Structural Studies of *N*-Alkyl-*N*-nitrosoanilines by Nuclear Magnetic Resonance[1a,b]

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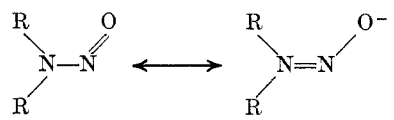
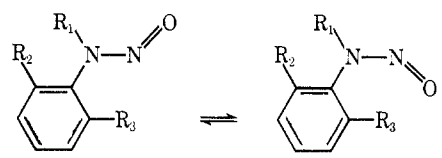
Configurations, and in most cases preferred conformations, were assigned to nine *N*-alkyl-*N*-nitrosoanilines from analysis of their nmr spectra. The syn:anti ratio was found to be most sensitive to the size of the *N*-alkyl substituent, although ortho substitution was also found to alter these ratios somewhat. Conformations of *N*-isopropyl groups were found to be very sensitive to ortho substitution on the ring. The enthalpy of activation for rotation about the N–N bond was determined for *N*-isopropyl-*N*-nitrosoaniline and was found to be similar to previously determined values for *N*-nitrosodimethylamine and *N*-benzyl-*N*-nitroso-2,6-xylidine, lending further support to the conclusion that the benzene ring contributes little to the partial double bond character of the N–N bond in this compound.

Nuclear magnetic resonance has been used extensively to study problems arising from restricted rotation about partial double bonds. *N*-Nitrosamines have been shown previously[2] to exhibit restricted rotation due to contributions from a polar resonance form. This barrier to rotation is readily observed in the nmr spectra of these compounds since the R groups,



located in different magnetic environments, have differing chemical shifts. In the *N*-nitrosoanilines, the partial double bond character of the N–N bond gives rise to two isomeric forms, syn and anti,[3] which are in dynamic equilibrium at room temperature.



syn anti

The nmr spectra of the nitrosoanilines give the patterns expected of molecules with partial double bonds, with the *N*-alkyl substituents of each isomer giving rise to its own set of resonances. Assignment of peaks as arising from either the syn or anti isomer has been greatly simplified by the earlier work of Karabatsos and Taller,[3] who showed that the protons usually resonate at higher fields when cis than when trans to the oxygen.

In coordination with our uv work on these compounds,[1a] we have extended the earlier work of Karabatsos and Taller[3] to a series of nine *N*-alkyl-*N*-nitrosoanilines. Configurational assignments (syn:anti) have been made in all cases; for most compounds, conformational assignments were also possible. The energy barrier restricting rotation about the N–N bond was also determined for one of the nitrosoanilines.

Experimental Section

Preparation of the nitrosoanilines has already been reported.[1a] They were either vacuum distilled or recrystallized from absolute ethanol prior to use.

All nmr spectra were obtained on a Varian Associates, Inc., Model A-60 spectrometer equipped with a V-6057 variable temperature system and a Hewlett–Packard side-band oscillator calibration. Chemical shifts were obtained on 0.1 mol-fraction solutions in CCl_4 relative to TMS as an internal standard and the τ values are accurate to ± 0.02. The neat compounds (or saturated CCl_4 solutions) were used for determination of isomer population by integration of the spectra; the reported values are accurate to $\sim 5\%$.

High temperature coalescence studies on **4** were carried out on a 0.2 mol-fraction solution, with 1-bromonaphthalene as solvent and hexamethylbenzene as the internal reference. Chemical shift separations for ethylene glycol and methanol were used to measure temperatures above and below ambient, respectively; relative temperature variation during the coalescence work was less than $\pm 1°$. Line shape measurements were run at a sweep rate of 1 cps.[2] The rf field amplitude was redetermined for each temperature and kept below the value where saturation broadening of signals occurred. All spectra were taken at least four times at each temperature to ensure no field or temperature variations during a given sweep.

The calculation of nmr line shapes was accomplished using the method of Alexander,[4] with an adaptation of a program graciously provided by Dr. J. D. Roberts, California Institute of Technology. The spectra were calculated on an IBM 7040 computer and plots of these spectra were obtained on a Calcomp plotter.

