3-Ethylidino-2-oxo-1,4-benzodioxane (23). Reaction of catechol with **5b** at 25° for 72 hr in the presence of KI gave **23** (18% yield): mp 74–75° (95% ethanol); nmr ($CDCl_3$) δ 6.99 (s, 4, aromatic), 6.29 (q, 1, J = 7.6 Hz, CH=), 1.88 (d, 3, J = 7.6 Hz, CH_3). *Anal.* Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.54. Found: C, 67.96; H, 4.51. The nmr spectrum of the crude reaction mixture indicated the presence of about 20–25% of a mixture of **12a** and **12b** and 30% of unreacted **5b**, which were removed by fractional distillation.

cis- **and** *trans*-**1-methyl-1,2,3,4,5,6-hexahydrobenzo[*b*]-*p*-dioxino[3,4-*e*]pyrid-2(2*H*)-one (14a and 14b)** were prepared by treating catechol with 1-methyl-3-bromo-1,2,5,6-tetrahydro-2(2*H*)-pyridone (**7**) in the usual manner. Column chromatography of the residue following work-up on neutral alumina with benzene–dichloromethane gave **14b**: mp 218° after recrystallizations from acetone; 220-MHz nmr ($CDCl_3$) δ 6.93 (m, 4, aromatic), 4.35 (d, 1, J = 9.4 Hz, C-2 OCH), 4.18 (m, 1, C-3 OCH), 3.39 (m, 2, NCH_2), 2.99 (s, 3, NCH_3), 2.45, 2.13 (m, 2, CH_2). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.75; H, 5.97; N, 6.87. Found: C, 65.67; H, 5.92; N, 6.66.

Subsequent fractions gave **14a**: mp 136–137° after recrystallizations from benzene; nmr ($CDCl_3$) δ 6.93 (m, 4, aromatic), 4.66 (d, 1, J = 2.8 Hz, C-2 OCH), 4.57 (m, 1, C-3 OCH), 3.62, 3.25 (m, 2, NCH_2), 2.93 (s, 3, NCH_3), 2.37, 2.38 (m, 2, CH_2). *Anal.* Calcd for $C_{12}H_{13}NO_3$: C, 65.75; H, 5.97; N, 6.87. Found: C, 65.76; H, 5.96; N, 6.29.

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Registry No.—**3**, 5459-35-8; **4**, 920-37-6; **5a**, 51263-38-8; **5b**, 51263-39-9; 7, 51263-41-3; **9**, 609-11-0; **10**, 4739-94-0; **11**, 1008-92-0; **12a**, 51263-58-2; **12b**, 51263-59-3; **14a**, 35528-83-7; **14b**, 35528 84-8; **20**, 51263-60-6; **21a**, 6065-32-3; **22**, 51263-61-7; **23**, 51263-62-8; 2-piperidone, 675-20-7; 1-methyl-2-piperidone, 931-20-4; 3,3-dibromo-1-methyl-2-piperidone, 49785-78-6; 1-methyl-3-chloro-1,2,5,6-tetrahydro-2(2*H*)-pyridone, 51263-48-0; catechol, 120-80-9; ethyl 4-bromo-2-methyl-2-butenoate, 51263-63-9.

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1,4-Benzoxathians. 1. Reactions of *o*-Mercaptophenol with α-Halo Michael Acceptors

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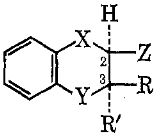
α-Halo Michael acceptors react with *o*-mercaptophenol in the presence of potassium carbonate to form substituted 1,4-benzoxthians, wherein the S atom may be α or β to the activating function. α-S substitution predominates when there are β-alkyl substituents present in the α-halo Michael acceptor, while β-S substitution occurs when the α carbon is unsubstituted. Both α- and β-S-substituted products were obtained in the reaction of *o*-mercaptophenol with 3-bromo-1,2,5,6-tetrahydro-2(2*H*)-pyridone, the α-S-substituted product having a trans configuration and the β-S-substituted product a cis configuration.

