x_2 greater than x_1, it was possible to submit the isolated product **1** (with $[\alpha_1]_D$) obtained from the experiment with an extent of reaction of x_1 to a further photolysis under the same conditions. In this way, if a photolysis of reaction extent x' is achieved from this already optically active product **1** ($[\alpha_1]_D$) the remaining product has a new optical rotatory power ($[\alpha_2]_D$). The corresponding extent of reaction x_2 of the photolysis starting with (±)-**1** is given by

$$x_2 = 1 - (1 - x_1)(1 - x') = x_1 + x'(1 - x_1)$$

This procedure was also used by Mitchell.[25]

We checked that the enantiomeric purity of the remaining compound in the partial photoresolution was the same either by achieving directly the reaction extent x_2, or by achieving x_1 and then x', separately. This procedure was used in the photolysis of both α-azido-*N*,*N*-dimethylpropionamide and camphor.

(±)-Camphor. Racemic camphor provided by the Delaire Co. (France) was recrystallized twice from hexane and then sublimed. Its glc analysis showed a purity greater than 99% and the optical activity was $[\alpha]^{25}D$ −0.14° (*c* 6, hexane).

This racemic camphor was obtained by a synthesis starting from naturally occurring optically active α-pinene and since one of the steps of this synthesis was a racemization, the slight residual optical activity observed in the final product was probably due to incomplete racemization.

A sample of camphor ($[\alpha]_D$ −0.14°) purified by the above procedure was submitted to preparative glc, and there was no difference in the specific rotation of the highly purified camphor collected. The presence of an optically active impurity was therefore ruled out, so that the slight optical activity observed was due to an enantiomeric excess of 0.25% in the camphor. For our experiments requiring completely racemic material, we adjusted the rotatory power of the nearly racemic compound to $[\alpha]_D$ 0.005 ± 0.005° by the addition of optically pure (+)-camphor [$[\alpha]^{25}D$ +52.9° (*c* 2.5, hexane)].

Partial Kinetic Photoresolution of Racemic Camphor. A solution of 6 g of racemic camphor in 360 ml of *n*-hexane was placed in the irradiation cell (diameter 100 mm, volume 360 ml) which was closed with a glass stopper and magnetic stirring was maintained during the course of the irradiation. For the determination of the extent of the photodecomposition, 1-ml samples were taken, a known weight of a standard (*n*-hexadecane) was added, and the mixture was analyzed by glc (column A temperature 120°, carrier N_2 25 ml/min); thus, the disappearance of camphor was determined by measurement of the peak areas of camphor and the standard. When the desired extent of reaction had been achieved the irradiation was stopped. The solvent then was carefully removed avoiding sublimation of remaining camphor which was separated from the mixture of photoproducts by preparative glc (column B temperature 145°, carrier N_2 100 ml/min). Two such purifications by glc were necessary and the purified camphor was used for the determination of the optical purity. The optical rotatory power was measured in *n*-hexane. We checked that there was no change in the specific activity of a known sample of camphor under these chromatographic conditions. The experimental results are: $x = 25\%$, $y = 0.69 \pm 0.07\%$; $x = 62\%$, $y = 3.7 \pm 0.4\%$; $x = 85\%$, $y = 6.5 \pm 0.7\%$; $x = 90\%$, $y = 9.0 \pm 1\%$; $x = 97\%$, $y = 15.8 \pm 1.5\%$; $x = 99\%$, $y = 19.9 \pm 2\%$.

Computation. The program allowing the simulation of the chemical systems involved in this work was written in FORTRAN IV and used the classical method of numerical integration Runge-Kutta order 4. The computation was performed on Univac 1108 and 1110 computers of the Centre de Calcul de l'Université, Paris-Sud.

Acknowledgments. We thank Professor K. Mislow for giving us authorization to reproduce Figure 2 and Professors A. Horeau and J. Kagan and Dr. Fiaud for their helpful criticisms of the manuscript. We thank C.N.R.S. for financial support.

cis-Azoxyalkanes. IV. Preparation and Nuclear Magnetic Resonance Spectra[1]

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Abstract: A three-step high-yield procedure for the generation of a series of polycyclic *cis*-azoxyalkanes is described. ^{13}C and shift reagent nmr studies confirm the unsymmetrical nature of the NNO unit, while anisotropy calculations provide a basis for understanding the anomolous proton nmr spectra of the title compounds. The effect of both conformation and configuration is assessed and applied to a variety of acyclic azoxyalkanes.

Although azoxyalkanes have surfaced in the chemical literature from time to time[3] they first attracted serious attention with the discovery that two naturally occurring pretoxins, macrozamin[4a,b] and cycasin,[4c] contain glycosylated methylazoxymethanol. The aglycone portion has since been established as the trigger substance for a series of detrimental biological events.[5] It is of some historical interest that Captain James Cook's crew apparently fell victim to these plant-bound

(1) For part III, see J. P. Snyder, L. Lee, V. T. Bandurco, C. Y. Yu, and R. J. Boyd, *J. Amer. Chem. Soc.*, **94**, 3260 (1972).

(2) Camille and Henry Dreyfus Teacher–Scholar Grant recipient, 1971–1976; University of Copenhagen.

(3) J. G. Aston and D. M. Jenkins, *Nature (London)*, **167**, 863 (1951), and references therein.

(4) (a) B. W. Langley, B. Lythgoe, and N. V. Riggs, *J. Chem. Soc., London*, 2309 (1951); (b) N. Nishida, A. Kobayashi, and T. Nagahama, *Bull. Agr. Chem. Soc. Jap.*, **17**, 77 (1955); (c) N. V. Riggs, *Chem. Ind. (London)*, 926 (1956); B. H. Korsch and N. V. Riggs, *Tetrahedron Lett.*, 523 (1964).

(5) Enzymes (β-glycosidases) in the tissues of mammalian systems cleave the sugar residue from the aglycone fragment releasing methylazoxymethanol (MAM),[6a] a powerful mutagen and carcinogen.[6b] The latter has been implicated in the methylation of liver RNA and DNA at the 7 position of guanine.[7a] Similarly inhibition of DNA synthesis and degradation of cellular DNA occur upon exposure of bacteria (*e.g.*, mutant strains of *E. coli*) to MAM.[7b] Certain insect larvae, on the other hand, thrive on MAM by performing an *in vivo* synthesis of the relatively nontoxic cycasin from its components.[7c]

(6) (a) G. Laqueur, *Fed. Proc., Fed. Amer. Soc. Exp. Biol.*, **23**, 1386 (1964); A. Kobayashi and H. Matsumoto, *Arch. Biochem. Biophys.*, **110**, 373 (1965); (b) for reviews on these and other effects of MAM, see G. L. Laqueur and M. Spatz, *Cancer Res.*, **28**, 2262 (1968); M. Spatz, *Ann. N. Y. Acad. Sci.*, **163**, 848 (1969).

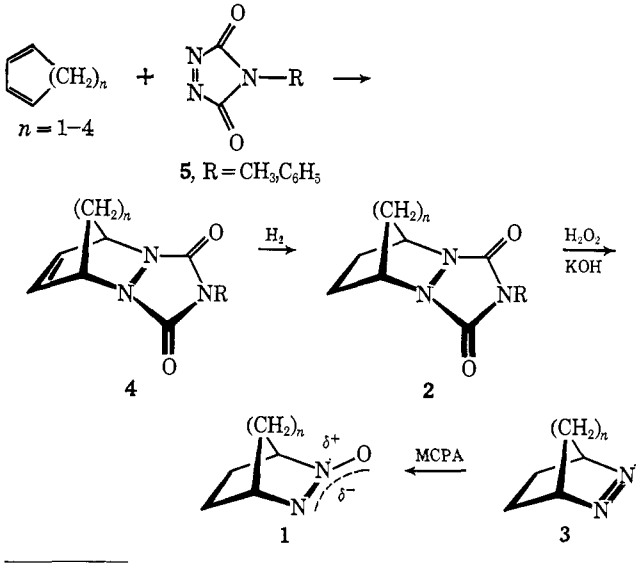
(7) (a) *In vivo*, R. C. Shank and P. N. Magee, *Biochem. J.*, **100**, 35 (1966); *ibid.*, **105**, 521 (1967); R. C. Shank, *Biochim. Biophys. Acta*, **166**, 578 (1968); *in vitro*, N. V. Riggs, *Nature (London)*, **207**, 623 (1965); H. Matsumoto and H. H. Higa, *Biochem. J.*, **98**, 20c (1966); B. Singer and H. Fraenkel-Conrat, *Biochemistry*, **8**, 3260 (1969); *ibid.*, 3266 (1969); (b) Dr. H. R. Rosenkrantz, Department of Microbiology, Columbia University, private communication; (c) H. J. Teas, *Biochem. Biophys. Res. Commun.*, **26**, 686 (1967).

toxins during their voyage of 1768–1771.[8] Furthermore, an α,β-unsaturated azoxyalkane unit occurs in the tuberculostatic antibiotic, Elaiomycin,[9] and an antifungal agent from *Streptomyces hinnulinus*.[10] These findings have stimulated the synthesis[11] and magnetic resonance evaluation[12] of a considerable number of acyclic *trans*-alkylazoxy compounds.

