

Carbodiimide-Sulfoxide Reactions. VII.¹

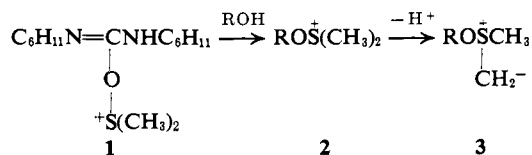
Synthesis of Stabilized Sulfonium Ylides

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Contribution No. 48 from the Institute of Molecular Biology, Syntex Research, Palo Alto, California. Received August 28, 1967

Abstract: A wide range of compounds containing reactive methylene groups flanked by carbonyl, ester, nitrile, amide, and phosphonate groups have been treated with dicyclohexylcarbodiimide and dimethyl sulfoxide, or other sulfoxides, in the presence of anhydrous phosphoric acid. The products from these reactions have been isolated in crystalline form and characterized as highly stabilized sulfonium ylides. The nuclear magnetic resonance spectra of certain of these ylides provide striking examples of magnetic nonequivalence of aliphatic methylene groups. Possible mechanisms of the reaction are discussed, and the X-ray crystallographic structure of one ylide is presented.

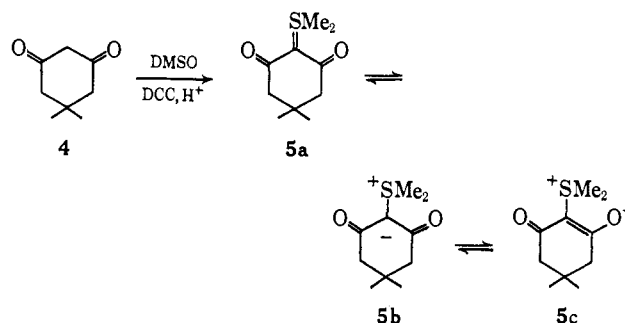
In earlier papers of this series we have described the mild, acid-catalyzed reactions of dimethyl sulfoxide (DMSO) and dicyclohexylcarbodiimide (DCC) with alcohols³ and with phenols.⁴ In the former case the reaction provides an extremely mild, yet powerful, method for the oxidative synthesis of aldehydes or ketones, while phenols lead to a variety of products in which thiomethoxymethyl groups are introduced in various ways. The mechanisms of both types of reaction appear to involve initial nucleophilic attack by the alcoholic or phenolic hydroxyl group upon the DMSO-DCC adduct **1** with formation of an alkoxy- or aryloxysulfonium compound **2**. Ready loss of a proton from one of the sulfonium methyl groups then gives a d orbital stabilized sulfonium ylide **3** which can collapse or rearrange to the observed products.



Recently, Torrsell⁵ has questioned the free existence of the alkoxy-sulfonium derivative **2** during oxidation of alcohols and has suggested a concerted termolecular mechanism which differs from our proposal only in the details of the proton abstraction step. Resolution of this question awaits further experimental evidence.

Further extension of this work has involved studies on the reactions of DMSO and DCC with a variety of other nucleophilic functional groups and in this paper we describe the results we have obtained with highly enolic compounds. To this end we have examined the reactions of DCC and DMSO, or other sulfoxides, with a wide range of "active methylene" compounds containing β -diketone, keto ester, cyano ester, diester, dinitrile, keto amide, and cyanophosphonate functions. In all cases the major product of the reaction was isolated in crystalline form (yields of 40–93%) and proved to be a stabilized sulfonium ylide. Thus, for example,

the reaction of dimedone (**4**) with DMSO, DCC, and anhydrous phosphoric acid led to the formation of the crystalline, water-soluble ylide 2-methylsulfuranylidene-5,5-dimethylcyclohexane-1,3-dione (**5**)⁶ in 59% yield.



The structure of **5** was derived from its elemental analysis and from spectral studies. Thus the nmr spectrum in deuteriochloroform showed only three sharp signals, a six-proton singlet ($>\text{CMe}_2$) at 1.03 ppm, a four-proton singlet (CH_2CO) at 2.29 ppm, and a six-proton singlet ($+\text{SMe}_2$) at 2.97 ppm. The infrared spectrum of **5** as a potassium bromide pellet showed an intense carbonyl band at 1540 cm^{-1} while that in dimedone was at 1615 cm^{-1} . The mass spectrum of **5** at 70 eV showed an intense molecular ion at m/e 200 (relative intensity 87%) with the other most intense peaks being at m/e 185 ($\text{M} - \text{CH}_3$, relative intensity 100%) and at m/e 62 (Me_2S , relative intensity 59%).⁸ At 15 eV, the molecular ion became the only significant peak. The ultraviolet spectrum was identical in both acidic and alkaline solution and showed λ_{max} 261 $m\mu$ (ϵ 17,100) while dimedone itself had $\lambda_{\text{max}}^{\text{H}^+}$ 259 $m\mu$ (ϵ 14,800) and $\lambda_{\text{max}}^{\text{OH}^-}$ 281 $m\mu$ (ϵ 24,000).

Similar types of reactions were applied to a variety of compounds containing active methylene groups and the physical, analytical, and spectral properties of the resulting ylides (**5–15**) are accumulated in Tables I and II and in the Experimental Section. It will be noted that a number of reactions have been run using sulfoxides other than DMSO. In these cases the products

(1) For part VI see A. F. Cook and J. G. Moffatt, *J. Amer. Chem. Soc.*, **89**, 2697 (1967).

(2) Syntex Postdoctoral Fellow, 1964–1965.

(3) (a) K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, **87**, 5661 (1965); (b) K. E. Pfitzner and J. G. Moffatt, *ibid.*, **87**, 5670 (1965); (c) A. H. Fenselau and J. G. Moffatt, *ibid.*, **88**, 1762 (1966).

(4) (a) M. G. Burdon and J. G. Moffatt, *ibid.*, **88**, 5855 (1966); (b) M. G. Burdon and J. G. Moffatt, *ibid.*, **89**, 4725 (1967).

(5) (a) K. Torrsell, *Tetrahedron Letters*, 4445 (1966); (b) K. Torrsell, *Acta Chem. Scand.*, **21**, 1 (1967).

(6) Use of the term "sulfuranylidene" as suggested by Ratts and Yao⁷ appears to offer the most versatile nomenclature for stabilized sulfonium ylides. In most cases it does not directly represent the most abundant tautomeric species present but the same defect is shared by other less convenient systems.

(7) K. W. Ratts and A. N. Yao, *J. Org. Chem.*, **31**, 1185 (1966).

(8) The mass spectra of all the ylides reported in this paper have been studied by Dr. Laszlo Tökés and will be reported in detail shortly.