As part of a continuing investigation of the base-catalyzed (anhydrous K_2CO_3) reactions of dibasic nucleophiles with α- and γ-halo Michael acceptors,[1,2] reactions of *o*-mercaptophenol with **1–5** were examined. Because of the greater nucleophilicity of sulfur as compared with oxygen and the greater acidity of thiophenols as compared with phenols,[3,4] it was anticipated that the thiophenolate anion generated in an alkaline medium would preferentially attack the double bond of an α-halo Michael acceptor. This would be followed by nucleophilic displacement of halide at the newly generated sp^3-hybridized α carbon to yield, preferentially, 1,4-benzoxathians wherein the S atom is β to the activating group. This prediction is supported by the work of Tsai, *et al.*,[5] who recently reported

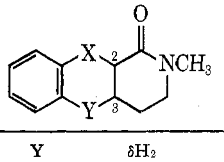
Table I
1,4-Benzoxathians. Yields and Product Ratios

Michael acceptor	Principal product(s)	Yield, %
1	**6**	78
2	**7**	90
3a	35% **8a**, 65% **8b**	44
3b	35% **8a**, 65% **8b**	54
4	**9**	65
5	80% **10a**, 20% **11b**	38

Table II
Nmr Data for 1,4-Benzoxathian Ring
(Protons in CDCl$_3$)



Compd	X	Y	Z	R	R′	δH$_2$	δH$_3$	$J_{2,3}$
6	O	S	CO$_2$Et	H	H	4.66	3.03	4.2
7	O	S	CN	H	H	6.13	2.83	5.4
8a	S	O	CO$_2$Et	CH$_3$	H	3.89	4.3[a]	2.4
8b	S	O	CO$_2$Et	H	CH$_3$	3.69	4.3[a]	6.0
9	S	O	CO$_2$Me	CH$_3$	CH$_3$	3.72		

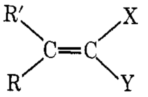


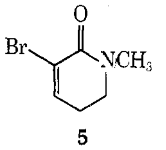
Compd	X	Y	δH$_2$	δH$_3$	$J_{2,3}$
10a (cis)	O	S	4.67	3.63	3.2
11b (trans)	S	O	4.00	4.18	9.4
19a (cis)	O	O	4.66	4.57	2.8
19b (trans)	O	O	4.35	4.18	9.5

[a] Overlapping resonances in mixture of two isomers prevents measurement of accurate chemical shifts of the H$_3$ protons of the respective isomers.

that ethyl 1,4-benzoxathian-2-carboxylate was the only isomer isolated from the reaction of ethyl 2,3-dibromopropanoate with *o*-mercaptophenol. Since we have strong evidence that this reaction proceeds through the intermediacy of ethyl α-bromoacrylate,[1] its selectivity is thus explained by the mechanism outlined above.

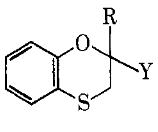
Reactions of *o*-mercaptophenol with the α-halo Michael acceptors **1** and **2** did, indeed, yield solely the anticipated 2-carbethoxy- and 2-cyano-1,4-benzoxathians **6** and **7**. However, when β-methyl and β,β-dimethyl substituents were present in the α-halo Michael acceptor, as in **3** and **4**, the 3-carbethoxy-1,4-benzoxathians **8** and **9** were obtained. Furthermore, the same mixture (Table I) of cis and trans 1,4-benzoxathians, **8a** and **8b**, respectively, was obtained from either **3a** or **3b**. This result contrasts with the stereoselectivity observed in reactions of catechol with **3a** and **3b**.[1]



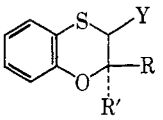


5

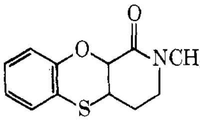
1, R = R′ = H; X = Br; Y = CO$_2$Et
2, R = R′ = H; X = Cl; Y = CN
3a, R = CH$_3$; R′ = H; X = Br; Y = CO$_2$Et
b, R = H; R′ = CH$_3$; X = Br; Y = CO$_2$Et
4, R = R′ = CH$_3$; X = Br; Y = CO$_2$Me



