211, 194, 168, 166 (base). Anal. Calcd for $C_{15}H_{12}N_2O_4$: C, 63.38; H, 4.25; N, 9.85. Found: C, 63.17; H, 4.29; N, 9.80.

9-Carbethoxy-2-cyano-3,8-methano-1-aza[10]annulene (6j). A solution of **6i** (122 mg, 0.43 mmol) in xylene (8 mL) was heated at reflux for 40 min. The solution was diluted with ether, washed with saturated $NaHCO_3$ and then brine, dried over Na_2SO_4, and evaporated. The residue was chromatographed (2:8 ethyl acetate/hexane) to give 59 mg (57%) of **6j**. Molecular distillation afforded the analytical sample: bp 140 °C (0.1 torr); ^{13}C NMR δ 164.24, 150.10, 132.67, 131.40, 130.72, 129.36, 128.57, 123.60, 119.00, 118.46, 114.76, 61.90, 33.68, 14.34; UV λ_{max} 397 nm (ε 3390), 354 (4360), 282 (20 400), 245 (20 800); IR (neat) 2970, 2220, 1710, 1500, 1290, 1230, 1100, 1060 cm^{-1}; MS, *m/z* 240 (M^+), 212, 211, 195, 167, 140 (base). Anal. Calcd for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.73; H, 5.05; N, 11.42.

9,10-Dicarbethoxy-1,2-dihydro-2-hydroxy-3,8-methano-1-aza[10]annulene (7). Preparative thin-layer chromatographic purification (3:7 ethyl acetate/hexane) of **6c** (28 mg) afforded 6 mg of **7**, which was isolated as a yellow crystalline solid: mp 107–109 °C; MS, *m/z* 305 (M^+), 259, 230 (base). For a combustion analysis see the preparation of **6c**. Alternatively, a solution of **6a** (44.8 mg, 0.13 mmol) in ethanol (5 mL) was treated with KOH (8.1 mg, 0.14 mmol) at room temperature for 16 h and then evaporated. To the residue in dry THF (5 mL) at 0 °C was added oxalyl chloride (120 μL, 1.4 mmol). After 1 h the solution was evaporated, the residue was dissolved in THF (3 mL) and the resulting solution was cooled to 0 °C. A solution of *tert*-butyl hydroperoxide (93 mg, 1 mmol) in pyridine (1 mL) was added. After 1 h, the solution was taken up in ether, washed with water and then brine, dried over Na_2SO_4, and evaporated to give a yellow oil weighing 20 mg. This oil was dissolved in toluene (5 mL), and the solution was heated at reflux for 30 min and then evaporated. Preparative thin-layer chromatography (3:7 ethyl acetate/hexane) afforded 2.4 mg (7%) of hydrate **7**.

Acknowledgment. We appreciate the assistance of Dr. Michael L. Maddox in obtaining and interpreting the NMR spectra. We are also grateful to Professor W. G. Dauben, Department of Chemistry, University of California, Berkeley, for permitting us to use the high-pressure apparatus and to Dr. A. Gottlieb for his invaluable assistance in its operation.

Registry No. **3**, 4646-69-9; **4a**, 74476-38-3; **4b**, 74476-39-4; **4c**, 74476-40-7; **4d**, 6498-02-8; **6a**, 74476-41-8; **6b**, 74476-42-9; **6c**, 74476-43-0; **6d**, 74476-44-1; **6e**, 88729-98-0; **6g**, 88729-99-1; **6h**, 88730-00-1; **6i**, 88746-41-2; **6j**, 88730-01-2; **7**, 88730-02-3; diethyl dioxosuccinate, 59743-08-7; cyanoformamidrazone, 54606-55-2.

Chemistry of Bis(alkoxycarbonyl)polysulfanes and Related Compounds[1]

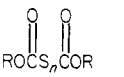
George Barany*[2] and Andrew W. Mott

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

Received August 29, 1983

Bis(alkoxycarbonyl)polysulfanes **3–6** with up to six sulfurs have been prepared by reaction of dichlorosulfanes with 2 equiv of *O,O'*-dialkyl thiocarbonates (**16**). This method is compared to several literature methods for the preparation of **1–6** together with some new methods, including the hydrolysis of bis(alkoxydichloromethyl)-polysulfanes **18–21** in turn derived from the chlorination of bis(alkoxythiocarbonyl)polysulfanes. Related chemistry provided (methoxycarbonyl)disulfanyl chloride (**15a**), (methoxydichloromethyl)disulfanyl chloride (**24a**), (chlorocarbonyl)disulfanyl chloride (**26**), and bis(chlorocarbonyl)trisulfane (**29**), all in good yields. Bis(alkoxycarbonyl)polysulfanes **1–9** with up to nine sulfurs were isolated from the alcoholysis of (alkoxycarbonyl)(alkoxydichloromethyl)di- and -trisulfanes **30, 31**, and **35** and (alkoxydichloromethyl)(chlorocarbonyl)polysulfanes **39–41**. The higher sulfanes **7–9** were identified by their HPLC behavior where a plot of log (retention time) against the number of sulfurs was found to be linear. Mechanisms for the formation of these products are proposed.

As part of the development of a general set of methods for the synthesis of bis(chlorocarbonyl)disulfane (**10**) and related compounds with a dithiocarbonyl function, we reported[3] the preparation of bis(alkoxycarbonyl)disulfanes (**2**); in a different context,[4] we observed bis(alkoxycarbonyl)trisulfanes (**3**). Ongoing studies[3,5] provided a variety of (alkoxydichloromethyl)sulfanes that have now been subjected to alcoholysis and shown to provide a series of bis(alkoxycarbonyl)polysulfanes **2–9**. Interest in this



1, *n* = 1 **4**, *n* = 4 **7**, *n* = 7
2, *n* = 2 **5**, *n* = 5 **8**, *n* = 8
3, *n* = 3 **6**, *n* = 6 **9**, *n* = 9

a, R = CH_3 b, R = C_2H_5

class of compounds led us to further investigate methods for their preparation. The products made according to prior literature methods, many of which date back more than 50 years, have been quantitatively analyzed by HPLC and compared to products made by several new techniques which are reported here. HPLC revealed the proportions of the different bis(alkoxycarbonyl)polysulfanes in the reaction mixtures, and the linearity of a plot of log (retention time) vs. number of sulfurs was taken as good evidence for the identity of the higher members of the homologous series.

Table I shows the structural formulas together with ^1H and ^{13}C NMR data for the compounds discussed in this

(1) A preliminary report of this work was presented at the 17th Great Lakes Regional Meeting of the American Chemical Society, St. Paul, MN, June 1–3, 1983. Financial support from the National Institutes of Health Grant GM 28934, Research Corporation (Leo H. Baekeland Grant), and Chicago Community Trust (Searle Scholars Program) is gratefully acknowledged.

(2) Searle Scholar, 1982; National Institutes of Health Research Career Development Award, AM 01099, 1982–1987.

(3) Barany, G.; Schroll, A. L.; Mott, A. W.; Halsrud, D. A. *J. Org. Chem.* **1983**, *48*, 4750–4761. This manuscript contains many of the general procedures of organosulfur chemistry as practiced in this laboratory, together with details on the preparations of several key starting materials.

(4) Barany, G.; Zalipsky, S. In "Peptides: Structure and Function: Proceedings of the Eighth American Peptide Symposium"; Hruby, V. J.; Rich, D. H., Eds.; Pierce Chemical Co.: Rockford, IL, 1983; pp 159–162.

(5) Barany, G. *Tetrahedron Lett.* **1983**, *24*, 5683–5686.

