References and Notes

(1) (a) Support of this work by U.S. Public Health Service Grant CA 08495, National Cancer Institute, is gratefully acknowledged; (b) presented in part as a preliminary communication: K. T. Potts, E. Houghton, and U. P. Singh, *Chem. Commun.*, 1128, 1129 (1969).
(2) K. T. Potts, E. Houghton, and U. P. Singh, *J. Org. Chem.*, **39,** 3619 (1974).
(3) (a) A recent review which summarizes earlier concepts and references is: M. Ohta and H. Kato in "Non-benzenoid Aromatics," J. P. Snyder, Ed., Academic Press, New York, N. Y., 1969, Chapter 4; (b) W. Baker and W. D. Ollis, *Quart. Rev., Chem. Soc.*, **11,** 15 (1957).
(4) Only oxygen is considered as the exocyclic atom here, the number of possibilities greatly increasing when sulfur, nitrogen, and carbon atoms are considered.
(5) M. Ohta, H. Chosho, C. Shin, and K. Ichimura, *J. Chem. Soc. Jap.*, **85,** 440 (1964).
(6) A. Shaikh, A. Chinone, and M. Ohta, *Bull. Chem. Soc. Jap.*, **43,** 453 (1970).
(7) (a) R. Huisgen, E. Funke, H. Gotthardt, and H. L. Pauke, *Chem. Ber.*, **104,** 1532 (1971); (b) H. Gotthardt and B. Christl, *Tetrahedron Lett.*, 4747 (1968).
(8) Z. Takayanagi, H. Kato, and M. Ohta, *Bull. Chem. Soc. Jap.*, **40,** 2930 (1967).
(9) K. T. Potts and S. Husain, *J. Org. Chem.*, **35,** 3451 (1970).
(10) K. Jensen and I. Crossland, *Acta Chem. Scand.*, **17,** 144 (1963).
(11) K. T. Potts and Syeda Husain, *J. Org. Chem.*, **36,** 3368 (1971); F. H. C. Stewart and N. Danieli, *Chem. Ind.*, 1926 (1963); H. U. Daeniker and J. Druey, *Helv. Chim. Acta*, **45,** 2426 (1962).
(12) G. M. Clarke and D. H. Williams, *J. Chem. Soc.*, 4597 (1965); R. A. Olofson and J. M. Landesberg, *J. Amer. Chem. Soc.*, **88,** 4263 (1966).
(13) P. Haake and W. B. Miller, *J. Amer. Chem. Soc.*, **85,** 4044 (1963).
(14) (a) R. Huisgen, *Angew. Chem. Int. Ed. Engl.*, **2,** 565 (1963); (b) J. Butler, S. Wassenaar, and R. M. Kellogg, *J. Org. Chem.*, **37,** 4045 (1972).
(15) K. T. Potts, A. J. Elliott, and M. Sorm., *ibid.*, **37,** 3838 (1972), and references listed therein.
(16) K. T. Potts and U. P. Singh, *Chem. Commun.*, 570 (1969); H. Gotthardt and B. Christl, *Tetrahedron Lett.*, 4743 (1968).
(17) T. Mukaiyama, K. Hagio, H. Takei, and K. Saigo, *Bull. Chem. Soc. Jap.*, **44,** 161 (1971).
(18) K. T. Potts and D. McKeough, *J. Amer. Chem. Soc.*, **95,** 2750 (1973).
(19) R. Helder and H. Wynberg, *Tetrahedron Lett.*, 605 (1972); K. Hafner and W. Kaiser, *ibid.*, 2185 (1964).
(20) (a) K. T. Potts, J. Baum, and E. Houghton, *J. Org. Chem.* **39,** 3631 (1974); (b) K. T. Potts, to be published.
(21) B. P. Stark and A. J. Duke in "Extrusion Reactions," Pergamon Press, Oxford, 1967, Chapter 6.
(22) S. Kapf and C. Paal, *Ber.*, **21,** 3053 (1888); E. Fromm, P. Fantl, and E. Leibsohn, *Justus Liebigs Ann. Chem.*, **457,** 267 (1927).
(23) Spectral characterizations were carried out with the following instrumentation: ir, Perkin-Elmer Model 421 and 137 infrared spectrophotometers; uv, Cary Model 14 spectrophotometer; nmr, Varian A-60 spectrometer using TMS as internal standard; mass spectra, Hitachi Perkin-Elmer RMU-6E mass spectrometer at 70 eV using the direct insertion probe at a temperature of *ca.* 150°. Evaporations were done under reduced pressure using a rotavap apparatus and melting points were determined in capillaries. Analyses are by Galbraith Laboratories, Knoxville, Tenn., and Instranal Laboratories Inc., Rensselaer, N.Y.
(24) We thank Dr. D. McKeough for this experiment.

Mesoionic Compounds. XXXII. Cycloaddition Reactions of the *anhydro*-4-Hydroxythiazolium Hydroxide System with Olefinic Dipolarophiles[1]

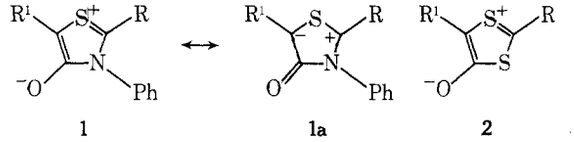
K. T. Potts,* J. Baum,[1a] and E. Houghton

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181

Received April 19, 1974

Di- and trisubstituted derivatives of the mesoionic *anhydro*-4-hydroxythiazolium hydroxide system underwent 1,3-dipolar cycloadditions *via* their thiocarbonyl ylide dipole giving stable 1:1 adducts of the substituted 1,2,3,4,5,6-hexahydro-3-oxo-1α,4α-epithiopyridine system with a wide variety of electron-deficient dipolarophiles. The stereochemistry of each adduct was determined by extensive nmr analysis and also by chemical methods. Several adducts lost the elements of H_2S upon treatment with sodium methoxide forming 4,5-disubstituted 1,3,6-triphenylpyrid-2-ones, and with *m*-chloroperbenzoic acid gave sulfoxide derivatives.

The title mesoionic ring system **1** has been shown[2] to undergo ready cycloaddition of acetylenic dipolarophiles to yield substituted 2-pyridones and thiophenes in good yields. The ring system contains a "masked" thiocarbonyl ylide dipole **1a** stabilized to some extent by an adjacent nitrogen atom. The same ylide is present in the *anhydro*-4-hydroxy-1,3-dithiolium hydroxide system **2** which has also



1 **1a** **2**

been shown to undergo cycloaddition of acetylenic dipolarophiles[3] to yield substituted thiophenes with elimination of carbonyl sulfide, as well as forming stable 1:1 cycloadducts with olefinic dipolarophiles.[4]

A study of the cycloaddition reactions of **1** was thus of particular interest. It would enable the effect of replacing the 3-sulfur atom in **2** with a nitrogen atom to be evaluated, as well as providing a novel series of bridged sulfur, bicyclic adducts incorporating a hexahydro-3-oxo-1α,4α-epithiopyridine system.

Electron-deficient olefins such as dimethyl maleate and fumarate, *N*-phenylmaleimide, maleic anhydride, methyl vinyl ketone, *trans*-dibenzoylethylene, ethyl acrylate, ethyl methacrylate, ethyl crotonate, acrylonitrile, and fumaronitrile all formed stable, 1:1 cycloadducts with di- and trisubstituted derivatives of **1** with relative ease. However, no major product was isolated from the reaction of **1** with norbornene, norbornadiene, tetracyanoethylene, 4-cyanopyridine, and chalcone, either in refluxing benzene or at room temperature. Similarly electron-rich olefins such as ethyl vinyl ether resulted in multi-component reaction mixtures from which no single product could be isolated.

The gross structural features of the 1:1 cycloadducts obtained from **1** and the dipolarophiles listed above were established from analytical, mass spectral, and other spectral data (Tables I–IV). All were consistent with the formation of a 1:1 adduct with the thiocarbonyl ylide dipole, and the stereochemistry of these adducts was established from their nmr spectra considered below in increasing order of complexity.

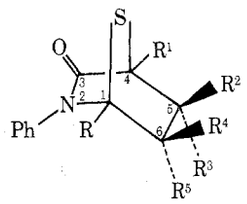
Cycloadducts from *anhydro*-2,3-Diaryl-4-hydroxythiazolium Hydroxide. *N*-Phenylmaleimide Adducts. Reaction of **1** (R = *p*-ClC_6H_4; R^1 = H) with *N*-phenyl-

Table I
Cycloadducts Derived from *anhydro*-2,3-Diaryl-4-hydroxythiazolium Hydroxide and Olefinic Dipolarophiles[a]

Compd no.	Yield, %	Mp,[b] °C	Molecular formula	M.+ (rel int)	Ir, cm^{-1}	uv max (CH_3OH), nm (log ε)
3 (R = *p*-ClC_6H_4)	35	270–273	$C_{25}H_{17}N_2ClO_3S$	460 (8)	1730, 1710 (CO)	220 sh (4.33)
3 (R = Ph)	60	265–267	$C_{25}H_{18}N_2O_3S$	426 (7)	1790, 1700 (CO)	
7 (R = *p*-ClC_6H_4)	38	225–230	$C_{31}H_{22}NClO_3S$	523 (3)	1720, 1690 (CO)	250 (4.23)
9 (R = $COCH_3$)	32	200–204	$C_{19}H_{16}NClO_2S$	357 (17)	1710, 1690 (CO)	224 (4.11)
9 (R = COOEt)	48	139–140	$C_{20}H_{18}NClO_3S$	387 (30)	1750, 1710 (CO)	224 (3.73)
13 (R = *p*-ClC_6H_4)	66	225–228	$C_{19}H_{12}NClO_4S$	385 (5)	1800, 1730 (CO)	245 sh (3.22), 223 (3.96)
15 (R = *p*-ClC_6H_4)	19	158–160	$C_{21}H_{13}NClO_5S$	431 (3)	1740, 1720 (CO)	222 (3.85)
15 (R = Ph)	70	164–165	$C_{21}H_{13}NO_5S$	397 (30)	1750, 1730, 1700 (CO)	205 (4.62)
16 (R = *p*-ClC_6H_4)	41	217–219	$C_{21}H_{13}NClO_5S$	431 (3)	1760, 1720 (CO)	222 (4.07)
16 (R = Ph)	63	219–220	$C_{21}H_{13}NO_5S$	395 (3)	1740, 1690 (CO)	240 (3.44), 206 (4.04)
17	97	235–240	$C_{25}H_{18}N_2O_4S$	442 (39)	1725 (CO), 1090 (SO)	277 (4.01)

[a] Satisfactory analytical values (±0.4% for C, H, N) were reported for all compounds in table: Ed. [b] All melting points accompanied by decomposition.