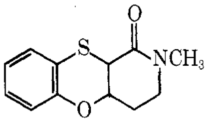
6, R = H; Y = CO$_2$Et
7, R = H; Y = CN



8a, R = CH$_3$; R′ = H; Y = CO$_2$Et
b, R = H; R′ = CH$_3$; Y = CO$_2$Et
9, R = R′ = CH$_3$; Y = CO$_2$Me



10a, cis
b, trans



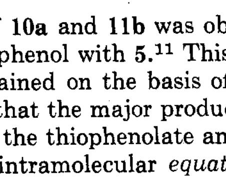
11a, cis
b, trans

A number of alternative mechanisms may be offered to explain both the formation of 3-carbethoxy-1,4-benzoxathians (instead of the expected 2-carbethoxy isomers) from **3a** and **3b** and the lack of stereoselectivity observed in these reactions. It is possible that β-alkyl substitution sufficiently hinders nucleophilic attack of the larger thiophenolate anion at the β carbon, but permits attack by the smaller phenolate ion to occur preferentially. Once **8a** and **8b** are formed, the α proton may be sufficiently acidic to allow equilibration between them, creating the observed isomer ratio. We do not favor this explanation, since **3** and **4** give good yields of **8** and **9**,[6] respectively, even at 25°, while much lower yields of the isomeric ethyl 3-methyl-1,4-benzodioxane-2-carboxylates are obtained from **3** and only a trace of ethyl 3,3-dimethyl-1,4-benzodioxane from **4** can be isolated from the corresponding catechol reactions at 55°.[1]

Alternatively, we propose that the formation of **8** and **9** may occur through the intermediate **12**. This intermediate could be formed by a direct nucleophilic substitution of bromide ion by *o*-mercaptophenol on the intermediate **13** (formed by prior migration of the double bond to the β,γ position[7]), followed migration of the double bond back into conjugation with the carbonyl group.[8] Or **12** could arise from the episulfonium ion intermediate **14**.[9] Since only the "normal" Michael addition products **6** and **7** are obtained from the α-halo Michael acceptors **1** and **2** lacking a β-methyl group, it appears unlikely that the "abnormal" products **8** and **9** result from a direct nucleophilic displacement[10] of bromide ion by *o*-mercaptophenol at the sp^2-hybridized carbon atom of **3** or **4**.

12

13

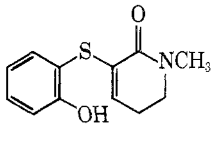


14

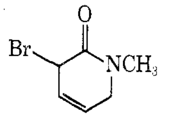
R = H; R′ = CH$_3$
R = R′ = CH$_3$

A 4:1 mixture of **10a** and **11b** was obtained in the reaction of *o*-mercaptophenol with **5**.[11] This somewhat curious result can be explained on the basis of two separate processes. It is likely that the major product **10a** is formed by the *axial* attack of the thiophenolate anion to the β carbon of **5**, followed by intramolecular *equatorial* addition of a proton to the α carbon and intramolecular nucleophilic displacement of bromide in a manner analogous to the catechol reaction.[1] The minor product **11b** is probably formed from the intermediate **15**, which could either arise from the reaction of *o*-mercaptophenol with the β,γ-unsaturated amide **16**[12] followed by double-bond migration, or *via* the episulfonium ion intermediate **17**.[9] It has been suggested that the normal product **10a** could be formed directly from **17**[9] stereospecifically.

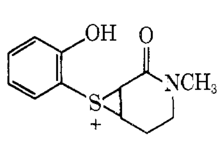
Attempts to epimerize either **10a** or **11b** in base failed. However, nmr evidence for the formation of the ring-opened compounds **15** and **18**, respectively, was obtained when **11b** and **10a** were each treated with potassium *tert*-butoxide in *tert*-butyl alcohol. Thus, **15** exhibited a triplet at δ 6.48 ppm (J = 5.2 Hz) and **18** gave a triplet at δ 6.12 ppm (J = 4.2 Hz).[13]



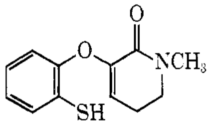
15



16



17



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Nmr data for the ring protons of 1,4-benzoxathians **7–13** and the tricyclic 1,4-benzodioxanes **19a** and **19b** are summarized in Table II. Chemical shift (δ) values for H_2 and H_3 permit unambiguous assignment of the positions of sulfur and oxygen atoms relative to the activating group (nitrile, ester, or amide) in all cases, since protons on carbon atoms adjacent to oxygen experience greater deshielding than those on carbon atoms adjacent to sulfur. Thus, δH_2 (doublet) for **6** is 4.66 ppm, while δH_2 doublets for **8a** and **8b** are 3.89 and 3.69 ppm, respectively, clearly establishing that H_2 is adjacent to oxygen in **6** and adjacent to sulfur in **8a** and **8b**. The coupling constants $J_{2,3}$ of 2.4 and 6.0 Hz are consistent with cis and trans geometries of **8a** and **8b**, respectively.