0022-3263/84/1949-1043$01.50/0

Table I. Numbering Scheme and Spectral Data

no.	structure	^{1}H NMR[a]	^{13}C NMR[b]
1a	MeO(C=O)S(C=O)OMe	3.89	54.5, 162.5
1b	EtO(C=O)S(C=O)OEt	1.34, 4.36 (7.1)	13.6, 64.2, 162.0
2a	MeO(C=O)SS(C=O)OMe	3.92	55.8, 166.7
2b	EtO(C=O)SS(C=O)OEt	1.34, 4.38 (7.1)	13.9, 65.6, 166.0
3a	MeO(C=O)SSS(C=O)OMe	3.94	55.7, 167.3
3b	EtO(C=O)SSS(C=O)OEt	1.35, 4.40 (7.2)	14.0, 65.6, 166.5
4a	MeO(C=O)SSSS(C=O)OMe	3.93	55.6, 167.1
4b	EtO(C=O)SSSS(C=O)OEt	1.36, 4.38 (7.1)	13.9, 65.5, 166.5
5a	MeO(C=O)SSSSS(C=O)OMe	3.95	
6a	MeO(C=O)SSSSSS(C=O)OMe	3.96	
10	Cl(C=O)SS(C=O)Cl		161.4
13a	$MeOCCl_2SCl$	3.76	57.0, 115.9
13b	$EtOCCl_2SCl$	1.38, 4.09 (7.1)	14.0, 67.5, 114.7
14a	MeO(C=O)SCl	3.97	55.9, 167.2
15a	MeO(C=O)SSCl	4.01	56.2, 165.1
16a	MeO(C=S)OMe	4.05	59.2, 197.2
16b	EtO(C=S)OEt	1.38, 4.50 (7.2)	13.5, 68.5, 195.2
17	MeO(C=O)SSS(C=O)OEt	3.93; 1.35, 4.40 (7.2)	55.8, 167.0, 167.0, 14.2, 65.9
18a	$MeOCCl_2SSSCCl_2OMe$	3.78	57.0, 117.7
18b	$EtOCCl_2SSSCCl_2OEt$	1.38, 4.12 (7.1)	14.0, 67.1, 116.5
	$MeOCCl_2SSSCCl_2OEt$	3.78; 1.38, 4.12 (7.1)	56.9, 117.7, 116.8, 13.9, 67.1
19a	$MeOCCl_2SSSSCCl_2OMe$	3.79	57.0, 117.6
19b	$EtOCCl_2SSSSCCl_2OEt$	1.39, 4.14 (7.1)	14.0, 67.1, 116.4
20a	$MeOCCl_2SSSSSCCl_2OMe$	3.80	57.1, 117.5
21a	$MeOCCl_2SSSSSSCCl_2OMe$	3.81	57.1, 117.5
22a	MeO(C=S)SS(C=S)OMe	4.24	61.5, 207.8
23a	MeO(C=S)S(C=S)OMe	4.22	60.4, 204.7
24a	$MeOCCl_2SSCl$	3.81	57.1, 117.5
24b	$EtOCCl_2SSCl$	1.39, 4.14 (7.1)	14.1, 67.4, 116.3
25a	MeO(C=S)Cl	4.18	63.1, 187.3
25b	EtO(C=S)Cl	1.46, 4.61 (7.1)	13.2, 73.7, 186.0
	Cl(C=O)SCl		160.8
26	Cl(C=O)SSCl		162.6
27a	MeO(C=S)SSS(C=S)OMe	4.29	61.4, 208.9
28a	MeO(C=S)SSSS(C=S)OMe	4.25	61.4, 208.6
29	Cl(C=O)SSS(C=O)Cl		163.0
30a	$MeOCCl_2SS(C=O)OMe$	3.75; 3.93	57.0, 117.0, 163.3, 55.7
30b	$MeOCCl_2SS(C=O)OEt$	3.75; 1.35, 4.39 (7.1)	57.0, 117.1, 165.6, 14.0, 65.7
31a	$EtOCCl_2SS(C=O)OMe$	1.32, 4.10 (7.1); 3.93	
31b	$EtOCCl_2SS(C=O)OEt$	1.32, 4.11 (7.0); 1.35, 4.39 (7.2)	
34	MeO(C=O)SS(C=O)OEt	3.92; 1.34, 4.38 (7.1)	55.6, 166.8, 165.9, 13.9, 65.7
35a	$MeOCCl_2SSS(C=O)OMe$	3.77; 3.93	56.8, 117.4, 167.5, 55.6
35b	$MeOCCl_2SSS(C=O)OEt$	3.77; 1.35, 4.39 (7.1)	
39a	$MeOCCl_2SS(C=O)Cl$	3.76	57.3, 116.1, 162.9
39b	$EtOCCl_2SS(C=O)Cl$	1.34, 4.11 (7.1)	13.9, 67.6, 114.9, 162.8
40a	$MeOCCl_2SSS(C=O)Cl$	3.78	56.9, 116.8, 163.2
40b	$EtOCCl_2SSS(C=O)Cl$	1.38, 4.13 (7.2)	13.9, 67.3, 115.5, 163.3
41a	$MeOCCl_2SSSS(C=O)Cl$	3.81	56.9, 116.7, 163.1
41b	$EtOCCl_2SSSS(C=O)Cl$	1.39, 4.13 (7.2)	13.9, 67.3, 115.5, 163.3
45	Ph(Me)N(C=O)SSN(Me)Ph	3.38; 3.35; 7.14-7.41 (Ph)	
46	MeO(C=O)SSN(Me)Ph	3.79; 3.32; 6.75-7.45 (Ph)	
47	MeO(C=O)SSS(C=O)N(Me)Ph	3.87; 3.39; 7.1-7.5 (Ph)	

[a] In $CDCl_3$, ppm downfield from tetramethylsilane (accuracy ±0.01 ppm). Chemical shifts are listed to match assignments with the structure as written. The shifts for the CH_3 and CH_2 protons of an ethyl group are listed together followed by the coupling constant in parentheses. Phenyl groups in compounds **45–47** showed multiplets in the indicated regions. [b] The resonances are listed in the same order as the corresponding carbons in the structure as written. Chemical shifts (accuracy ±0.1 ppm) were normalized to $CDCl_3$ = 77.0 ppm.

paper. In the table, compounds are listed in numerical order; names are given at their first mention in the text.

Results and Discussion

Literature Methods for the Preparation of Bis(alkoxycarbonyl)polysulfanes (Table II). Compounds **2–6** have been reported to result from treatment of *O*-alkyl potassium monothiocarbonates (Bender's salts) **11** with iodine,[6] SCl_2,[7] S_2Cl_2,[7] S_3Cl_2,[8] and S_4Cl_2.[8] Compounds **2** or **3** formed by the oxidation of **11** with iodine or sulfur dichloride were found to be essentially pure by HPLC, whereas the reaction of **11** with sulfur monochloride yielded **4** containing the disproportionation products **3** and **5**.[9] The results of these and other literature methods have

(6) (a) Winter, G.; Woods, R. *Separation Science* **1973**, *8*, 261–267. (b) Klaeser, K.; Gattow, G. *Z. Anorg. Allg. Chem.* **1981**, *481*, 135–142.

(7) Twiss, D. *J. Am. Chem. Soc.* **1927**, *49*, 491–494.

(8) Fehér, F.; Becher, W.; Kreutz, R.; Minz, F. R. *Z. Naturforsch. B: Anorg. Chem., Org. Chem., Biochem., Biophys., Biol.* **1963**, *18B*, 507–508.

(9) Contrary to the case reported (ref 10) for bis(alkoxythiocarbonyl)polysulfanes, disproportionation of bis(alkoxycarbonyl)polysulfanes was slow under the HPLC conditions (MeOH–H_2O, 68:32 and 85:15). For example, a sample of **6a** isolated by preparative HPLC (MeOH–H_2O, 85:15) contained less than 3% of **5a** when rechromatographed.

(10) Honeyman, R. T.; Schrieke, R. R. *Anal. Chim. Acta* **1980**, *116*, 345–351.

(11) (a) Meyer, V. *Ber. Dtsh. Chem. Ges.* **1869**, *2*, 297–299. (b) Gurvich, S. M.; Belova, R. Y. *Zh. Obsh. Khim.* **1961**, *31*, 1631–1635; *Chem. Abstr.* **1961**, *55*, 22129c.

Table II. Literature Methods for the Preparation of Bis(alkoxycarbonyl)polysulfanes[a]

method	ref	yield, %	product distribution, % 1	2	3	4	5	6	7
MeO(C=O)Cl (12a) + Na_2S	3, 11	64	**100**						
MeO(C=O)S^-K^+ (11a) + I_2	6	80		**100**					
EtO(C=O)S^-K^+ (11b) + I_2	6	100		**100**					
MeO(C=O)S^-K^+ (11a) + SCl_2	7	71*			**98**	2			
EtO(C=O)S^-K^+ (11b) + SCl_2	7	77			**97**	3			
MeO(C=O)S^-K^+ (11a) + S_2Cl_2	7	98			9	**83**	8		
EtO(C=O)S^-K^+ (11b) + S_2Cl_2	7	85			11	**79**	10		
Cl(C=O)SS(C=O)Cl (10) + MeOH	3	93		**100**					
Cl(C=O)SS(C=O)Cl (10) + EtOH	3	90		**100**					
$MeOCCl_2SCl$ (13a) + KI	12	21*		**60**	21	10	6	3	
MeO(C=O)SCl (14a) + KI	13, 14	74*		**97**	2	1			
EtO(C=O)SCl (14b) + KI	13, 14	74		**97**	3				
MeO(C=O)SSCl (15a) + KI	14	60*			**43**	42	11	3	1

[a] Yield is for conversion, in our hands, of starting material to the total product mixture by following the literature procedures as cited. An asterisk (*) next to the yield means that more detail is in the Experimental Section. Product distribution is by HPLC analysis (details in legend to Figure 1) with the anticipated product, based on the literature where a pure product was claimed, in **bold face**.

Table III. Additional Methods for the Preparation of Bis(alkoxycarbonyl)polysulfanes[a]

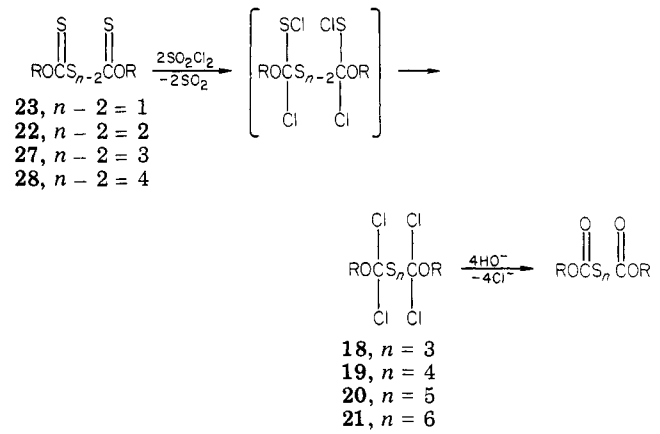
method	precedent	yield, %	product distribution, % 1	2	3	4	5	6	7	8	9
2MeO(C=S)OMe (16a) + SCl_2	3	67			**98**	2					
2EtO(C=S)OEt (16b) + SCl_2	3	89			**98**	2					
2MeO(C=S)OMe (16a) + S_2Cl_2	3	90			9	85	6				
2MeO(C=S)OMe (16a) + S_3Cl_2	3	86			4	4	**56**	12	24		
2MeO(C=S)OMe (16a) + S_4Cl_2	3	100			34	0	17	**49**			
$MeOCCl_2SSSCCl_2OMe$ (18a) + NaOH(aq)	19b	55			**70**	11	13	3	3		
$MeOCCl_2SSSSCCl_2OMe$ (19a) + NaOH(aq)	19b	78			9	**78**	9	4			
$MeOCCl_2SSSSSCCl_2OMe$ (20a) + NaOH(aq)	19b	79[b]			13	22	**40**	17	8		
$MeOCCl_2SSSSSSCCl_2OMe$ (21a) + NaOH(aq)	19b	86[b]			22	16	23	**35**	4		
Cl(C=O)SSS(C=O)Cl (29) + MeOH	3	56			**83**	8	5	3	1		
MeO(C=O)Cl (12a) + Na_2S_2(aq)	11, 13a, 21	24	100	**0**							
MeO(C=O)Cl (12a) + $Na_2S_{5.5}$(aq)		77	100								
MeO(C=O)Cl (12a) + Li_2S_2	22	52	96	**4**							
MeO(C=O)SCl (14a) + Na_2S(aq)	13a	78		47	**31**	13	5	3	1		
MeO(C=O)SCl (14a) + Na_2S_2(aq)	13a	93	53	28	10	4	3	2			
MeO(C=O)SCl (14a) + H_2S		98		15	**44**	21	10	7	2	1	
MeO(C=O)SCl (14a) + H_2S_2		97			7	**50**	30	13			
MeO(C=O)SCl (14a) + EtOH		27	2	54	37	6	1				
MeO(C=O)SSCl (15a) + EtOH		87			39	38	15	6	2		
MeO(C=O)SSCl (15a) + SCl_2 + KI		100			12	26	24	19	10	6	3
MeO(C=O)SCl (14a) + S_2Cl_2 + KI		52		56	6	29	1	8			
MeO(C=O)SSCl (15a) + S_2Cl_2 + KI		84		7	6	55	8	13	3	5	3