Table II
Methine and Alkyl Group Chemical Shifts and Coupling Constants for Cycloadducts Derived from *anhydro*-2,3-Diaryl-4-hydroxythiazolium Hydroxides and Olefinic Dipolarophiles[a]

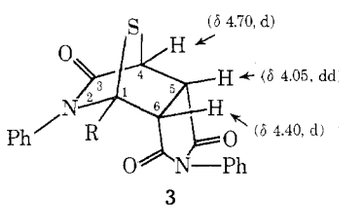


Compd no.	Chemical shifts (δ) R1	R2	R3	R4	R5	Coupling constants, Hz $J_{1,2}$	$J_{1,3}$	$J_{2,3}$	$J_{2,4}$	$J_{3,4}$
3, R = *p*-ClC_6H_4;[b] $R^3 = R^5$ = CONPhCO	4.70, d	4.05, dd		4.40, d		1.5			7.0	
3, R = Ph;[b] $R^3 = R^5$ = CONPhCO	4.69, d	4.09, dd		4.40, d		1.5			6.5	
7, R = *p*-ClC_6H_4;[b] $R^2 = R^5$ = COPh	4.43, d		4.83, t	5.80, d			4.0			4.5
9, R = *p*-ClC_6H_4;[b] $R^5 = COOCH_3$	4.27, dd	2.97, qd	2.52, qd	4.02, dd	*2.03*, s	1.0	3.5	12.5	8.0	4.5
9, R = *p*-ClC_6H_4;[c] $R^5 = COOCH_2CH_3$	4.22, dd	2.95, qd	2.71, qd	4.11, dd	3.91, q *0.97*, t	1.3	3.5	13.5	8.3	4.5
13, R = *p*-ClC_6H_4;[d] $R^3 = R^5$ = COOCO	4.97, d	4.70, dd		5.20, d		1.5			7.0	
15, R = *p*-ClC_6H_4; $R^2 = R^5 = COOCH_3$	4.48, d	*3.85*, s	4.08, t	4.42, d	*3.48*, s		3.8			4.3
15, R = Ph; $R^2 = R^5 = COOCH_3$	4.50, d	*3.83*, s	4.07, t	4.40, d	*3.42*, s		4.25			3.75
16, R = *p*-ClC_6H_4; $R^3 = R^5 = COOCH_3$	4.46, d	3.98, dd	*3.75*, s	4.37, d	*3.32*, s	1.0			9.0	
16, R = Ph; $R^3 = R^5 = COOCH_3$	4.51, d	4.00, dd		4.40, d		1.0			9.0	
17, R = Ph; $R^3 = R^5$ = CONPhCO	4.68, d	4.23, dd		5.17, d		1.5			9.0	

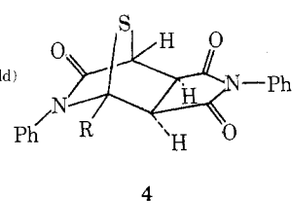
[a] Methyl resonances in italics. [b] Determined in $CDCl_3$. [c] Determined in acetone-d_6. [d] Determined in DMSO-d_6.

maleimide in refluxing anhydrous benzene gave a stable product corresponding to a 1:1 cycloadduct.

The structure of this adduct was assigned on the following basis. Infrared carbonyl absorptions were observed at 1730 and 1710 cm^{-1}, and the nmr spectrum (Table II) showed besides aromatic protons three aliphatic proton multiplets consisting of two groups of doublets (δ 4.40, 4.70) and one doublet of doublets (δ 4.05). These data are consistent with either the endo structure **3** (R = *p*-ClC_6H_4) or the exo structure **4** (R = *p*-ClC_6H_4). The stereochemistry of the 1:1 adduct is assigned the endo configuration by analogy with similar cycloadducts in the isobenzothiophene system[5] where with *N*-phenylmaleimide a mixture of endo, **5**, and exo, **6**,



3



4

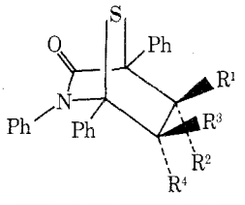
isomers was obtained. Assignments of the α-imido and bridgehead protons are as shown. It was postulated in this case that the difference in chemical shift between the protons α to the imide carbonyl from exo to endo was due to the deshielding effect of the sulfide

Table III
Cycloadducts Derived from *anhydro*-4-Hydroxy-2,3,5-triphenylthiazolium Hydroxides and Olefinic Dipolarophiles[a]

Compd no.	Yield, %	Mp, °C	Molecular formula	$M^{\cdot+}$ (rel int)	Ir, cm^{-1}	uv max (CH_3OH), nm (log ε)
19 (R = $COCH_3$)	17	180–182 dec	$C_{25}H_{21}NO_2S$	399 (2)	1700 (broad, CO)	
20	12.5	142–144 dec	$C_{25}H_{21}NO_2S$	399 (3)	1710 (broad, CO)	
21	17.5	148–150 dec	$C_{27}H_{25}NO_3S$	443 (21)	1750, 1720 (CO)	
22	17	170–172 dec	$C_{27}H_{25}NO_3S$	443 (6)	1740–1700 (broad, CO)	
24a	57.5	254–257 dec	$C_{25}H_{15}N_3O$	373 (100)	2240 (CN), 1680 (CO)	358 (3.83), 271 (3.82), 215 sh (4.29)
24b	87	290–293 dec	$C_{37}H_{25}NO_3$	531 (63)	1680, 1650 (CO)	340 (3.94), 254 (4.33)
24c	53.5	275–277	$C_{31}H_{20}N_2O_3$	468 (100)	1730, 1680 (CO)	362 (3.73), 287 (4.06)
24d	17	219–221 dec	$C_{27}H_{21}NO_5$	439 (100)	1745, 1670 (CO)	328 (3.74), 255 (3.64)
25a	70	198–200 dec	$C_{25}H_{17}N_3OS$	407 (4)	2250 (CN), 1720 (CO)	
25b	73	218–220 dec	$C_{37}H_{27}NO_3S$		1720, 1690, 1680 (CO)	250 (4.15)
25c	70	233–235	$C_{31}H_{22}N_2O_3S$	502 (2)	1790, 1710 (CO)	
25d	80	151–152	$C_{27}H_{23}NO_5S$	473 (5)	1735, 1725, 1700 (CO)	
25e	75	215–216	$C_{27}H_{23}NO_5S$	473 (4)	1750, 1700 (CO)	
28	84	250 dec	$C_{25}H_{17}NO_4S$	427 (2)	1780, 1710 (CO)	
29	48	240–242 dec	$C_{25}H_{19}NO_5S$		1750, 1740, 1690 (CO)	235 sh (3.59)
30	63	240–243 dec	$C_{37}H_{27}NO_4S$	581 (1)	1710, 1680 (CO), 1080 (SO)	251 (4.51)
31, 32	62	202–205	$C_{27}H_{23}NO_6S$	489 (1)	1740, 1720 (CO), 1085 (SO)	

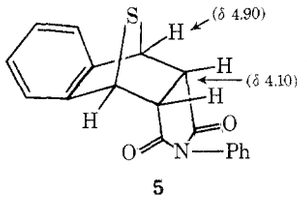
[a] Satisfactory analytical values (±0.4% for C, H, N) were reported for all compounds in table: Ed.

Table IV
Methine and Alkyl Group Chemical Shifts and Coupling Constants for Cycloadducts Derived from *anhydro*-4-Hydroxy-2,3,5-triphenylthiazolium Hydroxides and Olefinic Dipolarophiles

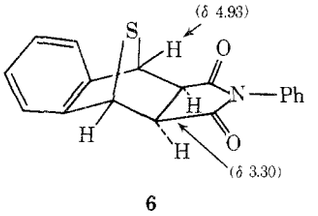


Compd no.	Chemical shifts (δ) R¹	R²	R³	R⁴	Coupling constants, Hz $J_{1,2}$	$J_{1,3}$	$J_{2,3}$	$J_{1,4}$	$J_{2,4}$
19, $R^4 = COCH_3$[a]	3.23, dd	2.80, dd	4.07, dd	*2.03*, s	13.5	8.5	5.0		
19, $R^4 = CN$[b]	3.47, dd	3.08, dd	4.76, dd		13.0	8.0	3.5		
20, $R^3 = COCH_3$[a]	3.40, dd	3.21, dd	*1.79*, s	3.88, dd	12.5			5.3	8.0
21, $R^1 = CH_3$;[a] $R^4 = COOCH_2CH_3$	*1.48*, d	3.52, dq	3.49, d	3.98, q[d] *0.99*, t	7.0		4.5		
22, $R^3 = CH_3$;[a] $R^4 = COOCH_2CH_3$	4.23, d	2.90, d	*1.70*, s	3.75, m[e] *0.77*, t	12.0				
25a, $R^1 = R^4 = CN$[a]		4.22, d	4.46, d				3.8		
25b, $R^1 = R^4 = COPh$[a]		5.18, d	5.70, d				6.0		
25c, $R^2 = R^4 = CONPhCO$[a]	4.17, d		4.54, d			6.5			
25e, $R^2 = R^4 = COOCH_3$[a]	4.31, d		4.52, d			9.0			
25d, $R^1 = R^4 = COOCH_3$[a]	*5.46*, s	4.29, d	4.52, d	*3.69*, s		4.5			
29, $R^2 = R^4 = COOH$[c]	4.47, d	12.40, s	4.78, d	12.40, s		8.5			

[a] Determined in $CDCl_3$, methyl resonance in italics. [b] Determined in acetone-d_6. [c] Determined in DMSO-d_6. [d] $J_{CH_2CH_3}$ = 7.0 Hz. [e] Nonequivalent methylene group.



5



6

bridge. These data are consistent with the data described above for the mesoionic *N*-phenylmaleimide adduct in an endo configuration. The coupling constant between the 4 and 5 protons in **3** (R = *p*-ClC_6H_4) was 1.5 Hz, indicating a trans coupling, and between the 5 and 6 protons it was 7.0 Hz, consistent with a cis coupling, these values being noteworthy in light of the following description of cycloadducts and their physical characteristics.

Under similar conditions 1 (R = Ph; R^1 = H) gave an analogous product whose physical constants are described in Tables I and II.

***trans*-Dibenzoylethylene Adduct.** The reaction of 1 (R = *p*-ClC_6H_4; R^1 = H) with *trans*-dibenzoylethylene gave a stable 1:1 cycloadduct, mp 225–230° dec, in moderate yield (38%), which may have either of the two possible isomeric configurations **7** or **8**.