Table I. Elemental Analyses of Sulfonium Ylides

Compd	Mp, °C	Formula	Calcd, %				Found, %			
			C	H	S	N	C	H	S	N
5	172.5–173 ^a	C ₁₀ H ₁₆ O ₂ S	59.98	8.05	16.00		60.07	8.00	16.20	
6	177–178	C ₁₂ H ₁₈ O ₂ S	63.70	8.02	14.14		63.86	7.92	14.35	
7a	190–191 ^b	C ₁₁ H ₁₆ O ₂ S	64.07	4.89	15.53		64.23	4.90	15.61	
7b	139–140	C ₁₃ H ₁₄ O ₂ S	66.65	6.02	13.66		66.82	5.96	13.82	
7c	64–66	C ₁₅ H ₁₈ O ₂ S	68.68	6.92	12.20		68.93	7.07	12.18	
7d	162–164	C ₁₃ H ₁₂ O ₂ S	67.23	5.21	13.78		67.37	5.32	13.90	
8a	166–167 ^c	C ₇ H ₁₂ O ₂ S	52.50	7.50	20.00		52.70	7.72	20.19	
8b	69–71	C ₁₁ H ₂₀ O ₂ S	61.09	9.32	14.81		61.41	9.16	14.63	
9	58–60 ^d	C ₈ H ₁₄ O ₃ S	50.52	7.37	16.85		50.38	7.00	17.12	
10	156.5–158	C ₁₂ H ₁₅ NO ₂ S	60.75	6.37	13.49	5.90	60.92	6.52	13.51	6.13
11	134–136 ^e	C ₉ H ₁₆ O ₄ S	49.09	7.27	14.55		48.96	7.11	14.72	
12a	158–160	C ₈ H ₉ NO ₂ S	45.28	5.70	20.11	8.80	45.42	5.69	20.29	8.68
12b	53–54	C ₁₀ H ₁₇ NO ₂ S	55.80	7.96	14.86	6.51	56.06	7.95	14.81	6.32
13a	99–100 ^f	C ₈ H ₈ N ₂ S	47.62	4.80	25.40	22.22	47.60	4.77	25.61	22.04
13b	84–85	C ₇ H ₁₀ N ₂ S	54.55	6.49	20.78	18.18	54.70	6.57	20.66	18.03
14	72–73	C ₈ H ₁₆ NO ₃ PS	40.50	6.80	13.49	5.90	40.15	6.83	13.20	6.32
15	266–268 ^g	C ₈ H ₈ N ₂ O ₃ S	38.30	4.29	17.04	14.89	38.57	3.93	16.99	14.89

^a Lit.^{15a} mp 172° by DMSO–Ac₂O. ^b Lit.^{14b} mp 190° by DMSO–Ac₂O. ^c Lit.^{15c} mp 168° by DMSO–Ac₂O. ^d Lit.^{15d} mp 64° by DMSO–Ac₂O. ^e Lit.^{15e} mp 135–137° from dimethylsulfonium methylide and ethyl chloroformate. ^f Lit. mp 99° by DMSO–Ac₂O^{14b} and by DMSO–P₂O₅.^{15e} ^g Lit. mp 263° via 5-bromobarbituric acid^{14c} and 273° by DMSO–Ac₂O.^{15b}

Table II. Spectral Properties of Dimethylsulfonium Ylides

Compd	Ultraviolet spectrum λ _{max} (ε) (solvent)	Infrared ^a ν _{max} (KBr), cm ⁻¹	Nmr spectrum (ppm, integrated intensity) ^b	
			Me ₂ S ⁺	Others
5	261 (18,600) (H ⁺ or OH ⁻)	1540, 1620, 1655	2.98 (6, s)	1.04 (6, s) (CMe ₂), 2.28 (4, s) (COCH ₃)
7a	215 (18,200), 220 (18,000), 253 (42,300), 261 (38,300), 370 (1500) (H ⁺ or OH ⁻)	1595, 1635	3.05 (6, s)	7.50 (4, s) (aromatic H)
8a	228 (6900), 271 (13,100) (H ⁺ or OH ⁻)	1560, 1605	3.00 (6, s)	2.33 (6, s) (COCH ₃)
9	225 (8700), 257 (12,600), (MeOH or OH ⁻)	1550, 1685	2.91 (6, s)	2.38 (3, s) (CH ₃ CO), 4.17 (2, q, J = 7 cps), 1.28 (3, t, J = 7 cps)
10	238 (19,900), 277 (17,500) (MeOH or OH ⁻)	1590, 1630	3.00 (6, s)	2.23 (3, s) (CH ₃ CO), 6.8–7.7 (5, m) (aromatic), 12.0 (1, br s)
11	233 (14,000) (EtOH or OH ⁻)	1635, 1670	2.88 (6, s)	4.17 (4, q), 1.29 (6, t)
12a	223 (11,400) (MeOH or OH ⁻)	1660, 2175	2.83 (6, s)	3.70 (3, s) (OMe)
13a	224 (5700) (MeOH or OH ⁻)	2155, 2190	2.82 (6, s)	
14	232 (5700) (MeOH)	2175	2.83 (6, s)	4.04 (4, p, J _{F,H} = 14 cps, J _{H,H} = 7 cps), 1.33 (6, t, J = 7 cps)
15	240 (13,800) (H ⁺), 250 (12,000) (OH ⁻)	1595, 1720	3.01 (6, s) ^c	

^a Only maxima in the carbonyl and nitrile regions are reported. ^b s, t, q, p, and m refer to singlet, triplet, quartet, pentuplet, and multiplet, respectively; e.g., 3.05 (6, s) refers to a six-proton singlet at 3.05 ppm downfield from an internal standard of tetramethylsilane. Except where indicated all spectra are in deuteriochloroform at 60 Mcps. ^c Determined in D₂O–NaOD.

were, once again, the corresponding sulfonium ylides (e.g., 6, 7b–d, 8b, 12b, and 13b), the products being characterized by analytical and spectral data.

In all the experiments reported in this paper, anhydrous orthophosphoric acid was used as the proton source. Other acids, such as pyridinium trifluoroacetate and dichloroacetic acid, which are effective during oxidation of alcohols, were found to be less efficient and led to unidentified by-products.

At the time that this work was done the only stable sulfonium ylides that had been described were 9-dimethylsulfuranylidene-fluorenes (e.g., 16)⁹ and 4-dimethylsulfuranylidene-pyrrolidine-2,3,5-trione (17)¹⁰ as well as several stable sulfoxonium ylides described by Corey¹¹ and König.¹² Since 1965, however, a

(9) (a) C. K. Ingold and J. A. Jessop, *J. Chem. Soc.*, 713 (1930); (b) E. D. Hughes and K. I. Kuriyan, *ibid.*, 1609 (1935).

(10) E. G. Howard, A. Kotch, R. V. Lindsey, and R. E. Putnam, *J. Amer. Chem. Soc.*, 80, 3924 (1958).

