the presence of the added diethyl fumarate.[22] The stereoselectivity of phenylsulfinyl carbene was determined in its addition to both Z-2-butene and cyclohexene. The ratio of anti addition to syn addition,[23] anti/syn, is 34/1 for addition to cyclohexene and >99/1 for addition to Z-2-butene. Compared to the stereoselectivities of other carbenes, these ratios are extremely large.[25-27]

Hoffman, Levin, and Moss,[28] on the basis of extended Huckel calculations, state that "in highly exothermic association reactions, where the transition state occurs at large separation of reaction partners, the activation energy for the path leading to the sterically more hindered product may be lower." They suggest that this may be the explanation for the contrathermodynamic syn stereoselectivity exhibited in the addition of many unsymmetrical carbenes to olefins. Although the data for benzenesulfinyl carbene seem to be contrary to their postulations, a closer examination reveals that the stereoselectivity data for sulfenyl, sulfinyl, and sulfonyl substituted carbenes provide a basis for further refinement of their theory.

The phenylsulfinyl substituent is large (A value of 1.9[29]) but the observation of a high degree of anti stereoselectivity is not simply a steric effect, since the sterically larger phenylsulfonyl group (A value of 2.5[30]) imparts no such selectivity to phenylsulfonyl carbene (anti/syn = 2.1 for addition to cyclohexene[31]). Electronically, the phenylsulfinyl substituent can stabilize the carbene center by delocalization of its lone pair into the empty orbital on carbon whereas the phenylsulfonyl substituent cannot.[32] Increased stability should lead to a more product-like transition state and to a higher degree of anti stereoselectivity. On the other hand, phenylsulfenyl carbene, though stable, is relatively nonstereoselective (anti/syn = 0.77 for addition to cyclohexene[24])· We believe that this lack of discrimination is due to the small steric size of the phenylsulfenyl group (A value of 0.8[34]). Thus, it appears that a substituent must be *both stabilizing and large* if it is to direct a high degree of anti stereoselectivity.

Further studies of diazo sulfoxides and sulfinyl carbenes are underway.

Acknowledgment. We thank the Robert A. Welch Foundation, Texas Christian University Research Foundation, and the Dow Chemical Company for financial support of this work.

References and Notes

(1) Part IV of a series, "α-Substituted Sulfoxides"; Part III, C. G. Venier and H. J. Barager, III, *Org. Prep. Proced. Int.*, **6**, 77 (1974).

(2) W. Kirmse, "Carbene Chemistry", 2nd ed, Academic Press, New York, N.Y., 1971.

(3) H. D. Hartzler, *J. Am. Chem. Soc.*, **95**, 4379 (1973); R. A. Moss and F. G. Pilkiewicz, *Synthesis*, 209 (1973); D. Seebach, *Chem. Ber.*, **105**, 487 (1972); R. H. Rynbrandt and F. E. Dutton, *Tetrahedron Lett.*, 1933 (1972); M. Makosza and E. Biatecka, *Tetrahedron Lett.*, 4517 (1971); A. Krebs and H. Kimling, *Angew. Chem., Int. Ed. Engl.*, **10**, 509 (1971).

(4) W. J. Baron, M. R. DeCamp, M. E. Hendrick, M. Jones, Jr., R. H. Levin, and M. B. Sohn, in "Carbenes", Vol. 1, M. Jones, Jr., and R. A. Moss, Ed., Wiley, New York, N.Y., 1973, Chapter 1.

(5) T. Durst, *J. Am. Chem. Soc.*, **91**, 1034 (1969).

(6) α-Diazo sulfoxides have been postulated, but not characterized, twice previously.[7,8]

(7) E. Ayca, *Rev. Fac. Sci. Univ. Istanbul, Ser. C*, **22**, 371 (1957); *Chem. Abstr.*, **53**, 11287*f* (1959).

(8) D. Hodson and G. Holt, *J. Chem. Soc. C*, 1602 (1968).

(9) For a recent attempted preparation of α-amino sulfoxides, see T. Numata and S. Oae, *Bull. Chem. Soc. Jpn.*, **45**, 2794 (1972).

(10) T. Kumamoto and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **41**, 2111 (1968).

(11) P. Yates, B. L. Shapiro, N. Yoda, and J. Fugger, *J. Am. Chem. Soc.*, **79**, 5756 (1957).

(12) A. M. Van Leusen and J. Strating, *Recl. Trav. Chim. Pays-Bas*, **84**, 151 (1965).

