made to sharpen the observed bands by changing the temperature of the sample.

The spectra of the ring protons in II, II′, II-O, and II′-O were analyzed in several steps with the aid of the Swalen–Reilly iterative method.[13] The complex spectrum from the nine interacting spins in each of these molecules was first simplified by simultaneously decoupling the nuclear spins of the phosphorus and the protons 1 and 6 (upfield multiplet). Under these conditions protons 7 and 8 gave a single line at their chemical shift and protons 2, 3, 4, and 5 gave an AA′BB′ pattern that was readily analyzed[13] to give accurate chemical shifts and interproton spin–spin coupling constants (see Table I). The chemical shift of protons 1 and 6, their spin–spin couplings to protons 2 and 5 and to the phosphorus, were obtained directly from the splittings in the upfield multiplet due to protons 1 and 6. The interproton coupling constants for protons 1, 6, 7, and 8 were obtained from the BB′ portion of the AA′BB′CC′ pattern from spins 1, 6, 7, 8, 2, and 5 with P decoupled. This procedure is believed to be valid because of the near-zero coupling of protons 7 and 8 (BB′) with protons 2 and 5 (CC′). A check on the correctness of the resulting parameters given in Table I was made by comparing the calculated P decoupled spectrum from the eight protons with that observed. Reasonable agreement was obtained as shown for example in Figures 1b and 1c for II. Improved values for some of the parameters quoted in Table I could undoubtedly be made by making an iterative analysis of the P decoupled spectrum (eight spins interacting). However, the results obtained as outlined above are adequate to establish the structure of II, II′, II-O, and II′-O.

For compounds II′ and II-O, in addition to the above analysis, the upfield multiplet from protons 1 and 6 was decoupled alone. The resulting AA′BB′CC′ portion of the AA′BB′CC′X pattern (X = P) was analyzed by a simple extension[79] of the Swalen–Reilly iterative method. Where possible to compare them, the results were in satisfactory agreement with the stepwise analysis given above. It was not possible to perform this analysis for II′-O because of incomplete decoupling of protons 1 and 6 from the remaining ones. Also, the sample of II available in solution had deteriorated too much by the time this decoupling could be done to permit meaningful results to be obtained. For this reason only estimated values for $J_{P_2} = J_{P_5}$ and $J_{P_3} = J_{P_4}$ can be given at this time for compounds II and II′-O.

Acknowledgments. We are grateful to the National Institutes of Health (MH-08912) and the Alfred P. Sloan Foundation for their support of this research at Columbia University. We thank Badische Anilin and Sodafabrik, A.G., for generous gifts of cyclooctatetraene.

(79) To be published separately.

N-Thionitrosoamines

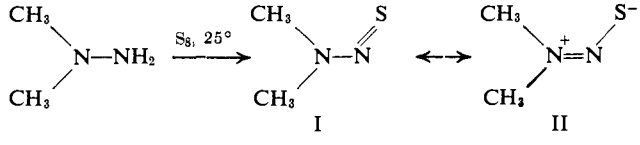
W. J. Middleton

Contribution No. 1210 from the Central Research Department, E. I. du Pont de Nemours and Company, Experimental Station, Wilmington, Delaware. *Received May 12, 1966*

Abstract: N-Thionitrosodialkylamines, which are organic compounds that contain a new functional group, the thionitroso unit (–N=S), have been prepared by reaction of 1,1-dialkylhydrazines with sulfur and by reduction of thionylhydrazines. The thionitrosoamines are highly colored compounds. Spectral evidence suggests that a dipolar resonance structure contributes to their over-all electronic structure.

Organic compounds that contain a nitrogen-to-divalent-sulfur double bond appear to be unknown. In particular, the sulfur analogs of common nitrogen–oxygen functional groups, such as nitro and nitroso, have never been reported.[1] Because of the difference in size between the nitrogen atom and the much larger sulfur atom, a π bond connecting these two atoms should be weak due to the restricted overlap of the π orbitals. However, it appeared possible that appropriately substituted thionitro and thionitroso compounds could exist, since thiocarbonyl compounds have a π bond between carbon and sulfur, and carbon is only slightly larger than nitrogen. Of the many classes that can be postulated, N-thionitroso secondary amines should be among the most stable because of the resonance stabilization possible. This paper reports the preparation and properties of amines containing the thionitroso unit (–N=S), a new functional group.