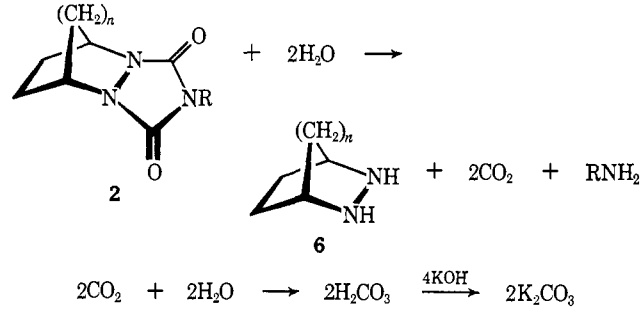
A selection of aliphatic *cis*-azoxy derivatives have likewise been synthesized by a variety of methods.[13–18] Some of the preliminary studies suggested an unusual divergence of spectroscopic properties for the cis and trans isomers,[14,17] in particular the nmr spectra. In order to probe these and anticipated chemical differences, we have undertaken a study of the preparation[17] and nmr spectra of a series of the title substances.

Synthesis

For the purpose of investigating the anisotropy of the *cis*-NNO moiety, it was desirable to obtain a series of compounds in which the location of protons α to nitrogen varied in a small but well-defined manner with respect to nitrogen. The bicyclic series **1** appeared ideal for this purpose. The required *cis*-azoxy compounds are obtained by suitable oxidation of the diazapolycyclic precursors **2** or **3**.



Adducts **4** are prepared from cyclic dienes and N-substituted triazoline diones **5** in good to excellent yields (53–95%). Generation of the heterodienophile **5** by nitrogen tetroxide oxidation[19] is convenient and generally results in improved adduct yields relative to other oxidants.[20a] Following hydrogenation (90–100% yield), an *in situ* hydrolysis and multiple oxidation of **2** with strongly basic hydrogen peroxide delivers the *N*-oxides **1**. Both a large excess of base and 30% hydrogen peroxide are employed. The former is necessary as a catalyst and as a neutralizing agent for the CO_2 liberated during hydrolysis. The stoichiometric relationship follows.



During our preliminary experiments with the *N*-phenyl adducts **2**,[17] a basic ethylene glycol–water mixture containing the latter was brought to reflux and then continuously treated dropwise with 30% H_2O_2 ([OH^-]/[C_6H_5–adduct] = *ca.* 7:1). Subsequent steam distillation removes the aniline formed. The corresponding unoptimized yields of azoxyalkanes are indicated in Table IV. Better yields are routinely obtained, however, by using the *N*-methyl derivative of **3** and a large excess of base ([OH^-]/[CH_3–adduct] = *ca.* 70:1); *cf.* Table I. Base-catalyzed decomposition of peroxide is suppressed under conditions with a favorable hydroxide–peroxide ratio.[20b] In the present application a more effective reagent medium results. Since methylamine is the nitrogenous by-product, steam distillation is unnecessary. Compounds **11** and **13** are prepared similarly; the precursor dienes are bicycloheptadiene and cyclooctatetraene dibromide, respectively. In the latter case debromination precedes hydrogenation.[21]

The hydrolysis of diaza diesters related to adducts **2** to hydrazines **6** is a well-known reaction.[22] Likewise bicyclic hydrazines are oxidized readily to azoalkanes by a variety of reagents including H_2O_2.[23–25] Thus it is

(8) "Journal of the Rt. Hon. Sir Joseph Banks during Cook's First Voyage in H. M. S. Endeavour in 1768–1771," J. D. Hooker, Ed., New York, N. Y., 1896, cited by M. G. Whiting, *Econ. Bot.*, **17**, 271 (1963); C. E. Searle, *Chem. Brit.*, **6**, 5 (1970). We are grateful to Professor Searle for pointing out the Whiting reference to us.

(9) C. L. Stevens, B. T. Gillis, J. C. French, and T. K. Haskell, *J. Amer. Chem. Soc.*, **80**, 6088 (1958); C. L. Stevens, B. T. Gillis, and T. H. Haskell, *ibid.*, **81**, 1435 (1959).

(10) (a) W. J. McGahren and M. P. Kunstmann, *J. Amer. Chem. Soc.*, **91**, 2809 (1969); **92**, 1587 (1970); (b) *J. Org. Chem.*, **37**, 902 (1972).

(11) (a) D. W. Langley, B. Lythgoe, and L. S. Rayner, *J. Chem. Soc., London*, 4191 (1952); (b) B. T. Gillis and K. F. Schimmel, *ibid.*, **27**, 413 (1962); B. T. Gillis and J. D. Hagarty, *J. Org. Chem.*, **32**, 95 (1967); (c) B. T. Gillis and K. F. Schimmel, *ibid.*, **32**, 2865 (1967); (d) B. T. Gillis and M. P. Montague, *ibid.*, **33**, 762 (1968); R. A. Moss and M. T. Landon, *Tetrahedron Lett.*, 2897 (1969); (e) R. A. Moss, M. J. Landon, K. M. Luchter, and A. Mamantov, *J. Amer. Chem. Soc.*, **94**, 4392 (1972); R. A. Moss and G. M. Love, *ibid.*, **95**, 3070 (1973).

(12) J. P. Freeman, *J. Org. Chem.*, **28**, 2508 (1963).

(13) (a) J. P. Freeman, *J. Org. Chem.*, **27**, 1309, 2881 (1962); (b) W. Luttke, *Justus Liebigs Ann. Chem.*, **687**, 236 (1965); (c) W. R. Dolbier, Jr., and W. M. Williams, *J. Amer. Chem. Soc.*, **91**, 2818 (1969); W. M. Williams and W. R. Dolbier, Jr., *ibid.*, **91**, 3955 (1972).

(14) F. D. Greene and S. S. Hecht, *Tetrahedron Lett.*, 575 (1969).

(15) J. Swigert and K. G. Taylor, *J. Amer. Chem. Soc.*, **93**, 7337 (1971).

(16) K. G. Taylor and T. Riehl, *J. Amer. Chem. Soc.*, **94**, 250 (1972).

(17) J. P. Snyder and V. T. Bandurco, *Tetrahedron Lett.*, 4643 (1969).

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

(19) J. C. Stickler and W. H. Pirkle, *J. Org. Chem.*, **31**, 3444 (1966).

(20) (a) R. C. Cookson, S. S. Giliani, and I. D. Stevens, *Tetrahedron Lett.*, 615 (1962); B. T. Gillis and J. D. Hagarty, *J. Org. Chem.*, **32**, 330 (1967); J. Sauer and B. Schröder, *Chem. Ber.*, **100**, 678 (1967); (b) F. R. Duke and T. W. Haas, *J. Phys. Chem.*, **65**, 304 (1961).

(21) D. G. Farnum and J. P. Snyder, *Tetrahedron Lett.*, 3861 (1965).

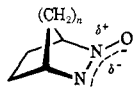
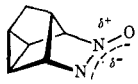
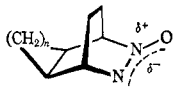
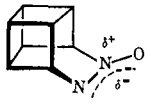
(22) S. G. Cohen and R. Zand, *J. Amer. Chem. Soc.*, **84**, 586 (1962); B. Franzus and J. H. Surridge, *J. Org. Chem.*, **27**, 1951 (1962); P. G. Gassman, K. T. Mansfield, G. N. Taylor, and K. B. Wiberg, *Org. Syn.*, **49**, 1 (1969); E. Allred, J. Hinshaw, and A. Johnson, *J. Amer. Chem. Soc.*, **91**, 3382 (1969); J. A. Berson and S. S. Olin, *ibid.*, **91**, 777 (1969); W. P. Lay, K. MacKenzie, and J. R. Telford, *J. Chem. Soc. C*, 3199 (1971); R. Askani, *Tetrahedron Lett.*, 3349 (1970); B. M. Trost and R. C. Cory, *J. Amer. Chem. Soc.*, **93**, 5572 (1971); R. M. Moriarity, C. Yeh, and N. Ishibi, *ibid.*, **93**, 3085 (1971); E. A. Allred and K. J. Voorhees, *ibid.*, **95**, 620 (1973).

