(M^+, 45), 384 (20), 383 (20), 369 (3), 368 (2), 367 (2), 366 (2), 365 (6), 284 (27), 271 (10), 259 (8), 253 (8), 247 (17), 165 (42), 162 (32), 136 (100), 135 (28), 119 (40), 118 (88).

Anal. Calcd for $C_{35}H_{51}N_3O_2$: C, 77.02; H, 9.15. Found: C, 76.75; H, 9.44.

Treatment of Adduct 7 with Alkali. Adduct **7** (800 mg) in a mixture of ethylene glycol (30 ml), water (30 ml), and KOH (630 mg) was heated at reflux under N_2 for 40 min. The mixture was cooled and extracted with ether, and the extract washed with water and saturated NaCl, dried (Na_2SO_4), and evaporated. The product (300 mg) was separated by preparative TLC (ethyl acetate/hexane 1/2) and the major product isolated. The product (110 mg) was identical with 5,6-*trans*-cholecalciferol (**4**), prepared by an alternative method.[4] No cholecalciferol or products obtained by treatment of cholecalciferol under the above conditions were detected.

Acknowledgments. This work was supported by Grant AM 17057 from the National Institute of Arthritis, Metabolism, and Digestive Diseases. We are indebted to Dr. Henry M. Fales, National Heart and Lung Institute, for the mass spectrum of compound **14**.

Registry No.—**1**, 67-97-0; **6**, 4233-33-4; **7**, 58581-83-2; **8a**, 15971-69-4; **8b**, 53959-00-5; **9**, 58617-26-8; **14**, 58581-84-3; **15**, 58581-85-4; **16**, 58617-27-9; **17**, 58581-86-5; cyclohexene, 110-83-8.

References and Notes

(1) (a) L. F. Fieser and M. Fieser, "Steroids", Reinhold, New York, N.Y., 1959, pp 90–168; (b) E. Havinga, *Experientia*, **29**, 1181 (1973).
(2) (a) H. K. Schnoes and H. F. DeLuca, *Vitam. Horm. (N.Y.)*, **32**, 385 (1974); (b) A. W. Norman and H. Henry, *Recent Prog. Horm. Res.*, **30**, 431 (1974).
(3) (a) I. T. Boyle, L. Miravet, R. W. Gray, M. F. Holick, and H. F. DeLuca, *Endocrinology*, **90**, 605 (1972); (b) I. T. Boyle, J. L. Ohmdahl, R. W. Gray, and H. F. DeLuca, *J. Biol. Chem.*, **248**, 4174 (1973).
(4) M. F. Holick, M. Garabedian, and H. F. DeLuca, *Biochemistry*, **11**, 2715 (1972); W. H. Okamura, M. N. Mitra, D. A. Proesal, and A. W. Norman, *Biochem. Biophys. Res. Commun.*, **65**, 24 (1975); A. W. Norman, M. N. Mitra, W. H. Okamura, and R. M. Wing, *Science*, **188**, 1013 (1975).
(5) A. W. Norman, K Schaefer, H. G. Grigoleit, D. von Herrath, and E. Ritz, Ed., "Vitamin D and Problems Related to Uremic Bone Disease", Walter de Gruyter, New York, N.Y., 1975.
(6) J. J. Partridge, S. Fater, and M. R. Uskoković, *Helv. Chim. Acta*, **57**, 764 (1974); T. A. Narwid, K. E. Cooney, and M. R. Uskoković, *ibid.*, **57**, 771 (1974); T. A. Narwid, J. F. Blount, J. A. Iacobelli, and M. R. Uskoković, *ibid.*, **57**, 781 (1974); M. Morisaki, J. Rubio-Lightbourn, N. Ikekawa, and T. Takeshita, *Chem. Pharm. Bull.*, **21**, 2568 (1973); C. Kaneko, A. Sugimoto, Y. Eguchi, S. Yamada, M. Ishikawa, S. Sasaki, and T. Suda, *Tetrahedron*, **30**, 2701 (1974); C. Kaneko, A. Sugimoto, S. Yamada, M. Ishikawa, S. Sasaki, and T. Suda, *Chem. Pharm. Bull.*, **22**, 2101 (1974); S. M. Sine, T. E. Conklin, and W. H. Okamura, *J. Org. Chem.*, **39**, 3797 (1974); M. N. Mitra, A. W. Norman, and W. H. Okamura, *J. Org. Chem.*, **39**, 2931 (1974); D. Freeman, A. Archer, and Y. Mazur, *Tetrahedron Lett.*, 261 (1975); R. M. Moriarty, H. Paaren, and J. Gilmore, *J. Chem. Soc., Chem. Commun.*, 927 (1974).
(7) D. J. Aberhart, J. Y.-R. Chu, and A. C.-T. Hsu, *J. Org. Chem.*, **41**, 1067 (1976).
(8) R. Harrison, B. Lythgoe, and P. W. Wright, *J. Chem. Soc., Perkin Trans. 1*, 2654 (1974).
(9) D. H. R. Barton, T. Shioiri, and D. A. Widdowson, *Chem. Commun.*, 937 (1970); *J. Chem. Soc. C*, 1968 (1971).
(10) D. Crowfoot and J. D. Dunitz, *Nature (London)*, **162**, 608 (1948); D. Crowfoot Hodgkin, M. S. Webster, and J. D. Dunitz, *Chem. Ind. (London)*, 1149 (1957).
(11) A. Windaus and W. Thiele, *Justus Liebigs Ann. Chem.*, **521**, 160 (1936).
(12) J. G. Martin and R. K. Hill, *Chem. Rev.*, **61**, 537 (1961).
(13) Even ergosterol gives products with maleic anhydride resulting from both α- and β-face attack: D. N. Jones and I. Thomas, *J. Chem. Soc.*, 5206 (1964).
(14) R. C. Cookson, S. S. H. Gilani, and I. D. R. Stevens, *J. Chem. Soc. C*, 1905 (1967).
(15) D. R. James, G. H. Birnberg, and L. A. Paquette, *J. Am. Chem. Soc.*, **94**, 7465 (1974).
(16) M. Sheves and Y. Mazur, *J. Am. Chem. Soc.*, **97**, 6249 (1975).

