peptide, tetrapeptide), 8 min (pentapeptide), and 25 min (hexapeptide).

The phenyl ester method is an integral part of our program in the synthesis of lysozyme analogs, and therefore we expect to report results of its more extensive application in due course. It should be noted that acylation, coupled with deacylation by peroxide anion, provides a *potentially general method for protection of phenolic hydroxyl groups.*

Acknowledgment. We are grateful to Drs. P. M. Hardy and J. R. McDermott for preliminary studies in this area and to Dr. R. C. Sheppard for helpful discussions.

(14) Fellow of the Canadian Medical Research Council.

G. W. Kenner,* John H. Seely[14]
The Robert Robinson Laboratories, University of Liverpool
Liverpool, England
Received October 22, 1971

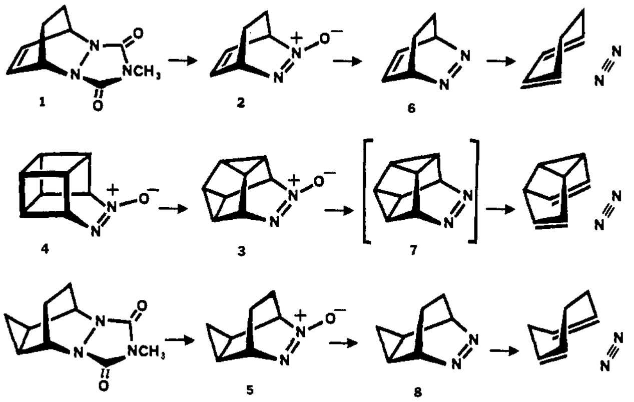
cis-Azoxyalkanes. III. A Dichotomy in the Thermal Stability of Azo- and Azoxyalkanes

Sir:

cis-Azoxyalkanes belong to a compound class of recent vintage. Although a variety of saturated examples exist,[1] only a few highly condensed derivatives[1a,2] and no unsaturated cases are known. We now report the synthesis of two new examples and elaborate on the remarkable stability of azoxyalkanes relative to their deoxy relatives, the azoalkanes.

Diels–Alder addition of *N*-methyl-1,2,4-triazolinedione and cyclohexadiene proceeds smoothly to give adduct **1**.[1a] Careful oxidative hydrolysis (ethylene glycol-water (1:1), excess 30% aqueous H_2O_2, 120°) generates 2,3-diazabicyclo[2.2.2]octadiene *N*-oxide (**2**) in a single experimental step (57% yield; mp 48.5–49.5°; ir ν (KBr) 1230 (s, NNO), 1485 cm^{-1} (s, NNO); nmr ($CDCl_3$) τ 3.46 (2 H, unsym t), 4.65 (2 H, envelope), 7.75–8.65 (4 H, envelope)). Alternatively, heterocycle **3**, 9,10-diazapentacyclo[$3.3.2.0^{2,4}.0^{3,7}.0^{6,8}$]decane *N*-oxide (60% yield; mp 133–134°; ir ν ($CHCl_3$) 1502 (s, NNO), 1265 cm^{-1} (s, NNO); nmr ($CDCl_3$) τ 4.4–5.0 (2 H, envelope), 7.3–8.1 (6 H, envelope)), arises by silver ion promoted rearrangement of diazabasketene *N*-oxide (**4**)[2] ($AgBF_4$, refluxing $CHCl_3$, inert atmosphere, 5 days). This conversion may be viewed as an allowed [${}_{\sigma}2_s + {}_{\sigma}2_s$] sigmatropic reorganization.[3] The structure of compound **3** follows from its spectroscopic properties and facile conversion to semibullvalene as discussed below.

