PHOTOCHEMICALLY INDUCED 1,3-DIPOLAR CYCLOADDITIONS OF 3-AMINO-2H-AZIRINES

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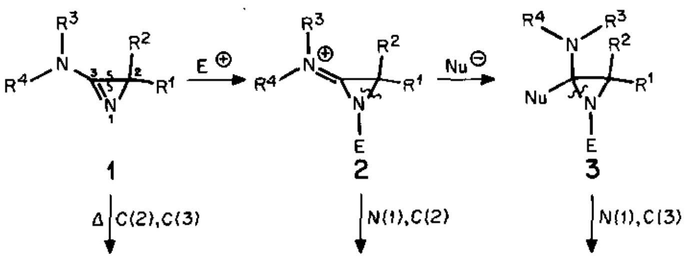
Abstract - Irradiation of 3-(N-methylanilino)-2H-azirines in dimethoxyethane solution in the presence of dipolarophiles leads to five-membered heterocycles in 40-60% yield. A reaction mechanism via splitting of the C(2),C(3)-bond and formation of a nitrilio methanide which then undergoes a thermal 1,3-dipolar cycloaddition is reasonable.

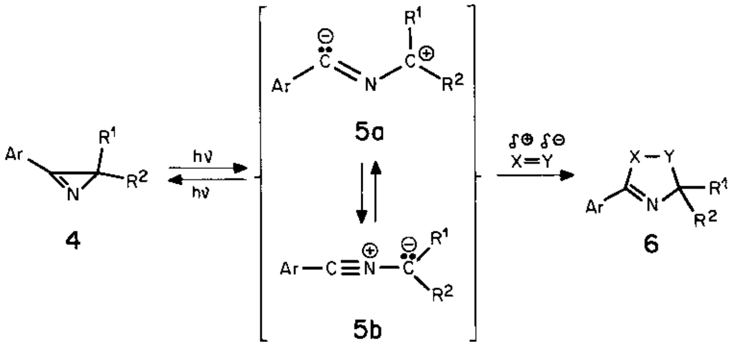
Three-membered cyclic amidines with an endocyclic double bond, the 3-dialkylamino-2H-azirines of type 1, are known since 1970 [1]. It has been shown, that they are useful molecules in the synthesis of heterocyclic compounds (cf. [2] and literature cited therein). Many examples for reactions proceeding by cleavage of the N(1),C(2)-single bond or of the N(1),C(3)-double bond are known (Scheme 1, cf. [3]). But only one example for the splitting of the C(2),C(3)-bond has been reported, namely the gas-phase thermolysis of 2-alkyl derivatives of 1 ($R^1 = CH_3$, CH_2CH_3), leading to 2-aza-1,3-butadienes [3,4].

Scheme 1



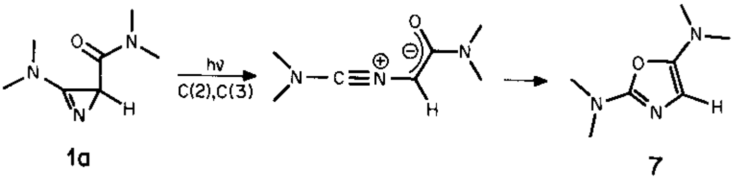
On the other hand it is well known, that irradiation of 3-aryl-2H-azirines leads to a reactive intermediate, which can be trapped with a variety of dipolarophiles to give five-membered heterocycles 6 [5,6]. The mechanism given in Scheme 2 is accepted for the formation of these products. Photolytical cleavage of the azirine C,C-bond leads to the nitrilio methanide 5, which then undergoes a thermal 1,3-dipolar cycloaddition to the dipolarophile. The regioselectivity of the addition reaction can be rationalized most easily by the dipolar structure 5a of the intermediate [6].

Scheme 2



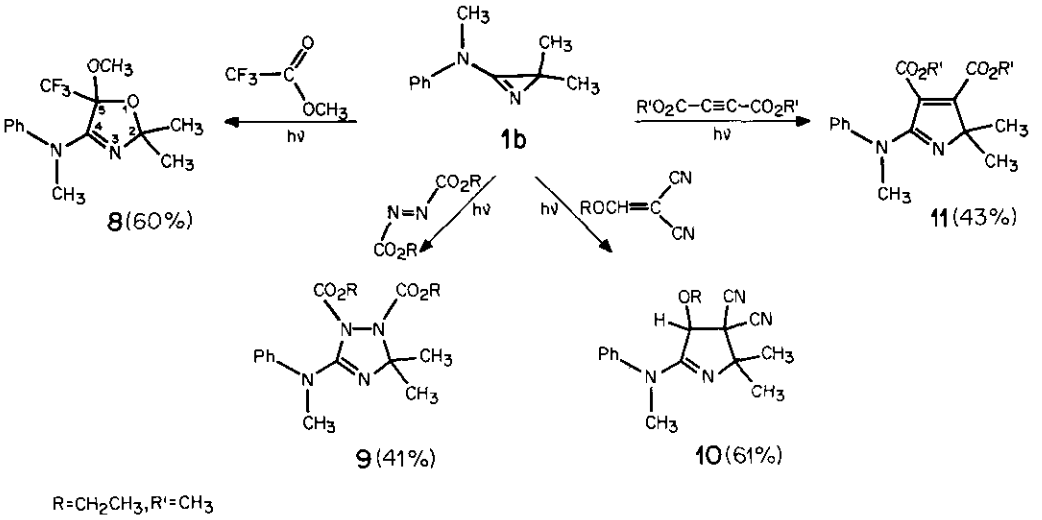
In view of the usefulness of the photoreaction of 3-aryl-2H-azirines, we tried to extend this synthetically potent reaction to aminoazirines of type 1. Irradiation of 1a [7] in acetonitrile with a mercury low pressure lamp gives the oxazole 7 in about 60% yield (Scheme 3). This reaction corresponds to the second step of the well known photochemical isoxazole-oxazole rearrangement [8]. Thus, the C(2),C(3)-bond of 1a is broken to give a dipolar intermediate, which via 1,5-dipolar electrocyclization (cf. [9,10]) leads to 7. All attempts to trap the intermediate with dipolarophiles like methyl trifluoroacetate [11] failed.