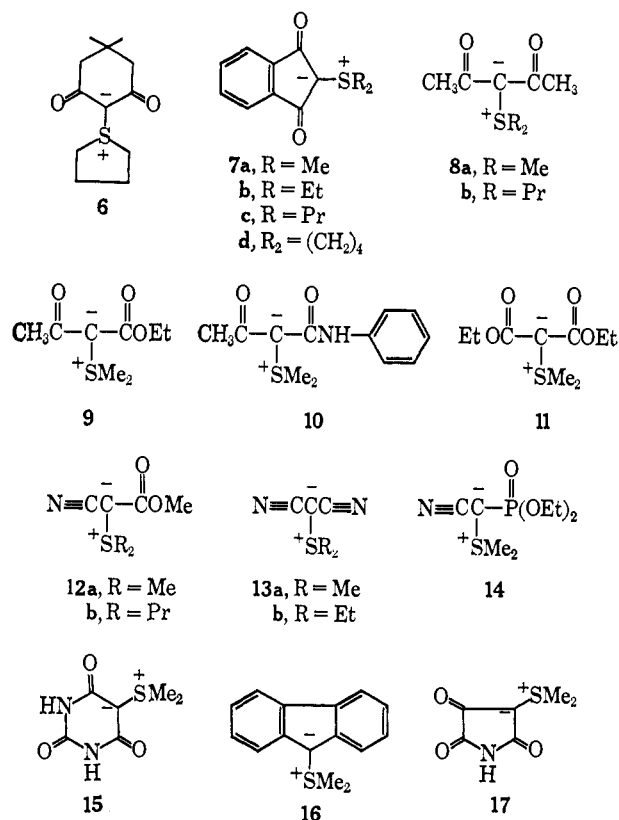
(11) (a) E. J. Corey and M. Chaykovsky, *Tetrahedron Letters*, 169 (1963); (b) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 86, 1640 (1964).

number of laboratories have shown a lively interest in the synthesis and properties of stabilized sulfonium ylides. These compounds have been primarily prepared by three different routes as follows: (1) base treatment of sulfonium salts bearing electron-withdrawing substituents at one or both of the α positions (reaction A);¹³ (2) mineral acid catalyzed condensation of sulfoxides with active methylene compounds or activated halides (reaction B);¹⁴ (3) condensation of

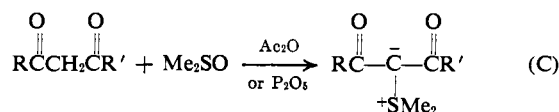
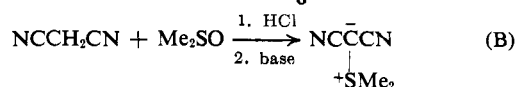
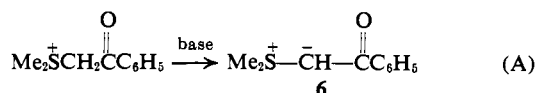
(12) (a) H. König and H. Metzger, *Tetrahedron Letters*, 3003 (1964); (b) H. König and H. Metzger, *Chem. Ber.*, 98, 3733 (1965).

(13) (a) H. Nozaki, K. Kondō, and M. Takaku, *Tetrahedron Letters*, 251 (1965); (b) H. Nozaki, M. Takaku, and K. Kondō, *Tetrahedron*, 22, 2145 (1966); (c) H. Nozaki, D. Tunemoto, S. Matubara, and K. Kondō, *ibid.*, 23, 545 (1967); (d) H. Behringer and F. Scheidl, *Tetrahedron Letters*, 1757 (1965); (e) A. J. Speziale, C. C. Tung, K. W. Ratts, and A. Yao, *J. Amer. Chem. Soc.*, 87, 3460 (1965); (f) A. W. Johnson and R. T. Amel, *Tetrahedron Letters*, 819 (1966); (g) C. P. Lillya and P. Miller, *J. Amer. Chem. Soc.*, 88, 1560 (1966).

(14) (a) A. Hochrainer and F. Wessely, *Tetrahedron Letters*, 721 (1965); (b) A. Hochrainer and F. Wessely, *Monatsh. Chem.*, 97, 1 (1966); (c) W. J. Middleton, E. L. Buhle, J. G. McNally, and M. Zenger, *J. Org. Chem.*, 30, 2384 (1965).



sulfoxides with active methylene compounds in the presence of acetic anhydride^{14b,15} or phosphorus pentoxide^{15c} (reaction C).



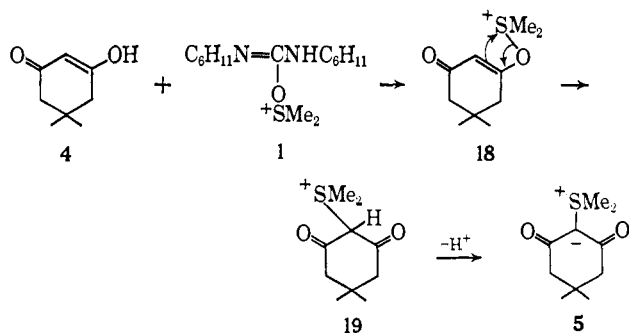
In addition several stabilized ylides have been prepared by special methods such as condensation of DMSO with diethyl acetylenedicarboxylate,¹⁶ reaction of dialkyl sulfides^{14c} and thiocarbonyl compounds¹⁷ with highly activated oxiranes, and acylation of less stabilized sulfonium ylides.^{13c} A recent Japanese review has carefully covered the literature.¹⁸

Hochrainer and Wessely^{14b} have prepared the dimethylsulfonium ylide of Meldrum's acid in 40% yield by condensation of the active methylene compound with DMSO and DCC in the presence of anhydrous orthophosphoric acid, but Nozaki, *et al.*,^{15c} have reported that such reactions do not occur in the desired way. In our experience, the DMSO-DCC reaction provides a more reactive system for the synthesis of sulfonium ylides than does the DMSO-acetic anhydride mixture. Thus, while diethyl malonate and ethyl

cyanoacetate have been reported to give no product^{14b} and a 2% yield^{15c} respectively, using the DMSO-acetic anhydride method, both types of compounds have reacted satisfactorily using DCC. Also, while diethyl cyanomethylphosphonate gave crystalline **14** in 46% yield using the DCC method, no trace of this product could be detected by thin layer chromatography using acetic anhydride. Considerable activation of the methylene group is, however, necessary for ylide formation. Thus less acidic compounds such as phenylacetonitrile, fluorene, and tetraethyl methylenebisphosphonate were completely inert under the usual reaction conditions.

