

*Anal.* Calcd. for  $C_{17}H_{11}N_4O_4$ : C, 58.94; H, 6.40. Found: C, 58.88; H, 6.70.

The second fraction, amounting to 0.2 g., was an oil and is identified as 2-( $\delta$ -methoxybutyl)-cycloheptanone (XVI);  $\bar{\nu}$  1710, 1118  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{12}H_{22}O_2$ : C, 72.68; H, 11.18. Found: C, 72.98; H, 11.09.

**N,N'-Dicarbethoxy-N,N'-dinitroso-1,4-butanediamine (Ib) and Acetone.**—The crude reaction product from 25 ml. (0.34 mole) of acetone and 43.5 g. (0.15 mole) of Ib was distilled to give 5.05 g. of a colorless oil with b.p. up to 58° (30 mm.) and 3.40 g. of a slightly yellow oil boiling up to 56° (0.3 mm.). Vapor phase chromatography of the lower-boiling fraction yielded two components, the first of which amounted to 2.4 g. (14.5%) of a colorless oil which is identified as 2,5-dimethylcyclopentanone, b.p. 146° (reported<sup>47</sup> 143–144°),  $n_D^{25}$  1.4305 (reported<sup>47</sup> 1.4322),  $\bar{\nu}$  1736  $cm^{-1}$ . It formed a 2,4-dinitrophenylhydrazone with m.p. 174–175° (reported<sup>47</sup> 172–172.5°).

*Anal.* Calcd. for  $C_{13}H_{16}N_4O_4$ : C, 53.42; H, 5.52. Found: C, 53.26; H, 5.55.

The second component from the lower-boiling fraction amounted to 1.0 g. of a colorless oil identified as 3-methyl-6-methoxyhexanone-2 (XVII);  $n_D^{25}$  1.4264;  $\bar{\nu}$  1710, 1118  $cm^{-1}$ .

*Anal.* Calcd. for  $C_9H_{16}O_2$ : C, 66.63; H, 11.18. Found: C, 66.87; H, 11.05.

**Deuterium Exchange Experiments.** (A) 10-Ketobicyclo[5,2,1]decane(II).—A solution from 1.0 g. of sodium metal in anhydrous methanol was evaporated to dryness. The sodium methoxide residue was added to 1 g. of the ketone mixed with 10 ml. of deuterium oxide (99.8%  $D_2O$ ). The mixture was refluxed for 12.5 hr. and then worked up to give

(47) R. W. Kierstead, R. P. Linstead and B. C. L. Weedon, *J. Chem. Soc.*, 3616 (1952).

ketone of m.p. 100–112°. Deuterium analysis indicated this material to have 1.75 atom-equivalents of deuterium.

(B) 9-Ketobicyclo[4,2,1]nonane (VIII).—A 0.5-g. sample of VIII after treatment with sodium methoxide and deuterium oxide as described above incorporated 0.14 atom-equivalent of deuterium. This small but apparently real deuterium uptake is ascribed to impurities rather than to the [4,2,1]-ketone.

(C) 1-Ketobicyclo[6,3,0]undecane (XV).—A 0.5-g. sample of XV after treatment with sodium methoxide and deuterium oxide as described above incorporated 2.80 atom-equivalents of deuterium.

**Cyanohydrin Equilibrium Constants.**—The method of Prelog and Kobelt<sup>50c</sup> was employed for the determination of the hydrogen cyanide present at equilibrium. The ketones were carefully purified by passage through the preparative vapor phase fractometer. The temperature for the establishment of equilibrium was held constant at  $\pm 0.1^\circ$ , and the titrations were carried out at the same temperature. The mixtures were allowed to stand for 24 hr. in the constant temperature bath before titrations were carried out. Several determinations were made with each ketone, and the data reported in Table I are the averaged values with an indication of the extreme values.

**Nuclear magnetic resonance spectra** were measured with a Varian high resolution spectrometer equipped with a Varian model V4311 fixed frequency rf unit operating at 56.4 Mc. The "side-band" technique employing an audio oscillator equipped with a frequency counter was used to determine the positions of the resonance lines relative to the reference compound. Area measurements were made by graphical means on spectra obtained at sufficiently low rf values to minimize saturation errors. In all cases the measurements were made on solutions containing 10% of the ketone, 89% carbon tetrachloride and 1% tetramethylsilane, the latter serving as the reference material. All of the solutions were thoroughly de-gassed before the spectra were obtained.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

## Transannular Interaction between Sulfide and Ketone Groups<sup>1</sup>

BY NELSON J. LEONARD, TERRY W. MILLIGAN<sup>2,3</sup> AND THEODORE L. BROWN

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This study has demonstrated the possibility of S-C=O transannular interaction in medium-ring thiaketones by the examination of the properties of a representative compound, 1-thiacyclooctan-5-one (I). The existence of interacted as well as non-interacted conformations of the ring in solution was demonstrated by a study of its infrared spectrum in the  $6\mu$  region, while the conformational equilibrium was studied as a function of solvent polarity in a qualitative manner. The charge separation implied in this interaction was emphasized by excitation of the molecules with ultraviolet light, the energy required for the transition (at 226–242  $m\mu$ ,  $\epsilon$  2400–2800) also being a (linear) function of solvent polarity as measured by the Z-parameter. Chemical evidence for the abnormal electron distribution was furnished by the isolation of several bicyclic sulfonium salts (IX, X, XI) formed by transannular reaction. These salts were reversibly dissociated in aqueous solution, and the dissociation constant of one of them (5-hydroxybicyclo[3.3.0]octane-1-thianium perchlorate) was measured ( $pK_a$  0.2) spectroscopically. The dissociation was also detected by nuclear magnetic resonance spectroscopy. By contrast, the oxygen analog, 1-oxacyclooctan-5-one (II), exhibited no such transannular effects in the infrared spectrum, even though its dipole moment indicated the preponderance of the requisite folded conformation of the ring. It would not form stable transannular salts, but was cleaved easily with hydrochloric acid to 1,7-dichloro-4-heptanone in a reaction which may proceed through such a salt as an intermediate.

