Photochemical Perturbation of $Z \rightleftharpoons E$ Equilibria in Nitrosamines[†]

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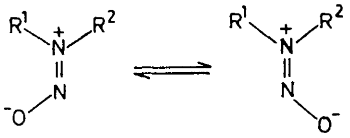
Summary Five dialkylnitrosamines have been isomerized about the partial double bond of the nitrosamino-function *via* the excited $n \rightarrow \pi^*$ singlet state.

N-nitroso-compounds having $R^1 \neq R^2$ may exist as mixtures of (*E*) and (*Z*) conformers (equation 1).[1] We have been seeking methods for perturbing the equilibrium between the two, both to study the kinetics and energetics of the re-equilibration process, and to facilitate isolation of the individual conformers in pure form for biological and chemical studies. We report that the desired change in nitrosamine stereochemistry can often be achieved by photochemical means.

We first studied methyl(acetoxymethyl)nitrosamine (I), which is of special interest as a progenitor of the presumed carcinogenic metabolite of dimethylnitrosamine.[2] Irradiation in a Pyrex n.m.r. tube of the equilibrium mixture containing only 5% of the (*Z*) conformer gave a photostationary state containing 38% (*Z*)-(I). The presence of a triplet sensitizer (benzophenone) or quenchers (piperylene and oxygen) failed to influence the photoisomerization appreciably, suggesting that a singlet $n \rightarrow \pi^*$ excited state was the reactive species.

Several other unsymmetrical nitrosamines also proved amenable to photoisomerization (Table). In all cases, the major n.m.r. spectral changes were reversible on allowing the solutions to stand in the dark. Preliminary data on the dynamics of return to thermal equilibrium reveal that $(Z) \rightarrow (E)$ interconversion barriers in (III)—(V) are of the magnitude expected for dialkylnitrosamines[3] [$t_{\frac{1}{2}}$ *ca.* 2 h for (IV) at 36 °C], while the activation energies for isomerization of (I) and (II) are surprisingly small [$t_{\frac{1}{2}}$ *ca.* 1 h for (I) at 1·5 °C].



(1)

The stability of compounds (I)—(V) in these experiments is also noteworthy, in view of the reported photolability of *N*-nitroso-compounds under certain conditions.[4,5] Some of our reaction mixtures were photoisomerized repeatedly, for a total of 8 h or more in a 700 W reactor, but no evidence of decomposition could be found in any n.m.r. spectrum

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[†] *Caution*: Most *N*-nitroso-compounds are potent carcinogens.

Table. Mole fractions of (*Z*) conformer for MeN(NO)R at thermal equilibrium and in the photostationary state.

Compound	R	Solvent	Mole fraction of (*Z*) conformer	
			At thermal equilibrium (36—43 °C)	In photostationary state[a]
(I)	$AcOCH_2$	$(CD_3)_2CO$	$0{\cdot}0_5$	$0{\cdot}3_8$
(II)	$MeOCH_2$	$C_6D_5CD_3$	$0{\cdot}0_2$	$0{\cdot}3_4$
(III)	$PhCH_2CH_2$	$C_6D_5CD_3$	$0{\cdot}2_7$	$0{\cdot}4_0$
(IV)	Cyclohexyl	CD_3CN	$0{\cdot}1_2$	$0{\cdot}2_8$
(V)	$PhCH_2$	CD_3CN	$0{\cdot}2_7$	$0{\cdot}4_0$

[a] Values given are the mole fractions of (*Z*) conformer after 6 h irradiation in Pyrex n.m.r. tubes with a high pressure (700 W) xenon lamp at <0 °C. That these values closely approximate the photostationary state composition was verified in several cases by showing that the total change in mole fraction was 2—4 times as great after the first 2 h as it was after the next 4 h. Standard solute concentration was 0·5 mmol g^{-1} of solvent.

except in that of (V), which contained a few percent of some unidentified degradation product(s) after 6 h irradiation.

Chow and his co-workers[5] have reported evidence suggesting the possibility of $(E) \rightarrow (Z)$ photoisomerization in *N*-nitrosamides. Their results, together with the present data, indicate that photochemical stereoisomerization may be a general property of *N*-nitroso-compounds. In any case, photoisomerization appears to provide a useful complement to existing methods[6,7] for separating (*Z*) and (*E*) conformers of compounds containing the $\geq$N–N=O group.

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