The highly polar nature of the sulfonium ylides generally makes them quite water soluble and necessitates removal of excess DMSO by evaporation under high vacuum prior to isolation of the product. Using sulfoxides other than DMSO, however, the ylides frequently are extracted out of water by organic solvents and chromatography on silicic acid is necessary in order to remove excess DCC and dicyclohexylurea. Such chromatographic separations are generally very easy to perform, particularly in those cases (*e.g.*, with di-*n*-propyl sulfoxide and tetramethylene sulfoxide) where the excess sulfoxide can be removed by aqueous extraction. Ylide formation still readily occurs using di-butyl sulfoxide but separation of the excess sulfoxide from the product by chromatography has proved difficult. Diphenyl sulfoxide does not appear to be sufficiently reactive to form ylides by this method.

Two distinct possibilities exist for the mechanism of these reactions. If, as has been unequivocally shown in the reactions of alcohols^{3c} and phenols,^{4a} we assume that the DMSO-DCC adduct **1** is indeed the first reactive intermediate, then this species can undergo nucleophilic attack by either the enolate anion or the carbanion of the active methylene compound. Attack by the enolate anion would give the enol sulfonium derivative, *e.g.*, **18**, which could rearrange to the diketo sulfonium salt **19**. Loss of a proton from **19** would occur spontaneously in a polar medium to give the ylide **5**.¹⁹



The rearrangement of the sulfonium group from oxygen to carbon finds analogy in the well-known conversion of O-acetyldimmedone to 2-acetyldimmedone upon treatment with pyridine or sodium acetate.²⁰ In addition, it has been shown that the tendency toward O-

(15) (a) A. Hochrainer, *Monatsh., Chem.*, **97**, 823 (1966); (b) R. Gompper and H. Euchner, *Chem. Ber.*, **99**, 727 (1966); (c) H. Nozaki, Z. Morita, and K. Kondō, *Tetrahedron Letters*, 2913 (1966).

(16) E. Winterfeldt, *Chem. Ber.*, **98**, 1581 (1965).

(17) W. J. Middleton, *J. Org. Chem.*, **31**, 3731 (1966).

(18) H. Nozaki, M. Takaku, D. Tunemoto, Y. Yamamoto, and K. Kondō, *Nippon Kagaku Zasshi*, **81**, 1 (1967).

(19) In work that will be described shortly (unpublished observations of A. F. Cook and J. G. Moffatt) we have shown that crystalline hydrochlorides of stabilized sulfonium ylides can be prepared in nonpolar solvents but that these salts revert to the parent ylide in the presence of water.

(20) W. Dieckmann and R. Stein, *Ber.*, **37**, 3370 (1904).

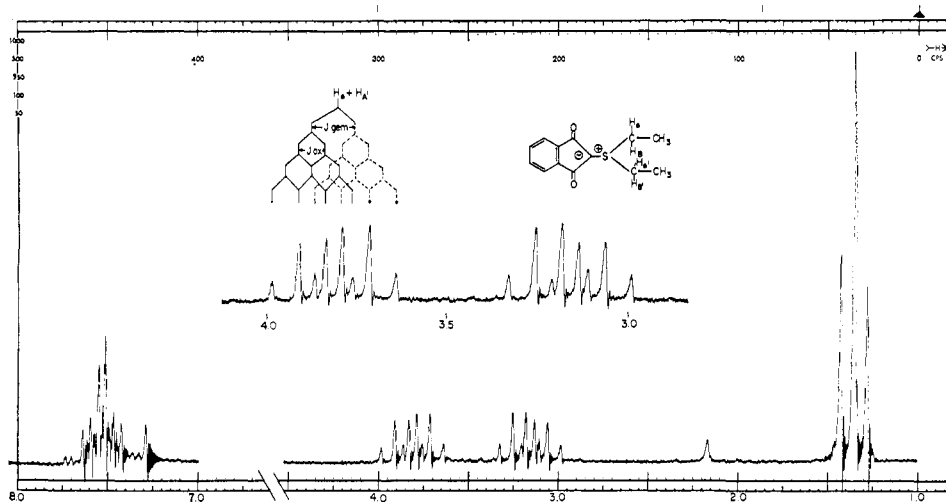
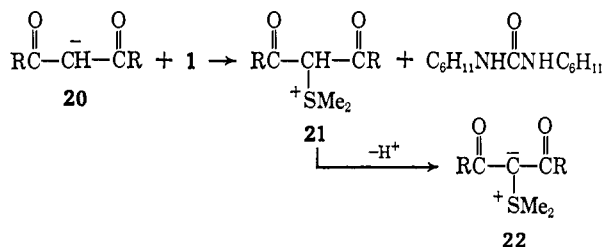


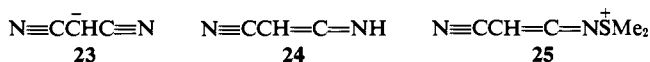
Figure 1. Nuclear magnetic resonance spectrum of 2-diethylsulfuranylidene-1,3-indanedione (**7b**) in deuteriochloroform at 100 Mcps. The insert is run using an expanded scale.

alkylation of ambident anions is greatly increased in aprotic dipolar solvents such as DMSO.²¹

Alternatively, nucleophilic attack by the carbanion **20** upon **1** would directly provide the sulfonium salt **21** and thence the ylide **22**.



In certain cases the latter would appear to be the only reasonable mechanism for ylide formation. Thus, in the case of malononitrile, nucleophilic attack by the carbanion **23** would readily lead to the ylide **13a**. The tautomeric ketenimine form **24** could, however, conceivably react by nitrogen attack but the resulting product **25** would be sterically incapable of rearrangement to **13a** via a cyclic mechanism due to the linear geometry of the ketenimine system.

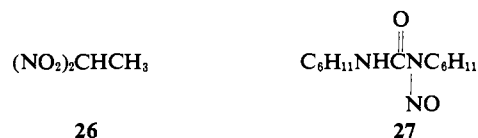


In more flexible systems it is not as yet possible to distinguish between these two mechanisms and it is not unlikely that both may be operative.

We have also attempted to react several α -substituted 1,3-dicarbonyl compounds such as 2-acetylcyclohexanone, 5-methylbarbituric acid, and 2-ethylcyclopentane-1,3-dione with DMSO, DCC, and anhydrous phosphoric acid under the usual conditions but in no case were we able to isolate any new products. In the case of 2-acetylcyclohexanone both thin layer and vapor phase chromatography showed only unreacted diketone together with DMSO, DCC, and dicyclohexylurea, whereas the other two compounds gave colored reaction mixtures that streaked badly on thin layer chromatography. The analogous reaction with 1,1-dinitroethane

(21) (a) G. Brieger and W. M. Pelletier, *Tetrahedron Letters*, 3555 (1965); (b) W. J. le Noble and J. E. Puerta, *ibid.*, 1087 (1966).