A systematic study of transannular interaction between tertiary amino nitrogen and ketone carbonyl in mesocyclic<sup>4</sup> aminoketones and aminoacyloins has led to an understanding of the modi-

fication in the properties of these donor-acceptor functional groups and the limitation of N-C=O interaction by steric, electronic and structural factors.<sup>5,6</sup> The prediction was made, in 1954, that transannular S-C=O and O-C=O interaction might be detected in heterocyclic ketones of appropriate size.<sup>7</sup> Preliminary announcements of

(1) Supported in part by a research grant (NSF-G6040) from the National Science Foundation.

(2) Sinclair Refining Co. Fellow in Organic Chemistry, 1957–1958. Work done under the sponsorship of the Sinclair Research Laboratories, Inc.

(3) Allied Chemical and Dye Corp. (Barrett Division) Fellow, 1958–1959.

(4) "Mesocycle" is here suggested as a concise descriptive term to serve as a possible alternative to designate a "medium sized ring" (8–11 members).

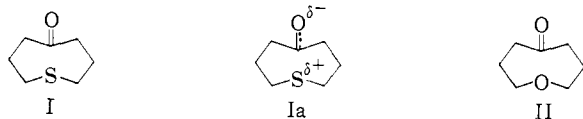
(5) For the most recent article on transannular N-C=O interaction, see N. J. Leonard, J. A. Adamcik, C. Djerassi and O. Halpern, *This Journal*, **80**, 4858 (1958).

(6) For a review of the subject, see N. J. Leonard, *Rec. Chem. Progress*, **17**, 243 (1956).

(7) N. J. Leonard, R. C. Fox and M. Ōki, *This Journal*, **76**, 5708 (1954).

the detection of S-CCO interaction have appeared only recently.<sup>8-10</sup>

Two medium-ring ketones, 1-thiacycloöctan-5-one (I) and 1-oxacycloöctan-5-one (II), have been synthesized and have been examined for evidences

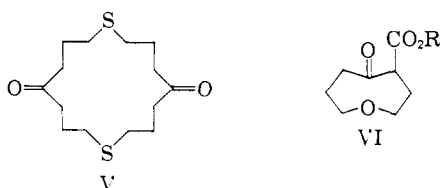


of S-SCO and O-CCO transannular interaction (e.g., Ia). These compounds were chosen first because of the favorable geometry for such interactions of the 8-membered ring with diametrically opposed functional groups, and, second, to check the predicted  $N > S > O$  order in the magnitude of the resulting modification of chemical and physical properties.

The Dieckmann cyclization was selected for the synthesis after preliminary attempts to cyclize 1,7-dichloro-4-heptanone (III) and 1,7-dichloro-4-ethylenedioxyheptane (IV) by reaction with alcoholic sodium sulfide had failed to produce products containing more than a few per cent. of sulfur. The conditions for the Dieckmann reaction included the use of slow addition (63-110



hours) of the starting diesters, diethyl  $\alpha, \alpha'$ -thia-bis-butyrates and diethyl or dimethyl  $\alpha, \alpha'$ -oxa-bis-butyrates to a rapidly stirred mixture of potassium *t*-butoxide in a large volume of refluxing xylene under nitrogen, conditions which had been employed previously in this Laboratory for the synthesis of similar aminoketones<sup>6,11</sup> and medium- and large-ring cycloalkanones.<sup>12</sup> The isolation and purification of the 1-thiacycloöctan-5-one, m.p. 53.2-54.2°, followed the hydrolysis and decarboxylation of the intermediate ketoester. A by-product, when the addition rate of the sulfide diester was relatively rapid (25 hours),<sup>13</sup> was the sixteen-membered ring compound, 1,9-dithia-cyclohexadecane-5,13-dione, m.p. 65-66° (V).



(8) N. J. Leonard, T. L. Brown and T. W. Milligan, *THIS JOURNAL*, **81**, 504 (1959).

(9) C. G. Overberger and A. Lusi, *ibid.*, **81**, 500 (1959).

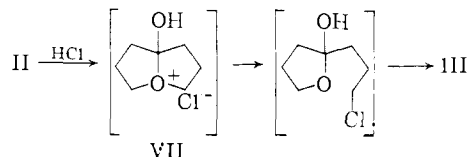
(10) See also A. Lusi, Master's Thesis, Polytechnic Institute of Brooklyn, 1959.

(11) N. J. Leonard and R. C. Sentz, *THIS JOURNAL*, **74**, 1704 (1952).

(12) N. J. Leonard and C. W. Schimelpfenig, Jr., *J. Org. Chem.*, **23**, 1708 (1958).

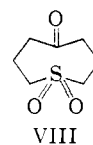
(13) N. J. Leonard, M. Ōki and S. Chiavarelli, *THIS JOURNAL*, **77**, 6234 (1955).

The isolation of 1-oxacycloöctan-5-one (II) from the intermediate  $\beta$ -ketoester VI (R = CH<sub>3</sub> or C<sub>2</sub>H<sub>5</sub>) could not be accomplished by hydrolysis-decarboxylation in aqueous hydrochloric acid, which was used for 1-thiacycloöctan-5-one (I). The compound isolated instead of II was 1,7-dichloro-4-heptanone, indicating a facile ether cleavage which may proceed through an intermediate transannular oxonium salt VII, sensitive to nucleophilic attack by chloride ion.<sup>14</sup> The



desired ketone was obtained by hydrogenolysis of the benzyl  $\beta$ -ketoester (VI, R = CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), which was formed in an exchange reaction between the methyl  $\beta$ -ketoester and benzyl alcohol. Decarboxylation of the resultant  $\beta$ -ketoacid occurred at room temperature to give the oxaketone II directly.