The 5-exo,6-endo configuration **7** was demonstrated by the nmr spectrum, with doublets at δ 4.43 (H_4) (J = 4.0 Hz) and δ 5.80 (H_6)

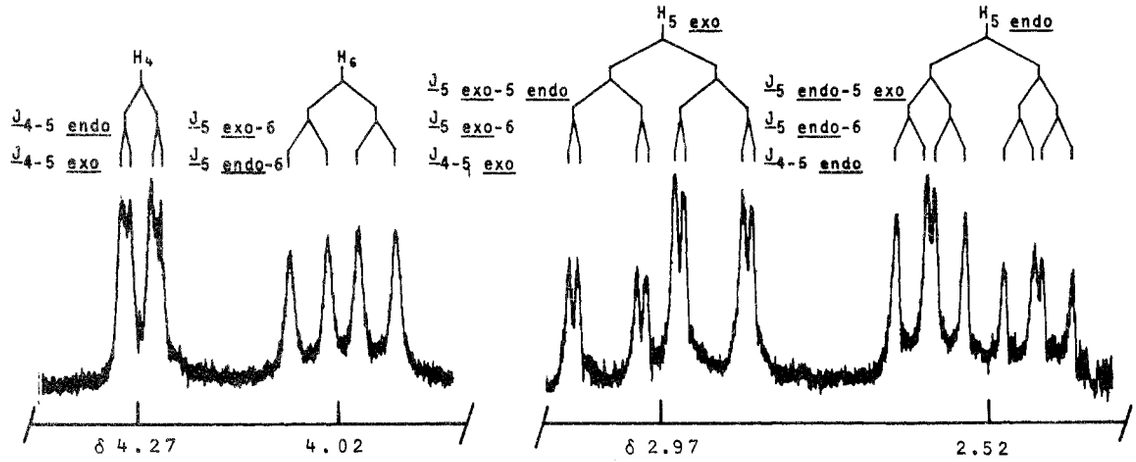
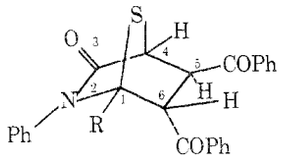
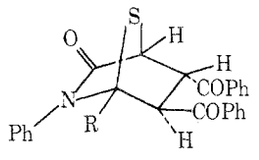


Figure 1. 100-MHz nmr spectrum of 6β-acetyl-1-*p*-chlorophenyl-1,2,3,4,5,6-hexahydro-2-phenyl-1α,4α-epithiopyrid-2-one.



7

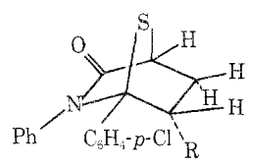


8

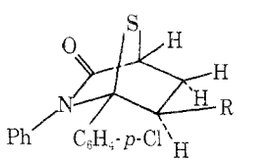
(J = 4.5 Hz) and a triplet at δ 4.83 being consistent with the trans arrangement of protons as shown. Additional evidence was provided from the nmr data of the *trans*-dibenzoylethylene adducts derived from 2,3-diphenylindenone oxide and also isobenzofuran[6] in which the 7-exo proton resonates at lower field relative to the corresponding 7-endo proton due in part to the deshielding by the oxide bridge. Since the sulfur bridge is expected to be more deshielding than an oxide bridge,[6] the 6 proton at δ 5.80 in **7** is in accord with the above results.

Methyl Vinyl Ketone Adduct. Methyl vinyl ketone allows a study of the effect of an asymmetrical olefin upon the course of the cycloaddition reaction, in particular the orientation(s) of any products isolated. The reaction of **1** (R = *p*-ClC_6H_4; R^1 = H) in refluxing methyl vinyl ketone proceeded smoothly, giving a 1:1 adduct in 32% yield with ν_{CO} at 1710 and 1690 cm^{-1} and an absorption maximum at 224 nm (log ε 4.11). The four possible configurations of the primary cycloadduct are shown below, and the 100-MHz spectrum of the adduct is shown in Figure 1.

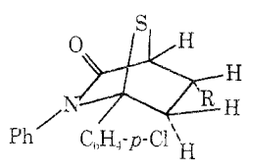
The doublet of doublets at δ 4.27 (J = 1.0 and 3.5 Hz), a second doublet of doublets at δ 4.02 (J = 4.5 and 8.0 Hz), a quartet of doublets at δ 2.97 (J = 1.0, 8.0, and 12.5 Hz), a second quartet of doublets at δ 2.52 (J = 3.5, 4.5, and 12.5 Hz), and a singlet at δ 2.03 allow structures **11** and **12** (R = $COCH_3$) to be eliminated immediately on the basis that the two high-field multiplets (δ 2.97, 2.52) show coupling to three protons whereas structures **11** and **12**



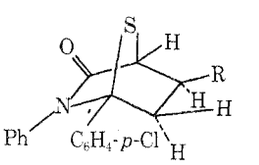
9



10



11



12

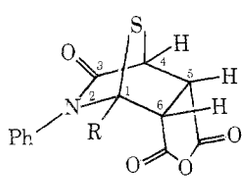
should show only one proton (H_5) coupled to three others. From this coupling information, proton 4 is assigned the multiplet at δ 4.27 since it is twice coupled in a trans fashion and falls in a chemical shift region consistent with other bridgehead protons. The δ 4.02 multiplet is assigned proton 6 since it would be anticipated to contain both a cis and trans coupling in either **9** or **10**, and be deshielded by an adjacent acetyl group. The proton at δ 2.97 is assigned to $H_{5\text{-exo}}$, being deshielded by the sulfide bridge relative to $H_{5\text{-endo}}$ which is now assigned at δ 2.52. It is also clear that $H_{5\text{-exo}}$ and H_6 are cis coupled (J = 8.0 Hz) and thus proton 6 must also be in the exo position. Following these arguments, the most plausible structure for the methyl vinyl ketone adduct is **9** (R = $COCH_3$) in which the acetyl group assumes an endo configuration.

Ethyl Acrylate Adduct. The reaction of **1** (R = *p*-ClC_6H_4; R^1 = H) with ethyl acrylate produced a colorless crystalline product, mp 139–140° dec, in 48% yield with the structural possibility of four different stereoisomers **9–12** (R = COOEt) above. Infrared absorptions (ν_{CO} 1750, 1710 cm^{-1}) and an ultraviolet absorption maximum at 224 nm (log ε 3.73) together with the nmr data (Table II) can best be accommodated in terms of structure **9** (R = COOEt).

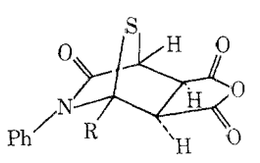
To obtain further information about the stereochemistry of these cycloaddition reactions, the series of cycloadducts described below which are capable of chemical interconversion was synthesized.

Maleic Anhydride Adduct. Maleic anhydride, at room temperature in dry benzene, afforded a primary cycloadduct in 66% yield with the following principal nmr characteristics.

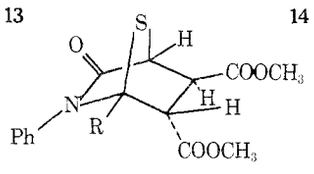
A doublet with a cis coupling (J = 7.0 Hz) at δ 5.20 must be assigned proton 6 in either the endo **13** or exo **14** structure, and a doublet at δ 7.94 with the small trans coupling (J = 1.0 Hz) is assigned the bridgehead proton 4. Proton 5 appears as a doublet of doublets at δ 4.70. These data are consistent with the endo structure **13** (R = *p*-ClC_6H_4).



13



14



15

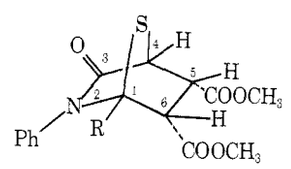
Dimethyl Fumarate Adduct. A primary 1:1 adduct, consistent with the structure **15** (R = *p*-ClC_6H_4) on the

basis of the spectral data immediately following was formed from 1 (R = *p*-ClC_6H_4; R^1 = H) and dimethyl fumarate in refluxing benzene.

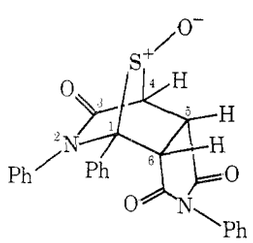
Nmr multiplets at δ 4.48 (d, J = 4.3 Hz) and δ 4.42 (d, J = 3.8 Hz) can be assigned to either H_4 or H_6 and a triplet at δ 4.08 can be assigned to H_5. That the carbomethoxy groups are in the 5-exo,6-endo configuration is postulated from the expectation that the proton 4-proton 5-endo coupling should be approximately 3–4 Hz, in analogy to the *trans*-dibenzoyl adduct 7.

The analogous product obtained from *1* (R = Ph; R^1 = H) and dimethyl fumarate (Tables I and II) was assigned a stereochemistry similar to **15**.

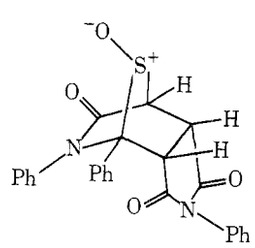
Dimethyl Maleate Adduct. Reaction of **1** (R = *p*-ClC_6H_4; R^1 = H) with diethyl maleate under reflux in dry benzene, gave a product that was identified as a 1:1 primary adduct **16** from its nmr spectrum (100 MHz).



16



17



18

Aliphatic resonance signals at δ 4.46 (d, J = 1.0 Hz), δ 4.37 (d, J = 9.0 Hz), δ 3.98 (dd), δ 3.75 (s), and δ 3.32 (s) were assigned to protons 4, 6, 5, and the two methoxycarbonyl methyl groups at carbons 5 and 6, respectively. These data support a structure **16** with an endo arrangement of methoxycarbonyl groups with respect to the sulfide bridge.

Reaction of dimethyl maleate with 1 (R = Ph; R^1 = H) resulted in a product analogous to **16** (Tables I and II).

Conversion of the Maleic Anhydride Adducts 13 into the Dimethyl Maleate Adduct 16. If the functional groups of the adducts **13** and **16** described above are similarly oriented, then opening of the anhydride moiety in **13** under suitable methylation conditions should give rise to an alternative synthesis of the dimethyl ester **16.** Diazomethane effected the interconversion of the cycloadducts in 98% yield, with the isolation of a product identical in all respects[7] with **16.** Thus the assigned endo stereochemistry is consistent within these two adducts and this stereochemistry most likely occurs in other cycloadducts of this type.

