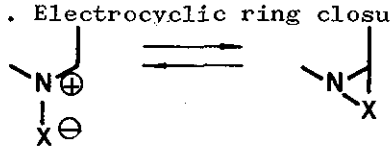
HETEROCYCLES, Vol. 6, Nos. 9, 10, 1977

PHOTOCHEMISTRY AS A TOOL IN HETEROCYCLIC SYNTHESIS: FROM PYRIDINIUM N-YLIDES TO DIAZEPINES AND BEYOND.

Jacques STREITH

Ecole Nationale Supérieure de Chimie de Mulhouse
Université du Haut-Rhin 68093 MULHOUSE France

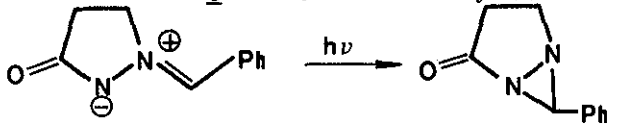
Electrocyclic ring closure of 4π electron 1,3-dipolar species 1, leading to the corresponding three-membered ring isomers 2, is permitted both by thermal and by photochemical processes according to symmetry selection rules (1). These latter ones should be preferred, since three-membered rings are usually unstable when heated, although some exceptions are known (2). In view of their aromatic counterparts three types of 1,3-dipoles 1 were of interest to us: azomethine ylides (X=CR_2); azomethine imines (X=NR) and nitrones (X=O). Electrocyclic ring closure would lead to the



1 2

corresponding three-membered rings 2: aziridines (X=CR_2), diaziridines (X=NR) and oxaziridines (X=O).

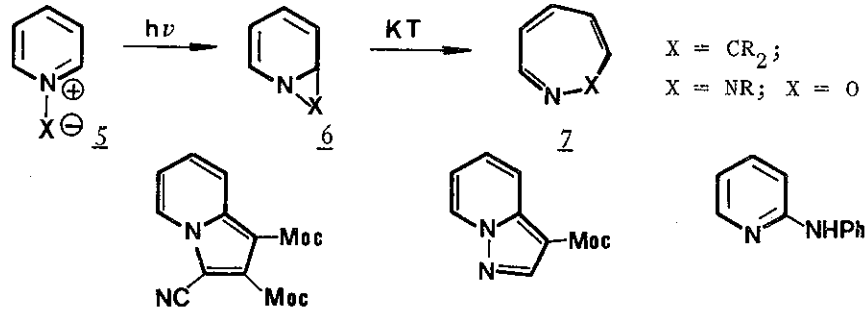
Stable azomethine imines lead photochemically to the corresponding diaziridines as was shown by Schultz (3) and by Moore (4). For example azomethine imine 3 leads to the bicyclic diaziridine 4(3)



3 4

Merely as a working hypothesis we postulated several years ago that pyridinium ylides 5 namely pyridinium methylides (X=CR_2), N-iminopyridinium ylides (X=NR) and pyridine-N-oxides (X=O),

should undergo photoinduced electrocyclic ring closure to the corresponding norcaradienes 6 in the same way the non-aromatic 1,3-dipolar species 1 underwent ring closure to their isomers 2 (5). Rapid thermal and disrotatory valence tautomerism of compounds 6 was expected to lead to the corresponding cycloheptatriene analogues 7. Predicting a similar behaviour for pyridinium ylides 5 and for 1,3-dipoles 1 in their excited state seemed reasonable in view of the fact that both types of compounds lead to 1,3-dipolar cycloaddition reactions (6): in the aromatic series pyridinium dicyanomethylide reacts with methyl acetylene dicarboxylate leading to the aromatic adduct 8 after HCN elimination (7). Likewise the non-substituted and rather unstable 1-iminopyridinium ylide reacts with methyl propynoate and gives adduct 9(7).Pyridine-N-oxide reacts with phenylisocyanate and leads to 2-phenylaminopyridine 20 via an oxadiazolidinone intermediate which expells CO_2 (7).



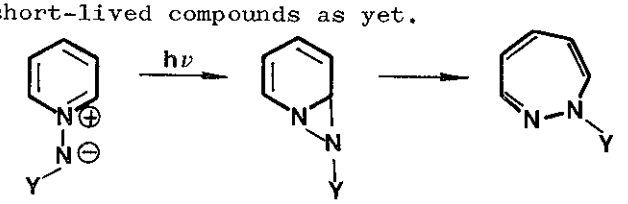
5 6 7

8 9 10

UV excitation of 1-iminopyridinium ylides leads to the expected 1,2-diazepines 7 . Pyridinium methylides and pyridine-N-oxides give pyrrole derivatives, the formation of which is best explained by assuming the intermediate occurence of 2H-azepines 7 ($X=CR_2$) and 1,2-oxazepines 7 (X=O) respectively.