Results

The *N*-alkyl-*N*-nitrosoanilines studied in this work are listed in Table I, along with the syn:anti ratios obtained by integration of the nmr spectra. With **3** and **5**, the very low population of one isomer prevented determination by integration, and the ratios were therefore estimated. In order to verify assign-

TABLE I

ISOMER POPULATIONS OF THE *N*-NITROSOANILINES[a]

Compd	R_1	R_2	R_3	syn:anti
1[b]	CH_2	CH_2	H	100:0
2	CH_3	H	H	100:0
3	C_2H_5	H	H	96:4
4	*i*-C_3H_7	H	H	65:35
5	*tert*-C_4H_9	H	H	1:99
6	CH_3	CH_3	H	83:17
7	*i*-C_3H_7	CH_3	H	36:64
8	CH_3	CH_3	CH_3	78:22
9	*i*-C_3H_7	CH_3	CH_3	29:71

[a] R groups refer to syn and anti structures in the text. [b] Fused ring analog, *N*-nitrosoindoline.

(1) (a) *Cf.* J. T. D'Agostino and H. H. Jaffé, *J. Amer. Chem. Soc.*, **92**, 5160 (1970). (b) Supported in part by National Science Foundation Grant GP 7551. (c) Procter & Gamble Fellow, 1967–1968.

(2) C. E. Looney, W. D. Phillips, and E. L. Reilly, *ibid.*, **79**, 6136 (1957).

(3) G. J. Karabatsos and R. A. Taller, *ibid.*, **86**, 4373 (1964).

(4) S. Alexander, *J. Chem. Phys.*, **37**, 967 (1962).

TABLE II

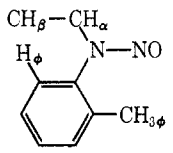
PROTON CHEMICAL SHIFTS (τ VALUES) OF NITROSOANILINES

	α CH_3		α CH_2		α CH		β CH_3		φ CH_3		φ H	
Compd	syn	anti	syn	anti	syn	anti	syn	anti	syn	anti	syn	anti
1			6.86						5.96[a]		2.80[b]	
2	6.67										2.13–2.89[c]	
3			6.01				8.69				2.57[b]	
4					4.91	5.13	8.85	8.57			2.64	2.98–3.25[c]
5							8.68	8.46				2.69[b]
6	6.74	6.01							7.78	8.08	2.75[d]	3.17–3.33[c]
7					5.00	5.23	8.91	8.55 8.47[e]	7.81	8.07	2.79[b]	3.12–3.30[c]
8	6.80	6.09							7.89	8.06	2.86	2.97
9					5.45	5.73	8.89	8.42	7.87	8.05	2.85	2.96

[a] *o*-Methylene protons. [b] Center of multiplet pattern. [c] Region of absorbance for the ortho proton(s). [d] Position of the larger peak in a distorted doublet. [e] Two doublets appear.

ment of these weak-intensity peaks as absorption of one isomeric form, the spectra of **3** and **5** were recorded at higher temperature (<100°); the weak signals were found to collapse into the more intense isomer peak for both cases and, upon cooling, the weak signals reappeared, thus confirming their assignment as due to isomeric absorption.

The nmr chemical shift data for the nitrosoanilines were obtained from CCl_4 solutions and appear in Table II. The notation used to distinguish the various protons is shown below, with each proton tabulated as syn or anti with respect to the isomeric form in which it appears.



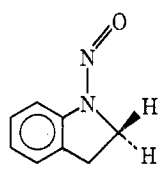
Discussion

A. Configurational Assignments.—The isomer ratios obtained for the nitrosoanilines are consistent with our knowledge of steric effects on the relative stabilities of geometric isomers.[5] The orientation of the NNO group is apparently most sensitive to the size of the R group to which it is cis; when R is methyl, the molecule exists 100% in the syn form, while changing R from ethyl to isopropyl results in an appreciable population of the anti isomer, and a *tert*-butyl group forces the molecule to exist almost completely (~99%) in the anti form.

The population of the anti isomer may also be increased by the substitution of *o*-methyl groups in the benzene ring; such substitution forces the ring to twist out of the NNO plane, thereby reducing the effective steric size of the phenyl group. This shifts the syn:anti equilibrium slightly in the direction of the anti isomer, accounting for its increased population. A second *o*-methyl group appears to be much less effective than the first in altering the syn:anti ratio.