The significant deshielding effect by a sulfoxide group on syn protons has been applied to configurational assignment in suitable pairs of stereoisomeric sulfoxides[8] and, conversely, formation of a sulfoxide by oxidation of a sulfide linkage should yield stereochemical information concerning proximinal protons in these cycloadducts. The proximity of a proton to a sulfoxide oxygen atom results[9] in a downfield shift in the nmr spectrum, as *e.g.*, with the β proton in thietane *S*-oxides.[10] When **3** (R = Ph) was treated with an equimolar amount of *m*-chloroperbenzoic acid in methylene chloride at room temperature, a colorless, crystalline oxidation product was isolated. A strong band at 1090 cm^{-1} in the infrared spectrum indicated a sulfoxide and two possible diasteromeric sulfoxide structures may be proposed, **17** where the S–O bond is syn to the *N*-phenylmaleimide moiety, and **18** in which the sulfoxide is oriented anti. The structure of the sulfoxide was established from nmr data shown below.

	Chemical shift (δ)			Coupling constants, Hz	
Structure	H_4	H_5	H_6	$J_{4,5}$	$J_{5,6}$
3 (R = Ph)	4.73	4.32	4.90	1.5	7.0
17	4.68	4.23	5.17	1.5	9.0

The significant downfield shift noted for H_6 indicating the proximity of the sulfoxide oxygen suggests that the structure of the oxidation product is **17.** The formation of this product is also consistent with steric considerations.

Oxidation of **15** (R = Ph) under similar conditions, however, gave a mixture of isomeric sulfoxides which were inseparable by recrystallization or chromatographic methods. The nmr data obtained from the mixture were consistent with the structural assignments above.

Cycloadditions with *anhydro*-4-Hydroxy-2,3,5-triphenylthiazolium Hydroxide (1, R = R^1 = Ph). In order to evaluate the effect of an additional substituent on the 1,3-dipolar activity of this mesoionic ring system, a series of cycloaddition reactions of (**1**, R = R^1 = Ph) with olefinic dipolarophiles was carried out.

trans-Dibenzoylethylene, *N*-phenylmaleimide, ethyl crotonate, dimethyl maleate, dimethyl fumarate, and maleic anhydride all gave stable 1:1 adducts, obtained in one stereochemical form. Methyl vinyl ketone, however, gave both exo and endo 1:1 adducts whereas acrylonitrile and ethyl methacrylate gave predominantly one isomer, a second isomer being observed by tlc. Fumaronitrile, on the other hand, gave a 1:1 adduct together with its H_2S elimination product, 2-oxo-1,3,6-triphenylpyridine-4,5-dicarbonitrile (**24a**), the relative proportions of these two products being dependent on the reaction time.

Introduction of a phenyl substituent into the 5 position of **1** (R = R^1 = Ph) significantly reduced the rate of reaction with *N*-phenylmaleimide, 3 days being required for its complete reaction, though the major portion of 1 (R = R^1 = Ph) had reacted in 15 hr. However, the stereochemical pattern of adduct formation did not alter the endo adduct **25c** (R^1 = R^3 = H; R^2 = R^4 = CONPhCO) being obtained exclusively. The chemical shifts of the ring junction protons (H_5, H_6) at δ 4.54 and 4.17 ($J_{5,6}$ = 6.5 Hz) (Table IV) can only be rationalized with protons in an exo configuration. This same stereochemistry can also be assigned to the other adducts described in Tables III and IV obtained with 1 (R = R^1 = Ph) in view of the consistency of the chemical shifts of the 5 and 6 protons.

This assumption is supported further by considering the exo and endo adducts obtained with methyl vinyl ketone. When **1** (R = R^1 = Ph) was refluxed in methyl vinyl ketone, the bright red color of the initial solution was discharged within 30 min and removal of excess dipolarophile *in vacuo* afforded a residue which contained two major components (tlc). Their separation was effected by preparative thin-layer chromatography and the two products isolated both corresponded to 1:1 primary cycloadducts. The structures of these adducts are assigned the endo configuration **19** (R = $COCH_3$) and the exo configuration **20** on the basis of spectral data. From the first fraction (R_f 0.5) isolated from chromatography, a colorless product, mp 180–182°, was obtained with carbonyl absorptions under a wide band centered at 1700 cm^{-1} and no absorption maxima above 203 nm. The nmr spectrum of this compound (Figure 2) clearly shows three proton multiplets. The doublet of doublets centered at δ 4.07 contains a trans coupling (J = 5.0 Hz) and a cis coupling (J = 8.5 Hz) and thus is assigned

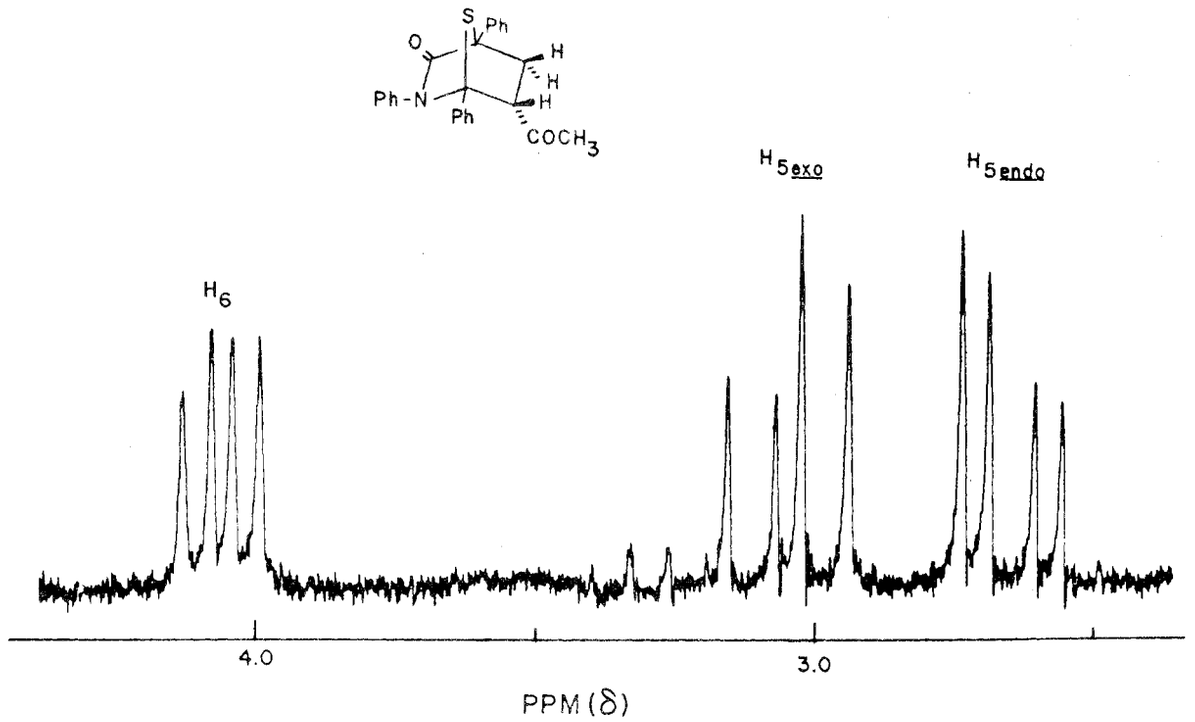


Figure 2. 100-MHz nmr spectrum of 6β-acetyl-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one.

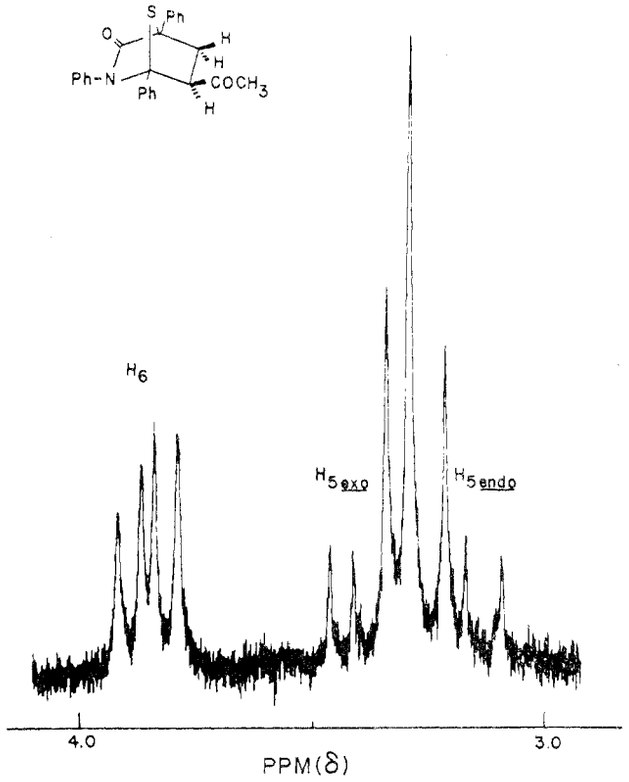


Figure 3. 100-MHz nmr spectrum of 6α-acetyl-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one.

the 6 proton. The doublet of doublets at δ 3.23 contains the cis coupling above, and a geminal coupling (J = 13.5 Hz). The third multiplet at δ 2.80 is both trans and geminally coupled. The δ 3.23 resonance multiplet is assigned the 5-exo proton since it would be expected to be further deshielded by the sulfide bridge than the 5-endo proton at δ 2.80. For the 6 proton to be cis coupled to $H_{5\text{-exo}}$ requires an endo acetyl group at carbon 6 and thus the assigned configuration is **19** (R = $COCH_3$).

The second isolated product (R_f 0.6) was obtained as colorless prisms, mp 142–144°, with an infrared spectrum very similar to **19** (R = $COCH_3$). The assignment of an exo configuration **20** for this compound was made on the basis of the nmr spectrum (Figure 3).

The data obtained (Table IV) shows that the furthest downfield multiplet at δ 3.88 (H-6) contains a trans (J = 5.3 Hz) and a cis (J = 8.0 Hz) coupling, the trans coupling being associated with the furthest downfield geminally coupled multiplet at δ 3.40 assigned to $H_{5\text{-exo}}$, and the cis coupling corresponding to the doublet of doublets at δ 3.21, $H_{5\text{-endo}}$. These data substantiate an exo arrangement of the acetyl group and thus the proposed structure is demonstrated to be **20**. It must be emphasized that the orientation of the adducts **19** (R = $COCH_3$) and **20** is based solely upon analogy to the corresponding methyl vinyl ketone adduct **9** described above.

