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SPECIFIC INTRAMOLECULAR NITROSAMINE PHOTOADDITION[1]

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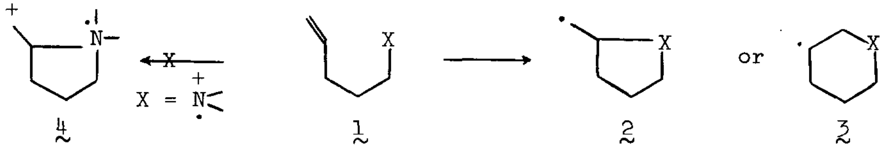
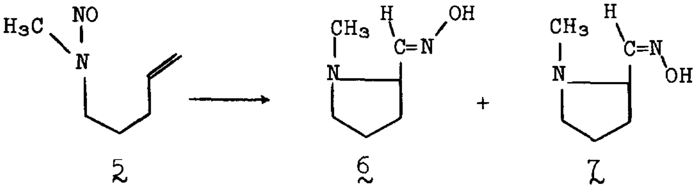
Radical initiated intramolecular addition appears to favor the formation of 5-membered rings over those possessing 6-members even in cases where the radical intermediate of the former (2) is clearly less stable than that of the latter (3).[2-4] An aminium radical generated from photolysis of a nitrosamine,[5]

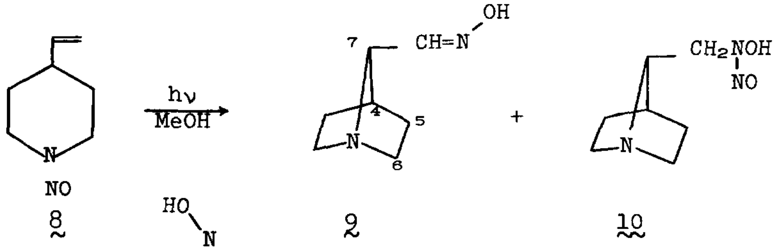


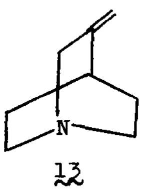
although it is very electrophilic due to its cationic charge, is required to react with an olefinic bond by a purely radical pathway (1 → 2 or 3) since the electrophilic addition (1 → 4) leads to a violation of Octet rule at the nitrogen center. The intramolecular photoaddition of nitrosamines 5 and 8 are now shown to be cleanly specific in forming 5-member azacyclics where from the radical pathway is indicated.[6]

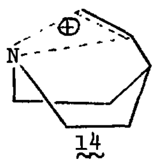
Photolysis[7] of 5 (1.00 g) in methanol (200 ml) containing 0.06 N HCl gave a mixture of syn-oxime 6 and anti-oxime 7 (ratio 4:1) as the basic extract (82%), the nmr spectrum of which exhibited two pairs of doublets [τ 2.75 (J = 7.5 Hz) and 3.25 (J = 6 Hz)] and two singlets [τ 7.67 and 7.40]. The major compound was shown to be the syn-oxime 6 which could be isolated in pure form by recrystallization from light petroleum ether: mp. 63-64°; ir. 2720, 1680, 1085, 1035, 935 and 925 cm^{-1}; nmr. τ 2.75 (d, 1H, J = 7.5), ~ 7.00 (m, 3H) and 7.67 (s, 3H); m/e 128.0944 (calc'd for $C_6H_{12}N_2O$; 128.0950), 111 and 84]. Decomposition of the tosylate of the crude oxime mixture in triethylamine gave N-methylpyrrolidine 2-nitrile[9] [ir. 2250 and nmr. τ 7.35 (s)].



Photolysis of 8 as above gave oxime 9 (24%), hydroxylamine 10 (22%), 4-vinyl-2-piperidone oxime (11, 10%), 4-vinylpiperidinoformamide (12, 5%) and the parent amine. 3-Quinuclidone oxime [13, m.p. 213 - 216°, τ 6.45 (s, 2H)] was not found in the photolysis. Oxime 9 [m.p. 171 - 172°; ir. 3200, 1650 and 960 cm^{-1}; m/e 140 (M^{+}), 123 (100%), 82, 69 and 38.7 (metastable)] exhibits the C-4 proton at τ 7.5 (t; J = 4.5 Hz) and the aldoxime proton at τ 2.18 (d, J = 5 Hz) which is coupled with the C-7 proton at τ 6.70 (d, J = 5 Hz): the C-4 and C-7 protons are weakly coupled as detected by decoupling experiments. Hydroxylamine 10 [mp. 200 - 201°; ir. 3380, 1510, 1240 and 945 cm^{-1}] showed the C-8 methylene protons at τ 5.5 - 6.1 (as the AB part of ABX system) and the C-4 proton at τ 7.05 (q, J = 4). The mass spectra (20 eV) of both 9 and 10 exhibits similar peak pattern below m/e 140 with identical major mass peaks [for example 123, 82, 69 and 54] in the comparable ratios indicating the similarity in the skeletons. The ring closure to the azabicyclo system in







this case is obviously less facile accounting for the formation[11] of secondary reaction products **10** - **12**.

For comparison the ring closure by nitrenium route[12] was also investigated. Treatment of the chloramine analogue of **5** (NO=Cl) with $AgNO_3$ in methanol solution gave, among other products, N-methyl-3-methoxypiperidine **15** as the major product.[13] However, a similar treatment of the chloramine analogue of **8** (NO=Cl) did not yield ring closure products; only the starting amine was recovered. This appears to indicate that a bridged ammonium ion, such as **14**, is an important intermediate in this π-route ring closure; the strain energy of **14** is sufficiently high to prevent the ring closure process.

The present results have demonstrated that intramolecular photoaddition of nitrosamines proceeds specifically to give 5-membered azacyclics. This also suggests that the intramolecular attack of an aminium radical at the δ-trigonal carbon center is favored by a large entropy gain and irreversible process.

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Notes and References

(1) Part XVI in series "Photochemistry of nitrosocompounds in solution". For Part XV see Y.L. Chow, C.J. Colón and D.W.L. Chang, Can. J. Chem., **48**, 1664 (1970).

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(6) See also Y.L. Chow, R.A. Perry and B.C. Menon, the succeeding paper.

(7) Both nitrosamines **5** and **8** exhibit the expected spectral characteristics in agreement with the published result [See Y.L. Chow and C.J. Colón, Can. J. Chem., **46**, 2627 (1968)]; the syntheses will be described in the full paper.

(8) The definition of the *syn*- and *anti*-oximes and the assignment of their configuration by nmr spectroscopy follow the correlation described [Y.L. Chow and C.J. Colón, J. Org. Chem., **33**, 2598 (1968)].

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(10) Compound **11** (mp. 135 - 136°) and compound **12** (mp. 76 - 77°) have been fully characterized and will be described in the full paper.

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(13) Among other products, the starting amine and N-methyl-2-methoxymethylpyrrolidine [τ 6.68 (s) 6.7 (m) and 7.58 (s)] were also isolated; the latter compound however was obtained only in semipure state. The ratio of piperidine **16** [τ 6.68 (s, 3H), 7.68 (s, 3H), 6.56 (t of t, J = 8.5 and ~ 3Hz) and 7.0 - 7.4 (m, 2H)] to the pyrrolidine is ca. 5:1.