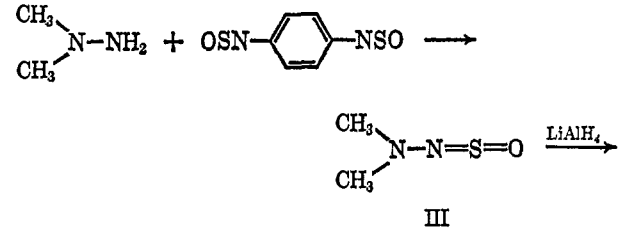
Preparation of N-Thionitrosoamines. These compounds have been prepared by two different procedures, one involving a sulfuration (oxidation) and the other a reduction. The most direct process consists in treating a 1,1-dialkylhydrazine with elemental sulfur. For example, N-thionitrosodimethylamine (I) is obtained



I II

from the reaction of 1,1-dimethylhydrazine with a heterogeneous suspension of sulfur in ether at 25°. This reaction is slow and requires 6 days for a 20% conversion of the hydrazine to product. Attempts to speed up the reaction by increasing the temperature or by increasing the concentration of dissolved sulfur by means of better solvents were unsuccessful owing to the instability of the thionitrosoamines under these conditions.

Compound I was also prepared by reduction of thionyldimethylhydrazine (III) with lithium aluminum hydride in ether. Even under the most favorable



III

(1) R. J. W. Le Fevré, *J. Chem. Soc.*, 2503 (1932), has reported several unsuccessful attempts to prepare thionitro compounds.

conditions tried, the reaction gave only a 24% yield of I. This low yield is due primarily to the fact that I is also reduced by hydride in a competing reaction to dimethylhydrazine. This reduction is an important part of the structure proof for I, indicating the thionitrosoamine does not have the isomeric rearrangement structure $(CH_3)_2N—S{\equiv}N$.[2]

The thionylhydrazine III used in the preparation of I was prepared by a transthionylation reaction of dimethylhydrazine with *p*-phenylenedi(thionylamine). Attempts to prepare this and other thionylhydrazines by direct reaction of thionyl chloride with the hydrazine were unsuccessful due to vigorous oxidation–reduction reactions that occurred.

Both of these synthetic methods for preparing thionitrosoamines have been used to prepare N-thionitrosopiperidine, and N-thionitrosohomopiperidine was prepared by the reaction of N-aminohomopiperidine with sulfur. However, neither of these thionitroso compounds was prepared in analytically pure form owing to their instability and lack of crystallinity. An attempt to prepare a phenylog of I by reduction of *p*-dimethylaminothionylaniline was unsuccessful.

Properties of N-Thionitrosoamines. N-Thionitrosodimethylamine is a deep purple, crystalline solid, mp 20–21°. Cryoscopic molecular weight measurements indicate that it is monomeric in benzene solution. It is stable at low temperatures (*ca.* $<-30°$) or in dilute solution in a nonpolar solvent, but neat liquid samples decompose in a few hours at room temperature. During decomposition, the purple color changes to yellow or orange, and a yellow solid precipitates. On two occasions, this yellow mixture detonated with considerable force. On one occasion, no detonation occurred, and some of the decomposition products were identified. The two major products were elemental sulfur and dimethyl sulfide. The nitrogen-containing products were not identified, but appeared to contain azides.

Compound I is also decomposed, quite rapidly, by acidic materials such as boron trifluoride, acetic acid, or mineral acids, with deposition of sulfur. Basic materials, such as pyridine, triphenylphosphine, and even aqueous sodium hydroxide, do not greatly accelerate or alter the course of the decomposition. The lack of reaction of I with triphenylphosphine and other bases is surprising, and may indicate that the dipolar resonance form II is important.