(**26**) was quite exothermic and thin layer chromatography showed rapid disappearance of the starting material and formation of a single ultraviolet absorbing product. This material was isolated in crystalline form in only 20% yield and characterized as 1-nitroso-1,3-dicyclohexylurea (**27**). This product was rather unstable and slowly decomposed with gas evolution upon storage at room temperature as well as during column chromatography or crystallization. The same compound was obtained in 72% yield through the reaction of dicyclohexylurea with isoamyl nitrite in glacial acetic acid. This suggests that **27** was formed via decomposition of 1,1-dinitroethane to nitrous acid under the reaction conditions. Dimethyl sulfoxide is apparently not necessary for this decomposition since **27** was also formed in similar reactions between **26**, DCC, and phosphoric acid using dimethylformamide or benzene as the solvent. In those cases, however, the



reaction was slow and required at least 15 hr to approach completion whereas using DMSO less than 15 min was sufficient.

The nuclear magnetic resonance spectra of certain of the sulfonium ylides described in this paper provide interesting examples of magnetic nonequivalence of methylene protons. By way of example, the 100-Mcps spectrum of 2-diethylsulfuranylidene-1,3-indanedione (**7b**) in deuteriochloroform is shown in Figure 1. From this spectrum it can be seen that the methyl groups of the diethylsulfonium moiety appear as a sharp triplet ($J = 7.5$ cps) at 1.35 ppm and are thus apparently equivalent. The methylene groups, however, appear as a pair of octets in the form of ABX_3 spectra ($J_{\text{AB}} = 12$ cps and $J_{\text{AX},\text{BX}} = 7.5$ cps) centered at 3.14 and 3.80 ppm. On the basis of spin-decoupling experiments it would appear that each octet represents the spectrum of one proton of identical chemical shift from each methylene group (*i.e.*, H_A and H_A' as one octet, H_B and H_B' as the other) rather than that of one complete

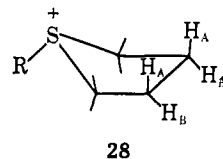
methylene group (H_A and H_B) which is magnetically nonequivalent to the other group ($H_{A'}$ and $H_{B'}$). The third possibility that, in fact, all four methylene protons are nonequivalent and each appears as a quartet with $J_{gem} = 0$ and $J_{AX} = J_{BX} = J_{A'X} = J_{B'X} = 7.5$ cps is shown to be invalid since the indicated geminal coupling of 12 cps is identical in spectra run at both 60 and 100 Mcps, thus confirming that this is true coupling rather than a difference of chemical shift. Irradiation at the center of the methyl triplet led to collapse of each octet into a quartet ($J = 3$ cps) and a singlet separated by 12 cps rather than to the expected doublet ($J = 12$ cps). Further studies on this unusual decoupling behavior are in progress. Irradiation at the center of either of the methylene octets led to collapse of the methyl triplet to a broadened doublet ($J = 7.5$ cps) which under optimal conditions began to show some further, as yet undefined, coupling of roughly 0.8 cps. Had each octet corresponded to a single methylene group then irradiation should reduce the signals due to the methyl groups to a superimposed singlet and triplet rather than to a doublet.

Recently there have been several reports of magnetic nonequivalence in methylene groups adjacent to polarized sulfur atoms in sulfonium ylides,²² sulfoxides,²³ and sulfonium salts.²⁴ While the compounds we have studied are different from those that have been previously described, the general nature of our spectra is in good agreement with what has been reported in these papers.

Most of the other ylides containing dialkylsulfonium groups larger than those in the parent dimethylsulfonium compounds show magnetic nonequivalence of the methylene groups. The magnitude of this nonequivalence is, however, quite variable and dependent upon the nature of the rest of the molecule and the solvent. Thus, while as described above, 2-diethylsulfuranylidene-1,3-indandione (**7b**) showed methylene protons separated by 0.66 ppm in deuteriochloroform, the corresponding 2-diethylsulfuranylidene malononitrile (**13b**) had completely equivalent ethyl groups appearing as a six-proton triplet ($J = 7.5$ cps) at 1.48 ppm and a four-proton quartet ($J = 7.5$ cps) at 3.01 ppm. 2-Dipropylsulfuranylidene-1,3-indandione (**7c**) also showed marked nonequivalence, the SCH_2 protons appearing as hextuplets ($J_{gem} = 12$ cps, $J_{AX} = 7.5$ cps) centered at 3.00 and 3.85 ppm as did 3-dipropylsulfuranylidene-2,4-pentanedione (**8b**) which showed hextuplets ($J_{gem} = 12$ cps, $J_{AX} = 7$ cps) at 2.89 and 3.91 ppm. The chemical shift difference between the methylene protons of methyl 2-dipropylsulfuranylidene cyanoacetate (**12b**), which is a considerably more compact molecule, was much less pronounced and led to partially overlapping hextuplets ($J_{gem} = 12$ cps, $J_{AX} = 7$ cps) at 2.88 and 3.32 ppm. It thus appears that protons adjacent to sulfonium ylide sulfur normally appear in a fairly narrow region of 2.82–3.14 ppm. In those cases where the structure of the molecule leads to magnetic nonequivalence, however, one of these methylene protons is shifted downfield and appears in the 3.32–

3.90-ppm range, the exact shift being dependent upon the nature of the molecule.

The spectra of the ylides **6** and **7d** are somewhat more complex since the chemical shift difference between the nonequivalent methylene protons adjacent to sulfur is relatively small and a complex multiplet results. Based upon spin decoupling studies on **7d** it appears that these methylene protons appear as octets centered at 3.37 and 3.63 ppm, with $J_{gem} = 12$ cps and couplings of 6 and 8 cps with the adjacent methylene protons. Because of the cyclic nature of the sulfonium group and the pyramidal structure of sulfonium sulfur the protons H_A and H_B in **28** also have different chemical shifts and appear as multiplets centered at 2.15 and 2.85 ppm.



It is also apparent that the extent of magnetic nonequivalence of methylene groups is solvent dependent. Thus, while in chloroform the ylide **12b**, as described above, exhibits pronounced nonequivalence, in dimethyl sulfoxide the methylene groups appear as a triplet ($J = 6$ cps) at 3.10 ppm which shows only a slight (0.5 cps) further splitting. Similarly the diethylsulfonium ylide **7b**, which showed a 0.66-ppm chemical shift difference between the methylene protons in chloroform, had only a variation of 0.06 ppm (3.56 and 3.62 ppm) in DMSO and this pattern was not further changed upon raising the temperature to 120°. A similar solvent dependence has been reported by Mislow²⁴ in certain sulfonium salts which showed nonequivalence in trifluoroacetic acid but not in chloroform, DMSO, or acetone. Roberts, *et al.*,²⁵ and Ratts²⁶ have also described a correlation between the degree of nonequivalence and solvent polarity in other types of compounds.

