

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 1.9²⁹) 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 2.5³⁰) imparts no such selectivity to phenylsulfonyl carbene (anti/syn = 2.1 for addition to cyclohexene³¹). 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, phenylsulfinyl carbene, though stable, is relatively nonstereoselective (anti/syn = 0.77 for addition to cyclohexene²⁴). We believe that this lack of discrimination is due to the small steric size of the phenylsulfinyl group (*A* value of 0.8³⁴). 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.

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- 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 $\text{C}_{11}\text{H}_{14}\text{OS}$: 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).
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- 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 norcaradiene is as follows: syn (ir(KBr), 1080, 1030 cm^{-1} (-S(O)-); NMR (δ), 1.1-2.5 (complex, 11 H, $J_{\text{H7-H1}} = 8.5 \text{ Hz}$ at ca. δ 2.3), 7.3 (m, 5 H); mp 95.5-97°. Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{OS}$: 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, $J_{\text{H7-H1}} = 4.5 \text{ Hz}$ at δ 2.0), 7.3 (m, 5 H); bp 132-133° (0.25 mm). Anal. Found: C, 70.83; H, 7.50.).
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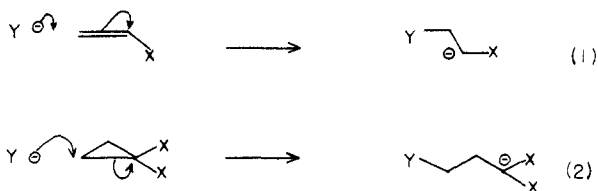
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A Highly Activated Cyclopropane for Homoconjugate Reactions

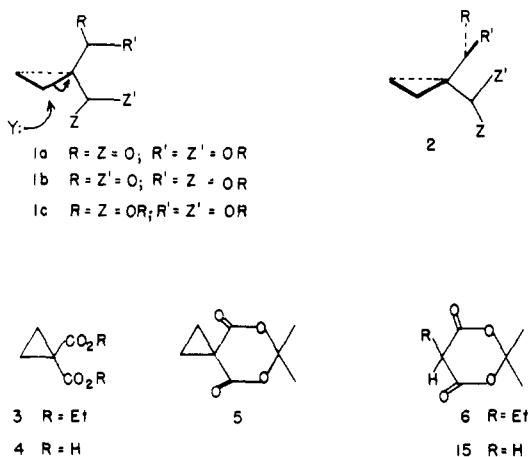
Sir:

In contrast to double bonds, which are susceptible to the Michael reaction¹ by virtue of one activating group (eq 1, $\text{X} = \text{CO}_2\text{R}$, 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 groups⁶⁻⁸ 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



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 acetal.¹⁴

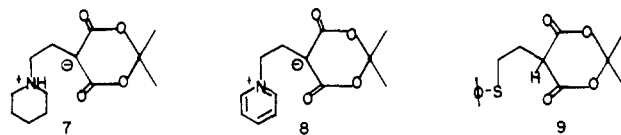


The diethyl ester, **3**, upon saponification gives diacid **4**,¹⁵ mp 139–141°, in 94% yield. Treatment of **4**¹⁶ with isopropenyl acetate in the presence of catalytic H_2SO_4 affords an 86% yield of **5**; mp 63.5–64.5°; $\lambda_{max}^{CHCl_3}$ 5.64 (sh); 5.70 μ ; δ $CDCl_3$ 1.82 (s, 3), 1.97 (s, 2) ppm. Compound **5** undergoes hydrogenation with H_2 -5% Pd/C-EtOAc at atmospheric pressure to give, quantitatively, the known¹⁸ **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 $^+CH_2CH_2CH(CO_2H)_2$.

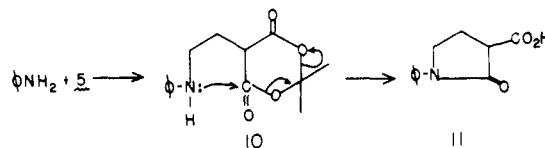
Compound **5** reacts exothermically with piperidine in benzene at room temperature. Hence, the addition was conducted by mixing the reactants at 5–10° for 30 min and then at room temperature overnight. A quantitative yield of the zwitterion, **7**,^{17a,b} mp 183–185°, was obtained. These mild conditions stand in striking contrast to those (110°, 20 hr) which have been used⁴ 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

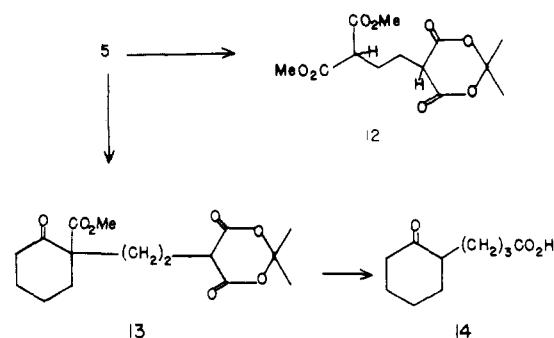
3 could be achieved only at ca. 80° in a relatively inefficient fashion.⁴



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.



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°).



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**, $R = H$; $pK_a \approx 5$)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 way¹⁴ 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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measured on facilities supported by RR 00292-03. Additional support from the Andrew Mellon Foundation is gratefully acknowledged.

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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

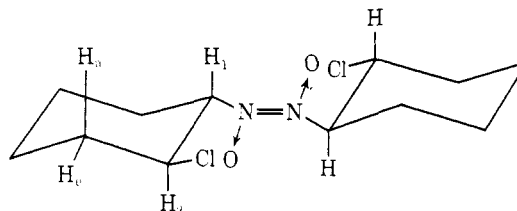
Sir:

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 controversy⁴⁻⁷ surrounding the nature of the chloronitroso dimer⁸ obtained by nitrosyl chloride addition to cyclohexene.

In previous reports by Ohno⁵ and by Zefirov⁶ 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 C₁-H and C₂-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 study⁵ 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 Ohno⁵ and Zefirov,⁶ they reported that the NMR spectrum at 100 MHz (deuteriochloroform) showed the C₁-H and C₂-H not as a pair of sextets,¹³ but as an octet and a multiplet.¹⁴ Ponder argued that the sextet for the C₁-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 conclusions⁷ 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 C₁₂H₂₀N₂O₂Cl₂ and the *uv* and *ir* spectra¹⁵ 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* spectra¹⁶ clearly established that this compound too was a nitroso dimer C₁₂H₂₀N₂O₂Cl₂ with the *E* configuration about the nitrogen-nitrogen dou-