1-Thiacycloöctan-5-one (I)<sup>15</sup> was characterized as its 1,1-dioxide VIII by oxidation with two moles of hydrogen peroxide in acetone. An accurate



molecular weight determination on I and a further indication of the structure was furnished by the mass spectrum, which showed a parent peak at 144 mass units. A study of dipole moments and of solvent effects on the infrared and ultraviolet absorption spectra of the thiaketone I leads to the conclusion that it exists in solution in non-polar solvents as a mixture of interacted and non-interacted conformations. The important finding is that the *conformational equilibrium is shifted as a function of solvent polarity* (Fig. 1).<sup>16</sup>

In non-polar solvents (cyclohexane, carbon tetrachloride) the major C=O band for I appears at the expected frequency for a cyclic ketone of this size, with a shoulder due to an interacted conformation(s). In passing through solvents of moderate polarity (trichloroacetonitrile, acetonitrile) to those with higher hydrogen bonding power (methylene chloride, chloroform), the band corresponding to interaction becomes stronger and finally dominant. The frequency also *shifts* to a degree greater than that of a number of model compounds in the same solvents, reflecting a change in the bond order of the carbonyl. These effects persist (in carbon tetrachloride and chloroform) in very dilute solu-

(14) H. Meerwein, *Angew. Chem.*, **70**, 630 (1958).

(15) This compound was identical with a sample of the same material concurrently synthesized by A. Lusi and kindly forwarded to us by Dr. Charles G. Overberger of the Polytechnic Institute of Brooklyn.<sup>9,10</sup>

(16) Cf. (a) J. Allinger and N. Allinger, *Tetrahedron*, **2**, 64 (1958); (b) K. Kazima, K. Sakashita and S. Maeda, *THIS JOURNAL*, **76**, 1955 (1954); (c) A. Tulinskie, A. DiGiacomo and C. P. Smyth, *ibid.*, **75**, 3552 (1953).

tions ( $10^{-2} M$ ), but unfortunately no quantitative information as to the equilibrium concentrations of the conformers could be obtained from the non-resolvable bands. The experimental results are listed in Table I, the lower entries in each block being values of  $10^3 (\Delta\nu/\nu)$ <sup>17</sup> based on the carbonyl frequency in cyclohexane. Model compounds were selected for comparison with I, including examples offering a "normal" carbonyl group in a ring of the proper size (cyclooctanone) and a carbonyl function separated from sulfide by three methylenic carbons, but not held in close proximity by a ring (5-methylmercapto-2-pentanone). It should also be noted that 4-oxothiepane (1-thiacycloheptan-4-one), with the sulfide two carbons away in a seven-membered ring, does not exhibit any splitting of the carbonyl band ( $\nu_{\max}^{\text{CCl}_4}$  1711  $\text{cm}^{-1}$ )<sup>8,18</sup>. By contrast with 1-thiacyclooctan-5-one, the oxygen analog II shows no transannular O-C=O interaction on examination by infrared spectroscopy. It has a sharp symmetrical band whose shape does not greatly change and whose frequency shifts with solvent in the same order of magnitude as cyclooctanone or the other model compounds described in Table I. Visual inspection of the infrared curves (carbonyl region) for 1-thiacyclooctan-5-one and 1-oxacyclooctan-5-one (Fig. 1) in various solvents discloses at once the source of the difference between these closely related compounds.

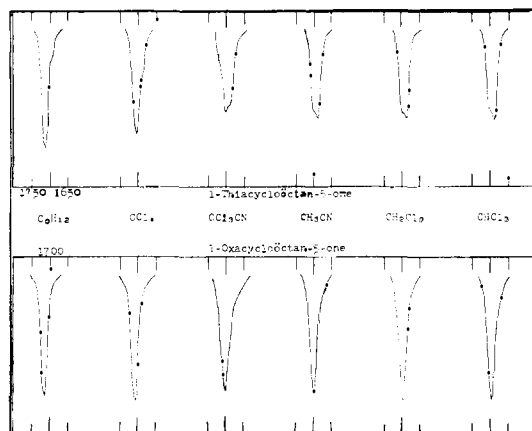
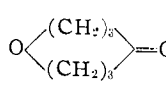
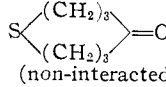
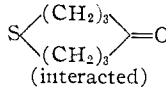


Fig. 1.—Solvent dependence of infrared carbonyl maxima (2.5% solns.).

quantity for a standard ketone, straight lines are usually obtained. In our work, cyclooctanone was selected as the standard and  $\Delta\nu$  was measured from the values of  $\nu$  in cyclohexane in the absence of gas phase measurements. These changes should have no effect on the general utility of the treatment since both the standard compound and the physical state where  $\Delta\nu = 0$  are arbitrarily chosen. Under these conditions a number of model compounds

TABLE I  
INFRARED SPECTRAL DATA FOR KETONES<sup>a</sup>

Values of $\nu_{\max}$ and $10^3 (\Delta\nu/\nu)$ for	C <sub>6</sub> H <sub>12</sub>	CCl <sub>4</sub>	CCl <sub>3</sub> CN	CH <sub>3</sub> CN	CH <sub>2</sub> Cl <sub>2</sub>	CHCl <sub>3</sub>
CH <sub>3</sub> COCH <sub>3</sub> <sup>17</sup>	1723	1719	..	1715	1713	1712
C <sub>6</sub> H <sub>5</sub> COCH <sub>3</sub> <sup>17</sup>	1696	1692	..	1687	1685	1683
(CH <sub>2</sub> ) <sub>5</sub> C=O <sup>17</sup>	1724	1719	1711 <sup>b</sup>	1709	1708	1705
(CH <sub>2</sub> ) <sub>7</sub> C=O	1707	1701	1694	1693	1693	1690
CH <sub>3</sub> S(CH <sub>2</sub> ) <sub>3</sub> COCH <sub>3</sub>	1728	1720	1713	1711	1711	1710
	1714	1705	1699	1699	1698	1695
	1713	1704 <sup>c</sup>	1700	~1701 <sup>d</sup>	~1698	~1696
(non-interacted)		0.528	0.883	0.883	0.942	1.12
	~1696	~1690 <sup>e</sup>	1691	1691	1689	1686
(interacted)		0.528	0.765	0.705	0.880	1.00
			1.30 <sup>f</sup>	1.30 <sup>f</sup>	1.42 <sup>f</sup>	1.60 <sup>f</sup>