Scheme 3



In order to generalize the photochemical C,C-splitting of aminoazirines of type 1, we tried to photolize the easily available tetraalkyl derivatives, e.g. the tetramethyl aminoazirine 1 (R^1-R^4 = CH_3). But in this case we had so far little success, probably because this azirine does not absorb above 230 nm. In order to get an aminoazirine which absorbs at longer wavelength, we synthesized the N-phenyl derivative 1b (Scheme 4) starting from N-methyl-N-phenyl-isobutyric thioamide (cf. [12]). Treatment of this thioamide with phosgene yields the corresponding α-chloroenamine, which with sodium azide at room temperature reacts to give 1b [13]. On irradiation (mercury low pressure lamp) of the dimethoxyethane solutions of 1b and an excess of the dipolarophiles shown in Scheme 4, the desired heterocyclic compounds 8-11 [14] are formed in 40-60% yield. The structures of the products have been elucidated from spectral data, especially ^{13}C-NMR, in comparison with the data of the corresponding 3-phenyl-2,2-dimethyl-2H-azirine adducts of type 6.

Scheme 4

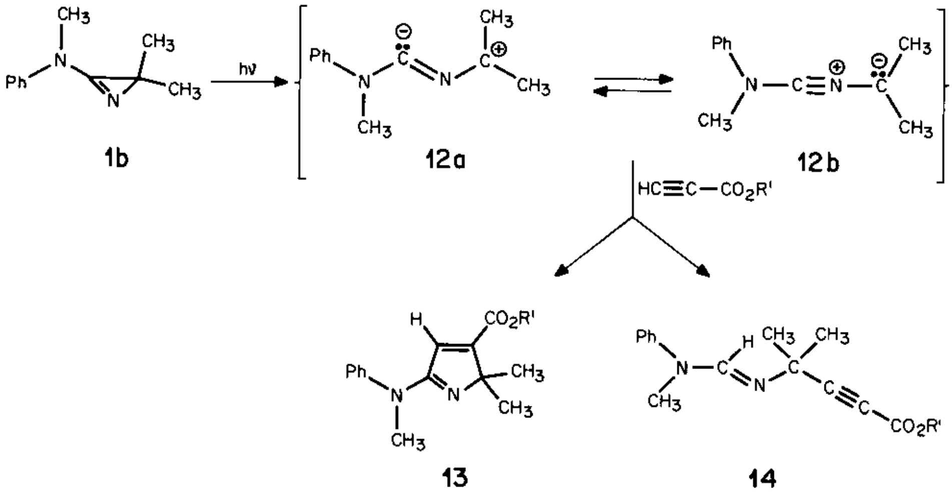


The photolysis of 1b in the presence of methyl trifluoroacetate and 2-ethoxy-1,1-dicyano ethylene, respectively, are of special interest, because in these two cases the formation of two regioisomers is possible. It is worthwile to mention that only 8 and 10 could be detected. The structures of the regioisomeric adducts are excluded considering the chemical shifts of the ring carbon atoms: The 3-oxazoline 8 shows absorptions at 153.5 ppm (C(4)), 105.1 ppm (C(2)) and 105.0 ppm (C(5)) (cf. [15])

and the signals of the 4,4-dicyano-1-pyrroline 10 appear at 159.8 ppm (C(2)), 88.0 ppm (C(3)), 73.0 ppm (C(5)) and 48.5 ppm (C(4)) [16] (cf. [17]).

Irradiation of 1b in the presence of ethyl propiolate gives a mixture of the two (1:1)-adducts 13 and 14 (Scheme 5) in a ratio of 5:2 (GLC) [18]. The structure of the 2H-pyrrole 13 has been elucidated again by comparison with the corresponding 4-phenyl-2H-pyrrole [15]. Again, formation of the possible regioisomeric 4-ethoxycarbonyl-2H-pyrrole could not be detected. The isomeric compound 14 shows a strong IR-absorption at 2240 cm^{-1} for the C,C-triple bond. In the NMR-spectra, the amidine proton absorbs at 8.33 ppm and the amidine C-atom shows a doublet at 151.5 ppm.

