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Synthesis and spectroscopic studies of
trans-bis-(3,5-dimethyl-4-nitrosopyrazole) dimer

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Abstract—Bis-(3,5-dimethyl-4-nitrosopyrazole) dimer was prepared by reaction of acetyl acetone with nitrous acid and condensation with hydrazine. Spectroscopic techniques, including IR, UV, ^{1}H NMR, and ^{13}C NMR, and CHN analysis were used to identify the product.
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Optically active nitroso compounds and nitrones have played significant roles in organic chemistry due to their broad utility, serving both as units for many biologically active compounds and as important chiral ligands or chiral auxiliaries for asymmetric synthesis.[1]

Nitroso compounds and nitrones can exist in the monomeric form **1** and in the cis- and trans-dimeric forms **2** and **3**, respectively.[1]
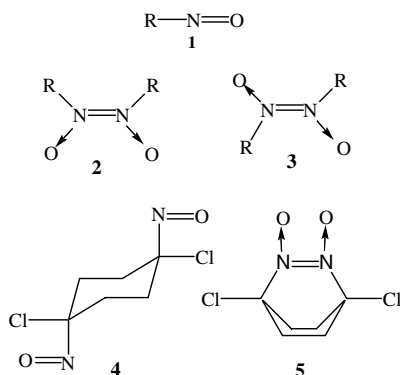
The monomers are green-blue in color and the dimers are colorless. The relative stabilities of the three forms are dependent upon the structure of R, the physical state, the temperature and, where appropriate, the solvent. In contrast to the extensive investigations on molecules containing one nitroso group **1** and dimers **2** and **3**, relatively little attention has been directed to the chemistry of molecules containing two independent monomeric nitroso groups. There is little, if any, experimental evidence for dinitroso alkanes, but it is well known that 1,4-dichloro-1,4-dinitrosocyclohexane can exist both as a stable trans-compound with two monomeric N=O groups **4** and as the internal cis-dimer **5**.[1] The cis-dimer may be characterized as an azodioxide compound or, more correctly, as a diazene-1,2-dioxide. Generally, the trans-dimer is more stable than the cis-dimer at room temperature in crystalline form or in solution. In general, trans-dimers are converted to cis-dimers by UV irradiation while heat isomerizes the cis-dimers to the trans-dimers.[2,3]

Although nitrosopyrazoles have been known for over 50 years,[4] relatively little spectroscopic information is available being confined to a study of the electron absorption spectrum of 3,5-dimethyl-4-nitrosopyrazole in water and dilute sodium hydroxide;[5] 4-nitrosopyrazole has also been reported.[6,7] In, addition, a small number of nitrosopyrazoles form nitroxides when used as free radical traps.[8] Extensive studies of the radiosensitivity of pyrazoles have revealed a number of biochemical and biological effects associated with their reductive metabolism.[9]

Nitrones and nitroso compounds are used in 1,3-dipolar cycloaddition reactions to synthesize compounds having interesting pharmacological activities and for the preparation of many stereochemically defined five-membered

heterocycles.[10–15] Due to their importance, we report herein the preparation of a new nitroso dimer.

Of further interest is a comparison between 3,5-dimethyl-4-nitrosopyrazole and 2,4,6-trimethylnitrosobenzene[16] with regard to the steric effects of the bulky groups upon the NMR chemical shift of the C–NO carbon. The geometry of the five-membered ring of the nitrosopyrazole implies that the steric hindrance between the nitroso group and the adjacent methyl groups is reduced compared with that for the similarly hindered nitroso benzene. The ^{13}C substituent shift of the C–NO group is increased considerably when it is flanked by bulky *tert*-butyl groups attached to the benzene ring.[17]

In our recent investigations[18,19] on the preparation of nitroso compounds, we demonstrated that the synthesis of these compounds in the solid state could generate persistent nitroso dimers which can be detected by electronic absorption, infrared and nuclear magnetic resonance spectroscopy. The synthesis of bis-(3,5-dimethyl-4-nitrosopyrazole) dimer is shown in Scheme 1.

The *trans*-bis-(3,5-dimethyl-4-nitrosopyrazole) dimer was prepared by treatment of acetylacetone with nitrous acid to give an oxime which was then condensed with hydrazine hydrate resulting in a white crystalline solid in 42% yield.