<sup>a</sup> Values of C=O stretching maxima (in  $\text{cm}^{-1}$ ) observed in 2.5% solutions. <sup>b</sup> W. B. Chipman, University of Illinois, personal communication. <sup>c</sup> 1703  $\text{cm}^{-1}$  in  $10^{-2} M$  solution. <sup>d</sup> ~ Denotes shoulder. <sup>e</sup> 1684  $\text{cm}^{-1}$  in  $10^{-2} M$  solution. <sup>f</sup>  $\Delta\nu$  calculated from the normal ketone value, 1713  $\text{cm}^{-1}$ .

The effect of solvent on the carbonyl bond in 1-thiacyclooctan-5-one ( $I \rightleftharpoons I_a$ ) is also exposed clearly by an analysis of the data (Table I) carried out in the style of Bellamy and Williams.<sup>17</sup> When the values of  $(\Delta\nu/\nu)$  for a particular compound (ketone) in various solvents are plotted *versus* the same

(17) L. J. Bellamy and R. L. Williams, *Trans. Faraday Soc.*, **55**, 14 (1959).

(18) C. G. Overberger and A. Katchman, *This Journal*, **78**, 1965 (1956).

(acetone, 5-methylmercapto-2-pentanone, cyclohexanone) do indeed give straight lines, as does 1-oxacyclooctan-5-one, indicating the normal response of each carbonyl group to environmental changes. The points for 1-thiacyclooctan-5-one, however, are divided into groups which form *two* linear segments. The first of these, based upon  $\nu$ -values obtained from the non-interacted (higher frequency) band, has a slope in the same range as

the model compounds. The other line segment, obtained from the "interacted" band (of increasing intensity in polar solvents) illustrates the changing nature of the carbonyl group as it becomes highly polarized in the interacted form (Figure 2).

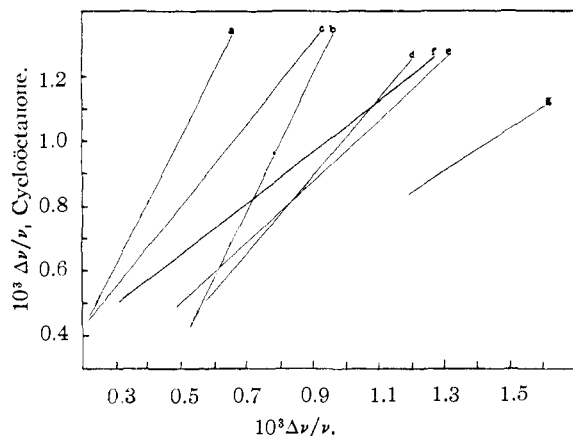


Fig. 2.—Analysis of infrared data according to the method of Bellamy and Williams. Slope of  $(\Delta\nu/\nu)$  vs.  $(\Delta\nu/\nu)$  (cyclooctanone) for: a, acetone, 2.04; b, 1-thiacyclooctan-5-one (non-interacted), 1.75; c, acetophenone, 1.25; d, 1-oxacyclooctan-5-one, 1.21; e, 5-methylmercapto-2-pentanone, 0.96; f, cyclohexanone, 0.81; g, 1-thiacyclooctan-5-one (interacted), 0.62.

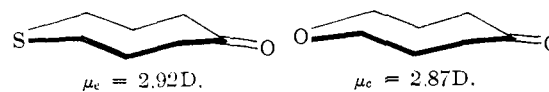
The infrared spectra of 1-thiacyclooctan-5-one and 1-oxacyclooctan-5-one in the 1500–1400  $\text{cm}^{-1}$  region are very similar and exhibit a group of four bands, each separated by about 20  $\text{cm}^{-1}$ . The quartet of bands was useful for the detection of these ring systems in crude mixtures. A similar complexity of spectra in the methylene-hydrogen deformation region has been observed in eight- and nine-membered cyclic sulfides.<sup>19</sup> Dipole moment measurements on these compounds and several models are summarized in Table II.

Compound (in benzene)	$\mu$ , Debye
Cyclohexanone	3.08 <sup>20</sup>
Tetrahydro-4H-thiopyran-4-one	1.73
4-Oxothiepane	3.04
1-Thiacyclooctan-5-one	3.81, 3.80 (CCl <sub>4</sub> )
1-Oxacyclooctan-5-one	4.09
Cyclooctanone	2.93 <sup>20</sup>

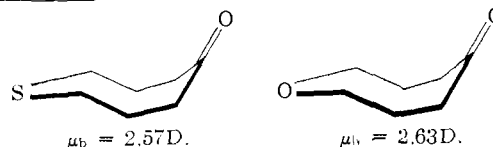
Although no reliable quantitative data on the percentage of interacted and non-interacted conformations present in solutions of 1-thiacyclooctan-5-one were obtained from the infrared spectra, a comparison of the observed results with the moments calculated for several extreme<sup>21</sup> conformations of the ring is instructive. The calculations for the crown, twisted boat and folded conformations