(23) *Cf.* citations in ref 29; for a theoretical study of electronic factors which govern the oxidation of cyclic hydrazines, *cf.* ref 24.

(24) J. P. Snyder, *Tetrahedron Lett.*, 2451 (1972).

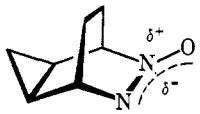
(25) M. L. Heyman and J. P. Snyder, *Tetrahedron Lett.*, 2859 (1973).

Table I. ^{13}C Azoxyalkane Chemical Shifts[a,b]

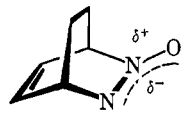
		n	Chemical shifts, δ
	7	1	112.2, 125.7, 150.5, 166.6, 167.7
	8	2	121.1, 135.1, 167.2 (2C), 168.9 (2C)
	9	3	119.1, 135.8, 164.7, 165.3, 170.1, 173.0, 173.9
	10	4	122.2, 135.1, 154.5, 167.8, 168.8 (2C), 169.7, 174.9
	11		106.7, 119.3, 142.2, 162.0, 168.0, 169.9, 171.7
	12	1	120.1, 135.2, 170.8, 171.9, 175.0 (2C), 180.9
	13	2	118.8, 132.5, 159.2, 159.7, 172.5, 174.2 (2C), 175.9
	25		126.0, 135.2, 152.4, 153.0, 155.7

[a] In ppm upfield from CS_2; natural abundance. Solvent $CDCl_3$. [b] Analogous results have been obtained for a fused four-membered ring azoxyalkane.[13c]

tempting to speculate that the oxidative hydrolysis of adduct **2** to azoxy **1** occurs by way of hydrazo and azo intermediates. However, the preparation of compounds **12** (see Experimental Section) and **14** by a



12



14

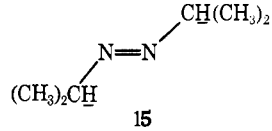
closely related procedure[1] suggests that an alternative pathway may interpose itself between starting adduct and azoxy product.

The azoalkanes corresponding to **14** ($t_{1/2}^{-78°} \leq 30$ sec)[26] and **12** ($t_{1/2}^{-3.5°} = 68$ min)[27] undergo extremely facile retrocycloadditions to nitrogen and cyclohexadiene and cycloheptatriene, respectively. It is unlikely that even in the presence of a large excess of oxidant they would survive temperatures from 80 to 100°, conditions under which the reaction proceeds.

Alternatively, *cis*-azoxyalkanes **7**–**13** can be prepared from the precursor azoalkanes **3** by direct oxidation with *m*-chloroperbenzoic acid.[14,28] Two recently developed high-yield routes utilize adducts **2** and the corresponding benzyl esters as starting substrates for series **3**.[25,29]

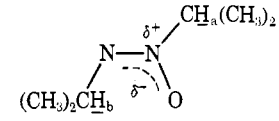
Nmr Spectra

Pmr chemical shifts have been of great utility in the classification of structural and geometrical isomers of azoxyalkanes. The early studies of Freeman in this area gave order to a variety of structural questions and in particular permitted facile assignment of the position of the N–O bond in *trans*-azoxyalkanes.[12] An important generalization was evolved in this work and has been cited a number of times since.[11c,e,14–16,30] Upon oxidation of an azoalkane, the alkyl group attached to the NO fragment of the subsequent azoxyalkane was predicted to shift to lower magnetic field in the nmr. By contrast alkyl hydrogens linked to unoxidized nitrogen were expected to experience a less strong paramagnetic shift or to move upfield. The latter was attributed to a possible diamagnetic effect arising from the shielding cone of the cis disposed N–O bond. For example, consider the azoisopropane system **15**. Oxidation to *N*-oxide **16** causes two significant changes in the chemical shifts for hydrogen α to nitrogen. First, the degeneracy of the precursor azoalkane α hydrogens is broken. Protons H_a(**16**) and H_b(**16**) are observed at τ 5.53 and 5.83. The lower field resonance has been associated with H_a, the proton nearest oxidized nitrogen. The second important modification of the pmr spectrum upon oxidation of azo **15** is that both α hydrogens are shifted downfield. Thus the generalization works well in the trans series and is in accord with a host of other electronegativity effects routinely applied in pmr spectroscopy. However, as discussed below, it cannot generally be used to compare trans-azo compounds with acyclic *cis*-azoxyalkanes. Furthermore, the rule breaks down completely for polycyclic and cyclic cis-azo/azoxy cases.



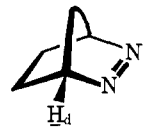
15

τ 6.43[15]



16

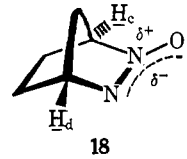
τ 5.83 τ 5.53[15]



17

τ 4.91 ± 0.14 ppm

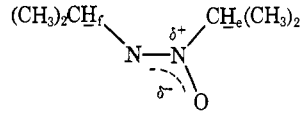
Δ τ (trans–cis) = 1.52 ppm



18

τ 5.41 ± 0.18 ppm

Δ τ = 0.12 (0.42) ppm



26

τ 5.90 τ 5.04[15]

Consider the conversion of a cyclic azo derivative to its *N*-oxide. Eight cases (Tables I and IV) are summarized in structures **17** and **18**. H_e(**18**) and H_d(**18**) are not only chemically equivalent but also shifted about 0.5 ppm upfield relative to the bridgehead protons of the azo precursor. In order to proceed with an analysis of this discrepancy, it is critical that the gross structure of the azoxy compounds be known with certainty. Static structures **19**, **20**, and **21** as well as a rapidly equilibrating constellation **22**/**22′** would permit a rationalization of both the equivalence of bridgehead hydrogens and the consistent upfield shift of these protons relative to the azo precursor.

Based on experiments with azoxyalkane **7** and *trans*-3,-

(26) N. Rieber, J. Alberts, J. A. Lipsky, and D. M. Lemal, *J. Amer. Chem. Soc.*, **91**, 5668 (1969).

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

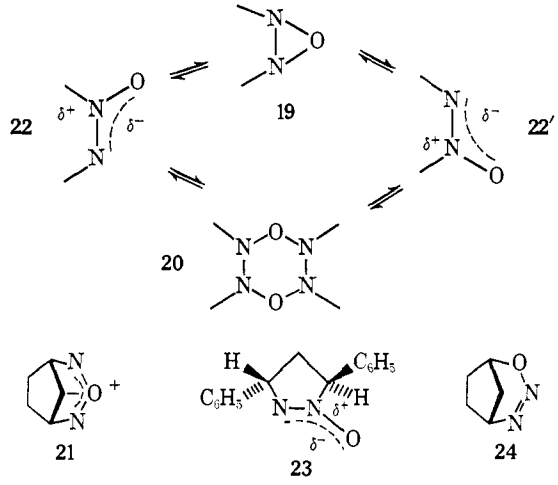
(28) M. L. Heyman and J. P. Snyder, unpublished results.

(29) M. L. Heyman, V. T. Bandurco, and J. P. Snyder, *Chem. Commun.*, 297 (1971).

(30) F. B. Mallory and A. Cammarata, *J. Amer. Chem. Soc.*, **88**, 61 (1966); B. T. Gillis and J. D. Hagarty, *J. Org. Chem.*, **32**, 95 (1967); P. E. Iversen, *Chem. Ber.*, **104**, 2195 (1971).

5-diphenylpyrazoline *N*-oxide (**23**), Greene and Hecht[14] have ruled out **19–22** and made a strong case for asymmetric, static azo *N*-oxide moiety.[31] Furthermore, structure **24** was eliminated on chemical grounds. Mild deoxygenation of the condensed and unsaturated azoxy derivatives **12** and **14**, respectively, supports this contention.[1]

In order to tie these observations firmly into the azoxy series **7–13**, additional confirmation concerning the asymmetry of **7** and related bicyclic derivatives has been obtained by recording the pmr spectra of *N*-oxides **7**, **8**, and **25**[18] in the presence of increasing quantities of tris(pivaloyl)europium.[32] In all cases the bridgehead protons are diamagnetically shielded and split into two peaks each integrating for a single proton. Assignment of the bridgehead bands at this time is complicated by uncertainty as to whether europium complexation occurs at nitrogen or oxygen. CNDO–MO–SCF calculations (*vide supra*) suggest a near equivalent distribution of negative charge between these two centers.