The thermal stability of *N*-oxides **2**, **3**, and **5** stands in stark contrast to that of the corresponding azo series **6**, **7**, and **8**. Compound **6**, generated at −78°, decomposes to cyclohexadiene rapidly upon formation ($t_{1/2}^{-78°} \leq 30$ sec).[4] The strained heterocycle **7** has been implicated as an unobserved intermediate in the formation of semibullvalene (<0°).[3a] Homolog **8** cycloreverts to 1,4-cycloheptadiene and nitrogen at room temperature ($k_1^{-3.5°} = 1.7 \times 10^{-4}$ sec^{-1}).[5] Azoxyalkanes **2**, **3**, and **5**, on the other hand, resist thermal change below 175° either neat or in solution. In fact the cis azo systems mentioned above are conveniently stored as their *N*-oxide derivatives. Treatment of each of the latter with excess hexachlorodisilane[6] in an nmr tube (25°) causes a mildly exothermic reaction which leads to the instantaneous disappearance of the azoxy spectrum. Only the corresponding hydrocarbon absorption (cyclohexadiene, semibullvalene,[7] and 1,4-cycloheptadiene, respectively) remains. Vacuum pyrolysis of compounds **2** (325°) and **5** (400°) over a quartz bed delivers 1,3-cyclohexadiene and 1,4-cycloheptadiene, respectively, as the exclusive products.



These observations suggest that the rate of nitrogen extrusion in a reverse [4 + 2] cycloaddition is at the very least 10^6 times that for N_2O expulsion.[8] The mechanism by which the heterocycles decompose is not altogether resolved. However, cis–trans isomers of 1,2-diaza-3,6-dimethylcyclohexadiene-1,4 and the corresponding azo cycles in which the carbon–carbon double bond is replaced by a cyclopropane moiety cyclorevert with a very high degree of stereospecificity.[9] Furthermore, the reactions proceed rapidly below room temperature analogous to the fates of compounds **6**, **7**, and **8**. Nitrogen loss by way of a single, concerted step is strongly suggested. If the potential surfaces associated with *N*-oxides **2**, **3**, and **5** are similarly constituted, the disparate thermal behavior of unsaturated or pseudounsaturated azo- and azoxyalkanes may be rationalized by considering the form of the molecular orbitals for nitrogen and nitrous oxide.

For purposes of analyzing the heteroextrusion reaction, the frontier orbitals[10] (Figure 1) are of singular importance. SCF-MO-CNDO calculations[11] indicate

---

(1) (a) J. P. Snyder and V. T. Bandurco, *Tetrahedron Lett.*, 4643 (1969); (b) F. D. Greene and S. S. Hecht, *ibid.*, 575 (1969); W. R. Dolbier, Jr., and W. M. Williams, *J. Amer. Chem. Soc.*, **91**, 2818 (1969); W. Luttke and V. Schabacker, *Justus Liebigs Ann. Chem.*, **687**, 236 (1969); J. P. Freeman, *J. Org. Chem.*, **27**, 1309, 2881 (1962).

(2) J. P. Snyder, L. Lee, and D. G. Farnum, *J. Amer. Chem. Soc.*, **93**, 3816 (1971).

(3) (a) R. M. Moriarity, C. Yeh, and N. Ishibi, *ibid.*, **93**, 3085 (1971); L. A. Paquette, *ibid.*, **92**, 5765 (1970); R. Askani, *Tetrahedron Lett.*, 3349 (1970); (b) W. G. Dauben, C. H. Schallhorn, and D. L. Whalen, *J. Amer. Chem. Soc.*, **93**, 1446 (1971).

(4) N. Rieber, J. Alberts, J. A. Lipsky, and D. M. Lemal, *ibid.*, **91**, 5668 (1969).

(5) M. Martin and W. R. Roth, *Chem. Ber.*, **102**, 811 (1969); E. L. Allred and J. C. Hinshaw, *J. Chem. Soc. D*, 1021 (1969).

(6) K. Naumann, G. Zon, and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7012 (1969).

(7) H. E. Zimmerman, R. W. Binkley, R. S. Givens, G. L. Grunewald, and M. A. Sherwin, *ibid.*, **91**, 3316 (1969).