(the latter leading to possible interaction) of the two mesocyclic ketones I and II are enumerated below. The assumptions are a C-S-C moment of 1.58 D., a C-O-C moment of 1.22 D. and a C=O moment of 2.93 D., from diethyl sulfide, diethyl ether and cyclooctanone, respectively; the angles between dipole vectors were measured on Dreiding scale models.<sup>22</sup>

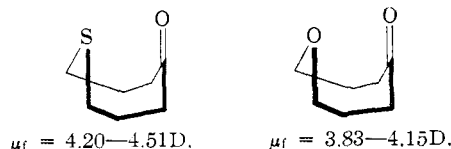
Crown,  $\theta = 105^\circ$



Twisted Boat,  $\theta = 118^\circ$



Folded,  $\theta = 45-0^\circ$  (variable)



The observed high electric moment of 1-thiacyclooctan-5-one (3.81 D.) is not surprising in the light of the infrared evidence concerning the presence of considerable amounts of the folded and interacted conformation. In addition, it should be realized that the partial charge separation accompanying interaction can in itself raise the moment of that form above the value obtained by simple vector addition, as observed in the case of the analogous 3°-aminoketone.<sup>23</sup> The most striking fact to be extracted from these calculations, however, is that the observed moment (4.09 D.) of 1-oxacyclooctan-5-one requires a preponderance of the folded conformation since it corresponds to the moment calculated for the folded form. This folding of the ring does not, however, cause an observable effect in the infrared spectrum. An explanation of this fact may lie in the decreased "nucleophilicity" of the divalent oxygen atom toward a carbonyl group as compared with that of divalent sulfur. The order of effective electron donor ability is compounded of several factors including electronegativity, effective orbital radius and resistance to ring flexion. The observed  $N > S > O$  order in donating ability in this series<sup>6,8</sup> is the same as that observed by Kochetkov in a series of 1-substituted 2-hexen-3-ones.<sup>24</sup> It is also consistent with the relative reactivities of comparable oxonium, sulfonium and 4°-ammonium salts<sup>25</sup> in reactions involving elimi-

(19) A. Müller, E. Funder-Fritzsche, W. Konar and E. Rintersbacher-Wlasak, *Monatsh. Chem.*, **84**, 1206 (1953).

(20) (a) T. Bürer and Hs. H. Günthard, *Helv. Chim. Acta*, **39**, 356 (1956); (b) E. Billeter, Th. Bürer and Hs. H. Günthard, *ibid.*, **40**, 2046 (1957); (c) Th. Bürer and Hs. H. Günthard, *ibid.*, **40**, 2054 (1957).

(21) N. Allinger and S. Greenberg, *THIS JOURNAL*, **81**, 5733 (1959). The authors are indebted to Dr. Allinger for a preprint of the article.

(22) W. Büchi, Glasapparate-Fabrik, Flawil, Switzerland.

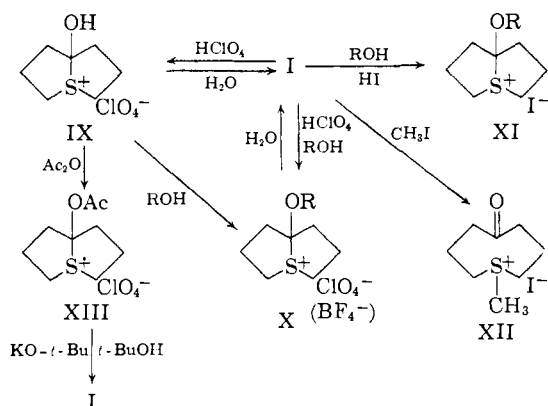
(23) N. J. Leonard, D. F. Morrow and M. T. Rogers, *THIS JOURNAL*, **79**, 5476 (1957).

(24) N. K. Kochetkov, M. I. Rybinskaya and A. N. Nesmeyanov, *Doklady Akad. Nauk S.S.S.R.*, **79**, 799 (1951); N. K. Kochetkov and V. N. Vinogradova, *Zhur. Obshchei Khim.*, **27**, 460 (1957); N. K. Kochetkov, *Izvest. Akad. Nauk S.S.S.R.*, 991 (1953).

(25) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter VIII.

nation of an ether, sulfide or amine, which reactions may be regarded as a reversal of the addition of these Lewis bases to an electrophilic center.

The monocyclic 1-thiacycloöctan-5-one (I) was converted to a bicyclic conjugate acid by *transannular reaction* involving protonation of the carbonyl oxygen. With 70% perchloric acid and compound I in ether the product was a new type of salt, 5-hydroxybicyclo[3.3.0]octane-1-thianium perchlorate (IX) containing the  $\overset{+}{S}-C-OH$  grouping. In the presence of alcohols the corresponding bridge-head alkoxy perchlorates (X, *e.g.*, R = CH<sub>3</sub>, C<sub>2</sub>H<sub>5</sub>) were obtained. A similar but less stable salt (XI) was obtained from I with methanol and hydriodic acid; the lower stability than the perchlorate may reflect the nucleophilic character of the iodide ion. The S-methylated isomer XII of XI was formed by the treatment of I with methyl iodide. 5-Acetoxybicyclo[3.3.0]octane-1-thianium perchlorate (XIII), obtained by acetylation of the hydroxy perchlorate IX with acetic anhydride, furnished the original ketone I on reaction with potassium *t*-butoxide in dry *t*-butyl alcohol, as did the hydroxy salt on treatment with aqueous sodium hydroxide.