We have also made several other physical studies on 2-dimethylsulfuranylidene malononitrile (**13a**). Firstly, the complete X-ray structure of the crystalline ylide has been determined by Dr. A. T. Christensen of the Institute of Steroid Chemistry of Syntex Research and will be reported in detail shortly.²⁶ The observed bond lengths and angles are shown in Figure 2. These data provide several pieces of evidence that extensive charge delocalization of the carbanion occurs in the crystalline state. Thus the $SC(CN)_2$ grouping was found to be planar while, if the negative charge resided exclusively on the central carbon, this atom would be isoelectronic with nitrogen and the arrangement would be expected to be pyramidal. Also the C–CN bond distances of 1.40 ± 0.01 Å are significantly shorter than those in other $sp-sp^2$ carbon-carbon bonds (1.42–1.46 Å) and indicate significant double-bond character due to the presence of the ketenimine anion tautomers. Similar conclusions have been arrived at from the crystal structure of the sodium salt of tricyanomethane by Thom and Klewe.²⁷ The sulfur atom of **13a** clearly showed the expected pyramidal structure. Extensive

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(23) (a) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, *J. Amer. Chem. Soc.*, **87**, 1958 (1965); (b) A. Rauk, E. Buncel, R. Y. Moir, and S. Wolfe, *ibid.*, **87**, 5498 (1965).

(24) K. Kondô and K. Mislow, *Tetrahedron Letters*, 1325 (1967), and references therein.

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(26) A. T. Christensen, *Acta Cryst.*, in press.

(27) E. Thom, Ph.D. Thesis, University of Oslo, 1965.

charge delocalization leading to the predominance of betaine structures for crystalline, stabilized phosphonium ylides has also been demonstrated by X-ray techniques.²⁸

The extreme polar nature of **13a** is also evident from dipole moment measurements for which we express our warmest thanks to Professor N. L. Allinger of Wayne State University. The observed moment of 8.077 ± 0.036 D in dioxane is consistent with a highly ionic structure and may be compared with values of 6.2 and 5.7 D, respectively, for 9-dimethylsulfuranylidene-fluorene (**16**)²⁹ and 5-dimethylsulfuranylidene-1,3-cyclopentadiene^{13d} that have been reported previously.

In a forthcoming paper in this series we will describe some chemical reactions that these highly stabilized ylides undergo.

Experimental Section

Methods. Thin layer chromatography was carried out on 0.25-mm layers of Merck silica gel GF, and the products were visualized by ultraviolet absorption or by spraying with a 5% solution of ammonium molybdate in 10% sulfuric acid followed by brief heating at 150°. Preparative thin layer chromatography was done on 20 × 100 cm glass plates coated with a 1.3-mm layer of Merck silica gel HF and column chromatography on Merck silica with 0.05–0.20-mm particles. Nuclear magnetic resonance spectra were obtained using solutions in deuteriochloroform (unless otherwise stated) and either a Varian A-60 or HA-100 spectrometer. Mass spectra were obtained on an Atlas CH-4 instrument with a direct inlet system. Instrumental analyses were performed by the staff of the Analytical Laboratory of Syntex Research. Crystallographic data were obtained using a Picker automatic diffractometer and an IBM 360-50 computer. Elemental analyses were obtained by Dr. A. Bernhardt, Mulheim, Germany. Unless otherwise presented, analytical and spectral data are to be found in Tables I and II, respectively. Molecular weights are determined by mass spectrometry.

2-Dimethylsulfuranylidene-5,5-dimethylcyclohexane-1,3-dione (5). Dimedone (1.4 g, 10 mmol) and dicyclohexylcarbodiimide (5.15 g, 25 mmol) were dissolved in a mixture of anhydrous dimethyl sulfoxide (DMSO, 10 ml)³⁰ and benzene (10 ml). Anhydrous orthophosphoric acid (1.0 ml of a 5 M solution in anhydrous DMSO, 5 mmol) was added and after a few minutes an exothermic reaction ensued. After storage overnight at room temperature ethyl acetate (50 ml) was added, and dicyclohexylurea was removed by filtration. The filtrate was extracted three times with water and the combined extracts were adjusted to pH 8 with lithium hydroxide. The solvent was then evaporated to dryness under high vacuum at 50° leaving a semicrystalline residue. This was extracted four times with warm acetone and the extracts were evaporated to dryness leaving a crystalline solid. Recrystallization from acetone at -10° gave 1.17 g (59%) of the ylide **5** of mp 172.5–173°; molecular weight, 200.

2-Tetramethylenesulfuranylidene-5,5-dimethylcyclohexane-1,3-dione (6). Dimedone (1.4 g, 10 mmol) was treated overnight at room temperature with DCC (5.15 g, 25 mmol) and anhydrous phosphoric acid (5 mmol) in a mixture of tetramethylene sulfoxide (10 ml) and benzene (10 ml). After addition of ethyl acetate, removal of dicyclohexylurea, and repeated extraction with water, the extracts were neutralized and evaporated to dryness under high vacuum at 50° leaving a white solid. Crystallization from acetone-ether gave 1.32 g (58%) of the ylide **6** as white needles of mp 177–178°; molecular weight, 226; $\lambda_{\text{max}}^{\text{MeOH}}$ 258 m μ (ϵ 18,500), unchanged in alkali; $\nu_{\text{max}}^{\text{KBr}}$ 1580 and 1610 cm⁻¹. The nmr spectrum (CDCl₃) showed a six-proton singlet (CMe₂) at 1.63 ppm and a four-proton singlet (COCH₂) at 2.31 ppm. The CH₂S group appeared as overlapping multiplets at 3.0–3.7 ppm and the other methylene groups as multiplets centered at 2.1 and 2.7 ppm.

(28) A. J. Speziale and K. W. Ratts, *J. Amer. Chem. Soc.*, **87**, 5603 (1965).

(29) G. M. Phillips, J. S. Hunter, and L. E. Sutton, *J. Chem. Soc.*, 146 (1954).

(30) Dried by distillation and storage over Linde Molecular Sieve, Type 4A.

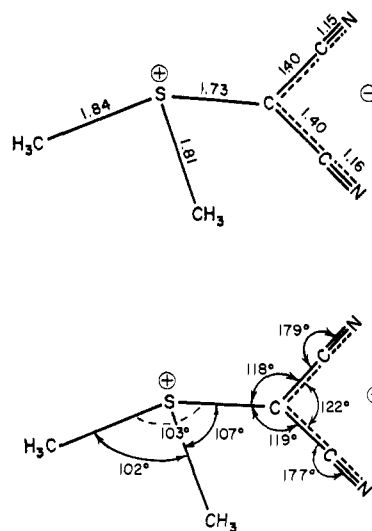


Figure 2. X-Ray crystallographic data on 2-dimethylsulfuranylidene-malononitrile (**13a**): (a) band lengths in Ångströms (± 0.01 Å), (b) bond angles. Details of this work will be published elsewhere.²⁸

2-Dimethylsulfuranylidene-1,3-indandione (7a). Indan-1,3-dione (1.46 g, 10 mmol), DCC (5.15 g, 25 mmol), and anhydrous phosphoric acid (5 mmol) were treated overnight in a mixture of DMSO (10 ml) and benzene (10 ml). The reaction was worked up exactly as above giving, after evaporation of the aqueous phase, an orange residue which was dissolved in ethyl acetate and chromatographed on a column containing 150 g of silicic acid. Elution with ethyl acetate removed some highly colored impurities and the desired compound was removed with acetone. Crystallization from acetone gave 1.66 g (80%) of the ylide **7a** as bright yellow crystals of mp 190–191°; molecular weight, 206.