[a] Detailed procedures in Experimental Section. Otherwise see note a to Table II. [b] The starting bis(alkoxydichloromethyl)polysulfanes had some initial heterogeneity prior to hydrolysis, see Experimental Section.

been listed together with the product distribution observed by HPLC.

New Methods for the Preparation of Bis(alkoxycarbonyl)polysulfanes (Table III). We recently reported[3] that the reaction of sulfenyl chlorides with *O,O'*-dialkyl thiocarbonates **16** yields the alkyl chloride plus the (alkoxycarbonyl)dithio compound. By an extension of this method, 2 equiv of **16** gave, with 1 equiv of SCl_2 or S_2Cl_2,[15] **3** and **4** in yields and purities similar to those obtained by reaction of the Bender's salts **11** with the same sulfur chloride. Also, the mixed (ethoxycarbonyl)(methoxycarbonyl)trisulfane (**17**) was obtained by reaction of *O,O'*-diethyl thiocarbonate (**16b**) with (methoxycarbonyl)disulfanyl chloride (**15a**); only trace amounts of the disproportionation products formed. Reaction of **16a** with

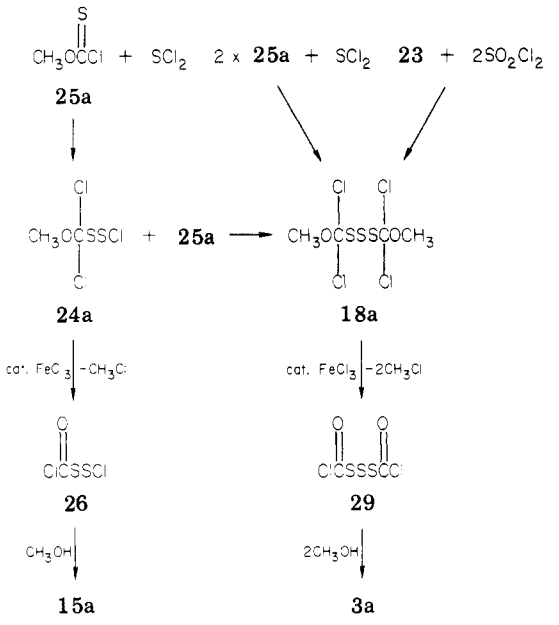
Scheme I[a]



[a] a, R = CH_3; b, R = C_2H_5.

(12) Douglass, I. B.; Marascia, F. *J. Am. Chem. Soc.* **1955**, *77*, 1899–1900.
(13) (a) Kobayashi, N.; Fujisawa, T. *J. Polym. Sci., Part A1* **1972**, *10*, 3317–3327. (b) Kobayashi, N.; Osawa, A.; Fujisawa, T. *J. Polym. Sci., Polym. Lett. Ed.* **1973**, *11*, 225–228.
(14) Böhme, H.; Steudel, H. P. *Liebigs Ann. Chem.* **1969**, *730*, 121–132.
(15) The specificity of these reactions is suggested by the following observations. An attempt was made to isolate **15a** by addition of **16a** to excess SCl_2, but only **3a** was obtained as a product. Similarly, the unknown three-sulfur analogue of **15a**, MeO(C=O)SSSCl, could not be prepared from **16a** plus S_2Cl_2.

Scheme II



S_3Cl_2[16a] or S_4Cl_2[16b] gave products containing about 50% of the desired **5a** or **6a** together with other bis(methoxycarbonyl)polysulfanes.

Phase-transfer-catalyzed hydrolysis of the bis(methoxydichloromethyl)polysulfanes **18a–21a** with sodium hydroxide gave mixtures of bis(methoxycarbonyl)polysulfanes with **3a–6a** as the major products, respectively (Scheme I). The tetrasulfane substrate **19a** was formed by chlorination[5,18] of bis(methoxythiocarbonyl)disulfane (**22a**). This transformation has already been noted,[19a] but as we suggested earlier[5,18] the presumed initial adduct, bis(methoxychloro(chlorothio)methyl)disulfane (Scheme I), which is the structure assigned in the literature, undergoes an intramolecular rearrangement to give the linear tetrasulfane. Similarly, trisulfane **18a** was obtained by careful chlorination of bis(methoxythiocarbonyl) sulfide (**23a**)[3] with sulfuryl chloride, as well as by independent routes from (methoxydichloromethyl)disulfanyl chloride (**24a**)[20] with methoxythiocarbonyl chloride (**25a**),[3] or sulfur dichloride with 2 equiv of **25a** (Scheme II). In addition, **24a** was converted with catalytic ferric chloride to (chlorocarbonyl)disulfanyl chloride (**26**), which reacted cleanly with methanol to give (methoxycarbonyl)disulfanyl chloride (**15a**) already known by a more laborious, low-yield route.[14] We now report details on the preparations of **15a**, **18a**, **19a**, and **26** and extend the methodology so that bis(methoxydichloromethyl)penta- and hexasulfanes (**20a** and **21a**) can be prepared by sulfuryl chloride treatments of bis(methoxythiocarbonyl)tri- and tetrasulfanes (**27a** and **28a**), respectively. Finally, the trisulfane **18a** was transformed by ferric chloride catalyzed loss of methyl chloride to bis(chlorocarbonyl)trisulfane (**29**), a new reagent which is the three-sulfur homologue of bis(chlorocarbonyl)disulfane (**10**). In analogy to the preparation[3] of **2a** from **10** and methanol, **29** prepared in situ reacted with methanol to give mainly **3a**. The fact that **18–21** and **29** can all be taken to the linear bis(alkoxycarbonyl)polysulfanes is strong evidence for the parent structures as written.

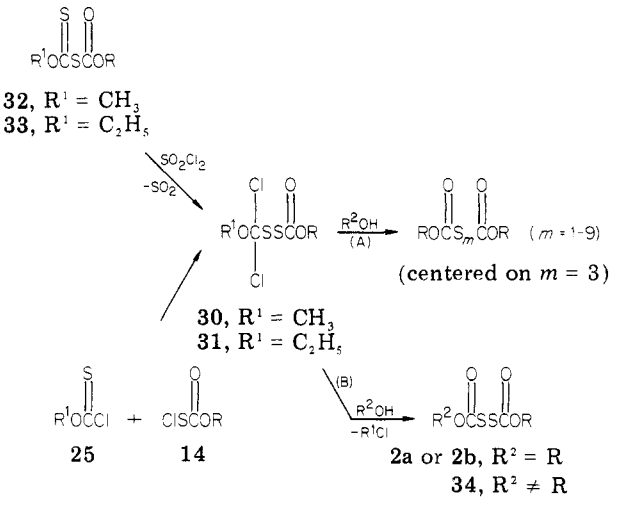
Some additional attempts (Table III, bottom half) to prepare bis(methoxycarbonyl)polysulfanes failed to yield the desired products as more than 50% of a mixture of the polysulfanes and often as a much lower percentage. As already mentioned (Table II), methyl chloroformate (**12a**) plus sodium sulfide gives **1a**, but attempts to prepare higher polysulfanes by reaction of **12a** plus sodium disulfide[16d,21] or sodium polysulfide[16e,21] proved unsuccessful with **1a** being the only product. Use of lithium disulfide[22] with **12a** caused little improvement; a mixture of **1a** and

Table IV. Alcoholysis of (Alkoxydichloromethyl)(alkoxycarbonyl)polysulfanes and (Alkoxydichloromethyl)(chlorocarbonyl)polysulfanes[a]

substrate	product distribution, %								
	1	2	3	4	5	6	7	8	9
$R^1OCCl_2SSCO_2R$[b]	4	4[b]	26	16	10	5	3	2	
$R^1OCCl_2SSSCO_2R$	0	0	13	12	45	11	11	5	3
$MeOCCl_2SSCO_2Me$ + 1 equiv of HCl	11	29	15	19	11	7	5	3	
$R^1OCCl_2SSCOCl$		36	13	20	11	9	6	5	
$R^1OCCl_2SSSCOCl$			11	12	42	17	14	4	
$R^1OCCl_2SSSSCOCl$			15	26	20	15	16	8	

[a] See Schemes III-V. The complete data, for all possible permutations of alkoxycarbonyl (R), alkoxydichloromethyl (R^1), and alcohol (R^2) radicals being Me and Et are provided in Tables VI and VII in the supplementary material; averages are provided here. Isolated yields were generally 50–90%, better with EtOH than with MeOH. [b] Numbers cited in this row add up to 70%. The remaining 30%, formed as in Scheme IIIB, was disulfane **2** (R^2 = R) or **34** ($R^2 \neq$ R).

Scheme III[a]



[a] a, R = CH_3; b, R = C_2H_5.