Comparison of chemical shift values δH_2 and δH_3 of **10a** and **11b** with the corresponding tricyclic cis and trans 1,4-benzodioxanes **19a** and **19b** compels reversal of the assignment of the positions of oxygen and sulfur atoms in the cis isomer **10a** *vs.* the trans isomer **11b**. Thus, δH_2 is virtually the same for the cis isomers **10a** and **19a** (4.67 and 4.66 ppm, respectively), while δH_3 for **10a** is 3.63 ppm compared to 4.57 ppm for **19a**. Cis geometries of **10a** and **19a** can be confidently assigned on the basis of coupling constants $J_{2,3}$ of 3.2 and 2.8 Hz, respectively. Likewise, $J_{2,3}$ values of 9.4 and 9.5 Hz, respectively, clearly establish trans geometries for **11b** and **19b**. The δH_3 multiplets for **11b** and **19b** have the same value of 4.18 ppm, indicating that in both H_3 is adjacent to oxygen and in an *axial* orientation. On the other hand, δH_2 for **11b** is in the relatively shielded position of 4.00 ppm, as compared to 4.35 ppm for **19b**, establishing the position of H_2 as adjacent to sulfur.

Experimental Section

Nmr spectra were determined on a Varian HA-100 spectrometer and (in special cases) on a Varian HR-220 spectrometer in $CDCl_3$ solution using tetramethylsilane as an internal standard. Chemical shift values are accurate to 0.01 ppm at 100 MHz and to 0.005 ppm at 220 MHz. Melting points were determined on a Thomas-Hoover melting point apparatus and are corrected.

Reactions of *o*-mercaptophenol with *α*-halo Michael acceptors were carried out using esentially identical procedures in every case. Therefore, one representative example will be described in detail and only physical data for the remaining compounds will be given.

Ethyl 1,4-Benzoxathian-2-carboxylate (6). A mixture of 6.9 g (0.055 mol) of *o*-mercaptophenol (Polysciences), 8.9 g (0.05 mol) of ethyl 2-bromopropenoate[1] (1), and 20.7 g (0.15 mol) of anhydrous K_2CO_3 in 200 ml of dry acetone was stirred under a blanket of nitrogen for 18 hr. After the acetone was removed the residue was taken up in methylene chloride, extracted (in turn) with water, 5% NaOH, 5% HCl, and saturated NaCl solutions, and dried over anhydrous Na_2SO_4. Evaporation of the residue afforded 9.6 g (78%) of **6**: bp 121–122° (0.2 mm) [lit.[5] bp 130° (0.5 mm)]; nmr ($CDCl_3$) δ 6.5 (m, 4, ArH), 4.66 (t, 1, J = 4.2 Hz, OCH), 4.21 (q, 2, J = 7.0 Hz, OCH_2), 3.03 (d, 2, J = 4.2 Hz, SCH_2), 1.22 (t, 3, J = 7.0 Hz, CH_3).

2-Cyano-1,4-benzoxathian (7) was obtained from the reaction of *o*-mercaptophenol with *α*-chloroacrylonitrile (Aldrich) under the above conditions in 90% yield as pale yellow flakes: mp 61–62° (acetone); nmr ($CDCl_3$) δ 6.9 (m, 5, ArH), 6.13 (t, 1, J = 5.4 Hz, OCH), 2.83 (d, 2, J = 5.4 Hz, SCH_2).

Anal. Calcd. for C_9H_7NOS: C, 61.01; H, 3.95; N, 7.90; S, 18.07. Found: C, 61.07; H, 3.96; N, 7.88; S, 18.19.

Mixtures of ethyl *cis*- and *trans*-2-methyl-1,4-benzoxathian-3-carboxylate (8a and 8b) were obtained from the reaction of *o*-mercaptophenol with ethyl *cis*-2-bromobut-2-enoate[1] (**3a**), 44% yield (35% **8a**, 65% **8b**); ethyl *trans*-2-bromobut-2-enoate[1] (**3b**), 54% yield (35% **8a**, 65% **8b**); and ethyl 2,3-dibromobutanoate, 48% yield (35% **8a**, 65% **8b**). Distillation of the mixture of **8a** and **8b** gave a colorless oil, bp 110–120° (0.12 mm). In the nmr spectrum of the mixture, doublets were observed at δ 3.89 (J = 2.4 Hz) and 3.69 ppm (J = 6.0 Hz) for the C-3 protons of **8a** and **8b**, respectively. Resonances for the C-3 methyl groups of **8a** and **8b** were observed as doublets at δ 1.45 (J = 6.4 Hz) and 1.48 ppm (J = 6.2 Hz), and the ester methyl groups were at δ 1.25 (J = 7.1 Hz) and 1.27 ppm (J = 1.27 Hz), respectively. Resonances of the aromatic and ester methylene protons of the two isomers overlapped.