The adducts obtained from ethyl crotonate and ethyl methacrylate (Tables III and IV) differed from each other in the position of the methyl substituent. However, this resulted in a significant and interesting change in their nmr spectra. In the 1:1 adduct from ethyl crotonate, ethyl 1,2,3,4,5,6-hexahydro-5α-methyl-1,2,4-triphenyl-1α,4α-epithiopyridine-6β-carboxylate (**21**), the ethoxycarbonyl group appeared as a quartet (δ 3.98) and a triplet (δ 0.99), these values being noteworthy in regard to the ethyl methacrylate cycloadduct described below. In the latter, ethyl 1,2,3,4,5,6-hexahydro-6α-methyl-3-oxo-1,2,4-triphenyl-1α,4α-epithiopyridine-6β-carboxylate (**22**), the ethoxycarbonyl methyl group was observed as a triplet at δ 0.77 and the adjacent methylene group did not appear as a normal quartet but rather as a complex 14-line pattern understandable in terms of the nonequivalency of these protons (Figure 4). The phenomenom of proton nonequivalency has been reported[11] in a variety of systems having the methylene group directly attached to an asymmetric center, such as in 2-chloro-4-ethyl-3-phenylcyclobut-2-enone (**23**), or in ethoxy groups attached at an asymmetric center, such as in cyclopropylmethylcarbinyl ethyl ether. The nonequivalence of the methylene protons in these cases is due to the asymmetric center of attachment which acts to favor one of the possible rotational conformations about the *O*-methy-

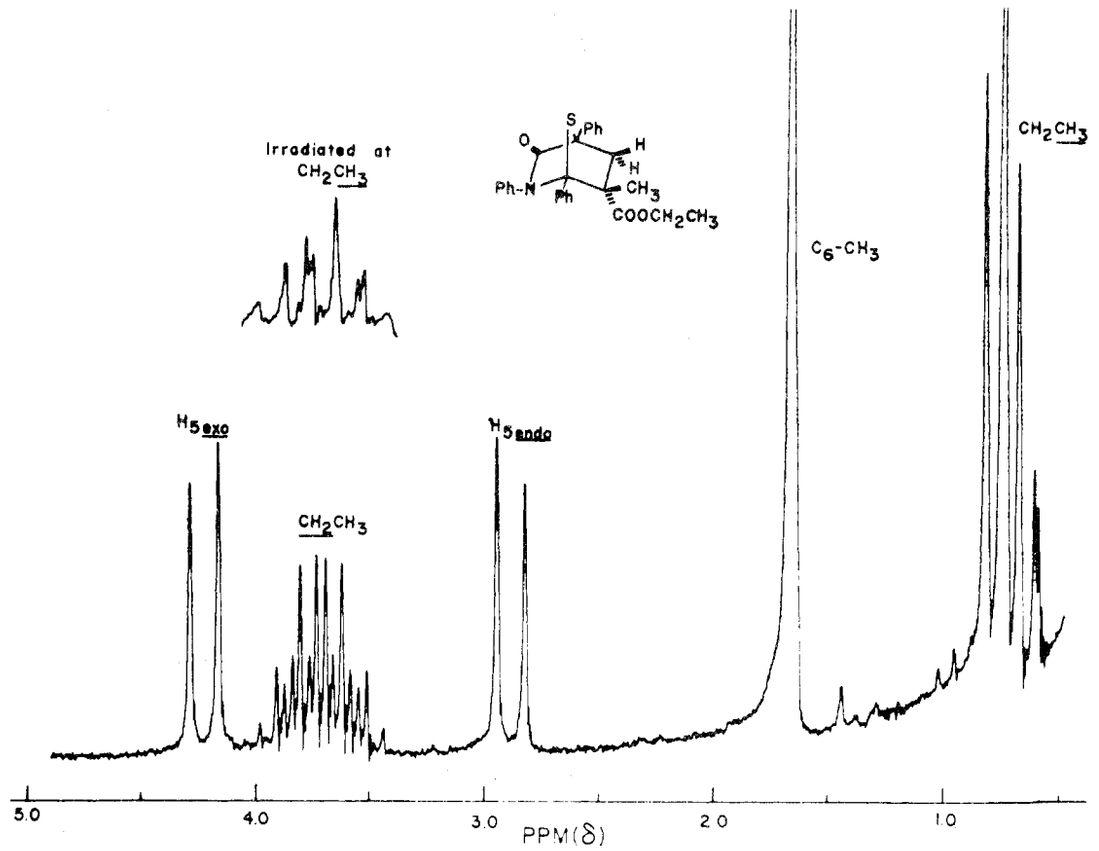
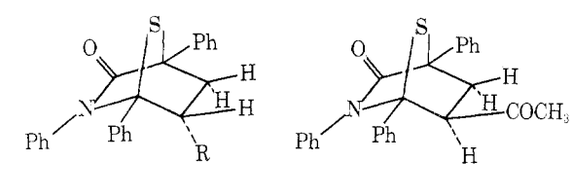
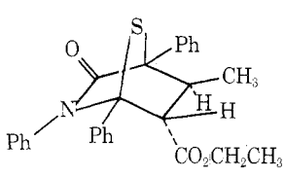


Figure 4. 100-MHz nmr spectrum of ethyl 1,2,3,4,5,6-hexahydro-6α-methyl-3-oxo-1,2,4-triphenyl-1α,4α-epithiopyridine-6β-carboxylate.

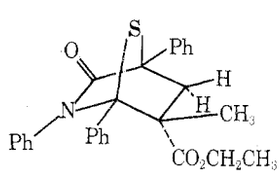


19

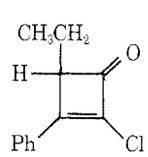
20



21



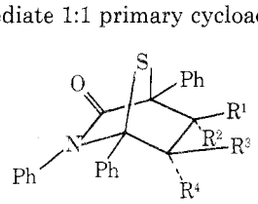
22

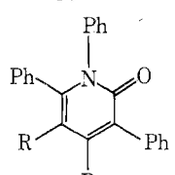


23

lene bond. In the case of the cycloadduct **22**, the asymmetric center at C-6, the bulkiness of the methyl group, and the rigidity inherent in the bicyclic ring system prevent free rotation about the O–CH_2 bond and thus an ABX_3-type pattern consisting essentially of a doublet of quadruplets arises. Theoretically a 16-line pattern is expected but overlapping of resonances reduces this to the observed 14-line multiplet. The exo methyl group at C-6 is apparently necessary for nonequivalence to occur since in the isomeric ethyl crotonate adduct **21**, a normal quartet–triplet ethyl pattern was observed. The ethoxycarbonyl methyl protons resonating as a triplet must be indicative of equal proton coupling between the methyl protons and the nonequivalent methylene protons. The result of a concentrated effort to decouple the methylene protons by irradiating at the center of the methyl resonance is shown in Figure 4, with the complex multiplet collapsing to the extent that a partial doublet of doublets was obtained.

Another interesting facet in these cycloaddition reactions was revealed in the reaction of fumaronitrile with **1** (R = R^1 = Ph) in refluxing benzene until the color of the reaction mixture had been discharged completely (89 hr). Removal of solvent and recrystallization of the crystalline residue did not afford a 1:1 primary adduct but rather 2-oxo-1,3,6-triphenylpyridine-4,5-dicarbonitrile (**24a**), a compound accountable in terms of loss of H_2S from an intermediate 1:1 primary cycloadduct **25a**. The pyridone **24a**



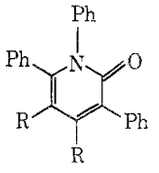


25a, $R^2 = R^3 = H$; $R^1 = R^4 = CN$
b, $R^2 = R^3 = H$; $R^1 = R^4 = COPh$
c, $R^2 = R^3 = H$; $R^2 = R^4 = CONPhCO$
d, $R^2 = R^3 = H$; $R^1 = R^4 = COOCH_3$
e, $R^1 = R^3 = H$; $R^2 = R^4 = COOCH_3$

24a, R = CN
b, R = COPh
c, R = CONPhCO
d, R = $COOCH_3$

has been prepared[12] by reaction of **1** (R = R^1 = Ph) with dicyanoacetylene in 0.5% yield, together with a 95.5% yield of 3,4-dicyano-2,5-diphenylthiophene. This excludes an initial oxidation step in the above reaction. A more plausible route may involve an initial base-catalyzed proton removal and opening of the sulfide bridge followed by a β elimination of H_2S to give **24**. Such a process has been observed with *N,N'*-diisopropyl-*N,N'*-diphenyl-2,4-thio-

Table V
4,5-Disubstituted Pyridones Derived from *anhydro*-4-Hydroxy-2,3,5-triphenylthiazolium Hydroxide Cycloadducts and Sodium Methoxide[a]



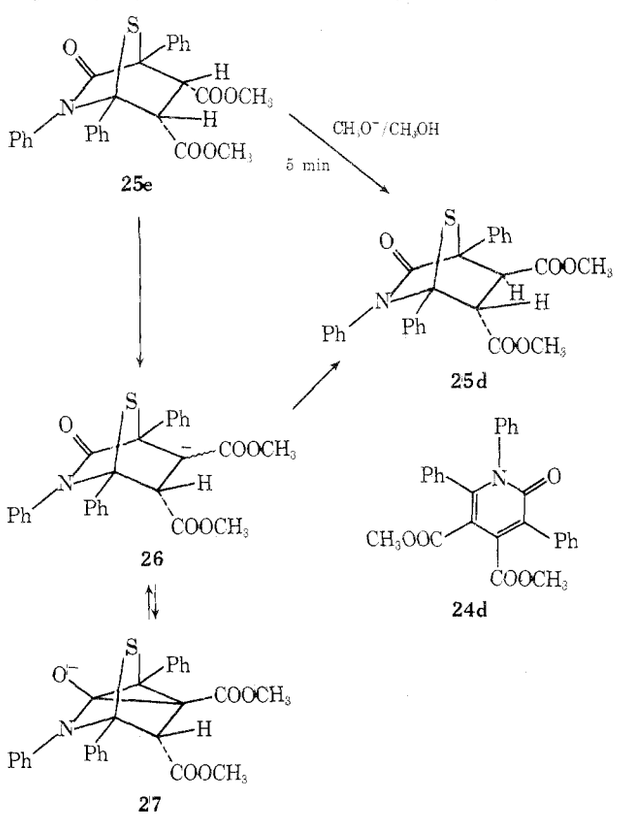
Compd no.	R	Yield, %	Mp, °C	Crystal habit and color[b]	Ir, cm^{-1}	uv max, nm (log ε)	$M^{\cdot+}$	Molecular formula
24a	CN	58	254–257dec	A	ν_{CN} 2240, ν_{CO} 1680	358 (3.83) 271 (3.82), 215 sh (4.29)	373 (100)	$C_{25}H_{15}N_3O$
24b	COPh	87	290–293dec	B	ν_{CO} 1650 (broad)	340 (3.94), 254 (4.33)	531 (63)	$C_{37}H_{25}NO_3$
24c	CONPhCO	54	275–277	B	ν_{CO} 1730, 1680	362 (3.73), 287 (4.06)	468 (100)	$C_{31}H_{20}N_2O_3$
24d	$COOCH_3$	17	219–221	C	ν_{CO} 1745, 1670	328 (3.74), 255 (3.64)	439 (100)	$C_{27}H_{21}NO_5$

[a] Satisfactory analytical values (±0.4% for C, H, N) were reported for all compounds in table: Ed. [b] A = colorless needles (benzene). [c] B = yellow needles (ethanol). [d] C = colorless needles (ethanol).

phenediamine and acrylonitrile in which the intermediate thiol was actually trapped by a second molecule of acrylonitrile.[13a] This mechanistic pathway cannot, however, be distinguished from an initial loss of elemental sulfur from **25a** followed by sulfur dehydrogenation of the intermediate. In limiting the reaction period to 26 hr, it was possible to isolate the intermediate **25a** (Tables III and IV) along with **24a** being observed in the filtrate.

