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NUCLEAR MAGNETIC RESONANCE SPECTRA OF N-NITROSOURETHANS

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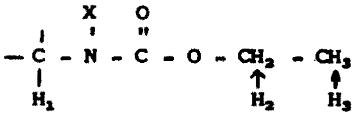
Despite long and continuing use of N-nitrosourethans as diazoalkane precursors, simple methods of monitoring the urethan-nitrosourethan conversion, and of non-destructively ascertaining product purity are not at hand. We report: (A) The nitrosation described by White (1) is applicable to a wide variety of urethans (2); (B) NMR comparison of urethans and N-nitroso derivatives permits qualitative and quantitative analyses of the nitrosation; (C) Our data are consistent with recent proposals concerning the anisotropy of N-nitroso groups (3).

Chemical shifts of the indicated protons (structure I) are collected in Table I.



$$-\underset{\substack{| \\ H_1}}{\overset{|}{C}}-\overset{\overset{X}{|}}{N}-\overset{\overset{O}{\parallel}}{C}-O-\underset{\substack{\uparrow \\ H_2}}{CH_2}-\underset{\substack{\uparrow \\ H_3}}{CH_3}$$

I

(Ia, X=H; Ib, X=NO)

TABLE I[a]

Chemical Shifts of Selected Protons in Urethans and N-Nitrosourethans; PPM Downfield from Internal TMS

N-Alkyl Group	$(H_1)_{Ia}$	$(H_1)_{Ib}$	$(H_2)_{Ia}$	$(H_2)_{Ib}$	$(H_3)_{Ia}$	$(H_3)_{Ib}$
1. *cyclo*-C_3H_4-CH_2-	2.95t	3.50d	4.03	4.43	1.20	1.43
2. C_6H_5-CH_2-	4.30d	4.93s	4.08	4.35	1.10	1.30
3. 1,2-dipropyl-cyclopropenyl-carbinyl-	3.05t	3.65d	4.05	4.47	1.22	1.42
4. *n*-C_4H_9-	3.07q[b]	3.65t[b]	4.00	4.47	1.17	1.43
5. *n*-C_8H_{17}-	3.08q[b]	3.65t[b]	4.05	4.48	1.18	1.43
6. CH_2=CH-CH_2-	3.70t[c]	4.28d	4.07	4.53	1.20	1.43
7. *cyclo*-C_6H_{11}-	3.35m[d]	4.45m[d]	4.05	4.45	1.20	1.42
8. 3-*exo*[3.2.1.$0^{2,4}$] tricyclooctyl-	2.35m[d,e]	2.12t	4.03	4.43	1.20	1.42
9. *cyclo*-C_3H_5	2.53m[d]	2.31m	4.05	4.42	1,20	1.43
10. *i*-C_3H7	3.77m[d]	4.80m[d]	4.03	4.44	1.18	1.42

[a] Determined as dilute solutions in CCl_4, at *ca*. 25°, on Varian A-60 equipment. Urethans and nitroso derivatives were fully characterized; the latter, also by quantitative nitrogen elimination.[3] Signal integrals were satisfactory. s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet. All H_2 were quartets; all H_3 were triplets.

[b] Fine structure, ascribed to virtual coupling is observed.

[c] Coupling with methylene protons leads to a nultiplet.

[d] Approximate center of gravity of multiplet.

[e] Multiplet falls under broad signal of C_1 and C_5 protons. Assigned on basis of integral intensity, and in analogy to corresponding proton in <u>no</u>. 9.

Table II presents chemical shift differences attending nitrosation. These are reported as $[(H_i)_{Ib}-(H_i)_{Ia}]$; all data (except Table I, <u>nos</u>. 8 and 9, H_1) are positive; <u>i.e.</u>, nitrosation <u>deshields</u> the indicated protons.

TABLE II

Chemical Shift Differences of Selected Protons (Ib-Ia), PPM.

System[a]	H_1	H_2	H_3
1	0.55	0.40	0.23
2	0.63	0.47	0.20
3	0.60	0.42	0.20
4	0.58	0.47	0.26
5	0.57	0.43	0.25
6	0.58	0.46	0.23
7	1.10	0.40	0.22
8	-0.27	0.40	0.22
9	-0.22	0.37	0.23
10	1.03	0.41	0.24

[a] See Table I

Inspection of the Tables reveals:

(1) In urethans, near equivalence of J_{NH-H_1}, and J_{H_1}-carbonbound vicinal protons, determines H_1 multiplicity in a "simple" manner.

(2) Nitrosation of Ia reduces H_1 multiplicity as expected.

(3) Substantial alteration of chemical shifts accompanies nitrosation. Deshielding is observed for H_2, H_3 and (secondary)

H_1. The magnitude of the observed deshielding increases respectively, but is remarkably constant within each proton class. Tertiary H_1, however, experience greater deshielding than secondary H_1; while cyclopropyl H_1 are shielded.

