.*, 1985, **26**, 359.
9 J. C. Hayes and R. S. Sheridan, *J. Am. Chem. Soc.*, 1990, **112**, 5879.
10 E. Leyva, M. S. Platz, G. Persy and J. Wirz, *J. Am. Chem. Soc.*, 1986, **108**, 3783.
11 I. R. Dunkin and J. G. MacDonald, *J. Chem. Soc., Perkin Trans. 2*, 2984, 2079.
12 O. L. Chapman, R. S. Sheridan and J. P. LeRoux, *J. Am. Chem. Soc.*, 1978, **100**, 6245; *Recl. Trav. Chim. Pays-Bas*, 1979, **98**, 334.
13 M. Lynch, PhD Thesis, University of Strathclyde, 1992.