Nucleophilic and 1,3 Additions to Triazolinediones[1a]

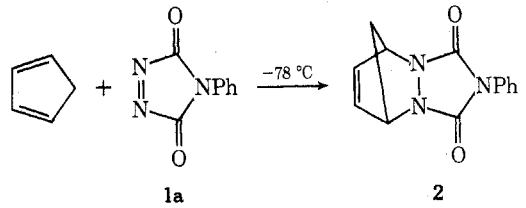
Alfred Hassner,* David Tang,[1b] and Joseph Keogh

State University of New York, Binghamton, New York 13901[1c]

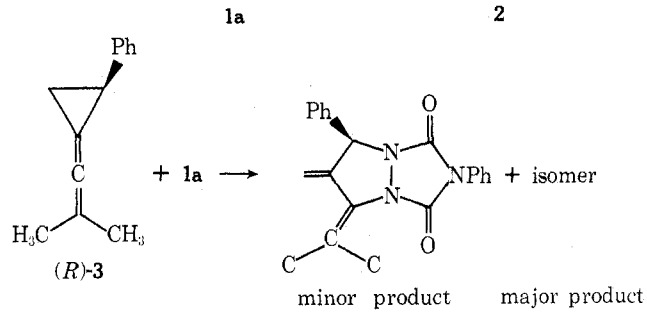
Received October 6, 1975

Triazolinediones **1** are shown to undergo cycloaddition to vinyl azides **5** in a 1,3 manner with loss of nitrogen to form novel bicyclic heterocycles **6**. Substituent effects on the vinyl carbons suggest nucleophilic attack by the β carbon of **5** on the N=N of **1**. Phosphorus ylides likewise undergo nucleophilic attack on **1** followed by proton abstraction to produce ylides **14**.

4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD, **1a**) has been shown in recent years to be one of the most powerful dienophiles.[2] For instance, cyclopentadiene reacts with **1a** at −78 °C in a 1,4 manner to produce **2**. On the other hand, allene **3** undergoes an addition with opening of the cyclopropane ring[2d] but to form an optically active adduct **4** and an isomer. These reactions were shown to occur in a concerted manner. Furthermore, a 1,2 addition of **1a** to a methylenecyclopropane has been reported.[2e]



1a **2**



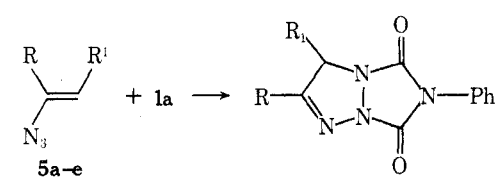
(*R*)-**3**

minor product major product

(*S*)-**4**

We now wish to report a 1,3 cycloaddition of **1a** with vinyl azides leading to the formation of novel heterocycles. This reaction can also be used as a method of derivatizing vinyl azides which are normally difficult to purify.