The proton nmr spectrum of I in carbon tetrachloride shows two singlets separated by 30 cps at τ 5.90 and 6.40.[3] This spectrum is similar to that of N-nitrosodimethylamine (two singlets 38 cps apart at τ 6.28 and 7.02) and indicates that the dipolar structure II, in which there is restricted rotation about the N-to-N bond, must contribute appreciably to the over-all electronic structure of I. The distance between the two peaks in the spectrum of I varies with both solvent and temperature. In saturated deuterium oxide, the peaks were only 23 cps apart at 25°. At 10% concentration in tetrachloroethylene, the signals were separated by 29 cps at 25° and 25 cps at 70°. On further heating, the sample decomposed before coalescence could be observed.[4]

The H^1 nmr spectrum of N-thionitrosopiperidine also indicates restricted rotation of the N-to-N bond, for the α hydrogens show as two broad multiplets of equal area at τ 5.7 and 6.2.

Solutions of the N-thionitrosoamines in nonpolar solvents are purple to blue. Solutions in polar solvents are orange to red. The bluish purple solution of I in cyclohexane is stable for weeks, but the orange-red solution in water is destroyed in a few minutes.

Table I shows the ultraviolet and visible spectra of I in three solvents. As can be seen from the table, the R band (probably, $n \rightarrow \pi^*$) of I shows a remarkable shift of 54 mμ in going from cyclohexane to ethanol. This large hypsochromic shift is strong evidence for extensive hydrogen bonding in ethanol and indicates that the dipolar structure II is an important contributor to the structure of I. The hypsochromic shift for N-nitrosodimethylamine, which has been regarded as a dramatic example of the effect of solvent on an $n \rightarrow \pi^*$ band, is only 14 mμ for the same solvents.[5] A very low-intensity, longer wavelength band observed in the spectrum of I also underwent a hypsochromic shift, although this shift was much less pronounced.

Table I. The Ultraviolet and Visible Spectra of N-Thionitrosodimethylamine

Solvent	Band	λ_{max}, mμ	ϵ
Cyclohexane		705	1.5
	R	587	27.3
	K	306	11,900
Carbon tetrachloride		685	1.8
	R	576	38
	K	309	12.300
Ethanol		680	1.0
	R	533	17.5
	K	306	10,800

Experimental Section

2,2-Dimethylthionylhydrazine. *p*-Phenylenedi(thionylamine)[6] (232 g, 1.16 moles) was slowly dissolved in 84 g (1.4 mole) of 1,1-dimethylhydrazine. The reaction mixture was distilled under reduced pressure to give 134 g (91%) of 2,2-dimethylthionylhydrazine as a light yellow liquid, bp 48–49° (10 mm), $n^{25}D$ 1.5407. The H^1 nmr spectrum of a neat sample showed a singlet at τ 6.63, and its infrared spectrum showed strong bands at 7.37 and 8.48 μ.

Anal. Calcd for $C_2H_6N_2SO$: C, 22.63; H, 5.70; N, 26.40; S, 30.20. Found: C, 22.37; H, 5.96; N, 26.96; S, 30.22.

N-Thionylaminopiperidine. A mixture of 10.0 g (0.1 mole) of 1-aminopiperidine[7] and 13.4 g of thionylaniline was distilled through an 18-in. spinning-band column under reduced pressure. There was obtained 8.7 g of aniline, bp 39–40° (0.5 mm), and 13.0 g (89%) of N-thionylaminopiperidine as a light yellow liquid,

(2) O. Glemser, *Angew. Chem. Intern. Ed. Engl.*, 1, 530 (1963). The structures of compounds formerly believed to be thionitrosyl chloride (Cl—N=S) and fluoride (F—N=S) have been shown to be thiazyl chloride (Cl—S=N) and fluoride (F—S≡N).

(3) Proton nmr spectra were measured at 60 Mc on a Varian A-60 spectrometer.

(4) A temperature of 180° was necessary to cause the two signals in the 40-Mc spectrum of N-nitrosodimethylamine to coalesce: C. E. Looney, W. D. Phillips, and E. L. Reilly, *J. Am. Chem. Soc.*, 79, 6136 (1957).

(5) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1962.

(6) O. Wichterle and J. Rocek, *Chem. Listy*, 47, 1768 (1953); *Collection Czech. Chem. Commun.*, 19, 282 (1954).