The hydroxy perchlorate IX could be converted to the methoxy compound (X, R = CH<sub>3</sub>) by simple recrystallization from methanol. This provided the first clue that the hydroxy perchlorate was dissociated in solution to the ketone and perchloric acid. Confirmation of the dissociation was obtained by three physical methods. The infrared spectra of all these salts as Nujol mulls were free of C=O bands. However, both the hydroxy and methoxy perchlorates exhibited a carbonyl band at 1667 cm.<sup>-1</sup> in deuterium oxide solution, confirming the presence of free ketone. The dissociation was also detectable by proton magnetic resonance spectroscopy, the n.m.r. spectrum of the salts in heavy water being that of the ketone, except for solvent effects on the resonance peaks (triplet, centered on  $\delta = 2.05$  p.p.m. rel. to water in CCl<sub>4</sub>;  $\delta = 1.80$  p.p.m. in D<sub>2</sub>O) due to the methylenes alpha to the thioether group, whose shielding characteristics are particularly sensitive to incipient protonation (deuteration) of the carbonyl. This interpretation is supported by the further shift in the presence of excess perchloric

acid (to  $\delta = 1.18$ ), the presence of a triplet with underlying fine structure at nearly the same field ( $\delta = 1.95$  in CCl<sub>4</sub>) in the spectrum of 1,5-dithiacycloöctane, and the fact that the similar triplet in the spectrum of 1-oxacycloöctan-5-one (II) appears at  $\delta = 1.15$  p.p.m. (in CCl<sub>4</sub>) because of the greater electronegativity of oxygen compared with sulfur. This last observation precludes assignment of this triplet to the methylenes alpha to the carbonyl. It is of interest that the dependence of the position of resonance peaks on the proton-donating power of the solvent may be useful in obtaining information as to the position of protonation in other compounds.

The  $pK_a'$  of 5-hydroxybicyclo[3.3.0]octane-1-thianium perchlorate (IX) could not be determined by potentiometric titration, but another indication of its extensive dissociation in solution was furnished by spectrophotometric measurement. The thiaketone I has an abnormal ultraviolet spectrum. The electronic transition appears at 226-242 m $\mu$ , the transition energy being an approximately linear inverse function of *Z*, a spectroscopic solvent polarity index.<sup>26</sup> The slope of the  $E_T$  vs. *Z* line (see Fig. 3) indicates that the excited electronic

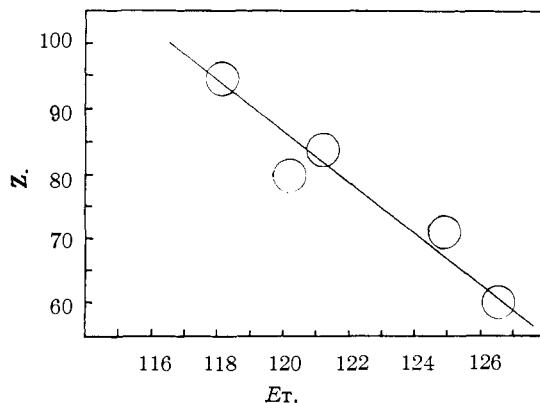


Fig. 3.—Electronic transition energies for 1-thiacycloöctanone in solvents of different *Z* values.

state has as a major contributor the extreme canonical form of Ia. The contribution of Ia to the ground state is manifested in the presence of interacting conformations of the ring with a lowered infrared carbonyl stretching frequency, as shown in Fig. 1. The intensity of the band (*ca.* 2400-2800) is also higher than that expected of a normal sulfide or carbonyl band. These deviations from the expected spectrum are a manifestation of transannular interaction resulting in a high degree of charge separation in the excited state. The "red shift" observed in passing from cyclohexane to solvents of higher polarity as measured by the Kosower *Z*-parameter is consistent with an excited state of higher dipole moment than that of the ground state. This fact seems to rule out an  $n \rightarrow \pi^*$  transition for which a "blue shift" would be expected under these conditions, and leads us to represent the excitation as an effective electron transfer from the divalent sulfur into the nearby carbonyl system. Thioesters, in which the sulfur

(26) E. M. Kosower, THIS JOURNAL, 80, 3253, 3261, 3267 (1958).

and carbonyl groups are connected by a direct covalent bond, have a similar ultraviolet spectrum, an example being acetylthiocyclohexane,  $C_6H_{11}SCOCH_3$ ,  $\lambda_{max}$  231.5  $m\mu$ ,  $\epsilon$  4500.<sup>27</sup> The dissociation of 5-hydroxybicyclo[3.3.0]octane-1-thianium perchlorate allowed an approximate determination of the  $pK_a'$  based on the intensity of the thiaketone ultraviolet band in aqueous solutions of the salt at different  $pH$  values.<sup>28</sup> The value was 0.2, about the same as that for trichloroacetic acid, making I a stronger base than any other ketone and nearly as strong as 2,6-dimethyl-4-pyrone ( $pK_a'$  0.28).<sup>29</sup> It also furnishes an explanation for the failure of the ketone to form a picrate, the conjugate acid of the ketone being a stronger acid than picric acid ( $pK_a$  0.8), while salts were formed easily with hydriodic and fluoboric acids as well as perchloric acid.<sup>30</sup>

A recent measurement<sup>31</sup> of the extent of the shift in the O-H stretching frequency of methanol caused by hydrogen bonding to di-*n*-butyl sulfide shows that it has the same effect as di-*n*-butyl ether, contrary to theoretical predictions based on the larger atomic radius of sulfur. The  $pK_a$  of di-*n*-butyl ether may be estimated by a similar spectroscopic measurement in  $CH_3OD$  and placed on a calibrated scale at a value of -2.3 using the data and empirical equation of Gordy.<sup>32</sup> Using the same method cyclooctanone has  $pK_a$  -3.0. Obviously the possibilities of charge distribution offered by transannular reaction make 1-thiacyclooctan-5-one much more basic (by 2.5-3.2  $pK_a$  units) than its isolated functional groups would indicate.<sup>33</sup> The ultraviolet maximum for 1-oxacyclooctan-5-one (II) in ethanol was indicative of a normal ketone function ( $\lambda_{max}^{EtOH}$  272  $m\mu$ ,  $\epsilon$  16.4).