When vinyl azides, **5**, were allowed to react with **1a** in

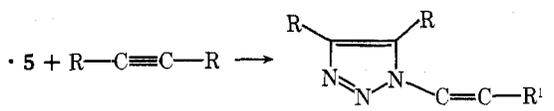


5a–e **6**

5	R	R′
a	Ph	H
b	Ph	CH_3
c	*p*-MeO—C_6H_4	H
d	H	*tert*-butyl
e	*p*-NO_2—C_6H_4	

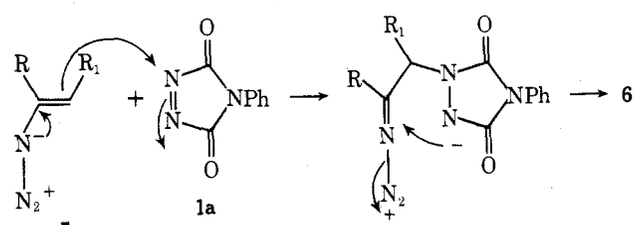
various solvents the formation of bicyclic triazolines **6** occurred readily at room temperature or below. The relative rates of reaction were in the order **5c** > **5a** > **5b** > **5d** >>> **5e** with electron-donating substituents favoring the addition.[3] The products **6** were stable solids and no imine–enamine tautomerization was evident by ir or attempted deuterium exchange studies.

Although alkyl and acyl azides are known to react with some dienophiles across the termini of the azide function and even vinyl azides **5** react with acetylenes in this manner to produce adducts **7**,[4] no analogous reaction was observed with PTAD.



7

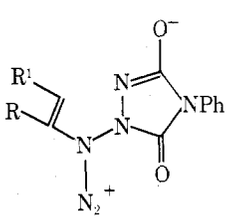
These results are best explained as proceeding via attack by the β carbon of the vinyl azide on the N=N of **1a** to lead to intermediate **8** which cyclizes to **6**.



5 **1a** **8**

Consistent with this interpretation is the fact that **5a** reacts about two times faster than **5b** which in turn reacts faster than **5d**, presumably owing to steric factors (R_1 = H, CH_3, or *t*-Bu). Likewise, the fact that the *p*-methoxy analogue **5c** reacts faster than **5a** whereas the *p*-nitro compound **5e** gave no detectable amount of cycloadduct can be rationalized on the basis of the changing nucleophilicity at the β carbon through resonance contributions from the para substituents of the α-substituted phenyl group. In analogy with this proposed mechanism are the reactions of vinyl azides with bromine[5] and ketenes[6] which have also been rationalized to have involved initial attack of the β carbon on the electrophile.

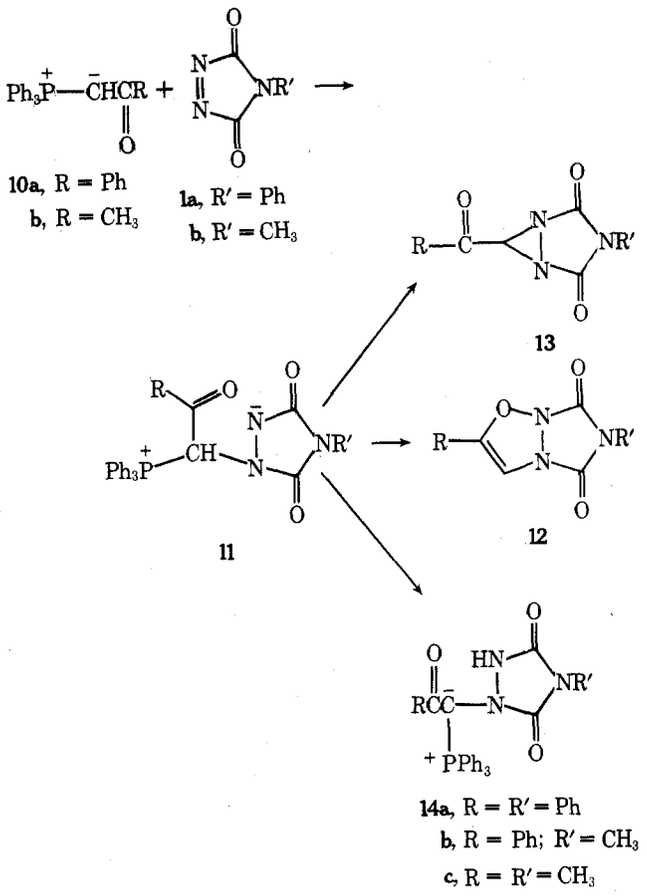
An alternative process which would involve attack by the azide N on **1a** followed by ring closure of **9** is inconsistent with the rate effects mentioned.