Anal. Calcd for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.46. Found: 60.62; H, 6.03; S, 13.40.

Methyl 2,2-Dimethyl-1,4-benzoxathian-3-carboxylate (9). Reaction of *o*-mercaptophenol with methyl 3-methyl-2-bromo-2-butenoate[1] (4) gave a 65% yield of **9** as colorless needles after recrystallizations from acetone: mp 61–62°; nmr ($CDCl_3$) δ 6.8 (m, 4, ArH), 3.72 (s, 1, SCH), 3.74 (s, 1, OCH_3), 1.49, 1.51 [d, 2, $C(CH_3)_2$].

Anal. Calcd for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92; S, 13.46. Found: C, 60.77; H, 6.06; S, 13.90.

***cis*-2-Methyl-3,4,4a,10a-tetrahydropyrido[3,4-*b*][1,4]benzoxathian-1(2*H*)-one (10a) and *trans*-2-methyl-3,4,4a,10a-tetrahydropyrido[4,3-*b*][1,4]benzoxathian-1(2*H*)-one (11b)** were prepared by treating *o*-mercaptophenol with a mixture of 1-methyl-3-bromo- and 1-methyl-3-chloro-5,6-dihydro-2(1*H*)-pyridone[1] (5) in the usual manner. Recrystallizations of the crude residue following work-up from the acetone gave a mixture consisting of 80% **10a** and 20% **11b** (38% total yield). Column chromatography of the mixture on neutral alumina with benzene-dichloromethane gave **11b**: mp 154–155° after recrystallization from acetone; nmr ($CDCl_3$) δ 6.94 (m, 4, ArH), 4.18 (m, 1, OCH), 4.00 (d, 1, J = 9.5 Hz, SCH), 3.43 (m, 2, NCH_2), 2.97 (s, 3, NCH_3), 2.48, 2.08 (m, 2, NCH_2).

Anal. Calcd for $C_{12}H_{13}NO_2S$: C, 61.27; H, 5.53; N, 5.95; S, 13.61. Found: C, 61.38; H, 5.47; N, 6.01; S, 13.70.

Subsequent fractions gave **10a**: mp 140–141° after recrystallizations from benzene; nmr ($CDCl_3$) δ 7.17 (m, 4, ArH), 4.67 (d, 1, J = 3.2 Hz, OCH), 3.63 (m, 1, SCH), 3.40 (m, 2, NCH_2), 2.90 (s, 3, NCH_3), 2.26 (m, 2, CH_2).

Anal. Calcd for $C_{12}H_{13}NO_2S$: C, 61.27; H, 5.53; N, 5.95; S, 13.61. Found: C, 61.04; H, 5.42; N, 5.76; S, 13.88.

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220-MHz nmr spectra were measured by the Physico-Chemical Measurements Unit, Harwell Didcot, Berkshire, England.

Registry No.—**1**, 5459-35-8; **2**, 920-37-6; **3a**, 51263-38-8; **3b**, 51263-39-9; **4**, 51263-40-2; **5**, 51263-41-3; **6**, 35143-10-3; **7**, 51263-42-4; **8a**, 51263-43-5; **8b**, 51263-44-6; **9**, 51263-45-7; **10a**, 51263-46-8; **11b**, 51263-47-9; **19a**, 35528-83-7; **19b**, 35528-84-8; *o*-mercaptophenol, 1121-24-0; ethyl 2,3-dibromobutanoate, 609-11-0; 1-methyl-3-chloro-5,6-dihydro-2(1*H*)-pyridone, 51263-48-0.

References and Notes

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(6) The higher isolated yield of **9** as compared with the mixture of **8a** and **8b**, although theoretically unexpected, probably resulted from the fact that **9** was isolated as a solid while the mixture of **8a** and **8b** was purified by distillation. As yet, attempts to separate **8a** and **8b** have been unsuccessful. Nmr of the reaction mixtures prior to purification failed to detect β-S-substituted reaction products.

(7) Although the α,β-unsaturated isomer is thermodynamically favored over the β,γ-unsaturated isomer, the $\Delta G°$ for the equilibrium is not large.

(8) The formation of unexpected products in the reaction of catechol with α-bromocrotonate esters has also been explained by these phenomena (see ref 1).

(9) We thank one of the reviewers for suggesting this intriguing possibility. Mechanistic studies are underway and will constitute the subject of a future report from our laboratory.

(10) G. Modena, *Accounts Chem. Res.*, **4**, 73 (1971).