(7) O. H. Anna and F. W. Schueler, *J. Am. Chem. Soc.*, 74, 3693 (1952).

bp 60–61° (0.2 mm), $n^{25}D$ 1.5603. The H^1 nmr showed multiplets centered at τ 6.15 (4 H) and at 8.35 (6 H).

Anal. Calcd for $C_5H_{10}N_2OS$: C, 41.07; H, 6.91; N, 19.16; S, 21.93. Found: C, 41.02; H, 6.78; N, 18.97; S, 21.67.

p-Dimethylaminothionylaniline. Thionylaniline, 13.9 g (0.1 mole), was added to a solution of 13.0 g (0.1 mole) of practical N,N-dimethylphenylenediamine in 100 ml of ether. The black mixture was heated at reflux for 10 min, and then cooled to −78°. The solid that separated was collected on a cold filter and washed with pentane. Recrystallization from hexane gave 4.7 g of *p*-dimethylaminothionylaniline as red-orange plates, mp 70–73°. The H^1 nmr spectrum in CCl_4 showed a singlet at τ 7.07 ($N(CH_3)_2$) and an A_2B_2 pattern with components centered at about 2.27 and 3.56. The visible spectrum showed $\lambda_{max}^{cyclohexane}$ 415 mμ (ε 29,000).

Anal. Calcd for $C_8H_{10}N_2OS$: C, 52.73; H, 5.53; N, 15.37; S, 17.59. Found: C, 53.01; H, 5.45; N, 15.26; S, 17.34.

N-Thionitrosodimethylamine. A. By Reduction of Dimethylthionylhydrazine. A stirred solution of 26.5 g (0.25 mole) of dimethylthionylhydrazine in 100 ml of ether was cooled to −75°, and 63 ml of a 1 *M* solution (0.063 mole) of lithium aluminum hydride in ether was added dropwise over a period of 1 hr. The reaction mixture was allowed to warm to room temperature, stirred for 1 hr, and then filtered under nitrogen. The purple filtrate was concentrated by distillation at room temperature and reduced pressure (0.01 mm) until no further distillate came over. The deep purple residue was dissolved in 25 ml of ether, and the solution was filtered. The filtrate was cooled to −78°, and the crystals that separated were collected on a cold filter, washed with cold ether, and dried under a stream of nitrogen in a pressure filter. There was obtained 4.9 g of thionitrosodimethylamine as deep purple crystals, mp 20–21°. The infrared spectrum contained strong bands at 6.78, 7.45, and 9.05 μ with weaker bands at 3.40, 6.91, 7.95, 9.40, and 10.92 μ. The H^1 nmr spectrum of a 10% solution in carbon tetrachloride showed two singlets at τ 5.90 and 6.40.

Anal. Calcd for $C_2H_6N_2S$: C, 29.14; H, 6.94; N, 31.02; S, 35.12; mol wt, 90.15. Found: C, 28.65; H, 6.67; N, 31.08; S, 35.57; mol wt (freezing point in benzene), 90.

B. By Reaction of Sulfur with Dimethylhydrazine. A mixture of 400 ml of ether, 64 g (2 g-atoms) of powdered rhombic sulfur, and 60 g (1 mole) of 1,1-dimethylhydrazine was stirred at room temperature (*ca.* 25°) for 6 days. The reaction mixture slowly became deep purple during this time. The reaction mixture was filtered, and 35 g of undissolved sulfur was recovered. The purple filtrate was evaporated to dryness under reduced pressure. The residue was recrystallized from ether at low temperature (−78°), and then dried under vacuum at 0° to give 13.65 g (15% conversion) of N-thionitrosodimethylamine, mp 20–21°. The product was soluble in water to give an orange solution, which could be extracted with ether to give a purple ethereal solution.