(13) A. Ledwith and E. C. Friedrich, *J. Chem. Soc.*, 504 (1964).

(14) B. Eistert, M. Regitz, G. Heck, and H. Schwall, in "Methoden der Organischen Chemie", 4th ed, E. Muller, Ed., Georg Thieme Verlag, Stuttgart, 1968, pp 473–893.

(15) C. G. Venier and H. J. Barager, III, *J. Chem. Soc., Chem. Commun.*, 319 (1973).

(16) The four diastereomers of 1,2-dimethyl-3-phenylsulfinyl cyclopropane can be analytically separated from each other and from **1** by HPLC on Corasil with 15% chloroform in petroleum ether as the moving phase. Characterization of the 1,2-dimethyl-3-phenylsulfinylcyclopropanes is as follows: (1) *cis*-dimethyl-*syn*-phenylsulfinyl (ir(neat), 1080, 1030 cm^{-1} (–S(O)–); NMR (δ), 1.1–1.7 (complex multiplet dominated by methyl resonances at 1.3 and 1.5, 8 H), 2.25 (m, 1 H), 7.5 (m, 5 H); mp 66–68°. Anal. Calcd for $C_{11}H_{14}OS$: C, 67.99; H, 7.26. Found: C, 67.94; H, 7.18); (2) *cis*-dimethyl-*anti*-phenylsulfinyl (ir(neat), 1075, 1035 cm^{-1} (–S(O)–); NMR (δ), 1.0 (d, 6 H), 1.3–1.8 (m, 3 H), 7.5 (m, 5 H); bp, 82–83° (0.01 mm). Anal. Found: C, 67.76; H, 7.46); (3) *trans*-dimethyl (a mixture of two diastereomers) (ir(neat), 1080, 1030 cm^{-1} (–S(O)–); NMR (δ), 0.8–1.7 (complex, 8 H), 1.75–2.1 (m, 1 H), 7.5 (m, 5 H); bp 83–85° (0.05 mm). Anal. Found: C, 67.89; H, 7.28).

(17) R. Helder, T. Doornbos, J. Strating, and B. Zwanenburg, *Tetrahedron*, **29**, 1375 (1973).

(18) K. N. Houk, J. Sims, R. E. Duke, Jr., R. W. Strozier and J. K. George, *J. Am. Chem. Soc.*, **95**, 7287 (1973).

(19) K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Am. Chem. Soc.*, **95**, 7301 (1973).

(20) P. K. Kadaba and T. F. Colturi, *J. Heterocycl. Chem.*, **6**, 829 (1969).

(21) R. Huisgen, H. Stangl, H. J. Sturm, and H. Wagenhofer, *Angew. Chem.*, **73**, 170 (1961).

(22) Preliminary analysis suggests that the decrease in norcarane yield results in the formation of bis(phenylsulfinyl)ethene. Decomposition of the diazo compound by adding it to diethyl fumarate or cyclopentane gives this compound also.

(23) The syn and anti configurations of the cyclopropyl sulfoxides derived from cyclohexene and Z-2-butene were established by hydrogen peroxide oxidation to the corresponding sulfones, whose configurations had been previously determined.[24] Characterization of phenylsulfinyl norcaranes is as follows: syn (ir(KBr), 1080, 1030 cm^{-1} (–S(O)–), NMR (δ), 1.1–2.5 (complex, 11 H, $J_{H_7-H_1}$ = 8.5 Hz at ca. δ 2.3), 7.3 (m, 5 H); mp 95.5–97°. Anal. Calcd for $C_{13}H_{16}OS$; C, 70.91; H, 7.27. Found: C, 70.90; H. 7.30.); anti (ir(neat), 1080, 1040 cm^{-1} (–S(O)–), NMR (δ), 1.0–2.2 (m, 11 H, $J_{H_7-H_1}$ = 4.5 Hz at δ 2.0), 7.3 (m, 5 H); bp 132–133° (0.25 mm). Anal. Found: C, 70.83; H. 7.50.).

(24) U. Schöllkopf, G. J. Lehmann, J. Paust, and H.-D. Härtl, *Chem. Ber.*, **97**, 1527 (1964).

(25) Reference 2, pp 286–287.

(26) R. A. Moss, in "Carbenes", Vol. 1, M. Jones, Jr., and R. A. Moss, Ed., Wiley, New York, N.Y., 1973, Chapter 2.