A final and direct measure of the asymmetry of the azoxy unit in the bicyclic series is the natural abundance ^{13}C spectra of compounds **7–13** and **25** (Table I). All carbons are easily distinguishable with the exception of a pair each in the seven- and eight-carbon azoxy cases **10**, **12**, **13**, and **25**. Coincidence is most likely due to the distance of these centers from the perturbing NNO moiety.

The asymmetry of the NNO function for cyclic and bicyclic azoxyalkanes is thus firmly established. The photochemical transformation of acyclic azoxyalkanes unambiguously permits the same conclusion in the trans series.[15,16,33] Left unanswered, however, is the origin of the chemical shift differences between protons α to nitrogen in the corresponding *cis*-azo and *cis*-azoxy series. In short, the problem can be resolved into two separate components by considering the *cis*-/*trans*-azo compounds independently from the *cis*-/*trans*-azoxy series. Both cis types are anomalous. Azoisopropane and its *N*-oxide with tertiary hydrogens α to nitrogen would seem to be suitable models for comparison with the bicyclic systems.

In the case of the azoalkanes a remarkable deshielding of about 1.5 ppm at α hydrogen is evident in the formal transformation of *trans*-**15** to *cis*-**17**. Configurational isomers of acyclic analogs azoisobutane ($\Delta\tau_{CH_3}$(trans–cis) = 0.33 ppm (CH_3OD))[34] and azoisopropane (**15**) ($\Delta\tau_{CH_3}$(trans–cis) = 0.14 ppm, $\Delta\tau_{CH}$(trans–cis) = 0.49 ppm (CCl_4))[15] behave likewise while the parent, azomethane ($\Delta\tau_{CH_3}$(trans–cis) = −0.10 ppm (D_2O)),[35] falls outside the pattern. The intramolecular nature of the observed azo-shift values is supported by their invariance as a function of solvent.[36] Lone pair–lone pair interaction may be a contributing factor.[37] Whatever the cause, the apparent upfield chemical shift of the azoxy bridgehead protons relative to that for the corresponding azo hydrogens in fact reflects a previously unrecognized diamagnetic effect for the *cis*-azo functionality.[38]

For the *N*-oxides, the spatial relationship of H_a(**16**) and H_c(**18**) to the N–O bond can be considered geometrically congruent. Both types of protons have very similar chemical shifts with the bridgehead hydrogen falling slightly to lower field. By contrast hydrogen α to oxidized nitrogen for *cis*-azoxyisopropane (**26**) is found 0.49 ppm downfield from the trans isomer **16**. This suggests a decided conformational preference for the isopropyl group of **26** and/or NNC bond angles which differ considerably from the bicyclic cases.

Anisotropy Calculations

Hydrogen α to unoxidized nitrogen remains unchanged in the acyclic isomerization (H_b(**16**) → H_f(**26**)) but is shielded considerably in the hypothetical acyclic–cyclic isomerization (H_b(**16**) → H_d(**18**)). It is this differential shielding which is responsible for the fact that the bridgehead protons of bicyclic *cis*-azoxyalkanes experience identical or near identical chemical shifts. In an attempt at understanding the observations outlined above, anistropy calculations of the Pople type[40] have been carried out for *trans*-azoxymethane (**27**) and the cis-bicyclic model structure **28**.

In the Pople formalism the total nmr shielding tensor is defined within an LCAO scheme as the sum of three contributing terms (eq 1 and 2).[41]

(31) Although *N*-oxide **7** has been partially resolved by an elegant asymmetric induction experiment,[14] the nmr spectra of *N*-oxides **7** and **8** obtained in an optically active medium ($CDCl_3$/D-α-pinene, 1:1) are indistinguishable from those recorded in $CDCl_3$ alone.

(32) For recent reviews, see J. Reuben, *Progr. Nucl. Magn. Resonance Spectrosc.*, **9**, 1 (1973); B. C. Mayo, *Chem. Soc. Rev.*, **2**, 49 (1973).

(33) (a) S. S. Hecht and F. D. Greene, *J. Amer. Chem. Soc.*, **89**, 6761 (1967); (b) F. D. Greene and S. S. Hecht, *J. Org. Chem.*, **35**, 2482 (1970).

(34) T. Mill and R. S. Stringham, *Tetrahedron Lett.*, 1853 (1969).

(35) R. F. Hutton and C. Steel, *J. Amer. Chem. Soc.*, 86, 745 (1964).

(36) For example for **3** (n = 2), $\tau_{bridgehead}$ = 5.08 ± 0.15 ppm for solvents with the dielectric constant range 2.23–32.6.

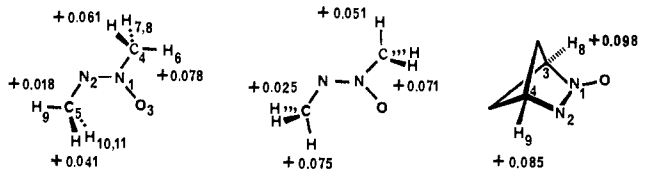
(37) E. Haselbach, J. A. Hashmall, E. Heilbronner, and V. Hornung, *Angew. Chem., Int. Ed. Engl.*, 8, 878 (1969); M. B. Robin, H. Basch, N. A. Kuebler, K. B. Wiberg, and G. B. Ellison, *J. Chem. Phys.*, **51**, 45 (1969); E. Haselbach and E. Heilbronner, *Helv. Chim. Acta*, **53**, 684 (1970); E. Haselbach, E. Heilbronner, A. Mannschreck, and W. Seitz, *Angew. Chem., Int. Ed. Engl.*, **9**, 902 (1970); R. J. Boyd, J. C. Bünzli, J. P. Snyder, and M. L. Heyman, *J. Amer. Chem. Soc.*, **95**, 6478 (1973); E. Heilbronner, F. Brogh, W. Eberbach, E. Haselbach, V. Hornung, and D. M. Lemal, *Helv. Chim. Acta*, **56**, 1933 (1973); H. Schmidt, A. Schweig, B. Trost, H. Neubold, and P. Scudder, *J. Amer. Chem. Soc.*, **96**, 622 (1974).

(38) Comparative ^{13}C chemical shifts for azoxyalkanes **7**, **8**, and **25** and the corresponding azo compounds (**3** (n = 1, 2), deoxy-**25**) do not reflect the proton result.[39]

(39) J. P. Snyder, unpublished results.

(40) J. A. Pople, *J. Chem. Phys.*, **37**, 53 (1962); *Discuss. Faraday Soc.*, **No. 34**, 7 (1962).

(41) The interpretation of the equation used here is due to W. G. Laidlaw, University of Calgary, private communication; see, for example, C. J. MacDonald, Ph.D. Thesis, University of Calgary, 1966.



27a 27b 28

Figure 1. Computed hydrogen charge densities (SCF–MO–CNDO).

$$\sigma^{T} = (e^2/3mc^2)\sum_{\mu}^{occ} c_{\mu p}c_{\mu p}\overline{(r^{-1})} - 2N^{-1}\langle r^{-3}\rangle_{A}\chi_{p}^{A} + (1/3N)\sum_{B\neq A}(R_{B}^{-3})\sum_{\alpha=x,y,z}(\chi_{p}^{B})_{\alpha\alpha}(1 - 3\cos^2\gamma_{\alpha}) \quad (1)$$

$$\sigma^{T} = \sigma^{d} + \sigma^{p} + \sum_{B\neq A}\sigma^{AB} \quad (2)$$

The first term, σ^{d}, represents the self-atom diamagnetic contribution, a function of the electron density on a given atom A (Figure 1). The self-atom paramagnetic component, σ^{p}, is determined by the magnetic anisotropy of atomic orbitals about atom A and is necessarily zero for proton calculations. The third term, σ^{AB}, sums the combined anisotropy effect by neighboring atoms on atom A and can be derived from computed bond orders and molecular geometry. It may be either paramagnetic or diamagnetic in character; σ^{T} is thus the total shielding of atom A in a molecular framework relative to atom A in isolation.

The requisite wave functions were obtained by a CNDO–MO–SCF scheme,[42] certain of the bond lengths and angles for structures **27** and **28** being derived by minimization of the total bonding energy (see Experimental Section). Manipulation of the resultant density matrix (*i.e.*, charge densities, bond orders) according to the above equation leads to the values tabulated in Table II.