(8) Calculated on the basis of a 1%/week (25°) decomposition of azoxyalkanes **2**, **3**, and **5**. It should be noted that the latter appear to be stable indefinitely at ambient temperature.

(9) J. A. Berson and S. S. Olin, *J. Amer. Chem. Soc.*, **91**, 777 (1969).

(10) (a) K. Fukuii, *Accounts Chem. Res.*, 4, 57 (1971); (b) R. G. Pearson, *ibid.*, 4, 152 (1971).

(11) R. J. Boyd and M. A. Whitehead, *J. Chem. Soc. A*, 3579 (1971); *J. Chem. Soc., Dalton Trans.*, 73, 78, 80 (1972); core repulsion and in-

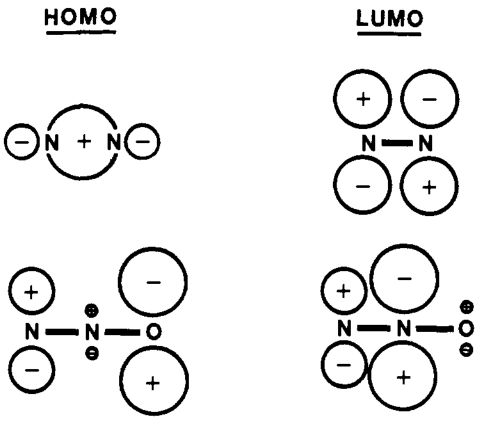


Figure 1. Highest occupied and lowest unoccupied molecular orbitals for nitrogen and nitrous oxide.

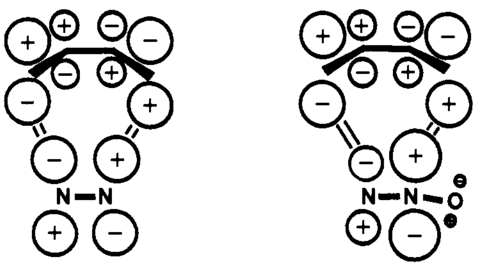


Figure 2. Orbital interactions beween N_2 LUMO and N_2O LUMO and a typical diene HOMO at the transition state for heteroextrusion.

the nitrogen HOMO to be strongly bonding between nitrogens, whereas the low-symmetry nitrous oxide HOMO is only weakly bonding between these centers.[12] In the transition state associated with N_2 expulsion, orbital interactions between the departing heterofragment and the incipient diene are equally distributed between each nitrogen and symmetry allowed. The more important[10b] N_2 LUMO and diene HOMO interaction is illustrated (Figure 2).

The analogous transition state for the nitrous oxide releasing reaction may be assumed to involve a slightly nonlinear N_2O unit.[14] Dominant interactions between N_2O and the virtual diene are undoubtedly characterized by electron flow from the hydrocarbon to the hetero moiety. Thus, the diene HOMO and bent N_2O LUMO (Figure 2) are strongly bonding between carbon and central nitrogen, but less strongly between carbon and terminal nitrogen. Similar conclusions may be drawn for the diene LUMO and nonlinear N_2O HOMO interactions. Reduced bonding between carbon and nitrogen when N_2 is replaced by N_2O is expressed implicitly by the symmetry conservation principle.[16] In general, HOMO–LUMO′ and HOMO′–LUMO pairs with the same symmetry experience a maximum bonding interaction. A reduction in symmetry, as caused by the strong oxygen perturbation in N_2O in the present case, diminishes orbital overlap and hence raises the interaction energy. The reaction consequently may be categorized as partly forbidden. In the limit, of course, the complete absence of congruent HOMO–LUMO symmetry results in zero overlap; the reaction is forbidden. It appears, therefore, that nitrous oxide loss as described above may well entail a symmetry-imposed barrier which augers against facile thermal decomposition.[17] Potential surface calculations are underway in order to more fully evaluate this postulate.