(27) R. A. Moss in "Selective Organic Transformation", Vol. 1, B. S. Thyagarajan, Ed., Wiley, New York, N.Y., 1970, pp 35–88.

(28) R. Hoffmann, C. C. Levin, and R. A. Moss, *J. Am. Chem. Soc.*, **95**, 629 (1973).

(29) E. L. Eliel, E. W. Della, and M. Rogic, *J. Org. Chem.*, **30**, 855 (1965).

(30) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis", Wiley, New York, N.Y., 1965, p 439.

(31) R. A. Abramovitch and J. Roy, *Chem. Commun.*, 542 (1965).

(32) That sulfur lone pairs can stabilize carbenes is well documented in the divalent sulfur series.[2] For example, $(CH_3S)_2C$ is so stable that it does not insert into normal olefins.[33]

(33) U. Schöllkopf and E. Wiskott, *Angew. Chem., Int. Ed. Engl.*, **2**, 485 (1963).

(34) E. L. Eliel and M. H. Gianni, *Tetrahedron Lett.*, 97 (1962).

(35) Texas Christian University Research Foundation Predoctoral Fellow, 1970–1971; Dow Fellow, 1971–1973; Robert A. Welch Foundation Predoctoral Fellow, 1973–1974.

(36) Texas Christian University Undergraduate Scholar, 1972; Dow Fellow, 1973–1975.

Clifford G. Venier,* Howard J. Barager, III,[35] Mark A. Ward[36]
Department of Chemistry, Texas Christian University
Fort Worth, Texas 76129

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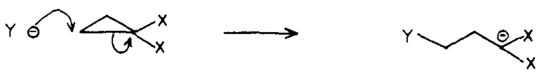
A Highly Activated Cyclopropane for Homoconjugate Reactions

Sir:

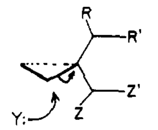
In contrast to double bonds, which are susceptible to the Michael reaction[1] by virtue of one activating group (eq 1, $X = CO_2R$, CN, etc), cyclopropanes require two such activating groups for homoconjugate addition. The process formalized in eq 2 for nucleophiles has been reported for enolates,[2a-c] amines,[3] mercaptans,[3] enamines,[4] and cuprates.[5] However, the severity of the conditions usually required for the intermolecular process even with two activating groups[6-8] has sharply reduced its attraction as a synthetic method.[9-13]

We considered the case of compound **1** in which both activating groups are esters, the most widely studied system in

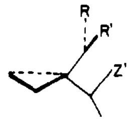

(1)


(2)

homoconjugate reactions. It is seen that both alkoxycarbonyl groups can participate in the delocalization of the emerging carbanion only in those conformations *where the plane of the cyclopropane is orthogonal to the O═C—OR planes of both esters.* These arrangements are termed the exo-exo (**1a**, R = Z = O; R′ = Z′ = OR), exo-endo (**1b**, R = Z′ = O; R′ = Z = OR), and endo-endo (**1c**, R = Z = OR; R′ = Z′ = O), conformers. Presumably, these conformers would be disfavored on obvious dipolar and steric grounds relative to conformers of the type **2**, where only one ester (Z′-C-Z) is disposed to facilitate reaction. We have therefore immobilized conformer **1a** through connection of R′ and Z′ as a cyclic acylal.[14]



1a R = Z = O; R′ = Z′ = OR
1b R = Z′ = O; R′ = Z = OR
1c R = Z = OR; R′ = Z′ = OR



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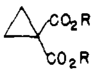
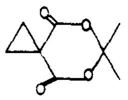


3 R = Et
4 R = H



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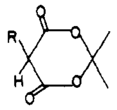
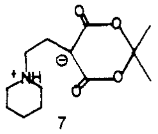


6 R = Et
15 R = H

The diethyl ester, **3**, upon saponification gives diacid **4**,[15] mp 139–141°, in 94% yield. Treatment of **4**[16] with isopropenyl acetate in the presence of catalytic H_2SO_4 affords an 86% yield of **5**: mp 63.5–64.5°;[17] $\lambda_{max}^{CHCl_3}$ 5.64 (sh); 5.70 μ; δ $CDCl_3$ 1.82 (s, 3), 1.97 (s, 2) ppm. Compound **5** undergoes hydrogenation with H_2-5% Pd/C-EtOAc at atmospheric pressure to give, quantitatively, the known[18] **6**. Under these conditions, cyclopropane **3** undergoes no reaction. Below are described a series of additional reactions which demonstrate the amazing double bond like character of **5** in its reactions with nucleophiles. Compound **5** is thus established as a versatile synthetic equivalent of $^{+}CH_2(CH_2)_2CO_2H$ and $^{+}CH_2CH_2CH(CO_2H)_2$.