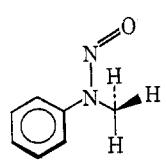
B. Conformational Analysis.—By studying the changes in chemical shift for chemically equivalent protons in the *N*-nitrosoaniline series, one can obtain information about the preferential orientation of such protons in the overall geometry of the molecule. In the case of the nitrosoanilines, this is possible because the π electron clouds of the NO and phenyl groups have anisotropic effects which may enhance (or diminish) the shielding properties in the environment of a given proton.

In the nitrosoanilines, the α protons of *N*-alkyl substituents appear to be most sensitive to these anisotropic effects. Table II reveals that the *N*-alkyl protons of **1** resonate at higher field strengths than are observed for such protons in any of the other nitrosoanilines. This is not surprising, since our knowledge of the geometry of this molecule requires that the α-methylene protons lie above and below the plane of the NNO and phenyl groups. In this configuration, these protons are relatively shielded by the anisotropy of both groups and therefore resonate at comparatively high field strengths.



syn-**1**

From a comparison of the ultraviolet absorption spectra of **1** and **2**, it has been shown[1a] that the benzene ring in **2** is not coplanar with the NNO group. The α-methyl protons (which characteristically have higher chemical shifts than methylene protons) resonate 0.19 ppm *lower* in **2** than in **1**. This can best be explained by considering that addition of a third proton to an oriented α-methylene group which staggers the oxygen requires that it be in the NNO plane and not far removed from the plane of the benzene ring. When the chemical shift of this deshielded proton is averaged with the relatively shielded values comparable to those of **1**, the result for the freely rotating methyl group is a chemical shift slightly lower than that observed for **1**.



syn-**2**

Conformational analysis of *syn*-**3** requires some information from the aliphatic nitrosamines. Table III lists the chemical shifts of α protons on methyl,

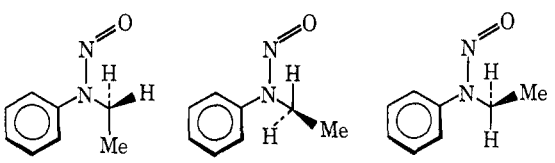
(5) R. T. Morrison and R. N. Boyd, "Organic Chemistry," Allyn and Bacon, Boston, Mass., 1962.

TABLE III
EFFECT OF A BENZENE RING ON THE CHEMICAL SHIFTS OF α PROTONS

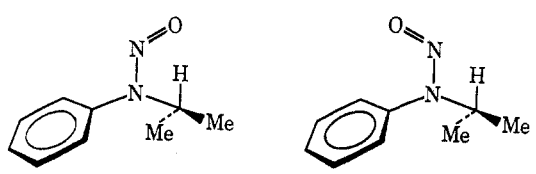
R group	RMeNNO,[a] τ	RPhNNO, τ	Δτ
$-CH_3$[b]	7.04	6.67	0.37
$-C_2H_5$[b]	6.48	6.01	0.47
$-i-C_3H_7$[b]	4.97	4.91	0.06
$-i-C_3H_7$[c]	5.15	5.13	0.02

[a] These data taken from ref 3. [b] R group is cis to the oxygen. [c] R group is trans to the oxygen.

ethyl, and isopropyl groups for aliphatic and aromatic nitrosamines. The tabulation is intended to show that, for R group cis to the oxygen, the presence of the benzene ring significantly deshields the α protons in **2** and **3**, while having very little effect on the chemical shift in **4**. The similar behavior of **2** and **3** to the presence of the ring suggests that, of the three most likely conformations for the ethyl group given below, structure A contributes little, since such an orientation cannot account for the 0.47-ppm shift downfield that is observed. (This same conclusion may be reached by comparing the α-methylene chemical shifts of **3** and **1**.) While there is no evidence which allows us to conclusively distinguish between the remaining two conformations, the close similarity of the ultraviolet spectra of **2** and **3** suggests that introduction of a β-methyl group does not cause an increased twist of the benzene ring, as would be expected in B. Furthermore, the results of analysis on **4** suggest that structure B would give rise to a greater deshielding of the α protons than is actually observed. We therefore favor structure C as the preferred conformation for *syn*-**3**.[6]