9

In light of the above observations we have investigated the reaction of ylides **10** to PTAD which could lead to novel heterocyclic systems such as **12** or **13**.

However, the products were found to be 1:1 adducts that possess structure **14** as indicated by ir (NH at 3340–3400 cm^{-1}), ^1H NMR (NH at τ 1.77, exchangeable with D_2O), and ^{13}C NMR (for **14a** =C=O doublet at 188.2 and 189.1 ppm, J_{CP} = 22 Hz, C–P doublet at 68.0 and 73.2 ppm, J_{CP} = 129 Hz). The ylides **14** evidently arise from nucleophilic attack by the ylide carbon of **9** on **1** to form **11** which undergoes intramolecular proton transfer. Similar tautomerizations in other ylides have been reported.[7] When the possibility for proton migration was eliminated as in the case of **15**, only polymeric type products could be obtained from its reaction with **1**.

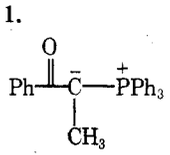


10a, R = Ph
b, R = CH_3

1a, R′ = Ph
b, R′ = CH_3

11 **12** **13**

14a, R = R′ = Ph
b, R = Ph; R′ = CH_3
c, R = R′ = CH_3



15

Experimental Section

General Procedure for the Reaction of 4-Phenyl-1,2,4-triazoline 2,5-dione (1a) with Vinyl Azides 5. A solution of 10 mmol of vinyl azide **5**[8] in 40 ml of dichloromethane was stirred at 0–5 °C and a solution of 10 mmol of PTAD in 70 ml of dichloromethane was added dropwise, over a 20-min period. After addition was complete the reaction mixture was stirred at room temperature for 1 h. Solvent was removed in vacuo and the resulting oil was recrystallized from CH_2Cl_2–MeOH. Adduct **6a** was prepared in 72% yield by the reaction of α-azidostyrene (**5a**) with PTAD at 0–5 °C: recrystallized from CH_2Cl_2–MeOH; mp 173–174 °C; NMR ($CDCl_3$) τ 5.08 (s, 2 H), 2.1–2.7 (m, 10 H); mass spectrum *m/e* 292 (M^+), 146, 117, 91, 90.

Anal. Calcd for $C_{16}H_{12}O_2N_4$: C, 65.75; H, 4.17. Found: C, 65.65; H, 4.17.

Cyeloadduct **6d** was prepared in 55% yield from PTAD and 1-azido-3,3-dimethyl-1-butene (**5d**): recrystallized from CH_2Cl_2–CH_3OH; mp 171–172 °C; NMR ($CDCl_3$) τ 8.92 (s, 9 H), 5.22 (d, *J* = 1.5 Hz, 1 H), 2.47 (m, 6 H); mass spectrum *m/e* 272 (M^+), 248, 216, 215, 188, 119.

Anal. Calcd for $C_{14}H_{16}O_2N_4$: C, 61.75; H, 5.92. Found: C, 61.41; H, 5.97.

Product **6c** was obtained in 78% yield from PTAD and α-azido-*p*-methoxystyrene (**5c**): mp 181–182 °C; NMR ($CDCl_3$) τ 6.15 (s, 3 H), 5.15 (s, 2 H), 3.03 (d, *J* = 8.5 Hz, 2 H), 2.52 (s, 5 H), 2.35 (d, *J* = 8.5 Hz, 2 H).

Anal. Calcd: C, 63.35; H, 4.34; N, 17.39; O, 14.90. Found: C, 63.29; H, 4.36; N, 17.32; O, 14.84.