1-Iminopyridinium ylides 2 proved to be the most interesting pyridinium ylides 11 in terms of preparative organic photochemistry. Furthermore the major photoproduct had the predicted seven-membered 1,2-diazepine structure 13 (8). According to our hypothetical mechanistic scheme 1,7-diazanorcaradienes 12 are suppo-

sed to be intermediates on the reaction pathway leading from 11 to 13 (5 and 9), although there is no clearcut proof in favour of such short-lived compounds as yet.

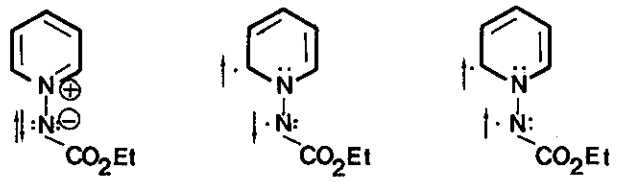


11 12 13

The synthesis of the zwitterionic and colourless pyridinium ylides 11 is based on nitrogen-nitrogen coupling reactions. They involve nitrene derivatives, which are obtained from azido compounds like ethyl azidoformate (10) or O-sulfonylated hydroxylamines, like hydroxylamine-O-sulfonic acid (11), or, even better, mesitylsulfonylhydroxylamine (12).

Various chromophores have been attached to the pyridine nitrogen atom: alkoxycarbonylimino-, benzoylimino- and tosylimino-groups. Ylides 11 all lead in high chemical yield to the corresponding 1,2-diazepines 13 when irradiated by means of high pressure mercury vapour lamps through Pyrex glass.

LCAO-SCF-CI calculations of the Pariser-Parr-Pople type predict π-π^* transitions for the photoactive part of the absorption spectrum: energies, relative intensities and polarization directions agree quite well with the experimental results, assuming an excited singlet state to be responsible for the photoisomerisation process (13). Experiments carried out so far suggest that this is indeed the case. The results obtained from theoretical calculations are that on excitation negative charge is being transferred from the exocyclic ylide nitrogen to the ring. In view of the strong negative solvatochromism, one may assume that intramolecular charge transfer occurs, leading to some sort of a diradical species. In its singlet this diradical could ring close to the diazanorcaradiene 12; intersystem crossing would lead to a triplet and thence to homolytic N-N bond cleavage.



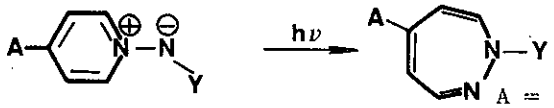
singlet state leading to isomerisation

Triplet state leading to N-N cleavage

The photochemical synthesis of 1,2-diazepines as described above is of preparative interest to organic chemists (14). Large batches of diazepines are prepared by using a 2000 watt dynamic thin film photoreactor.

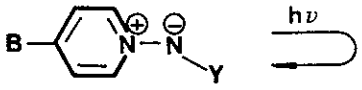
Ring monosubstituted pyridinium ylides are of interest to test substituent effects upon their photochemical reactivity. From data collected on Table 1 we deduce that the mesomeric effect of substituents attached to C-4 of the pyridinium ylide ring is pronounced indeed: electron-donating groups like dimethylamin, chlorine and phenyl permit photoinduced ring expansion, whereas electron-attracting groups like ketones, esters or nitriles inhibit this process (14).

Table 1 Photochemical behaviour of 4-substituted 1-iminopyridinium ylides.



Y = COPh or CO_2Et

A = CH_3	75%
A = C_6H_5	90%
A = Cl	80%
A = N Me_2	65%

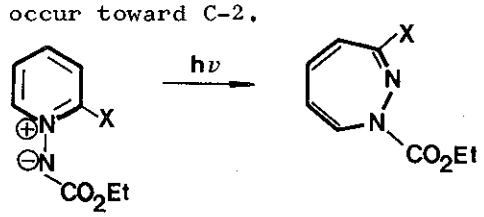


Y = COPh or CO_2Et

B = CO_2Et
B = CN
B = COAr

Substituents attached to C-2 or to C-3 of the pyridinium ring could lead to two isomeric diazepines depending upon the cyclisa-

tion direction of the exocyclic notrogen atom: toward C-2 or toward C-6. 2-Chloro- or 2-methoxypyridinium ylides could not be synthesized. 2-Cyanopyridinium ylide 14 (X=CN) undergoes in high yield a regiospecific ring enlargement leading exclusively to 3-cyano-1-ethoxycarbonyl-1,2-diazepine 15 (X=CN) (14). Rather unexpectedly the 2-methylpyridinium ylide 14 ($X=CH_3$) leads to the same type of result: again one observes a regiospecific ring enlargement to 1,2-diazepine 15 ($X=CH_3$). Methyl groups having no pronounced electronic effect upon π electrons, it is assumed that the regiospecific ring enlargement is mainly due to a steric effect which would prevent ring closure of the exocyclic nitrogen atom to occur toward C-2.