(16) Fehér, F. In "Handbook of Preparative Inorganic Chemistry", 2nd ed.; Brauer, G., Ed.; Academic Press: New York, 1963; Vol. 1. (a) pp 373–375, S_3Cl_2 freshly prepared from SCl_2 and H_2S, see note 17; (b) pp 375–376, S_4Cl_2 freshly prepared from SCl_2 and H_2S_2 (note 16c), see note 17; (c) pp 350–353, H_2S_2; (d) pp 361–363, aqueous solution of Na_2S_2 prepared from Na_2S and sulfur; (e) p 346, as note d but using more sulfur.

(17) Purities of SCl_2 and S_2Cl_2 were assayed by reaction with excess MeSH (1 M in CH_2Cl_2) followed by NMR and HPLC analysis of the resulting mixture of dimethylpolysulfanes (ref 3). However, reactions of S_3Cl_2 and S_4Cl_2 with MeSH yielded complex mixtures with equal or more disproportionation than the reactions with **16** (Table II).

(18) Larka, E. A.; Schroll, A. L.; Barany, G. In "Proceedings of the Thirty-First Annual Conference on Mass Spectroscopy and Allied Topics, Boston, MA", 1983, pp 577–578.

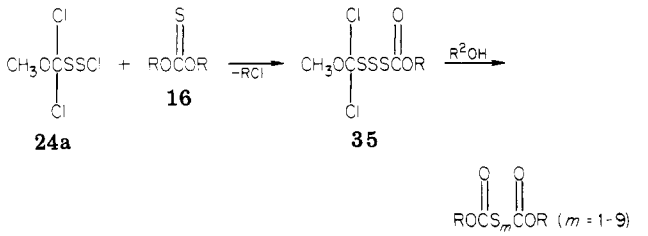
(19) (a) Shasha, B. S.; Doane, W. M.; Russell, G. R.; Rist, C. E. *J. Org. Chem.* **1969**, *34*, 1642–1645. (b) Shasha, B. S.; Doane, W. M. *Carbohydr. Res.* **1971**, *16*, 145–152.

(20) Böhme, H.; Brinkmann, M.; Steudel, H. P. *Liebigs Ann. Chem.* **1981**, 1244–1251.

(21) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, pp 1064–1065.

(22) Gladysz, J. A.; Wong, V. K.; Jick, B. S. *Tetrahedron* **1979**, *35*, 2329–2335. The lithium disulfide prepared according to this paper was checked by reacting it with iodoethane to give an excellent yield of diethyl disulfide, the identity and purity of which were confirmed by NMR and HPLC.

Scheme IV

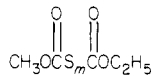


(centered on $m = 5$)

2a was obtained in a 96:4 ratio. Furthermore, **12a** did not react with hydrogen sulfide or disulfane.[16c] In contrast, (methoxycarbonyl)sulfenyl chloride (**14a**)[3] reacted with both hydrogen sulfide and disulfane to give **3a** and **4a**, respectively, together with considerable amounts of **2a–6a**. Compound **14a** with sodium sulfide or sodium disulfide also yielded mixtures of **2a–6a**.

Reduction of sulfenyl chlorides with aqueous iodide is a well-known method[23] for synthesis of disulfanes, and the results of applying this approach to **14** and **15** were shown (Table II). When these reductions were carried out in the presence of SCl_2 or S_2Cl_2, additional sulfur was introduced to the mixture of bis(alkoxycarbonyl)polysulfanes in units of one or two, respectively. These experiments allowed access to compounds with as many as nine sulfurs, with identifications based on HPLC retention times (see below). Finally, on treatment of **14a** and **15a** with ethanol, bis(methoxycarbonyl)polysulfane mixtures resulted with similar distributions to those obtained by iodide reduction.

Alcoholysis of Various (Alkoxydichloromethyl)sulfanes (Table IV). (Alkoxycarbonyl)(alkoxydichloromethyl)disulfanes **30** and **31** gave with alcohols a mixture of bis(alkoxycarbonyl)polysulfanes centered about the trisulfane **3** containing the original alkoxycarbonyl group (Scheme IIIA). Neither the alkyl group from the alkoxydichloromethyl moiety or from the alcohol was introduced into the products, except that some of the bis(alkoxycarbonyl)disulfanes **2** or **34**[3] were noted that arise by loss of alkyl chloride from **30** or **31** and subsequent esterification of the resulting acid chloride (Scheme IIIB). Alcoholysis of (alkoxycarbonyl)(alkoxydichloromethyl)trisulfanes **35** gave exclusively bis(alkoxycarbonyl)polysulfanes centered on the pentasulfane **5** (Scheme IV). When an equimolar mixture of **35a** and **35b** was treated with alcohol, the family of mixed (ethoxycarbonyl)(methoxycarbonyl)polysulfanes **17** and **36–38** was produced to-

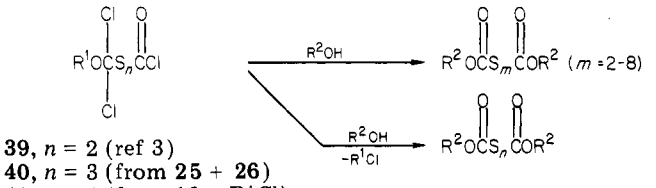


34, $m = 2$ **36**, $m = 4$
17, $m = 3$ **37**, $m = 5$
38, $m = 6$

gether with the bis(methoxycarbonyl) and bis(ethoxycarbonyl)polysulfanes. The major product was the pentasulfane **37**, and for every number of sulfurs (m) the binomial distrubition Me_2:MeEt:Et_2 = 1:2:1 was observed.

(Alkoxydichloromethyl)(chlorocarbonyl)polysulfanes **39–41** also gave mixtures of bis(alkoxycarbonyl)polysulfanes on alcoholysis (Scheme V). The trisulfanes **40** yielded a similar product mixture as did **35**, suggesting that initially **40** is esterified to **35**, which then undergoes the alcoholysis pathway already observed (compare Schemes IV and V). Alcoholysis of the tetrasulfane **41a** gave a mixture of bis(alkoxycarbonyl)polysulfanes with no one product dominating, implying that considerable disproportionation had taken place. The disulfane **39a** gave a mixture of the polysulfanes, with the disulfane **2a** (loss of MeCl followed by esterification) and the tetrasulfane **4a** as the major products. This result was different from that observed (Scheme III) for the alcoholysis of **30** or **31**. However, when **30a** was added to alcohol in the presence of HCl (1 equiv generated in situ by adding thionyl chloride to the alcohol), the product distribution observed (Table IV) was similar to that from **39a**. Lastly, the bis(alkoxydichloromethyl)polysulfanes **18–21** were subjected to alcoholysis, but the only nonvolatile product was elemental sulfur, amounting to a quantitative mass recovery of that element from the starting substrates.

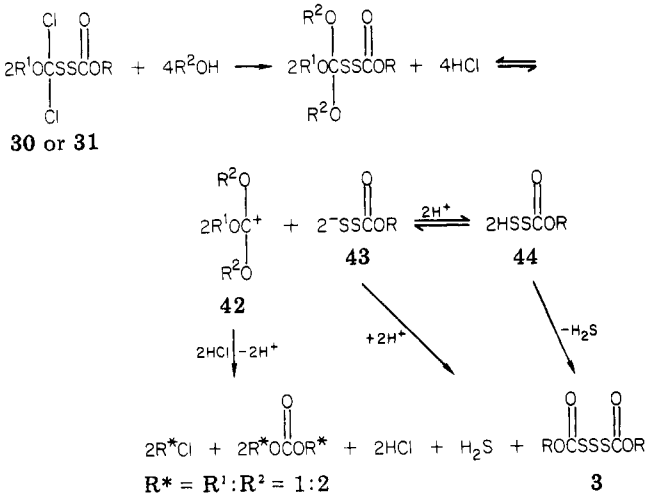
Scheme V[a]



39, $n = 2$ (ref 3)
40, $n = 3$ (from **25** + **26**)
41, $n = 4$ (from **19** − R^1Cl)

[a] a, $R^1 = CH_3$; b, $R^1 = C_2H_5$.

Scheme VI



$R^* = R^1:R^2 = 1:2$ **3**

Because the alkyl group of an alkoxydichloromethyl moiety did not become incorporated into isolable products during alcoholysis, it was of interest to establish the fate of that alkyl group and thereby develop insights into the mechanisms of these unusual transformations. This was accomplished by adding methanol or methanol-d_4 (2 equiv; found to be necessary for complete reaction) to solutions of **30** or **31** in $CDCl_3$ followed by NMR analysis (chemistry of Scheme III). For example, **30b** gave with methanol a mixture of bis(ethoxycarbonyl)polysulfanes (integral = 1.0 compared to starting **30b**, using toluene internal standard), MeO(C=O)OMe (1.9), MeCl (0.7), and with methanol-d_4, a mixture of bis(ethoxycarbonyl)polysulfanes (1.0), MeO(C=O)OMe plus MeO(C=O)OCD_3 (0.7), and MeCl (0.3). An acidic gas was evolved that was determined to contain HCl and H_2S. When **30a** was added to a large excess of methanol-d_4, the products seen by ^1H NMR were bis(methoxycarbonyl)polysulfanes (relative integral 1.0), MeO(C=O)OMe plus MeO(C=O)OCD_3 (0.3), and methanol-d (1.1); this last observation of methanol derived from the methoxydichloromethyl group indicates that some exchange with alcohol occurs before the final products are formed. Scheme VI is a summary of the stoichiometric reaction together with a possible mechanism that is consistent with the experimental observations. It seems

(23) Kharasch, N.; Wald, M. M. *Anal. Chem.* **1955**, *27*, 996–998.