N-Thionitrosopiperidine. A stirred solution of 9.7 g (0.067 mole) of N-thionylaminopiperidine in 25 ml of ether was cooled to −50°, and 18 ml of 1 *M* solution (0.018 mole) of lithium aluminum hydride in ether was added dropwise over a period of 15 min. The mixture was allowed to warm to room temperature and stirred for 1 hr. The reaction mixture was filtered, and the blue filtrate was concentrated by evacuation at 0.01 mm for 2 hr. Crude N-thionitrosopiperidine (3.25 g) was obtained as a purple oil, $\lambda_{max}^{CCl_4}$ 585 mμ (ε 13) and $\lambda_{max}^{CCl_4}$ 318 mμ (ε 14,500). H^1 nmr spectrum shows a multiplet centered about τ 8.4 (6 H), a broad band centered at 6.2 (2 H), and a broad band centered at 5.7 (2 H). This sample was not obtained in analytical purity. Attempts to further purify this material by recrystallization or distillation resulted in decomposition.

N-Thionitrosopiperidine was also obtained from the reaction of sulfur with N-aminopiperidine by a procedure similar to that described for the preparation of N-thionitrosodimethylamine from dimethylhydrazine and sulfur.

N-Thionitrosohomopiperidine. This compound was prepared in crude form by the reaction of N-aminohomopiperidine with sulfur in ether. It was obtained as a purple oil, λ_{max}^{ether} 700, 584, and 306 mμ.

Reduction of N-Thionitrosodimethylamine. A 1 *M* solution of lithium aluminum hydride was added dropwise to a stirred solution of 0.25 g of N-thionitrosodimethylamine in 10 ml of ether cooled to 0° with an ice bath. The addition was stopped when the purple color faded. A few drops of water was cautiously added to decompose the excess hydride, and then 10 ml of 30% sodium hydroxide was added. The ether layer was separated, and the aqueous layer was extracted twice with 5 ml of ether. The ether solutions were combined and dried over powdered potassium hydroxide. The ether was decanted, and a few drops of a saturated ethereal solution of *p*-nitrophenyl isocyanate was added. The white precipitate that formed upon cooling was collected on a filter and recrystallized from alcohol. There was obtained 0.108 g of 1,1-dimethyl-4-*p*-nitrophenylsemicarbazide as light yellow crystals, mp 204–205°. An identical sample was also prepared from authentic 1,1-dimethylhydrazine and *p*-nitrophenyl isocyanate.

Anal. Calcd for $C_9H_{12}N_4O_3$: C, 48.21; H, 5.40; N, 24.99. Found: C, 48.29; H, 5.55; N, 24.76.

Synthesis of Phosphatidylglycerol and Diphosphatidylglycerol[1,2]

Robin M. Saunders and Henry P. Schwarz

Contribution from the Department of Biochemistry, Philadelphia General Hospital, Philadelphia, Pennsylvania 19104. *Received February 28, 1966*

Abstract: 1′,3′-Di-O-(1,2-di-O-stearoyl-L-glycerol-3-phosphoryl)glycerol (IIa) has been synthesized and compared with ox heart cardiolipin. (1,2-Di-O-stearoyl-L-glycerol-3-phosphoryl)-3′-D-glycerol (IIIa), having the configuration of the naturally occurring phosphatidylglycerol, has been synthesized; previously other workers had synthesized only an alternative stereoisomer or a mixture of stereoisomers.

During studies in this laboratory of the effect of X-irradiation on phospholipids of rat liver,[3] a particularly noticeable effect was observed in the behavior exhibited by phosphatidylglycerol. This observation and other recent work here has prompted our interest in the interrelation of phosphatidylglycerol and cardiolipin and their metabolic roles. Certain other laboratories have reported interest in these topics. The above compounds IIa and IIIa have been synthesized as model substrates to aid in these investigations. It is expected that synthetic phosphatidylglycerol having the configuration of the natural material will be metabolically more active than other stereoisomers.

(1) This work was carried out under Contract NYO 1864-21 with the U. S. Atomic Energy Commission, and supported in part by National Institutes of Health Training Grant 5 TI GM 1116.

(2) "Phosphatidyl" is an abbreviation for (1,2-diacyl-L-glycerol-3-phosphoryl).

(3) H. P. Schwarz, L. Dreisbach, E. Polis, B. D. Polis, and E. Soffer, *Arch. Biochem. Biophys.*, **11**, 422 (1965).