(11) The failure to isolate **10b** and **11a** from the reaction mixture does not rule out their possible formation in small quantities (undetected by nmr).

(12) Similar double-bond migrations have been observed in 6-hydroxyhexenoic lactones [C. G. Overberger and H. Kaye, *J. Amer. Chem. Soc.*, **89**, 5640 (1967)] and in tetrahydro-2*H*-azepin-2-ones [H. K. Reimschuessel, J. P. Siblia, and J. V. Pascale, *J. Org. Chem.*, **34**, 959 (1969)].

(13) The isolation, characterization, and Michael-type ring closure reactions of **15** and **18** will be subject of a future publication from this laboratory.

Synthesis of ω-1,3-Dithianyl Carboxylic Acids *via* Cleavage of Cyclic α-Diketone Monothioketals

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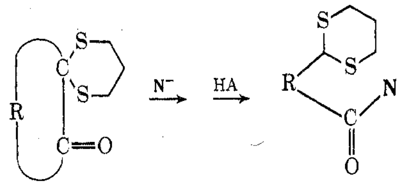
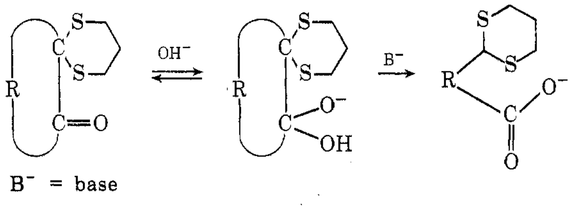
A number of cyclic (C_6–C_8) α-diketone monothioketals were prepared *via* hydroxymethylation of the parent monoketone followed by treatment with 1,3-propanedithiol ditosylate. Cleavage of these simple cyclic systems took place readily in KOH-*tert*-butyl alcohol to give, after acidification, ω-1,3-dithianyl carboxylic acids in 88–95% yield. The attempted cleavage of an α',α'-dimethylated cyclohexane-1,2-dione monothioketal with KOH-*tert*-butyl alcohol failed, apparently because of steric hindrance to carbonyl addition. A thioketal ketone derived from an α,β-unsaturated cyclohexanone likewise failed to cleave. In this case enolization took place leading to the β,γ-unsaturated ketone derivative. Methanolic sodium methoxide or methanolic potassium hydroxide were ineffective in the cleavage reaction. These findings are consistent with a mechanism involving hydroxide addition to the carbonyl followed by proton abstraction by *tert*-butoxide leading to a reactive dialkoxy anion which undergoes C–C bond cleavage.

In a preliminary report we described the apparent nucleophilic cleavage of α-diketone monothioketals to give ω-dithianyl carboxylic acid derivatives (eq 1).[1] Subsequent studies indicated that the above cleavage reaction most likely proceeds in two stages with initial attack by hydroxide on the carbonyl followed by subsequent proton abstraction of the presumed adduct (eq 2).[2] The essential features of eq 2 had previously been proposed by Gassman in connection with his studies on the Haller–Bauer-type cleavage of nonenolizable ketones.[3] Employing his reaction conditions (NaOH, NaO-*t*-Bu, *t*-BuOH, ether) we succeeded in obtaining ω-dithianyl carboxylic acids from certain unhindered decalones in over 90% yield.[2] We have now completed more definitive studies on this cleavage reaction which shed light on its scope and synthetic potential.



(1)

N = nucleophile



(2)

B⁻ = base

As noted above, Gassman's work and our own experience[2] indicated that a combination of hydroxide plus a strong (alkoxide) base afforded the highest yields of cleavage products. In an effort to simplify the experimental procedure we investigated the use of powdered potassium hydroxide in *tert*-butyl alcohol, a base system previously employed by Meyers, *et al.*[4] As shown below (Chart I), under appropriate conditions excellent results could be obtained using this base system with various cyclic α-diketone monothioketals. Optimum yields were realized when the temperature was maintained near 60°. Higher temperatures led to colored decomposition products and lower temperatures prolonged the required reaction times.

In contrast to the results obtained with decalone **9** and its angular methyl counterpart,[2] the dimethyldecalone **11** afforded only recovered starting material (98%) after 8 hr of reaction time. Evidently steric effects retard the postulated addition step of the cleavage reaction in this case. The apparent lesser reactivity of the cycloheptanone **3** and particularly the cyclooctanone **5** may be similarly explained. Likewise the conjugated keto thioketal **12** failed to yield a cleavage product. In this case a substantial pro-