The absence of significant deshielding for the α-methine protons in both *syn*- and *anti*-**4** relative to their aliphatic analogs (Table III) suggests that the α proton spends little time in the environment of the phenyl group for either isomer. For nitrosamines with an isopropyl group cis to the oxygen, Karabatsos[3] has shown that the α proton spends most of its time eclipsing the NO group, since this proton resonates at lower fields when cis than when trans to the oxygen, in contrast to α-methylene and α-methyl protons. By analogy with his observations,[3] we conclude that the α-methine proton of *syn*-**4** spends most of its time in the deshielding environment of the NNO plane. The marked similarity of α-proton chemical shifts in the *trans*-isopropyl compounds (Table III) allows the conclusion that the α proton is trans to the NO group in *anti*-**4**, by analogy to *syn*-methylisopropylnitrosamine.[3]

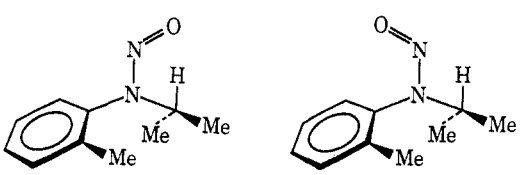


(6) Asterisks following a labeled structure indicate the preferred conformation.

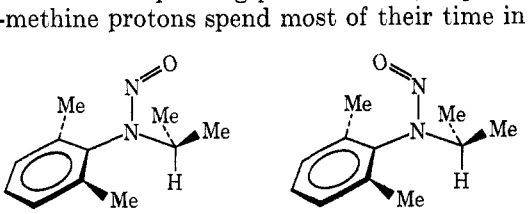
An examination of the phenyl protons in **4** indicates a pleasing agreement with observations from the uv spectrum of this compound. The phenyl pattern of *syn*-**4** approximates a singlet, in contrast to the more complicated multiplet patterns of *syn*-**2** and **3**. This observation is entirely consistent with our proposal[1a] of a highly twisted (probably >60°) benzene ring where the electronic interactions between the ring and NNO group are considerably reduced so that the ortho, meta, and para protons become more equivalent magnetically and the coupling between them is minimal.

Substitution of *o*-methyl groups on the benzene ring is expected to force the ring further out of the NNO plane and the spectra of **6** and **8** support this expectation. The aromatic protons give rise to a considerably simplified pattern which allows assignments of the signals arising from the syn and anti isomers. The small but definite upfield shift of the α-methyl signals (both syn and anti) in these compounds, relative to **2**, can be attributed to shielding from the twisted benzene ring. The increased shielding of these protons in **8** relative to **6** suggests that the benzene ring is more twisted in the former. The uv spectra of these two compounds support this conclusion.[1a]

The spectrum of **7** is unique among the nitrosoanilines studied because the two β-methyl groups of the anti isomer are magnetically nonequivalent, each giving rise to its own doublet; at 80°, the spectrum shows that the two doublets have coalesced into one averaged doublet for the anti isomer. This spectral behavior is similar to that observed for other highly substituted nitrosoanilines,[7] suggesting that rotation about the aromatic C–N bond is highly restricted in this isomer; hence the two β-methyl groups find themselves in differing aromatic environments with a rate of exchange which is slow on the nmr time scale so that each gives rise to its own distinct resonance. The largest contribution to this steric barrier appears to be the oxygen atom since the syn isomer failed to demonstrate any nonequivalence as far down as −60°. Comparison of chemical shifts for the α-methine protons in **7** with those in **4** suggests that they continue to remain close to the deshielding NNO plane for both isomers.



Finally, the 0.54- and 0.60-ppm field shifts for the α-methine protons of *syn*- and *anti*-**9**, respectively, relative to their corresponding positions in **4**, require that the α-methine protons spend most of their time in the

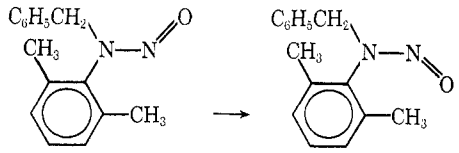


(7) A. Mannschreck and H. Muensch, *Tetrahedron Lett.*, 3227 (1968).

shielding environment of the benzene ring. Furthermore, molecular models show that steric interactions between the *o*-methyl and β-methyl groups of **9** are sufficient to force the β-methyl groups to stagger the NO group.