The elimination of H_2S was also observed when certain of these 1:1 adducts were treated with sodium methoxide yielding a series of 4,5-disubstituted 1,3,6-triphenylpyridones (Table V). Similar eliminations have been reported[13b] from maleic anhydride adducts of various substituted isobenzothiophenes using sodium hydroxide.

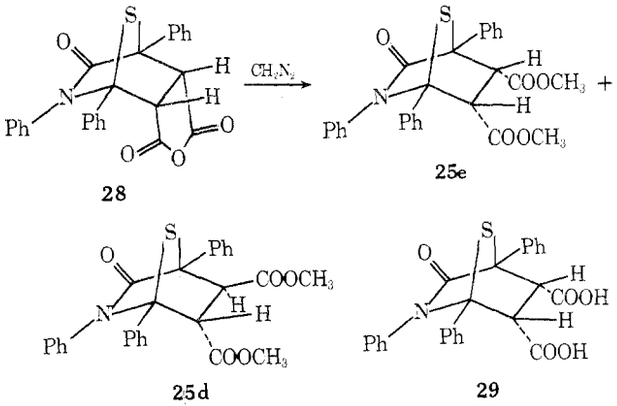
Treatment of the cis diester, dimethyl 1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyridine-5β,6β-dicarboxylate (**25e**) with sodium methoxide, however, followed a



different reaction pathway. Quenching the reaction after 5 min with water deposited a solid which was identical in every respect with the trans diester **25d,** synthesized in an alternative way by reaction of **1** (R = R^1 = Ph) with dimethyl fumarate (Table III). The epimerization was thought to occur at carbon 5 due to the expected acidity of the 5 proton.

A contribution from a transannular interaction of the carbanion at C-5 with the β carbonyl group, illustrated by **26** ⇄ **27,** may be significant but no data are available to substantiate this interaction. The filtrate of this reaction gave the 4,5-dicarbomethoxypyridone **24d** identical with an authentic sample but its isolation is not definitive as it could have been formed from either the cis or trans diesters or by electron rearrangement of the immediate carbanion **26.**

The stereochemical relationship between cycloadducts derived from **1** (R = R^1 = Ph) was determined by the reaction of the maleic anhydride adduct **28** with diazomethane. Treatment of **28** with an alcoholic–ethereal solution of diazomethane deposited crystals which were identical with an authentic sample of dimethyl 1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyridine-5β,6β-dicarboxylate (**25e**). From the filtrate of the reaction mixture was isolated a second crop of crystals whose behavior on Tlc and spectral data (ir, nmr) corresponded to a mixture of *cis*- and *trans*-dicarbomethoxy ester cycloadducts, **25e** and **25d,** re-



spectively. The formation of the trans diester **25d** can be attributed to reaction of **25e** with an excess of diazomethane, which may give rise to methoxide ion, and thus epimerize C-5 of the cycloadduct. That the cis diester is

formed reconfirms that a consistency of stereochemistry exists within cycloadducts of this mesoionic ring system.

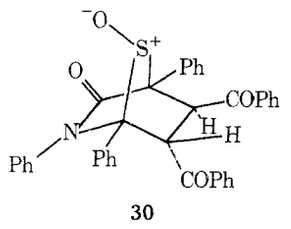
The ring opening of the maleic anhydride adduct **28** could also be achieved by base hydrolysis using sodium hydroxide, and resultant acidification of the reaction mixture produced 1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyridine-5β,6β-dicarboxylic acid (**29**) in 48% yield. Spectral data for this compound were consistent for the cis diacid structure **29** shown. Acidic protons were observed at δ 12.40 in the nmr spectrum and were exchanged with D_2O, and the 5,6-exo protons resonated at δ 4.47 and δ 4.78 (J = 8.5 Hz), respectively. Similar treatment of **29** with diazomethane afforded the cis diester **25e** identical with an authentic sample, but in this case no trans diester **25d** could be detected in the reaction mixture.

Oxidation to the corresponding sulfoxides also gave information regarding the stereochemistry of the cycloadducts. When the cycloadducts **25b** and **25d** were treated with *m*-chloroperbenzoic acid in methylene chloride, products were isolated which corresponded to oxidation of the sulfide bridge. Using the arguments advanced earlier, the orientation of the sulfoxide group was obtained from the nmr spectra. For the *trans*-dibenzoyl sulfoxide, **30**, and upfield shift of H_5 to δ 4.73, and a slight downfield shift for H_6 is consistent with the orientation of the S–O bond illustrated in **30**. This orientation might be expected on the basis of steric restraints imposed by the 5-benzoyl group. Further evidence for sulfoxide formation was obtained in the mass spectrum of **30** which had a very low intensity molecular ion (~1%) but the first fragmentation corresponded to a loss of SO.

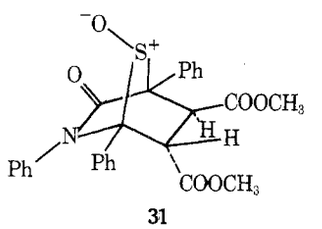
When the trans diester **25d** was oxidized, a compound homogenous on thin-layer chromatography was obtained but which corresponded to a mixture of diastereomeric sulfoxides **31** and **32** in the nmr spectrum. The resonances for the 5 and 6 protons in **25d**, **31**, and **32** are listed below. The

	Chemical shift (δ)		Coupling constant, Hz
Structure	H_5	H_6	$J_{5,6}$
25d	4.29	4.52	4.5
31	4.27	4.63	5.0
32	4.60	4.98	4.5

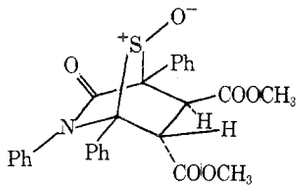
data show that a downfield shift was observed in sulfoxide **32**, the minor component in the nmr spectrum, for both H_5



30



31



32

and H_6 indicating that the sulfoxide group is proximinal to these protons, whereas a less intense effect can be observed with the major component, **31**. The mass spectral fragmentation is also indicative of sulfoxide formation, the molecular ion fragmenting with an initial loss of SO.

Experimental Section[14]

General Procedure for the Reaction of *anhydro*-4-Hydroxy-2,3-diarylthiazolium Hydroxide (1) with Olefinic Dipolarophiles. The Reaction of *anhydro*-2-*p*-Chlorophenyl-4-hydroxy-3-phenylthiazolium Hydroxide (1, R = *p*-ClC$_6$H$_4$; R^1 = H) with *N*-Phenylmaleimide. The mesoionic compound (1.4 g, 0.005 mol), *N*-phenylmaleimide (0.9 g, 0.005 mol), and dry benzene (50 ml) were refluxed overnight. The solvent was removed *in vacuo* and the residue crystallized from chloroform–petroleum ether (bp 60–80°) as colorless, irregular prisms of 1-*p*-chlorophenyl-*N*,2-diphenyl-1,2,3,4,5,6-hexahydro-3-oxo-1α,4α-epithiopyridine-5β,6β-dicarboximide (**3**, R = *p*-ClC$_6$H$_4$); 0.8 g (35%), mp 270–273° dec (Table I).

Variations of this procedure for a particular dipolarophile are shown in Table VI.

Reaction of 1-*p*-Chlorophenyl-1,2,3,4,5,6-hexahydro-3-oxo-2-phenyl-1α,4α-epithiopyridine-5β,6β-dicarboxylic Acid Anhydride (13; R = *p*-ClC$_6$H$_4$) with Diazomethane. The adduct (0.4 g, 0.01 mol) in anhydrous methanol (25 ml) was treated with an excess of an ethereal–ethanolic solution of diazomethane with stirring at room temperature. An initial exothermic reaction ensued and within 10 min a colorless solid separated which was filtered after stirring overnight. The isolated compound was identical[7] in all respects with **16** (R = *p*-ClC$_6$H$_4$); 0.42 g (97%), mp 216–217°.

Oxidation of 3 (R = Ph) with *m*-Chloroperbenzoic Acid. Equivalent amounts of the *N*-phenylmaleimide adduct **3** (R = Ph), and *m*-chloroperbenzoic acid in methylene chloride afforded the sulfoxide, 1,2,3,4,5,6-hexahydro-3-oxo-*N*,1,2-triphenyl-1α,4α-epithiopyridine-5β,6β-dicarboximide 7-oxide (**17**) as small, colorless needles from acetonitrile: yield 97%; mp 235–240° dec; ir (KBr) 1725 (CO), 1090 (SO) cm^{-1}; λ_{max} (CH_3OH) 277 nm (log ϵ 4.01); M·$^+$ 442 (39).

Anal. Calcd for $C_{25}H_{18}N_2O_4S$: C, 67.86; H, 4.10; N, 6.33. Found: C, 67.81; H, 4.17; N, 6.26.