Table II. Calculated Proton Shielding Terms for Azoxyalkane Models **27a**, **27b**, and **28** (ppm)[a]

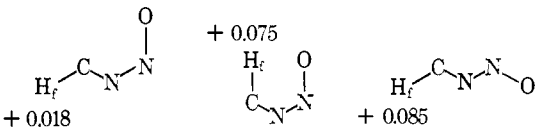
Proton type	*trans*-**27a**	*trans*-**27b**	*trans*-**27a**/*trans*-**27b**, 50:50	*cis*-**28**
		$CH_{3,n}$ or CH_n		
σ_n^{d}	−1.7	−1.7	−1.7	−2.5
σ_n^{AB}	−0.11	+0.09	−0.01	−0.17
σ_n^{T}	−1.8	−1.6	−1.7	−2.6
		$CH_{3,f}$ or CH_f		
σ_f^{d}	−0.84	−1.0	−0.94	−2.1
σ_f^{AB}	−0.29	−0.40	−0.34	−0.41
σ_f^{T}	−1.1	−1.4	−1.3	−2.5
		Δ_{n-f}		
$\Delta\sigma_{n-f}^{d}$	−0.83	−0.61	−0.72	−0.34
$\Delta\sigma_{n-f}^{AB}$	+0.18	+0.48	+0.33	+0.24
$\Delta\sigma_{n-f}^{T}$	−0.65	−0.13	−0.39	−0.10

[a] n = near, f = far.

Although the approximations involved in Pople's perturbation treatment as well as the CNDO method force us to attach only qualitative significance to the numerical results, previously unexplained trends can be identified. Of significance is the prediction in accord with experiment that the α hydrogens in the cis model experience nearly identical chemical shifts relative to the trans conformers ($\Delta\sigma_{n-f}^{T}$: cis, 0.10; trans, 0.13–0.65 ppm). The cis magnetic degeneracy can be seen in perspective by noting the consequence of molecular geometry on the terms σ^{AB} and σ^{d}. In order to simplify the discussion, hydrogens α to the N–O bond (**27**: H-6, H-7, H-8; **28**: H-8) are designated near (n), while those β to the same moiety (**27**: H-9, H-10, H-11; **28**: H-9) are labelled far (f). Table II illustrates that $\Delta\sigma_{n-f}^{AB}$ is nearly identical for both *trans*-**27a** and the cis structure **28** (0.18 and 0.24 ppm, respectively). The geometry of the cis α hydrogens and at least one of the trans methyl hydrogens relative to the NNO function is very similar. From the range of $\Delta\sigma_{n-f}^{AB}$ values it appears that anisotropy effects due to neighboring atoms are more sensitive to the relative conformation around carbon α to nitrogen than to cis–trans configuration about the N–N bond. The contrary is found for σ^{d}. As a measure of electron density on α H, this term is sensitive to configuration but much less so to conformation.

Azoxy Configuration and Conformation

The predicted influence of geometry becomes evident, if it is noted that $\Delta\sigma_{n-f}^{AB}$ and $\Delta\sigma_{n-f}^{d}$ are consistently opposite in sign for a given proton set (+ and −, respectively). Thus any tendency toward chemical shift degeneracy for α hydrogen near and far is a consequence of the relative magnitudes of the two terms. In the cis case they nearly cancel ($\Delta\sigma_{n-f}^{T}$ = 0.10 ppm). By contrast, rotation about the methyl–nitrogen bond for *trans*-**27a** and **-27b** upsets this balance and results in differential shielding ($\Delta\sigma_{n-f}^{T}$ = 0.13–0.65 ppm). In large measure the cis result can be traced to the relatively small $\Delta\sigma_{n-f}^{d}$ term which arises in turn directly from the calculated charge density values at H_n and H_f for *cis*-**28**. Remarkably, both protons have very similar predicted excess charge (+0.098 and +0.085, respectively). Intuitively it might be expected that the inductive effect of N–O should operate on the near proton, H-8, and much less so on the far proton, H-9. However, in the cis series **7**–**13** and **25** and in the *trans*-azoxymethane models **27** considered here, there are three orientations which hold the far α proton in a planar array with carbon and the NNO function, a, b, and c. According to the calculation, the U and W forms (b and c, respectively) transmit equally well the electronegative effect of the NO group. The skew geometry a, on the other hand, permits charge build-up to a much lesser extent.[43] In all the bicyclic *cis*-azoxyalkanes cited above, the far hydrogen is rigidly fixed as in c, whereas in the conformationally mobile trans compounds the U form b is diminished in importance by virtue of the contributions of the remaining nonplanar



a (**27a**) b (**27b**) c (**28**)

(42) R. J. Boyd and M. A. Whitehead, *J. Chem. Soc., Dalton Trans.*, 73 (1972); 78 (1972); 82 (1972).

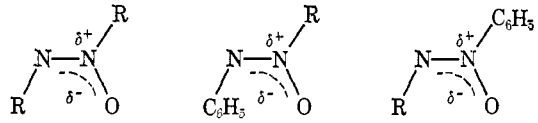
(43) This trend holds for calculations of other azoxy systems not reported here.[39]

methyl hydrogens or by the presence of other conformations (*e.g.*, a). Charge differences at H_n and H_f are consequently exaggerated for *trans*-azoxyalkanes thus giving rise to the observed chemical shift differences between these protons. The calculations suggest for the cis species, however, that while H_n(**28**) evidences a relatively "normal" shift position, H_f(**28**) is shifted downfield relative to a comparable acyclic trans derivative and most likely an analogous acyclic cis material as well. This interpretation is in remarkably good agreement with the observed τ values listed for compounds **16**, **18**, and **26**. It should be noted that the calculated effects of conformations a, b, and c are strongly reminiscent of the related geometrical dependence of coupling constants,[44] providing indirect support for our speculations.

Besides providing a rationale for the anomalous chemical shift behavior of *cis*-azoxyalkanes, the results of Table II accurately predict that the near hydrogen should fall downfield from the far in trans compounds (*i.e.*, σ^T). Likewise the relatively large shielding of H_n and H_f for **28** ($\sigma_n{}^T = -2.62$ ppm, $\sigma_f{}^T = -2.53$ ppm) compared to the methyl protons of **27a** and **27b** ($\sigma_n{}^T = -1.77$, -1.56 ppm; $\sigma_f{}^T = -1.12$, -1.44 ppm) is in agreement with the finding that tertiary and cyclobutyl hydrogens appear downfield from methyl hydrogen (experiment: 0.8–2.0 ppm;[44b] calcd: *ca.* 0.85–1.1 ppm).

Furthermore, order can be made of the variable proton nmr spectra of a variety of *trans*-azoxyalkanes. The early work of Freeman uncovered the unanticipated result that far protons were found either upfield or downfield from the corresponding hydrogens of the azo precursor.[12] Several examples are given in Table III.

Table III. Proton Nmr of *trans*-Azoxyalkanes (τ)[a]



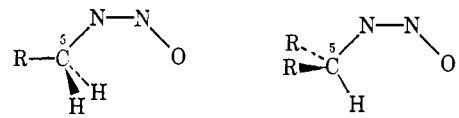
31 **32** **33**

R	δ_n	δ_f	$\Delta\delta_{n-f}$, ppm	*trans*-alkylazo	Δ_{azo-f}, ppm
CH_3, **31**	5.95[b]	6.93	0.98	6.32[b]	−0.61
32	5.81[c,d]	6.55[c,d]	0.74	6.10[b]	−0.45
33					
CH_3CH_2, **32**	5.68[c]	6.37[c,d]	0.69		
33					
$PhCH_2$, **31**	4.98[b]	5.65	0.67	5.15[b]	−0.50
$(CH_3)_2CH$, **31**	5.53[e]	5.83	0.30	6.43[e]	0.60
CH_3CH_2, **32**	8.41[c]	8.67[c,d]	0.26		
33					
$(CH_3)_3C$, **31**	8.52[b]	8.72	0.20	8.87[b]	0.15

[a] Solvent CCl_4 unless otherwise indicated. [b] Reference 12. [c] Reference 16. [d] Solvent $CDCl_3$. [e] Reference 15.

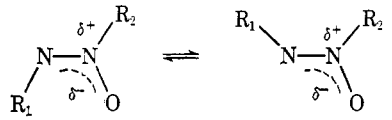
It is evident from the proton shift data that the difference in shielding between the near and far protons of *trans*-azoxyalkanes ($\Delta\delta_{n-f}$) decreases in the order primary, secondary, tertiary. Likewise $\Delta\delta_{n-f}$ not unexpectedly decreases with the distance of the proton from the perturbing NNO center: α-H > β-H. A less regular but similarly well-defined trend is followed by the shift differences between H_f and the corresponding azo protons (Δ_{azo-f}). Primary H_f azoxy protons are considerably upfield from the azo derivative hydrogens, while tertiary azoxy hydrogen is found equally far downfield.