C. Determination of the Rotational Barrier in 4.—The partial double bond character of the N–N bond has already been shown[3] to give rise to syn and anti isomeric forms in **4**. In the room temperature nmr spectrum of this compound, the magnetic nonequivalence of the isopropyl groups gives rise to two doublets for the β-methyl protons. At higher temperature, these doublets are found to broaden and, at 113°, coalesce into one very broad signal. From a line-shape study of these coalescing doublets, it was possible to determine the enthalpy of activation ($\Delta H^{\pm}$) for the rotation. For the process *syn*-**4** → *anti*-**4**, $\Delta H^{\pm}$ = 25.8 ± 0.8 kcal/mol, while, for the process *anti*-**4** → *syn*-**4**, $\Delta H^{\pm}$ = 24.1 ± 1.1 kcal/mol.

These enthalpies of activation are not unlike other values which have been determined for nitrosamines. Blears[8] found the $\Delta H^{\pm}$ for dimethylnitrosamine (mol fraction = 0.21 in 1-chloronaphthalene) to be 24 kcal/mol, while Mannschreck, *et al.*,[9] obtained a $\Delta H^{\pm}$ of 24.2 kcal/mol (in CCl_4) for the following process.



The close agreement between the enthalpy of activation for **4** and other such determinations suggests that there is little contribution from the phenyl group to the partial double bond character of the N–N bond. This conclusion is not surprising, however, since we know from both nmr and uv spectra[1a] of **4** that electronic interactions between the ring and NNO group have been considerably reduced because of twisting.

Registry No.—**1**, 7633-57-0; **2**, 614-00-6; **3**, 612-64-6; **4**, 24642-83-9; **5**, 24642-84-0; **6**, 10596-01-7; **7**, 24690-69-5; **8**, 24699-12-5; **9**, 24699-13-6.

Acknowledgment.—The authors would like to thank Professor F. Kaplan for many helpful discussions.

(8) D. J. Blears, *J. Chem. Soc.*, 6256 (1964).

(9) A. Manschreck, H. Muensch, and A. Mattheus, *Angew. Chem.*, **5**, 728 (1966).

Notes

Mass Spectra of Dimethyl Fumarate and Maleate

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A recent review of stereoisomeric effects on mass spectra,[1] coauthored by one of us, carried an introductory statement, since repeated elsewhere,[2] that "the most striking instance ... of stereoisomers with markedly different mass spectra is that of dimethyl fumarate and maleate." We have since found the literature report that led us to make this statement to be in error.

The statement was based on a report that the most abundant ion in the spectrum of dimethyl fumarate occurs at mass 112, corresponding to the loss of CH_3OH, in contrast to 113 in the spectrum of the maleate.[3] We have located two published spectra of dimethyl fumarate but none of the maleate. The first of the fumarate spectra,[4] which presumably furnished the basis for the qualitative statement above,[3] shows the strongest peak at mass 112 and an intensity at 113 of 21.02% that at 112. The other, presented in bar-chart form, shows the strongest peak at 113, an intensity at 114 about 21% that at 113, and nothing at 112.[5] The paper in which the latter spectrum appeared stated that the authors had measured the spectra of dimethyl maleate as well as fumarate and called attention to some spectral differences between the isomers. However, they said nothing about comparative intensities at 113 or 112, and they did not report the maleate spectrum.

We have now measured the two spectra, which are shown in Table I. Intensities are expressed as %Σ24, with all values ≥0.5% reported here. Intensity at 112 on this scale is less than 0.1% in both spectra. Evidently, the original qualitative statement contrasting the spectra was based on an error in reading the mass scale.

Nonetheless, our spectra do show significant differences. In each spectrum, the most abundant ion is $[M - CH_3O]^+$, and this species breaks down further by losing CO, as shown by a metastable peak. The

$$68.3 \quad 113^+ \longrightarrow 85^+ + 28$$

intensities of the resultant fragment ions at masses 113 and 85 in the two spectra differ substantially and these differences, coupled with the difference in geom-

* Research Department, Standard Oil Co., Naperville, Ill. 60540.

(1) S. Meyerson and A. W. Weitkamp, *Org. Mass Spectrom.*, **1**, 659 (1968).

(2) F. Benoit, J. L. Holmes, and N. S. Isaacs, *ibid.*, **2**, 591 (1969).

(3) F. W. McLafferty, "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press, New York, N. Y., 1963, Chapter 7.

(4) Uncertified Mass Spectral Data, The Dow Chemical Co., Midland, Mich., 1963, Spectrum No. 1309.

(5) J. H. Bowie, D. H. Williams, P. Madsen, G. Schroll, and S.-O. Lawesson, *Tetrahedron*, **23**, 305 (1967).