Oxidation of 15 (R = Ph) with *m*-Chloroperbenzoic Acid. Equivalent amounts of the trans diester **15** (R = Ph) and *m*-chloroperbenzoic acid in methylene chloride at room temperature gave, after extraction of the two-component mixture with 10% $NaHCO_3$, chromatography on preparative silica gel (chloroform–ethyl acetate 80:20), and recrystallization from ethanol, a mixture of the diastereomeric sulfoxides, 5α,6β-di(methoxycarbonyl)-1,2-diphenyl-1,2,3,4,5,6-hexahydro-1α,4α-epithiopyrid-2-one 7-oxides as colorless, prismatic needles: yield 78%; mp 180–181° dec (with gas evolution); ir (KBr) 3010, 2950 (CH), 1720 (broad, CO), 1085 (SO) cm^{-1}; λ_{max} (CH_3OH) none; nmr ($CDCl_3$, HA-100) major component δ 6.70–7.50 (m, 10, aromatic), 4.58 (d, 1, C_4-H, $J_{4,5}$ = 5.0 Hz), 4.33 (d, 1, C_6-H, $J_{5,6}$ = 3.8 Hz), 3.73 (dd, 1, C_5-H), 3.84 (s, 3, C_5-$COOCH_3$), 3.48 (s, 3, C_6-$COOCH_3$); minor component δ 4.74 (d, 1, C_6-H, $J_{5,6}$ = 4.0 Hz), 4.64 (d, 1, C_4-H, $J_{4,5}$ = 6.5 Hz), 4.35 (dd, 1, C_5-H), 3.88 (s, 3, C_5-$COOCH_3$), 3.50 (s, 3, C_6-$COOCH_3$); M·$^+$ 413 (6).

Anal. Calcd for $C_{21}H_{19}NO_6S$: C, 61.00; H, 4.63; N, 3.39. Found: C, 60.90; H, 4.68; N, 3.36.

General Procedure for the Reaction of *anhydro*-2-Aryl-4-hydroxy-3,5-diphenylthiazolium Hydroxide 1 (R = Ph or *p*-ClC$_6$H$_4$; R^1 = Ph) with Olefinic Dipolarophiles. *trans*-Dibenzoylethylene. The mesoionic compound[12] (3.0 g, 0.009 mol), *trans*-dibenzoylethylene (2.1 g, 0.009 mol), and dry benzene (100 ml) were stirred and refluxed for 24 hr. Removal of the solvent *in vacuo* and repeated crystallization of the residue from benzene afforded 5α,6β-dibenzoyl-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one (**25b**, R^2 = R^3 = H; R^1 = R^4 = COPh) as colorless needles; 3.7 g (73%), mp 218–220° dec (Table III). Variation of this procedure with several dipolarophiles is shown in Table VII and below.

Reaction of *anhydro*-4-Hydroxy-2,3,5-triphenylthiazolium Hydroxide (1, R = R^1 = Ph) with Methyl Vinyl Ketone. The mesoionic compound (1.5 g, 0.0045 mol) was refluxed in methyl vinyl ketone (30 ml) for 1 hr during which time the reaction mixture changed from a dark red to a light yellow color. Removal of excess methyl vinyl ketone under reduced pressure and crystallization of the resultant residue from chloroform–anhydrous ether afforded cream, irregular prisms. Chromatography by preparative tlc (5 × 1 mm plates, silica gel PF) using chloroform–ethyl acetate (9:1) as the developing solvent, isolation of the major band (R_f 0.5), and recrystallization from chloroform–anhydrous ether afforded the endo adduct 6β-acetyl-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-

Table VI
Reaction Conditions for the Cycloaddition of 1 (R = Aryl; R^1 = H) and Various Dipolarophiles[a]

Dipolarophile	Solvent	Reaction time, hr	Reaction temp	Crystallization solvent
trans-Dibenzoylethylene	Benzene	3	Reflux	Chloroform–petroleum ether (bp 60–80°)
Methyl vinyl ketone	XS reagent	17	Reflux	Benzene
Ethyl acrylate	XS reagent	14	Reflux	Benzene
Maleic anhydride[b]	Benzene	16	Room temp	Benzene
Dimethyl fumarate	Benzene	2	Reflux	Chloroform–ether
Dimethyl maleate[b]	Benzene	5.5	Reflux	Chloroform

[a] Reaction work-up involved concentration of the reaction mixture *in vacuo* and crystallization of the residue from the solvent shown except in *b* where the product crystallized. [b] Product crystallized.

Table VII
Reaction Conditions for the Cycloaddition of 1 (R = Aryl, R^1 = Ph) and Various Dipolarophiles

Dipolarophile	Solvent	Reaction time, hr	Reaction temp	Crystallization solvent
N-Phenylmaleimide (R = Ph)	Benzene	72	Reflux	Evaporation; chloroform–ether
Dimethyl maleate (R = Ph)	Benzene	24	Reflux	Chromatography, Kieselgel g; benzene–petroleum ether
Dimethyl fumarate (R = Ph)	Benzene	15	Reflux	Evaporation; chloroform–petroleum ether
Maleic anhydride (R = Ph)	Benzene	3	Reflux	Evaporation; ethanol
Ethyl crotonate (R = *p*-ClC_6H_4)	XS reagent	10	Reflux	Evaporation; chloroform–ether

1α,4α-epithiopyrid-2-one (**19**, R = $COCH_3$), as colorless, irregular prisms; 0.3 g (17%), mp 180–182° dec (Table III).

The filtrate from the initial crystallization of the endo isomer was evaporated *in vacuo* and the oily residue chromatographed on preparative tlc (5 × 1 mm plates, silica gel PF) using chloroform–ethyl acetate (9:1) as the developing solvent. The top, major band (R_f 0.6) was isolated, and trituration of the residual oil with anhydrous ether and standing overnight, afforded the exo adduct, 6α-acetyl-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one (**20**), as colorless prisms; 0.1 g (12.5%), mp 142–144° (Table III).

Reaction of *anhydro*-4-Hydroxy-2,3,5-triphenylthiazolium Hydroxide (1, R = R^1 = Ph) with Acrylonitrile. The mesoionic compound (2.0 g, 0.0063 mol) was refluxed in acrylonitrile (50 ml) for 3.5 hr. Excess acrylonitrile was removed under reduced pressure leaving a fluffy crystalline residue. Repeated chromatography on preparative silica gel (8 × 1 mm plates), using initially chloroform–ethyl acetate (11:1) and finally benzene–ethyl acetate (4:1) as the developing solvents, afforded the 1:1 adduct 6β-cyano-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one (**19**; R = CN) as colorless, irregular prisms from chloroform–petroleum ether (bp 60–80°); 1.3 g (22%), mp 98–102° dec (Table III).

Reaction of 1 (R = R^1 = Ph) with Ethyl Methacrylate. The mesoionic compound (1.5 g, 0.0045 mol) was stirred and refluxed in ethyl methacrylate (25 ml) for 12 hr. Evaporation of excess solvent *in vacuo*, chromatography of the residue on preparative tlc (4 × 1 mm plates, silica gel PF) using chloroform as the developing solvent, isolation of the major band (R_f 0.8), and trituration of the residual oil with anhydrous ether followed by standing overnight, yielded ethyl 1,2,3,4,5,6-hexahydro-6α-methyl-3-oxo-1,2,4-triphenyl-1α,4α-epithiopyridine-6β-carboxylate (**22**) as colorless prisms; 0.35 g (17%), mp 170–172° dec (Table III).

Reaction of 1 (R = R^1 = Ph) with Fumaronitrile. A. Isolation of the Primary Cycloadduct. The mesoionic compound 1 (R = R^1 = Ph) (1.5 g, 0.0045 mol), fumaronitrile (0.36 g, 0.0045 mol), and benzene (50 ml) were stirred under reflux for 26 hr. The solvent was removed *in vacuo* and the residue dissolved in a minimum amount of chloroform and let stand overnight. Crystals separated and were isolated by suction filtration. A second crop was obtained from the filtrate. The combined solids recrystallized from chloroform–anhydrous ether affording the 1:1 adduct 5α,6β-dicyano-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one (**25a**) as colorless, irregular prisms (tlc showed 4,5-dicyano-1,3,6-triphenylpyrid-2-one (**24a**) to be present in the initial filtrate); 1.3 g (70%), mp 198–200° dec (Table III).

B. Formation of 4,5-Dicyano-1,3,6-triphenylpyrid-2-one (24a). The mesoionic compound (1.0 g, 0.003 mol), fumaronitrile (0.24 g, 0.003 mol), and dry benzene (50 ml) were stirred and refluxed for 89 hr. The solvent was removed under reduced pressure, and the residue crystallized from chloroform–anhydrous ether as light brown, irregular prisms. Recrystallization from benzene gave 4,5-dicyano-1,3,6-triphenylpyrid-2-one (**24a**) as cream needles; 0.65 g (57.5%), mp 254–257° dec (Table V).

H_2S Elimination from the 1:1 Adduct, 5α,6β-Dicyano-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one (25a). Treatment of the 1:1 fumaronitrile adduct **25a** with an excess of sodium methoxide–methanol solution at room temperature afforded a colorless solid identical[7] in all respects with 4,5-dicyano-1,3,6-triphenylpyrid-2-one (**24a**); yield 89%, mp 254–256°.

Treatment of 25b with Sodium Methoxide. The *trans*-dibenzoyl adduct **25b** (1.0 g, 0.007 mol) was suspended in dry methanol (20 ml) and an excess of sodium was added with stirring. All solid dissolved and the reaction mixture turned a light orange. Solvent was removed *in vacuo*, the residue triturated with ethanol, and filtered. Recrystallization from methanol gave 4,5-dibenzoyl-1,3,6-triphenylpyrid-2-one (**24b**) as light yellow needles; 0.82 g (87%), mp *ca.* 290–293° dec (Table V).

Application of this procedure to the 1:1 adducts **25c–e** resulted in the pyridones **24c–d** (Table V).

Treatment of 28 with Diazomethane. To a stirring suspension of the maleic anhydride adduct **28** (0.2 g) in dry methanol (20 ml) was added at room temperature an excess of an alcoholic–ethereal solution of diazomethane. A colorless solid began to separate after 0.5 hr. After stirring overnight the reaction mixture was filtered yielding authentic[7] cis diester **25e** (30 mg). The filtrate when concentrated deposited a second crop of crystals shown by infrared, tlc, and nmr data to be a mixture of cis-**25e** and *trans*-**26d** diesters. The total yield of diester was 0.1 g (45%) of which the ratio between cis–trans was approximately 3:1.

Hydrolysis of 1,2,3,4,5,6-Hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one-5β,6β-dicarboxylic Acid Anhydride (28). The maleic anhydride adduct **28** (1.0 g, 0.0024 mol) was treated with sodium hydroxide (0.8 g) in water (25 ml) and heated on a steam bath for 15 min. The cooled reaction mixture was acidified with 3 *N* HCl causing a colorless solid to separate. Isolation and recrystallization from ethanol afforded 1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one-5β,6β-dicarboxylic acid (**29**) as colorless, clustered needles; 0.5 g (48%), mp 240–242° dec (Table III).