Intuitive applications of the orbital symmetry conservation principle[16] often assume that the removal of symmetry by introduction of substituents leaves the system essentially invariant. For many cases this assumption appears to be valid. However, a large substituent perturbation may cause sufficient electronic reorganization such that energy barriers to a given allowed reaction pathway are erected. Conversely, symmetry-forbidden reactions may be permitted under the influence of a similarly strong perturbation.[10b] The azoalkane–azoxyalkane and pyrroline–pyrroline *N*-oxide[19] decompositions, provided heteroextrusion is concerted, and the addition of HCl to an olefin[19b] are pertinent examples, respectively. Under these circumstances it is to be expected that alternate reaction pathways may operate.[19,20]

Acknowledgment. We are grateful to the National Institutes of Health (GM-15927) for support of the work. Professor David Harpp (McGill University) kindly provided computer time.

---

teratomic bonding parameters have been optimized to give molecular geometries and bonding energies which calibrate closely with experiment.

(12) Thus, AO's contributing to the frontier MO's are computed to have the following squared coefficients: N_2 HOMO, 0.50, 0.50; N_2O HOMO, N_1, 0.35, N_2, 0.05, O, 0.60; N_2 LUMO, 0.50, 0.50; N_2O LUMO, N_1, 0.40, N_2, 0.53, O, 0.07. The picture arising from the semiempirical method used here is very similar to that derived from more detailed *ab initio* calculations.[13]

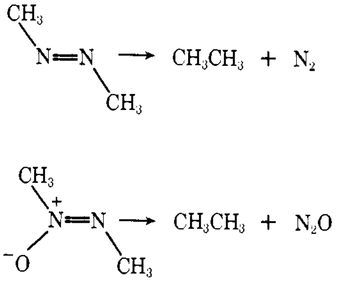
(13) M. Krauss, National Bureau of Standards Technical Note 438, Washington D. C., 1967.

(14) A result obtained for the calculated fragmentation of diazirine *N*-oxide to N_2O and singlet methylene.[15]

(15) J. P. Snyder, unpublished.

(16) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 8, 781 (1969).

(17) The variation in destruction rates discussed in the text can be ascribed *a priori* to a thermodynamic origin. This explanation is rendered less tenable, however, by reference to calculations for the following hypothetical transformations.[15]



	ΔH_{calcd},[11] kcal/mol	$\Delta\Delta H_{calcd}$
$CH_3N{=}NCH_3 \longrightarrow CH_3CH_3 + N_2$	−58.8	
		−3.9
$CH_3\overset{+}{N}(O^-){=}NCH_3 \longrightarrow CH_3CH_3 + N_2O$	−62.7	

Similar results are obtained for other azo–azoxy pairs. Given the operation of Hammond's postulate[18] in the present application, $\Delta\Delta H_{calcd}$ is far too small to account for the described kinetic discrepancies.

(18) G. S. Hammond, *J. Amer. Chem. Soc.*, 77, 334 (1955).

(19) D. M. Lemal and S. D. McGregor, *ibid.*, 88, 1335 (1966); S. D. McGregor and D. M. Lemal, *ibid.*, 88, 2858 (1966); L. A. Carpino, *Chem. Commun.*, 494 (1966).

(20) For example, 2,3-diazabicyclo[2.2.1]heptene-2 eliminates nitrogen exclusively in the mass spectrometer. The corresponding *N*-oxide expels both ethylene and N_2O: J. P. Snyder, M. L. Heyman, V. T. Bandurco, and D. N. Harpp, *Tetrahedron Lett.*, 4693 (1971).

(21) Recipient of the Camille and Henry Dreyfus Teacher-Scholar Grant.

James P. Snyder,*[21] Ling Lee, Victor T. Bandurco, C. Y. Yu
Belfer Graduate School of Science, Yeshiva University
New York, New York 10033

Russell J. Boyd
Mathematical Institute, University of Oxford
Oxford, OX1 3LB, England

Received September 16, 1971