Compound **5** *reacts exothermically with piperidine in benzene at room temperature.* Hence, the addition was conducted by mixing the reactants at 5–10° for 30 min and then at room temperature overnight. A quantitative yield of the zwitterion, **7**,[17a,b] mp 183–185°, was obtained. These mild conditions stand in striking contrast to those (110°, 20 hr) which have been used[4] in the case of the reaction of **3** with piperidine to achieve the analogous transformation in low yield.

Even the weakly nucleophilic pyridine reacts with **5** (chloroform, room temperature, 48 hr) to give the interesting yellow betaine, **8**,[17a] mp 166–168° dec, in 92% yield.[19] The introduction of nucleophilic sulfur in a 1,5-sense is also easily achieved. Compound **5** reacts with sodium thiophenoxide (dry dimethoxyethane, room temperature, 45 hr) to give, after acidification, the adduct, **9**,[17a,b] mp 150–153°, in 85% yield. Similar reactions in the case of **3** could be achieved only at ca. 80° in a relatively inefficient fashion.[4]



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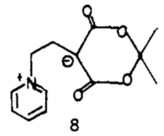

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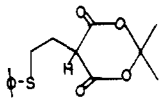
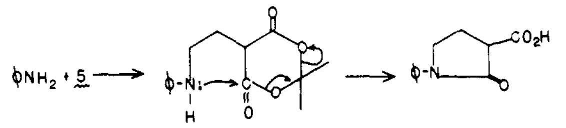


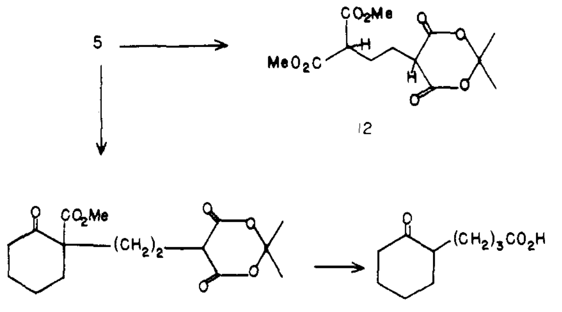
9

Extensive applications of compound **5** to heterocyclic synthesis may be envisioned. Sequential 1,5-addition and internal acylation (followed by extrusion of acetone) should provide access to various heterocyclic carboxylic acids. These possibilities are nicely foreshadowed in the reaction of **5** with aniline (neat, room temperature, 11 hr). A quantitative yield of lactam acid **11**,[17a] mp 143–145°, was obtained. A likely pathway, involving formation of intermediate **10**, is shown.



10 11

Reactions of **5** with enolates provide ready access to 1,6-dicarbonyl systems under mild conditions. The sodium salt of dimethylmalonate (prepared from the reaction of dimethyl malonate and sodium hydride) in dry dimethoxyethane reacts with **5** (room temperature, 39 hr) to give after neutralization and chromatography on silica gel, the tetraester **12**,[17] mp 71–72°, in 71% yield. Similarly, the sodium salt of 2-carbomethoxycyclohexanone reacts with **5** (dimethoxyethane, room temperature, 24 hr) to give, after acidification and chromatography (silica gel), an 88% yield of ketotriester **13**.[17a] The latter upon hydrolysis and decarboxylation (8% aqueous H_2SO_4, reflux, 28 hr) gives a 92% yield of 4-(2-cyclohexanone)butyric acid **14** (mp 56–57°, lit.[5] 56–58°).



12 13 14

Conformationally defined overlap, postulated above as a factor in the kinetic reactivity of **5**, may also be an important reason for the striking acidity of Meldrums acid (**15**, R = H; $pK_a \cong 5$)[20] and, indeed, for the enhanced acidity of cyclic β-dicarbonyl systems relative to their acyclic counterparts.[21] Whatever the cause of the massive acidity difference (ca. 10^7) between **15** and diethyl malonate, its mere existence can be used to rationalize the enormous reactivity of **5** relative to **3**.

The concept of improving the quality of a carbon leaving group in this way[14] may well have larger synthetic ramifications. Such possibilities, as well as further synthetic applications of compound **5** per se, are currently being studied.[22]

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References and Notes

(1) E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. React.*, **10**, 179 (1959).