Treatment of 29 with Diazomethane. To a stirring suspension

of the cis diacid **29** (0.2 g, 0.005 mol) in methanol (20 ml) was added an excess of an alcoholic–ethereal solution of diazomethane. A colorless solid began to separate after 10 min. After stirring overnight, filtration yielded a colorless solid (0.15 g, 46%) identical[7] in all respects with authentic cis diester **25e**. No trans diester **25d** could be detected by tlc of the isolated solid or of its filtrate.

Oxidation of 25b with *m*-Chloroperbenzoic Acid. The 1:1 cycloadduct **25b** (1.0 g, 0.0018 mol), 85% *m*-chloroperbenzoic acid (0.36 g, 0.0018 mol), and methylene chloride (40 ml) were stirred together overnight at room temperature. Extraction with 10% sodium bicarbonate, water, separation of the methylene chloride layer, drying over sodium sulfate, evaporation under reduced pressure, and recrystallization of the residue from acetonitrile gave 5α,6β-dibenzoyl-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one 7-oxide (**30**) as colorless prisms; 0.65 g (63%), mp 240–243° (Table III).

Oxidation of 25d with *m*-Chloroperbenzoic Acid. The trans diester **25d** (0.78 g, 0.0016 mol), 85% *m*-chloroperbenzoic acid (0.33 g, 0.0016 mol), and methylene chloride were stirred overnight at room temperature. Extraction in the usual manner and recrystallization of the resultant residue afforded a mixture of 5α,6β-di(methoxycarbonyl)-1,2,3,4,5,6-hexahydro-1,2,4-triphenyl-1α,4α-epithiopyrid-2-one 7-oxides (**31** and **32**) as colorless needles from ethanol; 0.5 g (62%), mp 202–205° (Table III).

Hydrolysis of *anhydro*-4-Hydroxy-2,3,5-triphenylthiazolium Hydroxide 1 (R = R¹ = Ph). From the reaction of the mesoionic compound with maleic acid in refluxing benzene was isolated after evaporation of the solvent, chromatography on preparative silica gel (chloroform), and recrystallization from ethanol, *S*-(*N*-phenylbenzimidoyl)mercaptophenylacetic acid as colorless needles: yield 25%; mp 165–167°; ir (KBr) 3280, 3050, 1660 cm^{-1}; λ_{max} (CH_3OH) 245 nm (log ε 4.38); nmr ($CDCl_3$) δ 7.03–8.33 (m, 15, aromatic), 5.60 (s, 1, CH).

Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.59; H, 4.93; N, 4.03. Found: C, 72.39; H, 4.82; N, 3.93.

Registry No.—**1** (R = *p*-ClC_6H_4, R^1 = H), 52730-97-9; **1** (R = R^1 = Ph), 18100-80-6; **1** (R = *p*-ClC_6H_4, R^1 = Ph), 52730-98-0; **3** (R = *p*-ClC_6H_4), 52730-99-1; **3** (R = Ph), 52731-00-7; **7** (R = *p*-ClC_6H_4), 52731-01-8; **9** (R = $COCH_3$), 52731-04-1; **9** (R = COOEt), 52731-05-2; **13** (R = *p*-ClC_6H_4), 52731-06-3; **15** (R = Ph), 52746-61-9; **15** (R = *p*-ClC_6H_4), 52795-10-5; **16** (R = *p*-ClC_6H_4), 52731-03-0; **16** (R = Ph), 52731-02-9; **17**, 52731-07-4; **19** (R = $COCH_3$), 52731-08-5; **19** (R = CN), 52731-09-6; **20**, 52731-10-9; **21**, 52731-11-0; **22**, 52748-26-2; **24a**, 52718-86-2; **24b**, 52731-12-1; **24c**, 52731-13-2; **24d**, 52731-14-3; **25a**, 52731-15-4; **25b**, 52748-27-3; **25c**, 52731-18-7; **25d**, 52731-16-5; **25e**, 52746-62-0; **28**, 52731-19-8; **29**, 52731-17-6; **30**, 52731-20-1; **31**, 52731-21-2; **32**, 52746-63-1; *N*-phenylmaleimide, 941-69-5; *trans*-dibenzoylethylene, 959-28-4; methyl vinyl ketone, 78-94-4; ethyl acrylate, 140-88-5; maleic anhydride, 108-31-6; dimethyl fumarate, 624-49-7; dimethyl maleate, 624-48-6; diazomethane, 334-88-3; *m*-chloroperbenzoic acid, 937-14-4; 5α,6β-di(methoxycarbonyl)-1,2-diphenyl-1,2,3,4,5,6-hexahydro-1α,4α-epithiopyrid-2-one 7-*syn*-oxide, 52731-22-3; 5α,6β-di(methoxycarbonyl)-1,2-diphenyl-1,2,3,4,5,6-hexahydro-1α,4α-epithiopyrid-2-one 7-*anti*-oxide, 52746-64-2; ethyl crotonate, 10544-63-5; acrylonitrile, 107-13-1; ethyl methacrylate, 97-63-2; fumaronitrile, 764-42-1; *S*-(*N*-phenylbenzimidoyl)mercaptophenylacetic acid, 52731-23-4.

References and Notes

(1) (a) Support of this work by U.S. Public Health Service Research Grant CA 08495, National Cancer Institute, is gratefully acknowledged; (b) NSF Predoctoral Trainee. Abstracted in part from the Ph.D. thesis of J.B. submitted to the Graduate School, Rensselaer Polytechnic Institute, Aug 1973

(2) K. T. Potts, E. Houghton, and U. P. Singh, *J. Org. Chem.*, **39**, 3627 (1974).

(3) K. T. Potts and U. P. Singh, *Chem. Commun.*, 569 (1969); H. Gotthardt and B. Christl, *Tetrahedron Lett.*, 4747 (1968); see also M. Ohta and M. Sugiyama, *Bull. Chem. Soc. Jap.*, **38**, 596 (1965); **36**, 1437 (1963).

(4) H. Gotthardt and B. Christl, *Tetrahedron Lett.*, 4751 (1968); K. T. Potts, A. J. Elliott, U. P. Singh, and E. Houghton, *J. Org. Chem.*, submitted for publication.

(5) M. P. Cava and N. M. Pollack, *J. Amer. Chem. Soc.*, **88**, 4112 (1966); however, see also F. H. M. Deckers, W. N. Speckamp, and H. O. Huisman, *Chem. Commun.*, 1521 (1970).

(6) J. W. Lown and K. Matsumoto, *Can. J. Chem.*, **49**, 3443 (1971).

(7) Identity of products was established by superimposable infrared spectra, identical R_f values, and mixture melting point determination.

(8) A. B. Foster, J. M. Duxburg, T. D. Inch, and J. M. Webber, *Chem. Commun.*, 881 (1967).

(9) U. Eisen, M. Z. Haq, J. Flippen, and I. Karle, *J. Chem. Soc. C*, 357 (1972), and references cited therein.

(10) C. R. Johnson and W. O. Siegl, *Tetrahedron Lett.*, 1879 (1969).

(11) F. Kaplan and J. D. Roberts, *J. Amer. Chem. Soc.*, **83**, 4666 (1961); P. Shafer, D. Davis, M. Vogel, K. Nagarajan, and J. D. Roberts, *Proc. Nat. Acad. Sci. U.S.*, **47**, 49 (1961); G. Whitesides, F. Kaplan, K. Nagarajan, and J. D. Roberts, *Proc. Nat. Acad. Sci. U.S.*, **48**, 1112 (1962); J. A. Elvidge and R. G. Foster, J. Chem. Soc., 981 (1964); W. L. Meyer, D. L. Davis, L. Foster, A. S. Levinson, V. L. Sawin, D. C. Shew, and R. F. Weddleton, *J. Amer. Chem. Soc.*, **87**, 1573 (1965).

(12) K. T. Potts, E. Houghton, and U. P. Singh, *J. Org. Chem.*, **39**, 3627 (1974).

(13) (a) J. P. Chupp, *J. Heterocycl. Chem.*, **9**, 1033 (1972); (b) R. Mayer, H. Kleinert, S. Richter, and K. Gewald, *Angew. Chem.*, **74**, 118 (1962); G. Wittig, E. Knauss, and K. Neithammer, *Justus Liebigs Ann. Chem.*, **630**, 10 (1960); O. Dann, M. Kokorudz, and R. Gropper, *Chem. Ber.*, **87**, 140 (1954).

(14) Spectral characterizations were carried out on the following instrumentation: infrared spectra, Perkin-Elmer Model 337 spectrophotometer; ultraviolet spectra, Cary 14 spectrophotometer; nmr spectra, Varian T-60 and HA-100 spectrometers, using TMS as internal standard; mass spectra, Hitachi Perkin-Elmer RMU-6E mass spectrometer at 70 eV, with a source temperature of *ca.* 150°. Melting points were determined in capillaries and all evaporations were carried out using a Rotovap apparatus. Microanalyses were performed by Instranal Laboratories, Inc., Rensselaer, N.Y., and Galbraith Laboratories, Inc., Knoxville, Tenn.

Synthesis of Olefins from Thionocarbonates by an Alkylation–Reduction Sequence

E. Vedejs* and E. S. C. Wu

Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

Received May 28, 1974

Thionocarbonates are alkylated at sulfur with concomitant ring cleavage by iodide to give vicinal iodo thiocarbonates. The latter are reductively cleaved to olefins by zinc dust reduction. Alkylation with methyl iodide at 90° gives the highest yields of thionocarbonate cleavage products. The method is well suited for preparation of cyclobutenes from the thionocarbonates. Stereochemistry of the starting diol is lost during the two-step procedure. Thus, either *meso*- or *dl*-hydrobenzoin thionocarbonates afford predominantly *trans*-stilbene, and either *cis*- or *trans*-cyclooctanediol thionocarbonates give only *cis*-cyclooctene.

Vicinal diol thionocarbonates are useful synthetic precursors to olefins. The procedure developed by Corey, *et al.*,[1] for thionocarbonate fragmentation with trivalent phosphorus reagents has been used successfully to generate highly strained alkenes including *trans*-cycloheptene,[1a] bicyclo[3.2.1]oct-1-ene,[2a] cyclobutene derivatives,[2b,c] as well as more routine olefins.[2d,f,g] The most common variation employs trialkyl phosphite at 110–160°, but lower reaction temperatures are feasible using 1,3-dibenzyl-2-methyl-1,3-diazaphospholidine (**1**) for desulfurization.[1b] Thionocarbonate decomposition can also be accomplished with zerovalent nickel and iron complexes.[3]