The origin of these shift values is suggested by the results of Table II. Three separate $\Delta\sigma_{n-f}{}^T$ quantities are tablulated for *trans*-azoxymethane (**27**). Methyl hydrogens experience the greatest differential shielding in the conformation represented by **27a** (0.65 ppm), the least by conformation **27b** (0.13 ppm), and an intermediate value for a 50:50 mixture (0.39 ppm). Inspection of models suggests that stepwise replacement of hydrogen by substituents at C-5 (H_f) should progressively favor conformation **27b**. Thus primary and secondary C-5 might be expected to promote a relatively high population of conformer **29**, while tertiary and quaternary C-5 would favor rotamer **30**. These conformational



29 **30**

preferences would seem to be reflected by the observations listed in Table III. In view of the correlations described here, the nmr spectra of cis–trans pairs **31**–**33** deserve comment.



31, $R_1 = i$-Pr; $R_2 = i$-Pr
32, $R_1 = CH_3$ or C_2H_5; $R_2 = C_6H_5$
33, $R_1 = C_6H_5$; $R_2 = CH_3$ or C_2H_5

As discussed above the conceptual transformation of a conformationally mobile trans acyclic azoxyalkane (**16**) to rigid cis isomers (**18**) causes a slight downfield shift of H_n but a marked paramagnetic shift of H_f. The minor change in H_n may be attributed to electron density effects, while we have argued that the inflexibility of the bicyclic system provides a conformational rationale for the altered pmr resonance of H_f.

Inversion of acyclic azoxy configuration causes yet a different set of proton shifts. If both substituents are alkyl, for example isopropyl (**31**, trans → cis), H_f remains essentially unchanged, while H_n displays an 0.58-ppm downfield shift (*cf.* structures **16** and **26**). The isopropyl derivative no doubt experiences a considerable degree of steric congestion in the cis configuration and a corresponding measure of conformational constraint. The relative paramagnetic position of H_n, in this case, is most likely a consequence of van der Waals deshielding,[45] while the stationary value for H_f may reflect a balance between two opposing effects. On the one hand, a high population of conformation **30** results

(44) (a) J. Meinwald and A. Lewis, *J. Amer. Chem. Soc.*, **83**, 2769 (1961); K. B. Wiberg, B. R. Lowry, and B. J. Nist, *ibid.*, **84**, 1594 (1962); A. Rassat, C. W. Jefford, J. M. Lehn, and B. Waegell, *Tetrahedron Lett.*, 233 (1964); K. L. Williamson, T. Howell, and T. A. Spencer, *J. Amer. Chem. Soc.*, **88**, 325 (1966); (b) J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution NMR Spectroscopy," Vol. 2, Pergamon Press, Oxford, 1966, pp 672 and 693; (c) S. Sternhell and J. R. Wilmshurst, *Aust. J. Chem.*, **18**, 1759 (1965).

(45) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, p 189; I. Fleming and D. H. Williams, "Spectroscopic Methods in Organic Chemistry," McGraw-Hill, London, 1966, p 85.

in the alteration of H_f/NNO geometry from a U to a skew relationship (**27b** → **27a**) in the trans to cis isomerization. An upfield shift should be the consequence. Van der Waals deshielding of a similar magnitude, operating mutually for H_n and H_f, could reverse the conformation effect causing a near net zero shift.

A third situation arises for the trans → cis conversion of an acyclic monophenyl azoxy derivative. In all cases consistent upfield alkyl proton shifts are observed (*i.e.*, **32**, **33**, trans → cis; $\Delta\delta_{alkyl}{}^{upfield}$ = 0.17–0.34 ppm).[16] Steric considerations require that the phenyl rings twist from planarity with the NNO moiety. Any conformationally determined downfield effects at CH_3 or C_2H_5 are clearly overwhelmed by the well-known diamagnetic influence of the aromatic π system.[16,44c]

A more definitive analysis awaits the availability of an appropriate series of geometrically constrained azoxyalkanes in connection with conformation studies.

Experimental Section

General. Melting points were taken on a Gallenkamp apparatus and are uncorrected. Spectra were recorded by means of the following instruments: infrared, Perkin-Elmer 257; proton nmr, Varian A60-A; carbon-13 nmr, Varian HA-100 or Bruker HX-90 E. Combustion analyses were performed by the Scandinavian microanalytical Laboratory, Herlev, Denmark. Calculations were carried out on an IBM-370 computer.

Unsaturated *N*-Phenylurazole Adducts 4. The following is a general procedure which applies to all adducts described in Table IV. All operations with the red triazolinedione were carried out under nitrogen.

Gaseous nitrogen tetroxide was passed through a narrow tube into a cold (0°) slurry of 4-phenylurazole (35.0 g, 196 mm) and anhydrous sodium sulfate (50 g) in methylene chloride (1800 ml) until all the urazole had dissolved. The solution was maintained at 0° during the reaction. Sodium sulfate was removed by filtration and the clear, red filtrate evaporated to dryness at reduced pressure under nitrogen. The red crystalline residue was taken up in acetone (50 ml).

Cyclic diolefin (200 mm) dissolved in dry acetone (20 ml) was added dropwise to the resulting red solution at room temperature. In most cases the discharge of color was nearly instantaneous. For a few dienes it is necessary to stir the reaction mixture at room temperature or over a steam bath for 10–15 min before the red color gives way to light yellow. Evaporation of the solvent under reduced pressure leads to a light yellow solid. In all cases the nmr spectrum of the crude product was virtually identical with the recrystallized material. Once washed with a small, cold portion of acetone, this preparation is usually suitable for further transformation. For recrystallization solvent and physical properties see Table IV. The *N*-methyl adducts were prepared similarly.

Hydrogenated Adducts 2. The following details are typical. A solution of the cyclopentadiene adduct **4** (*n* = 1, 12.6 g, 51.8 mm) in ethyl acetate[46] (520 ml) and 10% Pd/C (585 mg) was hydrogenated under *ca.* 60 lb of pressure on a Paar hydrogenation apparatus. Hydrogen was absorbed rapidly during the first 10 min. It was taken up only slightly in the next 3–4 hr. Uptake: 1225 ml at 18° and 760 mm; calculated for one double bond, 1235 ml. The mixture was filtered and the clear solution concentrated *in vacuo* to give a white solid. Nmr spectra of the hydrogenates were virtually superimposable with those of recrystallized samples. Yields and other data are listed in Table IV.

***cis*-Azoxyalkanes.** Both of the following methods represent the general procedure.

Method A. *N*-Phenyl Adducts. A mixture of tricyclic adduct **2** (*n* = 4, 75.3 g, 264 mm), ethylene glycol (690 ml), and a solution of potassium hydroxide (105.8 g, 1886 mm) in distilled water (690 ml) was refluxed for 24 hr.[47a] Aqueous hydrogen peroxide (30%, 1205 ml) was added dropwise over a period of 3 hr to the refluxing reaction mixture. The original pale yellow solution turned dark brown and then finally yellow. Removal of aniline by steam distillation left a residual yellow solution. The latter was extracted four times with chloroform (2 l. total) and combined extracts dried over calcium chloride and then magnesium sulfate. Removal of solvent under reduced pressure afforded a brown semisolid (39.0 g, 250 mm, 95%). Crystallization from ether–hexane (1:2) gave white solid (30.0 g, 195 mm, 78%), mp 133–134°. All purified azoxy products are white crystalline solids, some of which are hygroscopic (*i.e.*, *n* = 1, 3).

Method B. *N*-Methyl Adducts. A mixture of *N*-methyltriazolinedione adduct **2** (5 mm, *ca.* 1 g) and 35% hydrogen peroxide (30 ml) was treated with a solution of KOH (85% KOH, 20.0 g, *ca.* 350 mm) in distilled water (20 ml). The addition should be conducted with caution as it is frequently exothermic, particularly when larger quantities are employed. The reaction mixture was heated to 80–95° for 1 hr.[47b] During this period 35% H_2O_2 (25 ml) was added dropwise to maintain an excess of oxidant. The cooled mixture was extracted four times with chloroform (4 × 50 ml). Extracts were combined and dried over calcium chloride and then magnesium sulfate. Removal of solvent *in vacuo* produced an off-white solid or a light-brown oil. Nmr spectra of crude products revealed only azoxy compounds.