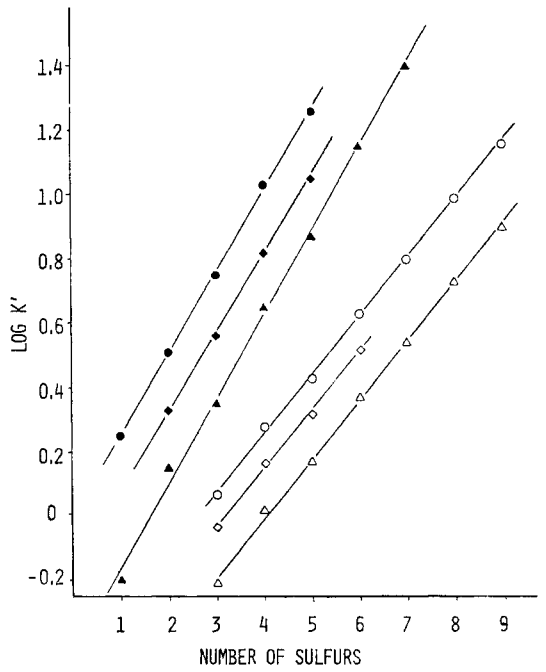


Figure 1. Relationship between HPLC retention (k', defined in ref 28) of $RO(C{=}O)S_n(C{=}O)OR'$ and the number of sulfurs (n) in the polysulfane chain, for R = R' = Me (△); R = Me, R' = Et (◇); R = R' = Et (○). Elution was with MeOH–H_2O (68:32) (solid symbols) or MeOH–H_2O (85:15) (open symbols). Integration constants relative to an equimolar amount of toluene at 210 nm varied with n (values in parentheses) as follows: 0.57 (*1*); 0.45 (*2*); 1.2 (*3*); 1.4 (*4*); 1.5 (*5–9*); further details are in Table VIII of the supplementary material.

reasonable to suggest an initial displacement of the labile chlorines[24] by alcohol followed by cleavage of the carbon–sulfur bond to give the stabilized trialkoxycarbonium ion **42**, which can then give, with chloride, alkyl chloride plus the dialkyl carbonate. Two of the (alkoxycarbonyl)disulfanyl ions **43** or disulfanes **44** could react further to provide the observed major product with $(2n-1)$ sulfurs plus H_2S. Further acid- or alcohol-catalyzed disproportionation[25] reactions would lead to the more complex mixtures of polysulfanes actually obtained.

HPLC and Other Characterizations of Bis(alkoxycarbonyl)polysulfanes. Reversed-phase HPLC has found wide application in the separation of polysulfanes, including aliphatic polysulfides,[26] bis(alkoxythiocarbonyl)polysulfanes,[10] and recently common inorganic sulfur itself.[27] Hiller[26] has reported that for aliphatic polysulfides log k'[28] increases linearly with (i) the number of sulfurs and (ii) the number of carbons and decreases linearly with (iii) the percentage of methanol in the methanol–water eluent. We have applied this analysis to the bis(alkoxycarbonyl)polysulfane series with very good correlation (Figure 1). The linearity of these plots is strong evidence for the identity of the previously unreported sulfanes **7–9**. It should be noted that for the same eluent, the lines for the Me_2, the MeEt, and the Et_2 series are parallel and equidistant.

Electron-impact mass spectroscopy was of some value for investigating the bis(methoxycarbonyl)polysulfane series (**a**); much less so for the MeEt and Et_2 series. MS on mixtures revealed ions regularly spaced (32 amu apart) up to m/e 342 ($M^{+\cdot}$ for **7a**). Pure **3a** and **4a** gave molecular ions at m/e 214 and 246, respectively, and no ($M^{+\cdot}$ – S) ions.

Table V. Representative Rates of Reactions[a]

sulfenyl chloride	with MeO(C=S)OMe product	with MeO(C=S)OMe k, L mol^{-1} s^{-1}	with MeO(C=S)Cl product	with MeO(C=S)Cl k, L mol^{-1} s^{-1}
SO_2Cl_2	**14a**	0.1	**13a**	3×10^{-5}
SCl_2	**3a**[b]	0.6	**24a**	4×10^{-3}
S_2Cl_2	**4a**[b]	4×10^{-3}	**19a**	4×10^{-5}
$MeOCCl_2SCl$ (**13a**)	**30a**	8×10^{-3}	*c*	
$MeOCCl_2SSCl$ (**24a**)	**35a**	7×10^{-2}	**18a**	2×10^{-4}
Cl(C=O)SCl	*d*	1×10^{-2}	**39a**	2×10^{-6}
Cl(C=O)SSCl (**26**)	*e*	4×10^{-2}	**40a**	5×10^{-4}
MeO(C=O)SCl (**14a**)	**2a**	0.2	**30a**	3×10^{-4}
MeO(C=O)SSCl (**15a**)	**3a**	0.1	**35a**	3×10^{-4}

[a] Reactants were 0.05–1.0 M in $CDCl_3$, with toluene as an internal standard, and were followed by ^1H NMR, at 25 °C. [b] See ref 15. [c] No reaction as written. The **13a** slowly loses MeCl to form Cl(C=O)SCl, which reacts as shown on line 6. [d] MeO(C=O)SS(C=O)Cl formed; see ref 3. [e] MeO(C=O)SSS(C=O)Cl formed initially but readily lost COS to form **15a**; 20% after 3 min, as followed by analytical-scale conversion to **47** and **46** (cf. method B for **15a**, Experimental Section).

Kinetics (Table V). The present paper extends to disulfanyl or bifunctional sulfenyl chlorides our reported methodology[3] for the addition of sulfenyl chlorides to alkoxythiocarbonyl compounds. Rate determinations showed that SCl_2 was the most reactive, over 100 times more so than S_2Cl_2. The disulfanyl chlorides **15**, **24**, and **26** were of comparable reactivities, which for the latter two compounds were substantially greater than the corresponding sulfenyl chlorides.

Experimental Section

General Methods. Most of the methods, instrumentation, and materials used have already been described.[3,29] SCl_2 was purified[30] just prior to use by distillation from PCl_3 (1% w/w) into a flask containing PCl_5. Analytical HPLC was performed with a Beckman-Altex 334 system on an Ultrasphere-ODS column (4.6 mm × 25 cm) eluted with MeOH–H_2O (68:32) for polysulfanes **1–6** or MeOH–H_2O (85:15) for polysulfanes **3–9** at a flow rate of 0.90 mL/min. Preparative HPLC was performed with the same system on a Zorbax-ODS column (9.4 mm × 25 cm) eluted with MeOH–H_2O (85:15) at 3 mL/min. All chloro compounds were stored at −20 °C.

Bis(methoxycarbonyl) sulfide (1a) (Table II, line 1) was prepared as already described[3] by the two-phase reaction of **12a** in $CHCl_3$ plus aqueous Na_2S: IR ($CDCl_3$) 1785 (s), 1720 (w), 1110 (vs), 810 (w) cm^{-1}; MS.

Bis(methoxycarbonyl)disulfane (2a). A,B (Table II, lines 2 and 8): as already described[3] by iodine oxidation of the Bender's salt (**11a**) or by reaction of bis(chlorocarbonyl)disulfane (**10**) with MeOH; MS. C (Table II, line 11): a solution of **14a** (2.21 g, 17.4 mmol) in $CHCl_3$ (30 mL) was stirred with a solution of KI (4.4 g, 26.5 mmol) in water (50 mL) for 3 h. The iodine was removed by addition of aqueous $Na_2S_2O_3$ (2 M, 20 mL), and the organic layer was separated, dried ($MgSO_4$), and evaporated to give a colorless oil (1.17 g, 74%): IR ($CDCl_3$) 1740 (s), 1720 (sh), 1190 (m), 1160 (sh), 1135 (vs), 810 (m) cm^{-1}. D (Table II, line 10): Following the procedure of Douglass,[12] **13a** (5 g, 27.5 mmol) was

(24) Gross, H.; Farkas, I.; Bogner, R. *Z. Chem.* **1978**, *18*, 201–210.
(25) Review: Parker, A. J.; Kharasch, N. *Chem. Rev.* **1959**, *59*, 583–628.
(26) Hiller, K. O.; Masloch, B.; Möckel, H. J. *Z. Anal. Chem.* **1976**, *280*, 293–297.
(27) Tebbe, F. N.; Wasserman, E.; Peet, W. G.; Vatvars, A.; Hayman, A. C. *J. Am. Chem. Soc.* **1982**, *104*, 4971–4972.
(28) $k' = (t_R - t_0)/t_0$; t_R = retention time sulfide, t_0 = retention time (void) of mobile phase = 2.7 min.
(29) MS or Anal. in Experimental Section mean, respectively, that a fully interpreted mass spectrum or the elemental analysis data in accord with theory were obtained and are presented in the supplementary material.
(30) Rosser, R. S.; Whitt, F. R. *J. Appl. Chem.* **1960**, 229–237.

added slowly to aqueous KI (1 M, 55 mL, 55 mmol) at 0 °C. After the vigorous reaction had subsided, the iodine formed was removed by addition of $Na_2S_2O_3$ (aq). The solution was extracted with ether (2 × 15 mL), and the organic phase was dried ($MgSO_4$) and evaporated to yield 0.61 g (21%) of a mixture of **2a** to **6a**.

Bis(methoxycarbonyl)trisulfane (3a). A (Table II, line 4): the Bender's salt **11a**[3] (4.11 g, 31.6 mmol) was suspended in ether (15 mL) at 0 °C and SCl_2 (1 mL, 15.8 mmol) was added dropwise with stirring. The mixture was warmed to 25 °C, filtered, and evaporated to yield the white solid **3a**, which was washed with petroleum ether (bp 30–60 °C) and dried: yield 2.41 g (71%): mp 65 °C (lit.[14] mp 59 °C); 98% pure by HPLC. B (Table III, line 1): freshly distilled SCl_2 (1.34 mL, 21 mmol) was carefully added to **16a** (4.45 g, 42 mmol), cooled sufficiently in dry ice–acetone to control the temperature but not freeze the starting material, with vigorous gas evolution and disappearance of the red color of SCl_2. The reaction mixture set solid at 25 °C, and the white needles were collected by filtration, washed with cold hexane, and dried to give **3a** (3.02 g, 67%): mp 65 °C, 98% pure by HPLC; IR ($CDCl_3$) 1740 (s), 1715 (m), 1135 (vs), 810 (m) cm^{-1}. Anal., MS.