Adduct **6b** was prepared in 73% yield from PTAD and α-azido-β-methylstyrene (**5b**): mp 158–159 °C; NMR ($CDCl_3$) τ 8.38 (d, *J* = 6.5 Hz, 3 H), 4.35 (q, *J* = 6.5 Hz, 1 H), 2.07–2.66 (m, 10 H); mass spectrum *m/e* 306 (M^+), 186, 158, and 130.

Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.72; H, 4.57. Found: C, 66.72; H, 4.67.

General Procedure for the Reaction of 1 with Ylide 10. A solution of 3.3 mmol of **1** in 50 ml of CH_2Cl_2 at 0 °C was added dropwise to 3.3 mmol of **9** in 50 ml of CH_2Cl_2. After the mixture was stirred at 25 °C for 1 h the solvent was evaporated and **14** was obtained as a white solid and recrystallized from CH_2Cl_2–pentane.

Ylide **14a** was prepared in 82% yield from **1a** and **10a:** mp 145–146 °C; ^1H NMR ($CDCl_3$) τ 2.93–3.06 (m); ir (KBr) 3320–3420 (NH), 1745 and 1695 cm^{-1} (C=O); ^{13}C NMR ($CDCl_3$) 68.03 and 73.17 (C–P, J_{CP} = 129.5 Hz), 150.24 and 151.27 (N_2C=O), and 188.19 and 189.07 ppm ((R–C=O, J_{CP} = 22 Hz); mass spectrum *m/e* M^+, 293 ($M^+ - Ph_3P$), and 262 (Ph_3P).

Product **14b** was prepared in 78% yield from **1b** and **10a:** mp 134–136 °C; ^1H NMR ($CDCl_3$) τ 7.45 (s, 3 H), 1.9–2.79 (m, 20 H), and 1.68–1.87 (br s, 1 H, exchangeable with D_2O); ir (KBr) 3320–3420 (NH), 1750 and 1700 cm^{-1} (C=O); ^{13}C NMR ($CDCl_3$) 24.56 (N–CH_3), 68.50 and 73.50 (C=P, J_{CP} = 126 Hz), 151.78 and 152.96 (N_2C=O), 187.6 and 188.5 ppm (R–C=O, J_{CCP} = 22 Hz); mass spectrum no M^+, *m/e* 262 (Ph_3P) and 231 ($M^+ - Ph_3P$).

Adduct **14c** was obtained in 85% yield from **1b** and **10b:** mp 120–122.5 °C; ^1H NMR ($CDCl_3$) τ 8.02 (s, 3 H), 7.33 (s, 3 H), 1.98–2.64 (m, 16 H); ir (KBr) 3310–3420 (NH), 1740 and 1695 cm^{-1} (C=O); ^{13}C NMR ($CDCl_3$) 23.70 and 24.20 (NCH_3 and CH_3C=O), 65.37 and 70.53 (C=P, J_{CP} = 129.5 Hz), 151.50 and 152.67 (N_2C=O), 189.66 and 190.61 ppm (R–C=O, J_{CCP} = 24 Hz); mass spectrum no M^+, *m/e* 262 (Ph_3P), 169 ($M^+ - Ph_3P$).

Acknowledgment. We are grateful for support of this research by a grant from the National Science Foundation.

Registry No.—**1a,** 4233-33-4; **1b,** 3274-43-6; **5a,** 16717-64-9; **5b,** 28022-21-1; **5c,** 34910-42-4; **5d,** 40168-86-3; **6a,** 58249-36-8; **6b,** 58249-37-9; **6c,** 58280-92-5; **6d,** 58249-38-0; **10a** charged form, 20913-05-7; **10a** neutral form, 859-65-4; **10b** charged form, 29942-64-1; **10b** neutral form, 1439-36-7; **14a** charged form, 58249-39-1; **14a** neutral form, 58249-40-4; **14b** charged form, 58249-41-5; **14b** neutral form, 58249-42-6; **14c** charged form, 58249-43-7; **14c** neutral form, 58249-44-8.