Each azoxyalkane possesses strong absorption in the infrared and the ultraviolet characteristic of the NNO functionality (Chart I). For yields and other physical data *cf.* Table IV.

Chart I

	1	**2**	**3**	**4**	**11**	**12**	**13**
ir (CCl_4), cm^{-1}	1287	1295	1295	1305	1280	1232	1225
	1514	1501	1509	1508	1510	1256	1250
						1498	1484
uv (96% EtOH)	227	230	233	235	223	231	232
λ_{max}, nm (ϵ)	(6670)	(6630)	(6180)	(6600)	(6070)	(6730)	(7418)

Cyclopropylazoxyalkane 12. 6,7-Diazatricyclo[3.2.2.0^{2,4}]-6-nonene *N*-Oxide. (a) Cycloheptatriene–Methylurazole Adduct (41). Cycloheptatriene (4.7 g, 61 mm) was added dropwise to a red solution of 3-methyl-1,2,4-triazoline-3,5-dione (6.8 g, 61 mm) in acetone (35 ml) at room temperature. The discharge of color was instantaneous. Evaporation of the yellow product solution to dryness at reduced pressure gave pale yellow crystals (9.0 g, 72%), mp 140–155°. Crystallization (ethyl acetate) afforded white needles (8.0 g, 64%): mp 178–180°; nmr ($CDCl_3$, TMS internal standard) τ 4.00 (2 H, t, J = 3.5 Hz), 4.90 (2 H, m), 7.03 (3 H, s), 8.42 (2 H, m), 9.32 (1 H, t), and 9.70 (1 H, t). The latter two bands are the AB part of an ABM_2 pattern: J_{AB} = 7.0 Hz; J_{AM} = 7.0 Hz; J_{BM} = 4.0 Hz.

Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.5; H, 5.4; N, 20.5. Found: 58.6; H, 5.5; N, 20.5.

(b) Preparation of Saturated Adduct 42 by Hydrogenation of 41. Hydrogenation (**41**: 5.7 g, 28 mm) takes place smoothly (EtOAc) as described above. Filtration, solvent removal, and recrystallization (EtOAc) lead to white needles (5.6 g, 27 mm, 96%): mp 115–116°; nmr ($CDCl_3$, TMS internal standard) τ 5.38 (2 H, broad s), 6.88 (3 H, s), 7.83–8.84 (4 H, m), 9.07–9.50 (4 H, m).

Anal. Calcd for $C_{10}H_{13}N_3O_2$: C, 58.0; H, 6.3; N, 20.2. Found: C, 58.0; H, 6.4; N, 20.3.

(c) Cyclopropylazoxyalkane 12. See *cis*-azoxyalkanes, method B, and Table IV.

Cyclobutylazoxyalkane 13. 7,8-Diazatricyclo[4.2.2.0^{2,5}]-7-decene *N*-Oxide. (a) Cyclooctatetraene Dibromide–Methylurazole Adduct (43). An acetone solution (100 ml) of *N*-methyltriazolinedione (from *N*-methylurazole, 14.0 g, 122 mm) was prepared as described above for the *N*-phenyl derivative. Cyclooctatetraene dibromide[48] (32.2 g, 122 mm) in dry acetone (100 ml) was added dropwise at −50 to −70°. The discolored solution was warmed to room temperature and evaporated to dryness. Light yellow crystals (37.3 g, 99 mm, 81%) with an nmr identical with that of the analytical sample were obtained. Crystallization (CH_3OH) produced a white solid (**43**): mp 225–226°; nmr ($CDCl_3$, TMS) τ 3.25 (1 H, septet), 3.65 (1 H, septet), 5.05 (2 H, m), 5.35 (1 H, m), 5.85 (1 H, m), 6.50 (2 H m), 7.05 (3 H, s).

Anal. Calcd for $C_{11}H_{11}N_3O_2Br_2$: C, 35.0; H, 2.9; N, 11.2; Br, 42.4. Found: C, 35.0; H, 3.1; N, 11.3; Br, 42.0.

(b) Reduction of Dibromide 43 to Diene 44. Dibromide **43**

(46) In order to effect complete solution, adducts **2** (*n* = 3 and 4) were hydrogenated in EtOH/$CHCl_3$ (5:1).

(47) (a) The more strained *N*-phenyl adducts (**2**, *n* = 1 and 2) may be converted in shorter reaction times, 1–6 hr; (b) likewise, *N*-methyl adducts **2** (*n* = 3 and 4) require a longer reaction period, 2.5 hr. A correspondingly greater quantity of H_2O_2 is added in both of the previous cases in order to maintain dropwise addition of the oxidant.

(48) A. C. Cope and M. Burg, *J. Amer. Chem. Soc.*, **74**, 168 (1952).

Table IV. Yields and Physical Properties of *N*-Phenyl Adducts 2 and 3 and Azoxyalkanes

Compd	*n*	Yield, %[a]	mp, deg (cryst solvent)	Lit. mp, deg	^{1}H nmr, τ (TMS)[c]	Calcd/found C	Calcd/found H	Calcd/found N
4 (R = C_6H_5)	1	84 (98)	145–147 (C_2H_5OH)	142–144[20a]	2.77 (5 H, s) 3.70 (2 H, unsym t) 4.99 (2 H, t) 7.74 (1 H, unsym, d) 8.15 (1 H, unsym, d)	64.6/64.6	$C_{13}H_{11}N_3O_2$ 4.6/4.7	17.4/17.2
	2	61 (69)	172–174 (CH_3CN)	172–174[20a]	2.52 (5 H, s) 3.43 (2 H, unsym, t) 5.00 (2 H, broad s) 7.5–8.6 (4 H, m)	65.9/65.8	$C_{14}H_{13}N_3O_2$ 5.1/5.0	16.5/16.3
	3	70 (93)	221–223 (CH_3CN)		2.3–2.8 (5 H, m) 3.72 (2 H, q) 5.03 (2 H, m) 7.8–8.5 (6 H, m)	66.9/66.8	$C_{15}H_{15}N_3O_2$ 5.6/5.5	15.6/15.8
	4	53 (70)	203–204 (CH_3OH)	207–208[20a]	2.1–2.7 (5 H, m) 3.77 (2 H, q) 4.95 (2 H, m) 7.0–8.7 (8 H, m)	67.8/67.6	$C_{16}H_{17}N_3O_2$ 6.0/5.8	14.8/14.7
2 (R = C_6H_5)	1	95 (91)	139–140 (EtOAc)		2.75 (5 H, s) 5.47 (2 H, broad s) 8.18 (6 H, broad s)	64.2/64.2	$C_{13}H_{13}N_3O_2$ 5.4/5.4	17.3/17.3
	2	95	216–217 (EtOAc)		2.49 (5 H, broad m) 5.50 (2 H, broad s) 7.5–8.5 (8 H, m)	65.4/65.4	$C_{14}H_{15}N_3O_2$ 5.9/6.1	16.1/16.1
	3	91	214–215 (EtOAc)		2.3–2.8 (5 H, m) 5.33 (2 H, broad s) 7.6–8.7 (10 H, m)	66.4/66.6	$C_{15}H_{17}N_3O_2$ 6.3/6.4	15.5/15.6
	4	93	178–180 (EtOAc)		2.0–2.7 (5 H, m) 5.20 (2 H, broad s) 7.3–8.6 (12 H, m)	67.3/67.5	$C_{16}H_{19}N_3O_2$ 6.7–6.9	11.2/11.1
7	1	78 (93)	93–95 (Et_2O–hexane)		5.32 (2 H, broad s, hw = 10 Hz) 7.6–8.5 (6 H, m); (4.85, hw = 5.5 Hz)	53.5/53.3	$C_5H_8N_2O$ 7.2/7.2	24.9/24.7
8	2	78 (100)	158–159 (C_2H_5OH)		5.55 (2 H, broad s, hw = 13 Hz) 8.17 (18 H, broad s); (4.90, hw = 6.5 Hz)	57.1/57.0	$C_6H_{10}N_2O$ 8.0/7.8	22.2/22.0
9	3	82 (97)	176–177 (Et_2O–hexane)		5.65 (2 H, broad s, hw = 12 Hz) 7.7–8.4 (10 H, broad m); (4.94, hw = 9.5 Hz)	59.9/59.6	$C_7H_{12}N_2O$ 8.6/8.8	20.0/19.8
10	4	78 (95)[b]	133–134 (Et_2O–hexane)		5.55 (2 H, broad s, hw = 14 Hz) 7.5–8.8 (2 H, broad m); (4.91, hw = 11.2 Hz)	62.3/62.3	$C_8H_{14}N_2O$ 9.1/9.1	18.1/17.9
11		78 (88)	55–56 (Et_2O–hexane)		5.61 (2 H, d, hw = 6 Hz) 7.40 (1 H, broad s) 8.0–8.2 (5 H, s); (4.77)	61.7/61.7	$C_7H_8N_2O$ 5.9/6.1	20.5/20.3
12		81 (100)	137–138 (C_2H_5OH)		5.32 (2 H, broad s, hw = 11 Hz) 8.0–8.8 (6 H, broad m) 8.7–9.3 (2 H, broad m); (4.80[e])	60.9/61.0	$C_7H_{10}N_2O$ 7.3/7.2	20.3/20.4
13		80 (100)	149–150 (Et_2O)		5.50 (2 H, broad s, hw = 15 Hz) 7.0–8.6 (10 H, broad m); (5.50)	63.1/63.3	$C_8H_{12}N_2O$ 7.9/7.9	18.4/18.5