Bis(ethoxycarbonyl)trisulfane (3b). A (Table II, line 5): SCl_2 was added to a suspension of **11b** (5 g, 34.7 mmol) in ether (50 mL) at 0 °C. The mixture was filtered and evaporated to give a colorless oil (2.92 g, 77%), 97% pure by HPLC. B (Table III, line 2): SCl_2 (0.24 mL, 3.85 mmol) was added to **16b** (1.0 g, 7.7 mmol) cooled in dry ice. After warming to 25 °C, the crude product (0.95 g) was distilled (bulb-to-bulb, oven temperature 95–105 °C, 0.08 mm) to give a white solid: yield 0.83 g (89%): mp 38–40 °C (lit.[7] oil), 98% pure by HPLC; IR ($CDCl_3$) 1745 (s), 1175 (sh), 1140 (vs) cm^{-1}. Anal., MS.

Bis(methoxycarbonyl)tetrasulfane (4a). A (Table II, line 6): prepared from S_2Cl_2 plus **11a** in a similar manner to the preparation of **3a**: yellow oil (98% yield). B (Table III, line 3): prepared from S_2Cl_2 plus **16a** in a similar manner to the preparation of **3a**: distilled (bulb-to-bulb, oven temperature 95–115 °C, 0.08 mm) yield of 92%; IR ($CDCl_3$) 1740 (s), 1715 (m), 1135 (vs) cm^{-1}. Anal., MS.

Bis(ethoxycarbonyl)tetrasulfane (4b) (Table II, line 7) from S_2Cl_2 and **11b** as in method A for **4a**: yellow oil (85% yield); IR ($CDCl_3$) 1745 (s), 1170 (sh), 1140 (vs) cm^{-1}. Anal.

Bis(methoxycarbonyl)pentasulfane (5a) and -hexasulfane (6a) (Table III, Lines 4 and 5). Following method B for **3a**, S_3Cl_2[16a] and S_4Cl_2[16b] were added to **16a**.

(Methoxycarbonyl)disulfanyl Chloride (15a). A. MeOH (2.2 mL, 54.6 mmol) was added dropwise to a stirred solution of **26** (8.48 g, 52 mmol) in dry ether (30 mL). After 8 h of reflux the ether was removed by distillation and the residual oil was distilled at reduced pressure to provide the yellow liquid **15a**: yield 56%; bp 41 °C (0.7 mm) [lit.[14] bp 72 °C (11 mm)]; ρ = 1.46; IR ($CDCl_3$) 1760 (s), 1435 (w), 1190 (s), 1145 (vs) cm^{-1}. Anal. After 5 weeks at 25 °C a sample had partially (16%) decomposed to MeO(C=O)SCl (**14a**). Pure **15a** was characterized by conversion to its *N*-methylanilide **46** (see later). B. Neat **26** (1.62 g, 9.9 mmol) and **16a** (1.1 g, 10.4 mmol) were mixed at −78 °C, allowed to warm to 25 °C, and analyzed by NMR to contain **15a** (8.1 mmol) and **3a** (2.2 mmol). Pure **15a** (0.75 g, 4.7 mmol, 48%) was obtained by short-path distillation, correct by NMR and IR, with crystalline **3a** obtained in the residue.

Potassium Iodide Reduction of (Methoxycarbonyl)disulfanyl Chloride (15a) (Table II, Line 13). A solution of **15a** (0.5 g, 3.9 mmol) in CH_2Cl_2 (10 mL) was shaken with a solution of KI (1 g, 6 mmol) and $Na_2S_2O_3$ (1.5 g, 6 mmol) in water (20 mL) for 15 min in accordance with the conditions of Böhme and Steudel.[14] The organic layer was separated, dried ($MgSO_4$), and evaporated to yield a colorless oil (0.25 g, 60%), comprised by HPLC of **3a** (43%), **4a** (42%), **5a** (11%), **6a** (3%), and **7a** (1%).

(Ethoxycarbonyl)(methoxycarbonyl)trisulfane (17). At 0 °C, **16b** (1 g, 8.5 mmol) was added to **15a** (1.34 g, 8.5 mmol), and the mixture was stirred for 24 h at 25 °C. The crude product (1.82 g, 94%) was distilled (bulb-to-bulb, oven temperature 65–70 °C, 0.06 mm) to give 1.39 g (77%) of colorless liquid **17**, 95% pure by HPLC. Anal.

Bis(methoxydichloromethyl)trisulfane (18a). A. A mixture of bis(methoxythiocarbonyl)sulfide (**23a**)[3] (10 g, 55 mmol) and SO_2Cl_2 (13.7 mL, 0.17 mol) in petroleum ether (bp 30–60 °C) (50 mL) was refluxed for 1 h, following which the solvent and excess reagents were removed at 20 mm through an 18-in. Vigreux column: yield 16.7 g (94%); IR (neat) 1270 (s), 1190 (m), 1120 (vs), 1050 (m), 940 (m), 830 (m) cm^{-1}. Anal., MS. B. (Methoxydichloromethyl)disulfanyl chloride (**24a**) (1.23 g, 6 mmol) was added to **25a** (0.5 mL, 6 mmol) to give after 16 h at 25 °C **18a** (1.86 g, 96%). Anal. C. At 25 °C, SCl_2 (1.5 mL, 23.6 mmol) was added slowly to **25a** (5.2 g, 47.1 mmol). After 24 h, the crude product (7.3 g, 96%) was found by NMR to contain **18a** (77%), **24a** (16%), and unreacted **25a** (7%). Distillation (bulb-to-bulb, oven temperature 80–85 °C, 0.15 mm) removed the **24a** and **25a** to leave pure **18a** (4.7 g, 63%) in the residue with no observed decomposition at these temperatures.

Bis(methoxydichloromethyl)tetrasulfane (19a). Exactly as in method A for **18a**, but using bis(methoxythiocarbonyl)disulfane (**22a**)[3] (60.4 g, 0.28 mmol) and SO_2Cl_2 (68 mL, 0.85 mol): yield 97.6 g (98%); IR (neat) 1270 (m), 1190 (s), 1110 (vs), 1050 (m), 930 (m), 820 (m) cm^{-1}. Anal., MS.

Bis(methoxydichloromethyl)pentasulfane (20a) and -hexasulfane (21a). As in method A for **18a**, bis(methoxythiocarbonyl)trisulfane (**27a**)[3] (15 g, 61 mmol) with SO_2Cl_2 (14.7 mL, 0.18 mol) gave a mixture (23.3 g, 103%) of **20a** (65%) and **21a** (35%), as judged by ^1H NMR, and bis(methoxythiocarbonyl)tetrasulfane (**28a**)[3] (14.1 g, 51 mmol) with SO_2Cl_2 (12.2 mL, 0.15 mol) gave a mixture (20.9 g, 104%) of **19a** (30%), **20a** (26%), and **21a** (44%). The above mixtures were used in the following hydrolysis experiments.

Hydrolysis of Bis(methoxydichloromethyl)polysulfanes (Table III, Lines 6–9). In general, a solution of the appropriate substrate **18a–21a** (1 g) in $CHCl_3$ (5 mL) was vigorously stirred at 25 °C with aqueous NaOH (1 M, 3.5 equiv) and Me_4NOH solution (0.5 mL, 10% w/v). After 14 h, during which the aqueous phase had become acidic, the organic layer was separated, washed with ether, dried ($MgSO_4$), and evaporated to yield yellow oils, which were analyzed by HPLC.

Bis(chlorocarbonyl)trisulfane (29) and Its Reaction with Methanol (Table III, Line 10). A solution of **18a** (1.55 g, 4.8 mmol) in $CDCl_3$ (2 mL) was carefully treated with $FeCl_3$ (10 mg) over a period of 2 h. Examination by ^{13}C NMR revealed that the conversion to **29** and MeCl was quantitative. The above solution was added to MeOH (40 mL) at 0 °C, followed by evaporation to give 0.58 g (56%) of primarily **3a** by HPLC. Attempts to isolate pure **29** by short-path distillation at high vacuum were unsuccessful.

Reaction of Methyl Chloroformate (12a) with Sodium Disulfide (Table III, Line 11). $Na_2S{\cdot}9H_2O$ (18 g, 75 mmol), elemental sulfur (2.5 g, 75 mmol), and water (20 mL) were stirred together at 70 °C until a red-brown solution of Na_2S_2 was formed. A solution of **12a** (2 mL, 25.9 mmol) in $CHCl_3$ (20 mL) was then added slowly at 0 °C to a portion of the disulfide solution (5.7 mL, 12 mmol). The mixture was allowed to warm to 25 °C and stirred for 3 h during which time the red color faded and sulfur was precipitated. The organic layer was separated, dried ($MgSO_4$), and evaporated to give 0.43 g (24%) of **1a**, as identified by ^1H NMR and HPLC retention data identical with those found previously for authentic **1a**.

Reaction of Methyl Chloroformate (12a) with Sodium Polysulfide (Table III, Line 12). Similarly to the experiment just described, **12a** (2 mL, 25.9 mmol) in $CHCl_3$ (20 mL) was added to a solution of sodium polysulfide[16e,21] prepared from $Na_2S{\cdot}9H_2O$ (2.9 g, 12.1 mmol) and sulfur (1.54 g, 48.1 mmol). Workup as before provided pure **1a** (1.39 g, 77%).