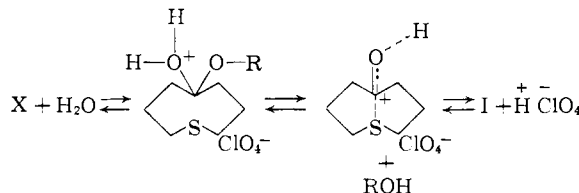
The values of the ultraviolet absorption maxima for solutions of the dissociating salts (IX, X) of 1-thiacyclooctan-5-one<sup>30</sup> as well as those for I were included in the plot of  $E_T$  vs.  $Z$  (Fig. 3). The spectral results are summarized in Table III. The best straight line calculated for these points by the method of least squares is  $E_T = -0.25456Z + 142.00$ .

(27) H. P. Koch, *J. Chem. Soc.*, 387 (1949).

(28) B. Eistert, E. Merkel and W. Reiss, *Chem. Ber.*, **87**, 1513 (1954).

(29) H. N. K. Rördam, *THIS JOURNAL*, **37**, 557 (1915).

(30) The presence of the free ketone was also detected in solutions of 5-methoxybicyclo[3.3.0]octane-1-thianium perchlorate (X, R =  $CH_3$ ) in methanol containing a trace of water. (At  $\lambda_{max}$  236  $m\mu$ ,  $\epsilon$  is variable and dependent on water content; anhydrous methanol produces no dissociation.) The requisite presence of water for the dissociation is logically accounted for by a sequence such as



(31) P. von R. Schleyer and R. West, *THIS JOURNAL*, **81**, 3164 (1959).

(32) W. Gordy, *J. Chem. Phys.*, **9**, 215 (1941); W. Gordy and S. C. Stanford, *ibid.*, **9**, 204 (1941).

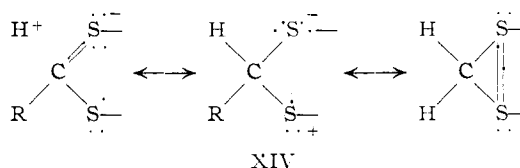
(33) We wish to record our appreciation of a helpful discussion with Dr. E. M. Arnett, University of Pittsburgh, on the basicities of sulfides and ketones.

TABLE III

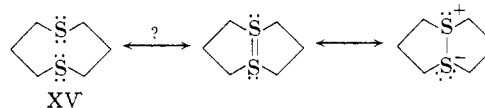
ULTRAVIOLET SPECTRUM OF 1-THIACYCLOOCTAN-5-ONE			
Solvent	Z	$\lambda_{max}$ , $m\mu$ ( $\epsilon$ )	$E_T$ , kcal. mole <sup>-1</sup>
Cyclohexane	60.1	226 (2445)	126.51 $\pm$ 0.5
Acetonitrile	71.3	229 (2690)	124.85
Methanol <sup>a</sup>	83.6	236 (variable) <sup>a,b</sup>	121.14
Ethanol	79.6	238 (2565)	120.14
Water <sup>c</sup>	94.6	242 (2775)	118.13

<sup>a</sup> From the dissociation of 5-methoxybicyclo[3.3.0]octane-1-thianium perchlorate. <sup>b</sup> Depends on water content of solvent; carefully dried methanol does not dissociate the salt. <sup>c</sup> From the dissociation of 5-hydroxybicyclo[3.3.0]octane-1-thianium perchlorate.

Ultraviolet maxima in the same wave length range but of much lower extinction were noted by Fehnel and Carmack<sup>34</sup> in the spectra of tetrahydro-4H-thiapyran-4-one ( $\lambda_{max}^{EtOH}$  235  $m\mu$ ,  $\epsilon$  355) and 1-ethylmercapto-2-propanone ( $\lambda_{max}^{EtOH}$  243  $m\mu$ ,  $\epsilon$  363; 298  $m\mu$ ,  $\epsilon$  257) and were attributed to interactions between -S- and C=O in the excited state. These authors also noted an anomaly ( $\lambda_{max}^{EtOH}$  235-240  $m\mu$ ,  $\epsilon$  6300) in the spectra of mercaptals, and suggested resonance structures (XIV) to account for this phenomenon. The postulate



of donor-acceptor interaction between two sulfide atoms led us to inspect the ultraviolet spectrum of 1,5-dithiacyclooctane (XV), synthesized previously by Meadow and Reid.<sup>35,36</sup>



Here the transannular proximity of the 1,5-atoms might be expected to lead to similar interactions (and spectrum) as found in the mercaptals. These expectations were not realized. No ultraviolet maximum appeared at a wave length longer than 202  $m\mu$  (apparent maximum),  $\epsilon$  ca. 3000 for XV in ethanol. This value for the extinction coefficient, although not accurate in the short wave length region, is about normal for a dialkyl sulfide ( $\epsilon$  ca. 1500 per C-S-C group). The band position is about 8  $m\mu$  lower than that for thiacyclohexane.<sup>34</sup> The absence of a higher wave length absorption maximum, as in the cyclic sulfides of six and fewer members,<sup>34,37</sup> is not consistent with the electron density on sulfur in compound XV when compared with cyclic sulfides of ordinary ring size, as revealed by the n.m.r.  $\delta$ -values for the  $\alpha$ -methylene groups. The value of 1.95 p.p.m. (relative to water, taken in carbon tetrachloride) indicates that in 1,5-dithiacyclooctane the electron density on sulfur is about the same magnitude<sup>38</sup>

(34) E. A. Fehnel and M. Carmack, *THIS JOURNAL*, **71**, 84 (1949).

(35) J. R. Meadow and E. E. Reid, *ibid.*, **56**, 2177 (1934).