[a] Values in parentheses represent crude yields for Method B; those not in parentheses are recrystallized. Isolated materials in each case, however, possessed nmr spectra virtually identical with the analytical sample. Yields for Method A are given in ref 17. [b] Method A. [c] Solvent $CDCl_3$ unless otherwise noted. [d] The final parenthetical band position belongs to the bridgehead ^{1}H chemical shifts (τ) for the corresponding azoalkane. All are broad singlets; *cf.* ref 29. [e] CCl_4; ref 27b.

(8.6 g, 23 mm) was added as a solid to a refluxing mixture of zinc–copper couple[49] (3.0 g, 46 mm) and absolute ethanol (50 ml). The reaction solution, boiled for 8 hr, was filtered hot and stripped of solvent to give an amber oil. This was taken up in methylene chloride (25 ml), washed twice with water (20 ml), and dried over calcium chloride. Solvent removal resulted in a colorless oil that crystallized when scratched with a glass rod. The near white powder (**44**) (3.8 g, 18 mm, 77%) was spectroscopically (ir) identical with the analytical sample. Double crystallization (methylcyclohexane) afforded silky white needles: mp 131–132°; nmr ($CDCl_3$, TMS) τ 4.02 (2 H, t), 4.13 (2 H, s), 5.21 (2 H, q), 6.82 (2 H, d), 7.10 (3 H, s).

Anal. Calcd for $C_{11}H_{11}N_3O_2$: C, 60.8; H, 5.1; N, 19.4. Found: C, 60.8; H, 5.2; N, 19.0.

(c) Hydrogenation of Diene 44 to Saturated Adduct 45. Reaction of **44** (2.5 g, 11 mm) proceeds on the Paar hydrogenation apparatus as described above (EtOAc, 200 ml) to yield white crystals (2.4 g, 11 mm, 100%). A portion crystallized (ether–petroleum ether) as colorless needles (2.0 g, 9.0 mm, 90%): mp 70–71°;

(49) R. D. Smith and H. E. Simmons, *Org. Syn.*, **41**, 72 (1961).

nmr ($CDCl_3$, TMS) τ 5.81 (2 H, m), 6.98 (3 H, s), 7.18 (2 H, m), 7.4–8.3 (8 H, m).

Anal. Calcd for $C_{11}H_{15}N_3O_2$: C, 59.7; H, 6.85; N, 19.0. Found: C, 59.9; H, 6.79; N, 19.1.

(d) Cyclobutylazoxyalkane 13. See *cis*-azoxyalkanes, Method B, and Table IV. For computations *cf.* ref. 42 for the CNDO paramaterization.

Azoxymethane (27a–b) and 2,3-Diazabicyclo[2.1.1]-hexene 2-*N*-Oxide (28). For the two conformations of *trans*-azoxymethane, **27a** and **27b**, five simplifying structural assumptions have been made: (1) r(CH) = 1.09 Å, (ii) tetrahedral carbon angles (109.47°), (iii) $\angle N_2N_1C_4 = \angle N_1N_2C_5$,[50] (iv) $r(N_1C_4) = r(N_2C_5)$,[50] and (v) planarity for all atoms except the four methyl hydrogens H-7, H-8, H-10, and H-11. Remaining bond lengths and angles have been derived by minimization of the bonding energy with respect to molecular geometry (**27a**/**27b**): r(NN) = 1.220/1.220 Å, r(NO) = 1.267/1.272 Å, r(NC) = 1.383/1.388 Å, $\angle$NNO = 125.8/126.7°, $\angle$NNC = 117.7/115.5°. A fixed geometry calculation for *N*-oxide (**28**) made use of the following input: r(NN) = 1.23 Å, r(NO) = 1.25 Å, r(NC) = 1.53 Å, r(CH) = 1.10 Å, $\angle$NNO = 121.4°.

(50) Separately minimized NNC bond angles fall within the very narrow range 117 ± 2.4°.[39] This compares well with the 115.5 and 117.7° angles for **27a** and **27b** obtained by using assumption iii. Likewise separately minimized r(NC) distances fall within the limits 1.384 ± 0.007 Å.[39]

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A Proton Nuclear Magnetic Resonance Study of 2-Aryl-2-norbornyl Cations. The Onset of "Nonclassical" Stabilization[1]

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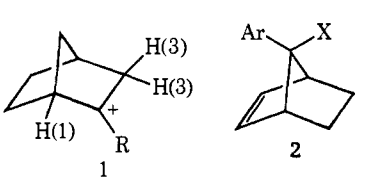
Abstract: A plot of the nmr chemical shifts of H(1) *vs.* H(3) (average) for a series of substituted 2-aryl-2-norbornyl cations shows a marked deviation from linearity for substituents on the aryl group more electron withdrawing than hydrogen. A similar plot for 2-arylbicyclooctyl cations is very closely linear over a wider range of substituents although some deviation is apparent for *p*-trifluoromethylphenyl. Calculation of the maximum concentration of rearranged classical ion that could be in equilibrium with unrearranged classical ion indicates that a rapid equilibration between classical ions accounts for no more than 1% of the deviation for the norbornyl cations. The results are consistent with the onset of C(1)–C(6) σ bond delocalization or "nonclassical" stabilization in those norbornyl cations more electron demanding than the 2-phenylnorbornyl cation. A rearrangement which exchanges H(1) and H(6) endo but not H(6) exo is detected in these cations by the "double irradiation spin saturation transfer" (DISST) technique. This experiment also reveals a large nuclear Overhauser effect (*ca.* 50% enhancement) for geminal hydrogens H(6) exo and endo.

Searching for nonclassical character in the norbornyl cation (**1**, R = H) has been a favorite pastime for hosts of chemists for many years. The often elusive, and sometimes recalcitrant, nature of the problem has extracted an enormous expenditure of time and energy, has trained a generation (perhaps two) of physical-organic chemists in the difficult art of casting subtle structural questions in experimental form, and has resulted in a mind-boggling flood of literature. To contribute to the flood at this point may seem curious, or even superfluous, but we enjoy making our ripple as much as the next man, and, because we had so much to learn, we learned much from the effort. Most of the literature has been reviewed recently,[2] and in an earnest desire to avoid confusing both ourselves and our readers, we have chosen to restrict ourselves to a brief discussion of the two contributions which seem to delineate most clearly the limited aspect of the nonclassical ion problem to which we want to direct our attention. We will try to avoid a pitfall of this approach, unrecognized bias, by stating our bias where it seems important and we are able.



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From an extensive study of the stable norbornyl cation (**1**, R = H) in solution in powerful acids, Olah

(1) Abstracted in part from the Ph.D. thesis of Anthony D. Wolf, Michigan State University, 1972. Supported by the National Science Foundation under Grants GP 10734 and GP 27994.

(2) H. C. Brown, *Chem. Brit.*, 199 (1966), *Chem. Eng. News.*, **45**, 87 (1967); G. D. Sargent, *Quart. Rev., Chem. Soc.*, **20**, 299 (1966); P. D. Bartlett, "Nonclassical Ions," W. A. Benjamin, New York, N. Y., 1965; T. D. Swartz, "Solvolytic Studies of Brendyl, Brexyl, and Norbornyl Systems," Ph.D. Thesis, Johns Hopkins University, Baltimore, Maryland, 1966; G. D. Sargent in "Carbonium Ions," Vol. III, G. A. Olah and P. v. R. Schleyer, Ed., Wiley-Interscience, New York, N. Y., 1972, p 1099.