The dimer dissolved on heating in ethanol to give an almost colorless solution which became green on cooling. Heating the solution dissociated the solid dimer to the monomer.

The existence of the *trans*-bis-(3,5-dimethyl-4-nitrosopyrazole) dimer in the solid phase or in solution was proved by studying its electronic and infrared spectra. The electronic absorption spectra were recorded in chloroform at room temperature and showed that the dimer exhibited two (π–π^*) transition bands, the first transition band at 296 nm being ascribable to the dimeric grouping (N_2O_2), and the other transition at 254 nm being due to the C=C and C=N bonds, Figure 1.

Analysis of the dimeric π–π^* transition revealed that a comparison between the electronic configuration of the monomers and the dimers suggested that the dimerization process required organization of the electron distribution in the R–NO subunit. Experimental evidence, indicated that this does indeed happen.[20]

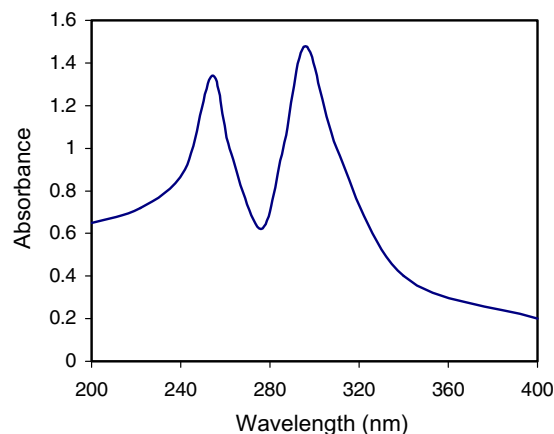The color of the monomers in solution might be due to a weak n–π^* transition, which involved an electron lone-

Figure 1. UV spectrum (CHCl$_3$) of *trans*-bis-(3,5-dimethyl-4-nitrosopyrazole) dimer.

pair localized on the nitrogen atom. This transition disappears when the nitrogen lone-pair of the monomer was used to form the N=N bond on dimerization.[21]

Many groups[22–24] have assigned the infrared N–O stretching frequencies of cis-and trans-nitroso dimers. Typically, the N–O stretch of cis-dimers appears as a strong double band absorption in the 1180–1320 cm^{-1} range, whilst trans-dimers exhibit a single strong stretching absorption in the same range. The IR spectral assignments are based on the CNOCNO grouping of the dimer and conform with group theory.[18] The infrared spectrum of the bis-(3,5-dimethyl-4-nitrosopyrazole) dimer prepared herein shows a single stretching frequency at 1220 cm^{-1} for the N–O group thus confirming that the solid nitroso pyrazole dimer existed in the trans form.

The CNOCNO group of the dimer skeleton has essentially C_{2h} symmetry and therefore the b_u skeletal frequencies for antisymmetric N–O and C–N stretching vibrations are for the cis-dimer. Due to the basic skeleton C_{2h} symmetry both the A_1 vibrations, which include the symmetric N–O and C–N stretching modes and the N–N stretching mode, and also the b_1 vibration, which includes the antisymmetric N–O and C–N stretches, are all expected to absorb above 900 cm^{-1} in the infrared region.

The conformation of the *trans*-bis-(3,5-dimethyl-4-nitrosopyrazole) dimer was further confirmed by analysis of the proton resonance signals.[20]

In the ^{1}H NMR spectrum, two resonances were observed at δ 2.34 and δ 7.20 ppm. That at δ 2.34 ppm
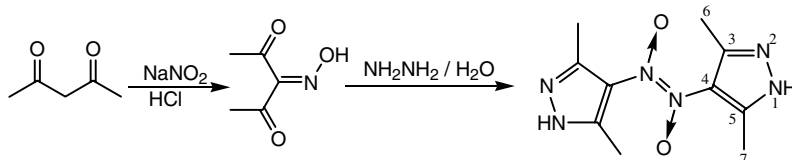
Scheme 1.
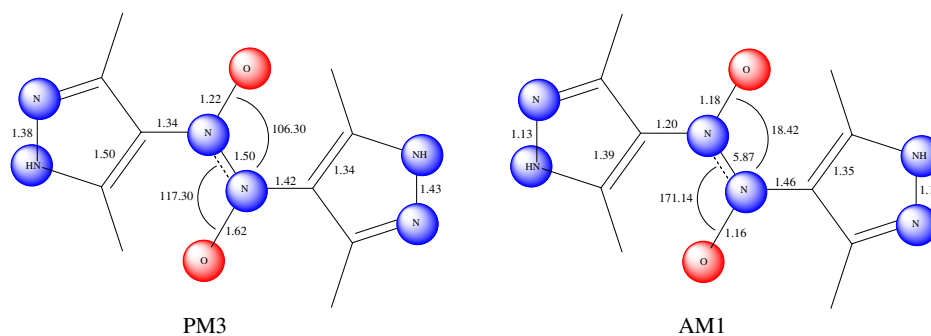
Figure 2. Structures of bis-(3,5-dimethyl-4-nitrosopyrazole) with bond lengths shown in Ångstroms (Å) and bond angles in degrees (°) computed using the semi-empirical AM1 and PM3 methods.