(2) (a) R. W. Kierstead, R. W. Linstead, and B. C. L. Weedon, *J. Chem. Soc.*, 3610 (1952); (b) P. L. Fuchs, *J. Am. Chem. Soc.*, **96**, 1607 (1974); (c) W. G. Dauben and D. J. Hart, *ibid.*, **97**, 1622 (1975).

(3) J. M. Steward and H. H. Westberg, *J. Org. Chem.*, **30**, 1951 (1965).

(4) J. E. Dolfini, K. Menich, P. Corlias, S. Danishefsky, R. Cavanaugh, and S. Chakrabartty, *Tetrahedron Lett.*, 4421 (1966).

(5) E. J. Corey and P. L. Fuchs, *J. Am. Chem. Soc.*, **94**, 4014 (1972).

(6) The only apparent exception to the requirement of two activating groups involves a thioprenoxide opening. See W. E. Truce and L. B. Lindy, *J. Org. Chem.*, **26**, 1463 (1961). It should also be noted that cyclopropanes contained in systems which increase the normal ring strain are also subject to nucleophilic ring opening by one activating group.[8]

(7) J. Meinwald and J. K. Crandall, *J. Am. Chem. Soc.*, **88**, 1292 (1966).

(8) A. Cairncross and E. P. Blanchard, *J. Am. Chem. Soc.*, **88**, 496 (1966).

(9) Intramolecular versions of this reaction involving the formation of three-,[10] five-,[11] and six-membered[12] rings can be achieved under relatively mild conditions.

(10) S. Danishefsky, J. Dynak, and M. Yamamoto, *J. Chem. Soc., Chem. Commun.*, 81, (1973).

(11) S. Danishefsky, J. Dynak, W. E. Hatch, and M. Yamamoto, *J. Am. Chem. Soc.*, **96**, 1256 (1974).

(12) S. Danishefsky and J. Dynak, *J. Org. Chem.*, **39**, 1979 (1974).

(13) One exception, wherein a diactivated cyclopropane is opened under relatively mild conditons, is that of cuprate addition to a 1-cyano-1-carbethoxy system.[8] Another is the case[3b] where one of the activating groups is a phosphonium function. Presumably this grouping does not exert strong conformational requirements for activation. Finally, there is some indication[4] that the rather inaccessible 1,1-dicarbonitrile system undergoes facile ring opening, though in very low yield. This finding would be in keeping with the conformational formulations projected above. However, both in terms of availability and flexibility the system shown here is far superior to the dinitrile, even if preliminary results with the dinitrile could be improved upon and generalized.

(14) For the use of a cyclic acylal of malonic acid in a conceptually related way see L. S. Melvin and B. M. Trost, *J. Am. Chem. Soc.*, **94**, 1790 (1972).

(15) P. I. Abell and R. Tien, *J. Org. Chem.*, **30**, 4212 (1965).

(16) Cf. (a) M. Jones, W. Ando, M. E. Hendrick, A. Kulczycki, P. M. Howley, K. F. Hummel, and D. S. Malamant, *J. Am. Chem. Soc.*, **94**, 7469 (1972); (b) P. J. Scheuer and S. G. Cohen, *ibid.*, **80**, 4933 (1958).

(17) This assigned structure is supported by its (a) infrared, NMR, and mass spectra and (b) combustion analysis.

(18) I. Schuster and P. Schuster, *Tetrahedron*, **25**, 199 (1969).

(19) Cf. K. Okhata, T. Sakai, Y. Kubo, and T. Hanafusa, *J. Chem. Soc., Chem. Commun.*, 581 (1974).

(20) K. Pihalaja and M. Seilo, *Acta Chem. Scand.*, **23**, 3003 (1969).

(21) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Menlo Park, Calif., 1972, pp 492–494.

(22) For a recent application of the acylal concept to lowering the activation of Diels-Alder reactions see W. G. Dauben, A. P. Kozikowski, and W. T. Zimmerman, *Tetrahedron Lett.*, 515 (1975).

(23) A Fellow of the Andrew Mellon Foundation.