2-Diethylsulfuranylidene-1,3-indandione (7b). Indan-1,3-dione (1.46 g, 10 mmol), DCC (5.15 g, 25 mmol), and anhydrous phosphoric acid (5 mmol) were treated overnight in a mixture of diethyl sulfoxide³¹ (10 ml) and benzene (10 ml). After removal of dicyclohexylurea the residue was partitioned between ethyl acetate and water. Chromatography of the dark colored organic phase on a column of silicic acid with acetone-ethyl acetate (2:1) gave 2.77 g (76%) of yellow crystalline ylide of mp 139–140°. Evaporation of the aqueous layer and chromatography of the yellow residue on silicic acid as above gave a further 0.40 g (total yield 93%) of pure **7b**. Recrystallization from acetone-ether did not change the melting point; $\lambda_{\text{max}}^{\text{MeOH}}$ 216 m μ (ϵ 23,400), 220 (24,000), 258 (29,500), 267 (28,500), and 370 (1300), all unchanged in alkali; $\nu_{\text{max}}^{\text{KBr}}$ 1590 and 1630 cm⁻¹. The nmr spectrum is shown as Figure 1; molecular weight, 234.

2-Dipropylsulfuranylidene-1,3-indandione (7c). 1,3-Indandione (1.46 g, 10 mmol), DCC (4.9 g), and anhydrous phosphoric acid (5 mmol) were treated overnight in a mixture of di-*n*-propyl sulfoxide (7.3 g, 55 mmol) and benzene (10 ml). After dilution with benzene and removal of dicyclohexylurea the filtrate was partitioned between water and ethyl acetate. The organic layer was washed with water and evaporated to dryness leaving a red syrup that was chromatographed on a column of silicic acid using ethyl acetate-acetone (1:1). After removal of minor colored impurities a yellow compound was obtained and crystallized from ether giving 1.99 g (76%) of the ylide **7c** of mp 64–66°, unchanged upon recrystallization; $\lambda_{\text{max}}^{\text{MeOH}}$ 216 m μ (ϵ 23,000), 220 (23,600), 257 (32,000), 266 (30,800), and 365 (1400), unchanged in alkali; $\nu_{\text{max}}^{\text{KBr}}$ 1590 and 1630 cm⁻¹. The nmr spectrum (CDCl₃) showed two hexuplets ($J_{\text{gem}} = 12$ cps, $J_{\text{ax}} = 7.5$ cps) at 3.85 and 3.00 ppm, the internal methylene groups as a multiplet centered at 1.75 ppm, the methyl group as a triplet ($J = 7$ cps) at 1.06 ppm, and the aromatic protons as a multiplet at 7.40–7.65 ppm; molecular weight, 262.

2-Tetramethylenesulfuranylidene-1,3-indandione (7d). The reaction between 1,3-indandione (1.46 g, 10 mmol), DCC (5.15 g, 25 mmol), and anhydrous phosphoric acid (5 mmol) in a mixture of tetramethylene sulfoxide (10 ml) and benzene (10 ml) was worked

(31) Prepared by oxidation of diethyl sulfide with hydrogen peroxide in acetone, bp 60° (0.1 mm).

up as above. The neutralized aqueous extracts were evaporated to dryness under high vacuum at 50° leaving a partially crystalline residue which was chromatographed on a column of silicic acid using acetone. The chromatographically homogeneous yellow product was crystallized from cold acetone giving 1.03 g (45%) of the ylide **7d** of mp 162–164°; $\lambda_{\text{max}}^{\text{MeOH}}$ 216 m μ (ϵ 23,500), 220 (23,500), 261 (25,500), 269 (30,000), 385 (1600); $\nu_{\text{max}}^{\text{KBr}}$ 1585 and 1625 cm $^{-1}$. The nmr spectrum is discussed in the text; molecular weight, 232.

3-Dimethylsulfuranylidene-2,4-pentanedione (8a). 2,4-Pentanedione (2.0 g, 20 mmol), DCC (10.3 g, 50 mmol), and anhydrous phosphoric acid (10 mmol) were treated overnight in a mixture of DMSO (20 ml) and benzene (20 ml). The mixture was worked up as above and the neutralized aqueous phase was evaporated to dryness under high vacuum at 50°. The resulting semicrystalline residue (2.4 g) was extracted with warm acetone and crystallized from a small volume of acetone giving 2.0 g (63%) of the ylide **8a** with mp 166–167°; molecular weight, 160.

Ethyl 2-Dimethylsulfuranylidene-3-ketobutyrate (9). The reaction of ethyl acetoacetate (1.45 g, 15 mmol), DCC (7.73 g, 37.5 mmol), and anhydrous orthophosphoric acid (7.5 mmol) in a mixture of DMSO (15 ml) and benzene (15 ml) was worked up as above. The neutralized aqueous extracts were evaporated to dryness leaving a brown syrup that was extracted with hot acetone. Evaporation of the extracts left a syrup that slowly crystallized. Recrystallization from acetone-ether gave 1.0 g (35%) of **9** as prisms of mp 58–60°; molecular weight, 190.

2-Dimethylsulfuranylideneacetoacetanilide (10). Acetoacetanilide (1.77 g, 10 mmol), DCC (5.15 g, 25 mmol), and anhydrous phosphoric acid (10 mmol) were treated overnight in DMSO (10 ml) and benzene (10 ml). Evaporation of the neutralized aqueous extracts left a semicrystalline residue that was crystallized from ethyl acetate giving 1.16 g (49%) of **10** with mp 156.5–158°; molecular weight, 237.

Diethyl 2-Dimethylsulfuranylidene malonate (11). Diethyl malonate (1.60 g, 10 mmol), DCC (5.15 g, 25 mmol), and anhydrous phosphoric acid (5 mmol) were treated overnight in DMSO (10 ml) and benzene (10 ml). The mixture was diluted with ether, filtered, and extracted four times with water. The aqueous extracts were neutralized to pH 7.5 with sodium hydroxide and evaporated to dryness leaving 0.80 g of a waxy solid that was extracted with chloroform and chromatographed on a column containing 80 g of silicic acid using chloroform-methanol (10:1). The crystalline ultraviolet absorbing product (0.875 g, 40%) could be recrystallized from acetone-ether with mp 134–136°; molecular weight, 220.