These relationships are easily made the basis for qualitative and quantitative analyses of the nitrosation reaction.

Discussion of the chemical shift changes must involve consideration of the anisotropy of the nitroso group, as well as of the conformations available to the urethan and its N-nitroso derivative.

Although, in amides, considerable double bond character exists between N and carbonyl-C, resulting in a restricted bond rotation, observable at room temperature via NMR (4), such seems not to be the case for urethans (5). N-nitroso compounds generally exhibit double bond character between both N-N and N-O, (3). But, again, in N-nitrosourethans, rotation about the N-carbonyl-C bond is probably free. [These ideas receive some support from our observation that the carbonyl frequency (IR) of the urethan is not altered upon nitrosation (ca. 5.70μ). Were the urethan to exhibit substantially restricted roation about the N-carbonyl-C bond, which decreased on nitrosation, a dramatic rise in carbonyl frequency would be expected (6).]

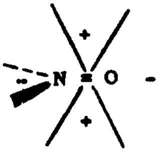
Lack of substantial restricted rotation about the N-carbonyl-C bond in both urethan and N-nitrosourethan suggests that the chemical shift changes accompanying nitrosation cannot be explained by conformational changes of carbonyl group as Ia is converted to Ib, but, rather, that the principal origin of these changes must reside in the anisotropy of the nitroso group.

According to Brown and Hollis, (3a), this anisotropy is represented by II. The theoretical basis of this proposal is the isoelectronic nature of carbonyl and nitroso groups. Protons situated in the region denoted (+) should be shielded, protons situated outside this region should be deshielded. For *N*-nitroso compounds, this model must be an oversimplification; there must also be anisotropic effects in the region of the N-N linkage, which has considerable double bond character (3b). Nevertheless, simple application of the Brown-Hollis model leads to predictions mostly in good agreement with observation.

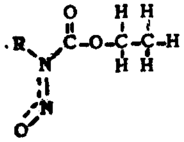
Molecular models constructed in accord with III, in which O, N, N, and carbonyl-C are coplanar, (7), demonstrate that H_2 and H_3 protons must fall in the deshielding region created by the nitroso anisotropy. Relative to their chemical shifts in the urethan, H_2 and H_3 will appear at lower field in the nitrosourethan.

Deshielding of H_1 in systems 1-6 may be explained similarly, IV. The circle superimposed on the nitroso group represents the cross-section of the shielding cone at that altitude (above the N-N-O plane) defined by H_1 at its closest approach to the shielding cone.

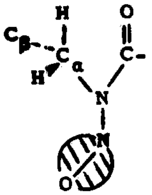
In systems 7 and 10, enhanced deshielding is observed for H_1. Models suggest that steric interaction of protons on C_β with unshared pairs on nitroso-oxygen will cause a confor-



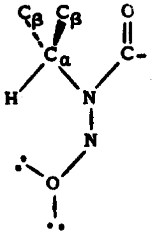
II



III



IV



V

mation such as V to be preferred. Here, H_1 is coplanar with N-N-O; an arrangement in which deshielding should be maximized. A parallel effect and analogous discussion for N-nitrosamines may be found in Karabatsos' study (3b).

Most difficult to understand, however, is the shielding of H_1 when the N-alkyl group is cyclopropyl (systems 8 and 9). Particularly noteworthy is the contrast between iso-propyl, no. 10 and cyclopropyl, no. 9. Although the β methyl interactions which cause no. 10 to assume conformation V are relieved in no. 9, no conformation, in which the coplanarities indicated in IV or V are maintained, predicts shielding for H_1 under simple application of the Brown-Hollis anisotropy model (8). A more exact knowledge of the anisotropy of the N-N-O group would seem to be required before H_1 shielding is understood.

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4. See: L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, 1959, p. 103.

5. The sole reported observation of restricted rotation seems to be: J. C. Breliere and J. M. Lehn, *Chem. Comm.*, 426 (1965). It is not clear whether the restriction can be observed at room temperature.

6. As is observed in the amide - *N*-nitrosamide case: K. Heyns and A. Heins, *Ann.* *604*, 133 (1957)

7. See the discussion in: R. Huisgen and J. Reinertshofer, *ibid.*, *575*, 197 (1952); R. Huisgen and H. Reimlinger, *ibid.*, *599*, 11 (1956). Evidence is presented for a preferred anti arrangement of nitroso-oxygen and carbonyl-C.

8. If, however, the nitroso-oxygen could deviate from the plane defined by C_α-N-N, shielding of H_1 could result. Such deviation should result in a loss of resonance energy, and therefore seems not to offer an attractive explanation for the observed shielding.