S. Danishefsky,* R. K. Singh[23]

Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260

Received February 24, 1975

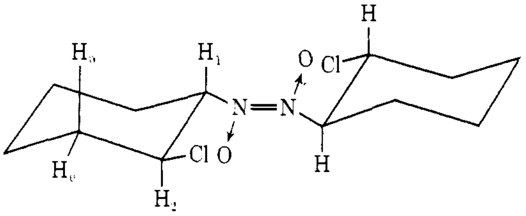
Homospecific and Heterospecific Dimerization of Nitroso Compounds. The Controversy Surrounding the Nature of the 2-Chloronitrosocyclohexane Dimer Obtained by Addition of Nitrosyl Chloride to Cyclohexene

Sir:

Despite existence of voluminous literature concerning the chemistry of nitrosyl chloride,[1-3] surprisingly little is known about the mechanism and the stereochemistry of nitrosyl chloride addition to a carbon-carbon double bond. Pending detailed discussion of both of these aspects in forthcoming papers, we should like to comment here on the controversy[4-7] surrounding the nature of the chloronitroso dimer[8] obtained by nitrosyl chloride addition to cyclohexene.

In previous reports by Ohno[5] and by Zefirov[6] and their coworkers the chloronitroso dimer obtained by nitrosyl chloride addition to cyclohexene in liquid sulfur dioxide or isopentyl nitrite-hydrochloric acid is described as (E)-1,1′-dioxidodiazenediylbis(*trans*-2-chlorocyclohexane),[12] mp 153° (ethanol)[5] or 132° dec,[6] respectively. Both groups assigned the configuration about the nitrogen-nitrogen double bond as E, and suggested that the addition of nitrosyl chloride occurred anti on the basis of 100-MHz proton NMR spectra. In both spectra the C_1-H and C_2-H appeared as a pair of triplets further split into doublets.[13] Ohno et al.[5] also reported that nitrosyl chloride addition to cyclohexene in methylene chloride, chloroform, or trichloroethylene occurred syn to give the corresponding (E)-1,1′-dioxidodiazenediylbis(*cis*-2-chlorocyclohexane), mp 133–135°.

More recently Ponder et al.[7] forcefully challenged Ohno's conclusions. They claimed that, in repeating Ohno's study[5] in the solvents he used as well as in a number of others, they were in no case able to find any evidence for the cis product. They reported that their nitrosyl chloride adduct, like Ohno's trans product, had mp 152–153° after three crystallizations from ethanol. However, contrary to Ohno[5] and Zefirov,[6] they reported that the NMR spectrum at 100 MHz (deuteriochloroform) showed the C_1-H and C_2-H not as a pair of sextets,[13] but as an octet and a multiplet.[14] Ponder argued that the sextet for the C_1-H observed in Ohno's spectrum would result only if $J_{12} = J_{23a} = J_{16a}$, but that "*this is clearly not the case, since we observed eight well resolved lines for this proton.*"[7] And yet Ponder et al. felt that their adduct was the same as Ohno's as "*verified by its ir and uv absorption, melting point and its elemental analysis.*"[7]



To our knowledge these conclusions[7] were questioned neither by Ohno nor by Zefirov. In a forthcoming paper we shall discuss in detail solvent dependence of the stereochemical course of the nitrosyl chloride addition to a carbon-carbon double bond. Here we present a reconciliation of the apparent discrepancies among Ponder's, Zefirov's, and Ohno's proton NMR spectra of the (E)-chloronitroso dimer.

Upon addition of nitrosyl chloride to cyclohexene in liquid sulfur dioxide at −20° we obtained, in over 90% yield, a slightly colored solid which precipitated partially during the reaction. Purification of this solid via preparative TLC (silica gel, benzene) revealed three components with R_f values of 0.45, 0.35, and 0.05. Compound **1** (R_f = 0.45) melted at 153° (ethanol). Elemental analysis and mass spectrum confirmed the molecular formula of a nitroso dimer $C_{12}H_{20}N_2O_2Cl_2$ and the uv and ir spectra[15] established that the configuration of the nitrogen-nitrogen double bond was E. A 100-MHz proton NMR spectrum in deuteriochloroform showed two single proton signals at δ 4.32 and 5.49 as a pair of sextets. Thus it appears that **1** was identical with Ohno's (E)-1,1′-dioxidodiazenediylbis(*trans*-2-chlorocyclohexane). Compound **2** (R_f = 0.35) melted at 142–144° (chloroform-hexane), and elemental analysis, mass spectrum, and the uv and ir spectra[16] clearly established that this compound too was a nitroso dimer $C_{12}H_{20}N_2O_2Cl_2$ with the E configuration about the nitrogen-nitrogen dou-