References and Notes

(1) (a) Cycloadditions. XXI. For the previous paper see A. Hassner and D. J. Anderson, *Synthesis*, 475 (1975). (b) NIH Postdoctoral Fellow, 1974–1975. (c) Work performed in part at the University of Colorado, Boulder, Colo.
(2) For selected examples see (a) R. A. Clement, *J. Org. Chem.*, **25**, 1724 (1960); **27**, 1115 (1962); (b) D. H. R. Barton, T. Shioiri, and D. A. Widdowson, *Chem. Commun.*, 939 (1970); (c) W. Ried and S. H. Lim, *Justus Liebigs Ann. Chem.*, 129 (1973); (d) D. J. Pasto and J. K. Barchardt, *J. Am. Chem. Soc.*, **96**, 6944 (1974); (e) D. J. Pasto and A. F. T. Chen, *Tetrahedron Lett.*, 2955 (1972).
(3) The red color of **1a** is discharged rapidly even at 0 °C in the reaction of **5a–c. 5c** reacted at least five times faster than **5b** at −15 °C and with **5d** the color discharge proceeded much more slowly even at 25 °C.
(4) G. L'Abbe, *Chem. Rev.*, **69**, 345 (1969).
(5) A. Hassner and A. B. Levy, *J. Am. Chem. Soc.*, **92**, 1672 (1970).
(6) A. Hassner and A. S. Miller, *J. Org. Chem.*, **37**, 2682 (1972).
(7) (a) G. Aksnes, *Acta Chem. Scand.*, **15**, 692 (1961); (b) C. Osuch, J. E. Franz, and F. B. Zienty, *J. Org. Chem.*, **29**, 3721 (1964); (c) H. Hoffmann, *Chem. Ber.*, **94**, 1331 (1961).
(8) The vinyl azides were prepared by the method of A. Hassner and F. W. Fowler, *J. Org. Chem.*, **33**, 2686 (1968).

Carbon-13 Nuclear Magnetic Resonance Chemical Shifts of Substituted Phenazines

Eberhard Breitmaier

Chemical Institute of the University of Tübingen, D-7400 Tübingen, Auf der Morgenstelle, Federal Republic of Germany

Ulrich Hollstein*

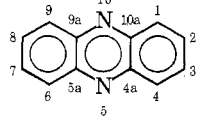
Department of Chemistry, The University of New Mexico, Albuquerque, New Mexico 87131

Received September 29, 1975

The ^{13}C chemical shifts of 16 phenazines, substituted in the 1, 1,6, and 1,9 positions, are reported. Signals are assigned by means of substituent effects on benzene shifts, by intensities, by molecular symmetry considerations, and by nuclear Overhauser enhancement for protonated carbons. Substituent effects of the substituent at carbon 1 are determined for carbons 1, 2, 3, and 4 and compared with those for benzene.

The ^{13}C NMR spectra of phenazines are of biological as well as of theoretical interest. Presently some 30 substituted phenazines have been isolated from microorganisms.[1] They possess antibiotic properties due to their interaction with deoxyribonucleic acid. Their ^{13}C spectra are useful in the elucidation of their biosynthesis. The electronic structure of phenazines, being diaza analogues of anthracene, is furthermore of interest and can be studied by ^{13}C NMR.[2]

We have measured the ^{13}C NMR spectra of 16 phenazines (**1**) in $CDCl_3$, Me_2SO-d_6, and mixtures thereof. The phenazines were substituted with various substituents in the 1, 1,6, or 1,9 position. Assignments were made by means of known benzene substituent effects,[3] by intensities, by molecular symmetry considerations, and by nuclear Overhauser enhancement for protonated carbons.



1

Phenazine itself measured in $CDCl_3$ as well as in $(CD_3)_2SO$ showed slightly lower chemical shifts than those reported in the literature.[2] The protonated carbons were measured at 0.70 ppm and the nonprotonated carbons at 0.55 ppm upfield from the reported values. The methyl substituent effects on benzene shifts (α, ortho, meta, para) were used in the assignment of the methylated phenazines. Similarly the benzene –OH, $-OCH_3$, –COOH, $-NO_2$, $-NH_2$, and $-COOCH_3$ substituent effects served to assign the correspondingly substituted phenazines. The symmetrically 1,6- or 1,9-disubstituted phenazines showed the expected reduced number of 6 instead of 12 skeleton signals for the mono- or unsymmetrically substituted phenazines. Nuclear Overhauser enhancement aided in distinguishing the protonated from the nonprotonated carbons. 1,6-Dimethylphenazine was only sparingly soluble in $CDCl_3$ and showed a signal:noise ratio for the quaternary carbons of less than 3:1. In 1,6-dimethoxyphenazine 5-oxide