Methyl 2-Dimethylsulfuranylidene cyanoacetate (12a). Methyl cyanoacetate (1.50 g, 15 mmol), DCC (7.73 g, 37.5 mmol), and anhydrous phosphoric acid (7.5 mmol) were treated overnight in DMSO (15 ml) and benzene (10 ml). The ylide **12a** was isolated from the aqueous solution and crystallized from acetone-ether giving 1.62 g (62%) of colorless product of mp 158–160°; molecular weight, 159.

Methyl 2-Dipropylsulfuranylidene cyanoacetate (12b). Methyl cyanoacetate (2.0 g, 20 mmol), DCC (8.2 g, 40 mmol), and anhydrous phosphoric acid (2.5 mmol) were treated overnight with di-*n*-propyl sulfoxide (4.0 g, 30 mmol) in benzene (10 ml). Following addition of ethyl acetate and removal of dicyclohexylurea, the filtrate was extracted several times with water. The organic layer was then chromatographed on a column of silicic acid with ethyl acetate, and the ultraviolet absorbing product was recrystallized from acetone-ether giving 1.76 g (41%) of **12b** of mp 53–54°; $\lambda_{\text{max}}^{\text{MeOH}}$ 222 m μ (ϵ 11,900) unchanged in alkali; $\nu_{\text{max}}^{\text{KBr}}$ 1655 and 2175 cm $^{-1}$. The nmr spectrum (CDCl₃) showed a three-proton singlet (OMe) at 3.68 ppm, the CH₂S group as hexuplets ($J_{\text{gem}} = 12$ cps, $J_{\text{ax}} = 7$ cps) centered at 2.88 and 3.32 ppm, the internal methylene groups as a broadened hexuplet at 1.82 ppm, and the methyl groups as a triplet ($J = 7$ cps) at 1.09 ppm; molecular weight, 215.

2-Dimethylsulfuranylidene malononitrile (13a). Malononitrile (9.9 g, 150 mmol), DCC (51.4 g, 250 mmol), and anhydrous phosphoric acid (7.5 g, 75 mmol) were treated overnight in DMSO (100 ml).

The product was isolated from the aqueous extracts in the usual way and crystallized from acetone-ether giving 10.84 g (57%) of **13a**, mp 99–100°; molecular weight, 126.

2-Diethylsulfuranylidene malononitrile (13b). Malononitrile (0.66 g, 10 mmol), DCC (5.15 g, 25 mmol), and anhydrous phosphoric acid (3.8 mmol) were treated overnight in diethyl sulfide (5 ml) and benzene (5 ml). After partitioning between water and ethyl acetate the product was located primarily in the organic phase. The ethyl acetate solution was evaporated and chromatographed on two 1-m long preparative thin layer plates using chloroform-ethyl acetate (1:1). Elution of the single ultraviolet absorbing band with acetone followed by evaporation to dryness left 1.09 g (71%) of crystalline, homogeneous ylide **13b** of mp 84–85°, unchanged upon recrystallization from acetone-ether; $\lambda_{\text{max}}^{\text{MeOH}}$ 235 m μ (ϵ 4800), unchanged in alkali; $\nu_{\text{max}}^{\text{KBr}}$ 2170 and 2195 cm $^{-1}$. The nmr spectrum in CDCl₃ showed only two equivalent ethyl groups as a triplet ($J = 7$ cps) at 1.48 ppm and a quartet ($J = 7$ cps) at 3.01 ppm; molecular weight, 154.

Diethyl 2-(Dimethylsulfuranylidene) cyanomethylphosphonate (14). Diethyl cyanomethylphosphonate (1.78 g, 10 mmol) was treated overnight with DCC (6.18 g, 30 mmol) and anhydrous phosphoric acid (5 mmol) in a mixture of DMSO (10 ml) and benzene (5 ml). After removal of dicyclohexylurea and partitioning between water and ethyl acetate the aqueous phase was evaporated to dryness under high vacuum and chromatographed on four 1-m long preparative silica plates using chloroform-methanol (9:1). The ultraviolet absorbing band was eluted with methylene chloride-methanol (4:1) giving 1.10 g (46%) of the pure ylide **14** which spontaneously crystallized. The product could be recrystallized from acetone-ether with mp 72–73° but was hygroscopic; molecular weight, 237.

1-Nitroso-1,3-dicyclohexylurea (27). a. 1,1-Dinitroethane (8.0 ml of a 30% solution in methylene chloride, 20 mmol) and DCC (12.36 g, 60 mmol) were dissolved in a mixture of DMSO (10 ml) and benzene (10 ml), and anhydrous phosphoric acid (10 mmol) was added. An exothermic reaction took place after a few minutes, and the mixture was stored for 30 min. Ether (50 ml) was added and, after filtration of dicyclohexylurea, the solution was extracted three times with water, dried, and evaporated to dryness leaving 6.9 g of an orange oil. This was chromatographed on a column of silicic acid using benzene which gave a single ultraviolet absorbing product in tubes 28–50 (20 ml each). Evaporation of these fractions left 1.76 g of a light yellow oil that was crystallized from hexane (some gas evolution during heating) giving 1.0 g (20%) of **27** as pale yellow crystals of mp 67–68°. Storage of the crystals at room temperature led to slow decomposition with gas evolution; $\lambda_{\text{max}}^{\text{MeOH}}$ 225 m μ (ϵ 5800); $\nu_{\text{max}}^{\text{KBr}}$ 1735 and 3365 cm $^{-1}$ (cf. 1-nitroso-1-methylurea $\nu_{\text{max}}^{\text{KBr}}$ 1730 cm $^{-1}$). The nmr spectrum showed only 20 aliphatic protons at 1.0–2.3 ppm and two nonexchangeable protons (=NCHR₂) as diffuse multiplets at roughly 3.8 and 4.6 ppm. The mass spectrum showed a molecular ion at m/e 253.

Anal. Calcd for C₁₃H₂₂N₂O: C, 61.63; H, 9.15; N, 16.59; O, 12.53. Found: C, 61.79; H, 9.09; N, 17.20; O, 11.95.

b. Dicyclohexylurea (1.12 g, 5 mmol) was dissolved with warming in glacial acetic acid (15 ml) and then cooled. Isoamyl nitrite (1 ml) was added giving a clear yellow solution. After 30 min the solvent was evaporated to dryness *in vacuo* leaving 1.35 g of a yellow oil that was dissolved in warm hexane (15 ml) and filtered from a little insoluble material. Upon cooling 905 mg (72%) of **27** of mp 67–68° separated and was identical with that above.

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