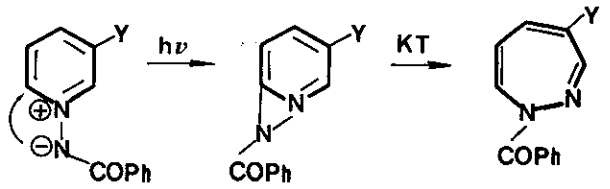
X = Me 80%

X = CN 86%

14 15

As can be seen from Table 2 electron-attracting groups like esters, amides and nitriles lead regiospecifically and in high yield to only one type of photoisomer, namely 4-substituted 1,4-diazepines.

Table 2 Regiospecific photochemical ring expansion of 3-substituted pyridinium ylides (Y = π electron-attracting groups)



$Y = CO_2Et$ 80%

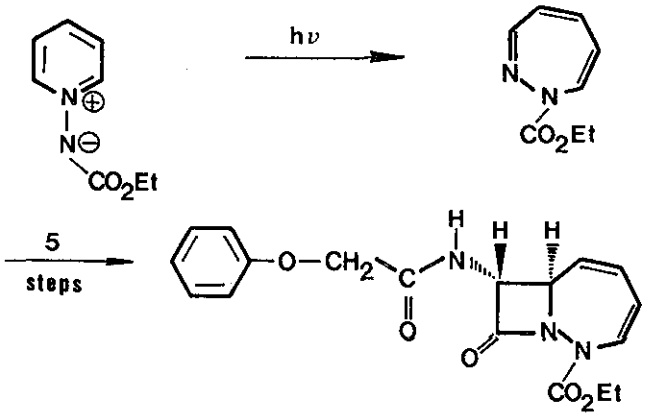
$Y = CONH_2$ 86%

Y = CN 84%

To the contrary, electron-donating C-3 substituents, which do not bear any acidic hydrogen atoms, lead in a non-regiospecific way in high yield to a mixture of the corresponding 4- and 6-

substituted 1,2-diazepines.

1,2-Diazepines being easily available by the aforementioned photoinduced ring expansion process, proved to be interesting synthons for the preparation of various polycyclic systems: acid catalysed dimerisation leads to tricyclic compounds (15); 1,3-dipoles add either to the Δ^4 or to the Δ^2 double bond leading for example to pyrazolino-diazepines and thence to homodiazepines (16) or to oxadiazolines (17); potential antibiotics have been synthesized in excellent yields starting from 1,2-diazepines, acyl chlorides and triethylamine (17, 18), to quote but a few examples.



REFERENCES

(1) R.B.Woodward and R.Hoffmann, Die Erhaltung der Orbitalsymmetrie, Verlag Chemie, Weinheim/Bergstrasse, 1970

(2) R.Huisgen, W.Scheer and H.Huber, J.Amer.Chem.Soc., 89, 1753 (1967)

(3) M.Schultz and G.West, Angew.Chem., 82, 265 (1970)

(4) M.G.Pleiss and J.A.Moore, J.Amer.Chem.Soc., 90, 4738 (1968)

(5) J.Streith, A.Blind, J.M.Cassal and C.Sigwalt, Bull.Soc.chim. France, 948 (1969)

(6) R.Huisgen, Bull.Soc.chim.France, 3431 (1965)

(7) R.Huisgen, Proc.Chem.Soc. (London), 357 (1961)

(8) J.Streith and J.M.Cassal, Angew.Chem.Inter.Ed.Engl., 7, 129 (1968)

(9) J.Streith and J.M.Cassal, Tetrahedron Letters, 4541 (1968)

(10) K.Hafner, D.Zinser and K.L.Moritz, Tetrahedron Letters, 1733 (1964)

(11) R.Gösl and A.Meuwsen, Ber., 92, 2521 (1959); T.Okamoto, M.Hirobe, C.Mizushima and A.Osawa, Yakugaku Zasshi, 83,309 (1963)

(12) Y.Tamura, J.Minamikawa, Y.Miki, S.Matsugashita and M.Ikeda, Tetrahedron Letters, 4133 (1972)

(13) R.Gleiter, D.Schmidt and J.Streith, Helv.chim.Acta, 54, 1645 (1971)

(14) J.Streith and J.M.Cassal, Bull.Soc.chim.France, 2175 (1969); A.Balasubramanian, J.M.Mc Intosh and V.Snieckus, J.Org.Chem., 35, 433 (1970); T.Sasaki, K.Kanematsu, A.Kaheki, I.Ichikawa and K.Hayakawa, J.Org.Chem., 35, 426 (1970); J.Streith, J.P.Luttringer and M.Nastasi, ibid., 36, 2962 (1971)

(15) B.Willig and J.Streith, Tetrahedron Letters, 4167 (1973)

(16) G.Taurand and J.Streith, Tetrahedron Letters, 3575 (1972)

(17) J.Streith and G.Wolff, Heterocycles, 5, 471 (1976)

(18) J.P.Luttringer and J.Streith, Tetrahedron Letters, 4163 (1973).