Scheme 5



In analogy to the photolysis of 3-aryl-2H-azirines of type 4, where the reactive intermediate 5 has been detected directly by UV-spectroscopy [15,19], we formulate a reaction mechanism with a dipolar intermediate 12 in the case of the 3-amino-2H-azirines too (Scheme 5). This 1,3-dipole, formed by splitting of the azirine C(2),C(3)-bond, undergoes a cycloaddition with electron deficient dipolarophiles to give five-membered heterocycles with an amidine function.

It is remarkable that the regioselectivity of these cycloaddition reactions is the same as in the case of the photolysis of 3-aryl-2H-azirines. Thus, the structure of the 1,3-dipole is best represented by formula 12a [20]. This structure is also responsible for the formation of 14: Protonation at the C(1)-atom of 12a by methyl propiolate, followed by an attack of the acetylide anion at the C(3)-atom of 12a, yields 14.

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REFERENCES

1. M. Rens and L. Ghosez, Tetrahedron Lett., 1970, 3765.
2. H. Heimgartner, Chimia, 1979, 33, 111.
3. L. Ghosez, A. Demoulin, M. Henriet, E. Sonveaux, M. Van Meerssche, G. Germain, and J.-P. Declercq, Heterocycles, 1977, 7, 895.
4. A. Demoulin, H. Gorissen, A.-M. Hesbain-Frisque, and L. Ghosez, J. Amer. Chem. Soc., 1975, 97, 4409.
5. A. Padwa, Accounts Chem. Res., 1976, 9, 371; A. Padwa, Chem. Rev., 1977, 77, 37.
6. P. Gilgen, H. Heimgartner, H. Schmid, and H.-J. Hansen, Heterocycles, 1977, 6, 145.
7. G.J. de Voghel, T.L. Eggerichs, B. Clamot, and H.G. Viehe, Chimia, 1976, 30, 191.
8. E.F. Ullman and B. Singh, J. Amer. Chem. Soc., 1966, 88, 1844; B. Singh and E.F. Ullman, ibid., 1967, 89, 6911; B. Singh, A. Zweig, and J.B. Gallivan, ibid., 1972, 94, 1199; A. Padwa, E. Chen, and A. Ku, ibid., 1975, 97, 6484; K. Dietliker, P. Gilgen, H. Heimgartner, and H. Schmid, Helv. Chim. Acta, 1976, 59, 2074.
9. E.C. Taylor and I.J. Turchi, Chem. Rev., 1979, 79, 181.
10. R. Huisgen, presented on the occasion of the 1st European Symposium on Organic Chemistry, Cologne, August 20-23, 1979.
11. P. Gilgen, H.-J. Hansen, H. Heimgartner, W. Sieber, P. Uebelhart, H. Schmid, P. Schönholzer, and W.E. Oberhänsli, Helv. Chim. Acta, 1975, 58, 1739.
12. L. Ghosez and J. Marchand-Brynaert, "Iminium Salts in Organic Chemistry", ed. by H. Böhme and H.G. Viehe, Vol. 9, Part I in the series "Advances in Organic Chemistry", ed. by E.C. Taylor, Wiley-Interscience, New York 1976, p. 421.

13. All described compounds give correct C,H and N analysis (± 0.3%). The UV-spectrum (hexane) of 1b shows a maximum at 254 nm ($\varepsilon = 17400$) with shoulders at 274, 283 and 291 nm whereas the tetramethyl derivative 1a shows only a shoulder at 225 nm ($\varepsilon = 3000$; $\varepsilon(245\ \text{nm}) < 80$).

14. All compounds have been isolated by preparative TLC (silica gel). The colourless oils 8 and 9 have been purified by distillation ($60\text{-}65^{\circ}\text{C}/10^{-3}$ Torr and $75\text{-}85^{\circ}\text{C}/10^{-2}$ Torr), the colourless solids 10 (mp 103.5-104°C) and 11 (mp 83-83.5°C) by crystallization from ethanol and heptane, respectively.

15. U. Gerber, H. Heimgartner, H. Schmid, and W. Heinzelmann, *Helv. Chim. Acta*, 1977, 60, 687.

16. ^{13}C-NMR-spectra were recorded at 25.2 MHz, ^{1}H-NMR-spectra at 90 MHz; chemical shifts are given in δ values (TMS = 0 ppm).

17. W. Stegmann, P. Gilgen, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, 1976, 59, 1018.

18. Multiple preparative TLC followed by distillation at $95\text{-}110^{\circ}/10^{-2}$ Torr lead to the pure isomers 13 and 14 as colourless oils in 16% and 5% yield, respectively.

19. A. Orahovats, H. Heimgartner, H. Schmid, and W. Heinzelmann, *Helv. Chim. Acta*, 1975, 58, 2662.

20. The problem of the structure of nitrilio methanides (nitrile ylides) has been discussed recently[21].

21. K.N. Houk, *Topics in Current Chemistry*, 1979, 79, 1.

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