Reaction of Methyl Chloroformate (12a) with Lithium Disulfide (Table III, Line 13). A solution of lithium triethylborohydride (Superhydride) (Aldrich) in THF (1 M, 5 mL, 5 mmol) was added under N_2 to sulfur (0.16 g, 5 mmol). After being stirred for 15 min, **12a** (0.71 mL, 10 mmol) was added to the yellow solution. The solution turned colorless and a white solid precipitated. After being stirred for 30 min, ether (25 mL) was added, and the solution was filtered and evaporated to give a colorless oil comprising **1a** (96%) and **2a** (4%) by HPLC; yield 0.39 g (52%).

Reaction of (Methoxycarbonyl)sulfenyl Chloride (14a) with Sodium Sulfide (Table III, Line 14). A solution of **14a** (3 mL, 32.9 mmol) in $CHCl_3$ (20 mL) was stirred with a solution of $Na_2S{\cdot}9H_2O$ (3.6 g, 15 mmol) in water (8 mL) at 25 °C for 4 h,

during which time yellow color due to **14a** faded. The organic layer was separated, dried ($MgSO_4$), and evaporated to give a pale yellow oil (2.74 g, 78%).

Reaction of (Methoxycarbonyl)sulfenyl Chloride (14a) with Sodium Disulfide (Table III, Line 15). In an analogous fashion to the reaction of **12a** with Na_2S_2, **14a** (3 mL, 32.9 mmol) plus Na_2S_2 (15 mmol) yielded a yellow oil (3.17 g, 93%).

Reaction of (Methoxycarbonyl)sulfenyl Chloride (14a) with Hydrogen Sulfide (Table III, Line 16). Hydrogen sulfide was bubbled slowly through a solution of **14a** (1 mL, 10.9 mmol) in CH_2Cl_2 (30 mL) at 25 °C until the yellow color disappeared (2 h). Evaporation of the solvent left a solid residue (1.25 g, 98%).

Reaction of (Methoxycarbonyl)sulfenyl Chloride (14a) with Disulfane (Table III, Line 17). Disulfane[16c] (1 mL, 20.8 mmol) was added to a solution of **14a** (5.06 g, 40 mmol) in CH_2Cl_2 (10 mL); vigorous gas evolution occurred. After being stirred for 2 h at 25 °C, the mixture was evaporated to yield a yellow oil (5.09 g, 97%).

Reaction of (Methoxycarbonyl)sulfenyl Chloride (14a) with Ethanol (Table III, Line 18). At 0 °C, **14a** (0.5 g, 4 mmol) was added with stirring into EtOH (10 mL). After 14 h the EtOH was evaporated to yield a yellow oil (0.11 g, 27%).

Reaction of (Methoxycarbonyl)disulfanyl Chloride (15a) with Ethanol (Table III, Line 19). In an analogous manner, **15a** (0.5 g, 3.15 mmol) was added to EtOH (10 mL). After 3 h, solvent was evaporated to yield a yellow oil (0.33 g, 87%).

Potassium Iodide Reduction of (Methoxycarbonyl)-sulfanyl Chlorides (14a and 15a) in the Presence of Sulfur Chlorides (Table III, Lines 20–22). A. A solution of **14a** (1 mL, 10.9 mmol) and S_2Cl_2 (1 mL, 12.5 mmol) in CH_2Cl_2 (20 mL) was shaken with an aqueous solution of KI (1 M, 20 mL, 20 mmol), and the resulting brown solution was washed with $Na_2S_2O_3$ solution until colorless. The organic layer was separated, dried ($MgSO_4$), and evaporated to yield a yellow oil (0.41 g, 35%). B. Similarly, a solution of **15a** (0.27 g, 1.7 mmol) and SCl_2 (0.63 g, 6.1 mmol) in $CHCl_3$ (5 mL) was shaken with the KI solution (6 mL, 6 mmol). Workup yielded a yellow oil (0.27 g, 100%). C. Similarly, a solution of **15a** (0.1 g, 0.63 mmol) and S_2Cl_2 (0.14 mL, 1.7 mmol) in $CHCl_3$ (5 mL) was shaken with the KI solution (6 mL, 6 mmol) to yield a yellow oil (0.07 g, 84%).

(Methoxydichloromethyl)disulfanyl Chloride (24a). At −30 °C, **25a** (34.8 g, 0.32 mol) was added dropwise with stirring to SCl_2 (20 mL, 0.32 mol). After the addition was complete, the mixture was warmed to 25 °C for 1 h, at which time the crude product (67.1 g, 100%) contained **24a** and **18a** in a 9:1 molar ratio (NMR). Distillation [bp 49–52 °C (0.15 mm) [lit.[20] bp 29 °C (0.09 mm)]] gave **24a** (41.5 g, 62%) pure by ^{13}C and ^1H NMR; ρ = 1.59; IR (neat) 1185 (m), 1120 (vs), 940 (s), 820 (m) cm^{-1}. Anal. A solution of **24a** in $CDCl_3$ after 1 week at 25 °C showed no MeCl or **26** by ^{13}C NMR.

(Ethoxydichloromethyl)disulfanyl Chloride (24b). Similarly to the procedure for **24a**, **25b** with SCl_2 gave a 100% crude and 66% distilled yield of pure **24b**: bp 70–79 °C (0.5 mm) [lit.[20] bp 41 °C (0.01 mm)]: ρ = 1.46. Anal.

(Chlorocarbonyl)disulfanyl Chloride (26). At 0 °C, $FeCl_3$ (40 mg, 0.7% w/v) was slowly added to freshly prepared **24a** (58.9 g, 0.29 mol). A vigorous evolution of gas occurred with a weight loss of 14.7 g (99% of theory). Distillation gave pure **26** [bp 49 °C (12 mm) [lit.[20] bp 53–54 °C (12 mm)]], free of S_2Cl_2 and Cl(C=O)SCl by *N*-methylaniline assay:[3,18] yield 37.7 g (80%); IR ($CDCl_3$) 1780 (s), 780 (vs) cm^{-1}; ρ = 1.64. Anal. Pure **26** was characterized by conversion to its *N*-methylanilide **45** (see later).

(Alkoxycarbonyl)(alkoxydichloromethyl)disulfanes (30 and 31). A. On a 10-mmol scale, **13a**[3,12] (1 equiv) was added to the appropriate **16** cooled in dry ice, to provide after warming to 25 °C the appropriate **30** in near quantitative yields. B. On a 5-mmol scale, SO_2Cl_2 (1.1 equiv) was added to the appropriate one of four alkoxycarbonyl alkoxythiocarbonyl sulfides (**32** or **33**)[3] cooled in ice. Gas evolution occurred, and the reactions were complete within 5 min. The title products were obtained in near quantitative yields, with the positioning of the alkyl groups as shown in Scheme III.[5] C: from **14** plus **25** as previously described.[3]

(Alkoxycarbonyl)(methoxydichloromethyl)trisulfanes (35). In a manner analogous to method A for the preparation of disulfanes **30**, **24a** (1 equiv) added to the cooled thiocarbonates **16** provided the trisulfanes **35**.

(Alkoxydichloromethyl)(chlorocarbonyl)trisulfanes (40). A. In analogy to the preparation[3] of **39** from **25** plus Cl(C=O)SCl, **26** (1 equiv) was added to **25**. The reactions, followed by ^{13}C and ^1H NMR, were complete after 14 h at 25 °C. B. A solution of **18b** (7.16 g, 20.3 mmol) in $CDCl_3$ (5 mL) was allowed to stand at 25 °C and followed by ^{13}C NMR. After 6 days, no starting material remained; neither was any **29** observed. Evaporation gave **40b** (5.35 g, 92%).

(Alkoxydichloromethyl)(chlorocarbonyl)tetrasulfane (41). A solution of **19** (20 mmol) in $CDCl_3$ (5 mL) was followed by ^{13}C and ^1H NMR. Loss of MeCl from **19a** to give **41a** was complete in 2 days at 25 °C, whereas loss of EtCl from **19b** to give **41b** took 6 days.

Alcoholysis of (Alkoxydichloromethyl)(alkoxy-carbonyl)polysulfanes and (Alkoxydichloromethyl)(chlo-rocarbonyl)polysulfanes (Table IV). A solution of the (alkoxydichloromethyl)-containing polysulfane **30**, **31**, **35**, **39**, **40**, or **41** (1 g) in $CHCl_3$ (1 mL) was added with stirring to MeOH or EtOH (10 mL) at 0 °C. After being stirred for 6–14 h at 25 °C, the solutions were filtered to remove small amounts of elemental sulfur and evaporated to give almost colorless to yellow oils. For an insight into mechanisms, MeOH or CD_3OD (50 μL, 2 equiv) was added to a solution of **30b** (0.15 g, 0.7 mmol) in $CDCl_3$ (3 mL) containing toluene (100 μL, internal standard) at 25 °C in a screw-capped tube. After 2 h the cap was removed to release an acidic gas that fumed with ammonia and blackened lead acetate paper. The proportions of products as determined by ^1H NMR are described in the Results section. In another experiment summarized earlier, **30a** (0.1 g) in $CDCl_3$ (0.1 mL) was added to excess CD_3OD (1 mL) in an NMR tube and the spectrum was recorded after 6 h at 25 °C. Finally, a mixture of **35a** and **35b** (0.5 g of each) in $CHCl_3$ (1 mL) was added to MeOH (10 mL) at 0 °C. After the usual workup, HPLC of the resulting product mixture (0.19 g) showed **3a**, **17**, **3b**, **4a**, **36**, **4b**, **5a**, **37**, **5b**, **6a**, **38**, and **6b** in a ratio 10:5:1:2:3:1:17:32:15:4:7:3.

(*N*-Methyl-*N*-phenylcarbamoyl)(*N*-methyl-*N*-phenyl-amino)disulfane (45). A solution of **26** (1 g, 6.1 mmol) in $CHCl_3$ (15 mL) was added to *N*-methylaniline (2.8 mL, 26 mmol) in $CHCl_3$ (15 mL) at less than 5 °C. After 1 h at 25 °C, the solution was washed with 1 N aqueous HCl (2 × 20 mL) and water (20 mL), dried ($MgSO_4$), and evaporated to give a pale yellow oil (1.65 g, 89%), which crystallized slowly on standing at 25 °C; mp 52–54 °C, HPLC pure. Anal., MS.