was due to the C-6 and C-7 methyl protons, which exist in analogous chemical environments. The second resonance can be attributed to the N-1 amino protons.

In the ^{13}C NMR spectrum of the trans-compound, three resonances were observed. These signals were due to the five carbon atoms, C-6, C-7 = 28.48 ppm, C-3, C-5 = 86.33 ppm, and C-4 = 132.59 ppm. ^{13}C NMR spectroscopy has provided interesting structural information on *C*-nitroso compounds, and the large difference (<20 ppm) between the C–NO and C–N$_2$O$_2$–C resonances clearly allows the prediction of monomeric N–O or dimeric N$_2$O$_2$ modes in the solid state.[25,26]

Figure 2 displays the geometry optimization of bis-(3,5-dimethyl-4-nitrosopyrazole) using semi-empirical AM1 and PM3 methods.[27] The figures show bond lengths in Angstroms (Å) and bond angles in degrees (°).

Preparation of trans-bis-(3,5-dimethyl-4-nitrosopyrazole) dimer: Acetyl acetone (10 g, 0.1 mol) was added to a solution of concentrated hydrochloric acid in water (9 ml HCl in 50 ml H$_2$O), and cooled in ice to 8 °C. Sodium nitrite (7.1 g, 0.1 mol) in 20 ml of water was added dropwise and the mixture was allowed to stand for 20 min. Hydrazine hydrate (5.4 g, 0.1 mol) was added with stirring, which resulted in immediate formation of a white crystalline precipitate of *trans*-bis-(3,5-dimethyl-4-nitrosopyrazole) dimer. This was filtered off, washed with ethanol, dried and then recrystallized from chloroform. Melting point (mp) = 114–116 °C, CHN analysis for C$_{10}$H$_{14}$N$_6$O$_2$ Calcd: C, 47.99; H, 5.64; N, 33.59%. Found: C, 47.52; H, 5.52; N, 33.50. UV (CHCl$_3$), λ_{max} 254 nm and 296 nm. IRv = 3103 (N–H), 2896 (CH$_3$), 1625 (C=N), 1508 (C=C), 1309 (N=N), 1220 (N–O), 1093 (C–N) cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$) δ_H = 2.34 (6H, s, 2 × CH$_3$) and 7.20 (2H, s, 2 × NH) ppm. ^{13}C NMR (100 MHz, CDCl$_3$) δ_C = 28.48, 86.33 and 132.59 ppm.

Acknowledgment

References and notes

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27. Semi-empirical self-consistent-field molecular orbital (SCF-MO) method at AM1 (Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902) and PM3 (Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209) levels within restricted Hartree–Fock (RHF) (Roothaan, C. C. J. *Rev. Mod. Phys.* **1951**, *23*, 69). Formalism has been considered to optimize fully the geometry of the bis-(3,5-dimethyl-4-nitrosopyrazole) dimer in its ground state. Geometry optimization was carried out by using a conjugate gradient method (Polak–Ribiere algorithm) (Fletcher, P., *Practical Methods of Optimization*, Wiley, New York, 1990). The SCF convergence was set at 0.001 kcal/mol and the RMS gradient was set to 0.001 kcal/(Å mol) in the calculations. We performed all the calculations using the HyperChem-7 program. (Hyperchem^{TM} release 7.52. Windows Molecular Modeling System, Hypercube, and Autodesk, Developed by Hypercube).