(Methoxyccarbonyl)(*N*-methyl-*N*-phenylamino)disulfane (46). With use of the same procedure for the conversion of **14a** to its *N*-methylanilide,[3] **15a** (0.5 g, 3.2 mmol) yielded a colorless oil **46** (0.67 g, 97%); HPLC pure. MS. After several months at 25 °C, a sample of **46** had completely decomposed to sulfur and MeO(C=O)N(Me)Ph.

(Methoxycarbonyl)(*N*-methyl-*N*-phenylcarbamoyl)tri-sulfane (47). A solution of *O*-ethyl *N*-methyl-*N*-phenylthiocarbamate[3] (0.31 g, 1.6 mmol) and **15a** (0.25 g, 1.6 mmol) in benzene (1.6 mL) was maintained overnight at 25 °C and concentrated to give the viscous yellow oil **47** (0.46 g, 100%), HPLC purity >95% and resolved from the corresponding disulfane.[3] MS.

Registry No. **1a**, 1190-35-8; **1b**, 36955-31-4; **2a**, 26555-39-5; **2b**, 6365-90-8; **3a**, 26555-41-9; **3b**, 88766-26-1; **4a**, 88766-27-2; **4b**, 88766-62-5; **5a**, 88766-28-3; **5b**, 88766-48-7; **6a**, 88766-25-0; **6b**, 88766-49-8; **7a**, 88766-31-8; **7b**, 88766-50-1; **8a**, 88766-51-2; **8b**, 88766-52-3; **9a**, 88766-53-4; **9b**, 88766-54-5; **10**, 51615-88-4; **11a**, 34520-64-4; **11b**, 35832-93-0; **12a**, 79-22-1; **13a**, 87463-08-9; **13b**, 87463-09-0; **14a**, 26555-40-8; **14b**, 26555-35-1; **15a**, 88766-29-4; **16a**, 1115-13-5; **16b**, 762-03-8; **17**, 88766-32-9; **18a**, 88766-33-0; **18b**, 88766-44-3; **19a**, 88766-34-1; **19b**, 88766-47-6; **20a**, 88766-35-2; **21a**, 88766-36-3; **22a**, 1468-37-7; **23a**, 18804-17-6; **24a**, 79598-17-7; **24b**, 79342-44-2; **25a**, 2812-72-8; **25b**, 2812-73-9; **26**, 79341-73-4; **27a**, 25170-09-6; **28a**, 74568-23-3; **29**, 88766-37-4; **30a**, 87462-95-1; **30b**, 87462-96-2; **31a**, 88766-38-5; **31b**, 88766-39-6; **32a**, 87463-06-7; **32b**, 26698-15-7; **33a**, 87463-07-8; **33b**, 3278-35-1; **34**, 87463-04-5; **35a**, 88766-40-9; **35b**, 88766-41-0; **36**, 88766-55-6; **37**, 88766-56-7; **38**, 88766-57-8; **39a**, 87462-91-7; **39b**, 87462-92-8; **40a**, 88766-42-1; **40b**, 88766-43-2; **41a**, 88766-45-4; **41b**, 88766-46-5; **45**, 88766-58-9; **46**, 88766-30-7; **47**, 88766-59-0; Na_2S, 1313-82-2; SCl_2, 10545-99-0; S_2Cl_2, 10025-67-9; S_3Cl_2, 31703-09-0; S_4Cl_2, 15731-86-9; SO_3Cl_2, 7791-25-5; Na_2S_2, 22868-13-9; Na_2S_8, 1344-08-7; Li_2S_2, 7783-06-4;

H_2S, 7783-06-4; ClC(O)SCl, 2757-23-5; MeOC(O)N(Me)Ph, 28685-60-1; PhN(Me)C(O)SEt, 40088-76-4; $MeOCCl_2SSSCCl_2OEt$, 88766-60-3; MeOC(O)SSC(O)Cl, 87462-93-9; MeOC(O)SSSC(O)Cl, 88766-61-4; disulfane, 13465-07-1; *N*-methylbenzamine, 100-61-8.

Supplementary Material Available: Tabulations of all UV, mass spectral, chromatographic, and analytical data, together with the complete data that is summarized in Table IV (6 pages). Ordering information is given on any current masthead page.

Probes for Narcotic Receptor Mediated Phenomena. 4.[1] Synthesis of (±)-2,3,4,5,6,6a-Hexahydro-3-methyl-8-hydroxy-1*H*-4,11b-methanobenzofuro-[3,2-*d*]azocine, an Oxide-Bridged 5-(*m*-Hydroxyphenyl)morphan†

Terrence R. Burke, Jr., Arthur E. Jacobson, and Kenner C. Rice*

Section on Medicinal Chemistry, Laboratory of Chemistry, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20205

J. V. Silverton

Laboratory of Chemistry, National Heart and Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland 20205

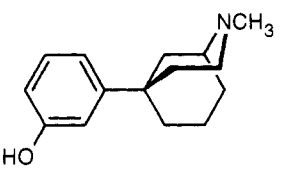
Received August 19, 1983

The synthesis of racemic 2,3,4,5,6,6a-hexahydro-3-methyl-3-hydroxy-1*H*-4,11b-methanobenzofuro[3,2-*d*]azocine (**2**) is described. The route utilized a key photochemical conversion of the aryloxy enone **7** to the hexahydrodibenzofuran **8**, which established the relative stereochemistry of the oxide and methano bridges of **2**. A 1,4-Michael-type addition of nitrogen to the β-carbon of the α,β-unsaturated compound **12** established the fourth and final ring. The title compound **2** represents an oxide-bridged derivative of the potent 5-(*m*-hydroxyphenyl)morphan class of opioid analgesics. Unlike the 5-(*m*-hydroxyphenyl)morphans, which have a freely rotating phenyl group, **2** has the phenyl ring conformationally restricted at an angle of 86° relative to atoms 1, 2, 4, and 12 of the piperidine ring as determined by X-ray analysis. The lack of in vivo agonist or antagonist activity of **2** in contrast to the parent 5-(*m*-hydroxyphenyl)morphan **1** suggests that the phenyl ring torsion angle is unsuitable for binding to the opioid receptor system.

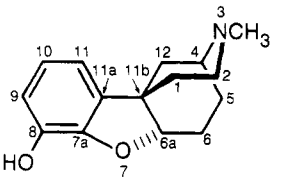
Opioid receptors are stereospecific, saturable, high-affinity binding sites in the mammalian central nervous system (CNS) that mediate the analgesic effects of morphine and its surrogates and probably also control certain aspects of the perception of pain, pleasure, and mood by interaction with opiate-like peptides (endorphins) produced in the CNS. In the first two reports of our study of the structure and function of these receptors,[2] we described the preparation of site-directed alkylating agents specific for individual subpopulations of opioid receptors and identification of a M_r 58000 subunit of the opioid δ-receptor. We have also begun examining the topographical features of the opioid receptor system through a structure–activity study based upon the 5-phenylmorphan class of opioid analgesics.[1]

Since the discovery of the 5-phenylmorphans by May in 1954,[3] certain of these compounds have been found to have morphine-like activity and potential therapeutic value. We have undertaken a synthetic study of the 2-methyl-5-(*m*-hydroxyphenyl)morphan nucleus to differentiate aspects of its structure that are important for its observed biological activity. Since the phenylmorphan ring system itself is rigid, we are examining the role of the phenyl ring torsion angle with respect to the fixed piperidine ring as it relates to biological activity and opioid receptor binding. The importance of the phenyl ring torsion angle has previously been cited as one factor effecting the enantiomeric difference in potency between prodine isomers.[4,5]

In our approach toward an unambiguous definition of the phenyl torsion angles for a homologous series of 2-methyl-5-(*m*-hydroxyphenyl)morphans, we have adapted the use of an oxide bridge to covalently link the 2-position of the phenyl ring with atoms 1, 12, or 6a of the morphan moiety in **2**. The arrangement of these sites about the



1



2

phenyl–morphan bond and the possibility of α,β isomers at each position results in six possible rotational isomers, with the phenyl ring of each isomer being rotated approximately 60° from that of the previous isomer (Figure 1).

The first isomer chosen for synthesis, **2**, has an oxide bridge distantly comparable to that of morphine, and in fact, the *O*-methyl ether of the 11-methyl analogue has previously been obtained by degradation of naturally occurring thebaine.[6] Examination of models indicated that

† Dedicated to Dr. Ulrich Weiss on the occasion of his 75th birthday.

(1) For the previous paper in this series, see: Burke, T. R., Jr.; Jacobson, A. E.; Rice, K. C.; Silverton, J. V. In "Problems of Drug Dependence 1983"; Harris, L. S., Ed.; NIDA Research Monograph: Washington, DC, in press.

(2) (a) Klee, W. A.; Simonds, W. F.; Sweat, F. W.; Burke, T. R., Jr.; Jacobson, A. E.; Rice, K. C. *FEBS Lett.* **1982**, *150*, 125 (paper 1 in this series) (b) Rice, K. C.; Jacobson, A. E.; Burke, T. R., Jr.; Bajwa, B. S.; Streaty, R. A.; Klee, W. A. *Science (Washington, D.C.)* **1983**, *220*, 314 (paper 2 in this series).

(3) May, E. L.; Murphy, J. G. *J. Org. Chem.* **1954**, *19*, 618.

(4) Larson, D. L.; Portoghese, P. S. *J. Med. Chem.* **1973**, *16*, 195.

(5) Portoghese, P. S.; Gomma, Z. S. D.; Larson, D. L.; Shefter, E. *J. Med. Chem.* **1983**, *16*, 199.