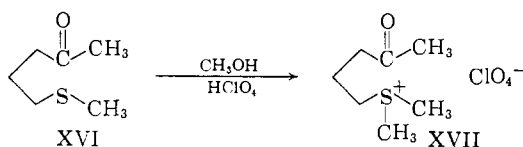
(36) Cf. W. Autenrieth and K. Wolff, *Ber.*, **32**, 1375 (1899).

(37) R. E. Davis, *J. Org. Chem.*, **23**, 1380 (1958).

(38) D. J. Anderson, University of Illinois, personal communication.

as in 1-thiacyclohexan-4-ol and its tosylate ( $\delta = 2.05, 2.02$  p.p.m.). Other compounds with similar  $\delta$ -values for methylenic hydrogen alpha to a sulfide include tetrahydro-4H-thiapyran-4-one ( $\delta = 1.90$  p.p.m.) and tetrahydro-4H-thiapyran-3-one ( $\delta = 1.97$  p.p.m.). Unfortunately a comparison with the  $\delta$ -values<sup>39</sup> of simple cyclic sulfides is ruled out by the different conditions used for their determination.

An interesting reaction appeared as a by-product of this investigation. 5-Methylmercapto-2-pentanone (XVI), the open-chain analog of 1-thiacyclooctan-5-one (I), by contrast, did not form a salt with methanolic perchloric acid at room temperature. When XVI was heated under reflux for several hours, however, a low-melting perchlorate salt was obtained, the structure of which was partially deduced, on the basis of infrared spectrum, positive iodoform test and the formation of a 2,4-dinitrophenylhydrazone of empirical formula  $C_{13}H_{19}ClN_4O_8S$ , as 5-dimethyl-



sulfonium-2-pentanone perchlorate (XVII). Unfortunately, it was not readily convertible to the independently synthesized methyl *p*-toluenesulfonate salt. The most probable explanation for the formation of XVII is alkylation of the sulfide by protonated solvent molecules, previously observed in the reaction of methionine with isopropyl alcohol and sulfuric acid<sup>40</sup> and in this series by Overberger and Lusi<sup>9</sup> in the formation of bicyclo[3.3.0]octane-1-thianium picrate from 1-thiacyclooctan-5-ol on treatment with phosphoric anhydride followed by picric acid.

**Acknowledgment.**—The authors are pleased to record the thanks due to Dr. Harold Boaz, Eli Lilly and Co., Indianapolis, Ind., and Dr. Everett J. Frazza, American Cyanamid Co., Stamford, Conn., for their help in providing data crucial to the success of this research.

### Experimental<sup>41</sup>

**Diethyl  $\gamma, \gamma'$ -Thia-bis-butyrate.**<sup>42</sup>—A mixture of 120 g. (0.625 mole) of ethyl  $\gamma$ -bromobutyrate<sup>43</sup> and 59 g. (0.35 mole) of sodium sulfide pentahydrate in 500 ml. of absolute ethanol was refluxed and stirred for 7 hours. The mixture was cooled to 30°, filtered, and concentrated under reduced pressure. The residue was partitioned between ether and water, and the aqueous phase was further extracted with two 50-ml. portions of ether. The combined ether layers were dried, the

solvent was removed, and the product was distilled, b.p. 119–122° (0.2 mm.),  $n_D^{25}$  1.4653, yield 40.3 g. (49%).

*Anal.* Calcd. for  $C_{12}H_{22}O_4S$ : C, 54.93; H, 8.45; S, 12.22. Found: C, 55.10; H, 8.18; S, 12.53.

**1-Thiacyclooctan-5-one (I).**—In a 3-l. Morton high dilution apparatus fitted with a high speed stirrer, a Hershberg addition funnel and a condenser of the spiral type with provision for removal of solvent by distillation was placed 800 ml. of dry xylene and 100 ml. of *t*-butyl alcohol, both previously distilled from sodium. Freshly cut potassium metal (9.38 g., 0.24 gram-atom) was added to the mixture while a stream of dry nitrogen was passed into the apparatus from the bottom of the stirrer. The mixture was stirred and warmed gently until all the potassium had reacted, 400 ml. of xylene was added, and the excess alcohol was distilled until the temperature of the distillate reached 134°. The volume was adjusted to about 1.2 l. by the addition of xylene, and then a solution of 34.6 g. (0.132 mole) of diethyl  $\gamma, \gamma'$ -thia-bis-butyrate in 400 ml. of xylene was added through the Hershberg funnel during 110 hours under a continuous stream of nitrogen. The volume was maintained approximately constant by the periodic addition of xylene and removal of alcohol by distillation. The mixture was heated and stirred for a further 2.75 hours, cooled to room temperature, and washed successively with 2.5 *N* hydrochloric acid, 5% aqueous sodium bicarbonate solution and water. The xylene was removed by evaporation under reduced pressure, leaving a residual orange oil which was refluxed for 3 hours with 190 ml. of 6 *N* hydrochloric acid to effect hydrolysis and decarboxylation. The acid solution was cooled to 5° and was maintained below 15° while being made strongly basic by the slow addition of a saturated potassium hydroxide solution. The cold, orange alkaline solution was extracted immediately with ether. The ethereal solution was dried and concentrated under reduced pressure, leaving 8.52 g. (45%) of an orange solid, m.p. 44–50.5°. Treatment of the crude product with charcoal in boiling ether, followed by the addition of pentane, afforded 3.78 g. (20%) of pure 1-thiacyclooctan-5-one, colorless needles, m.p. 53.2–54.2°, a second crop (0.88 g., 4.6%), m.p. 53–54°, and an impure third crop (0.62 g., 3.3%), m.p. 45–52°. The infrared spectrum (5.5% in carbon tetrachloride) had selected maxima at 1703, 1687(sh), 1460, 1440, 1422 and 1408  $cm^{-1}$ . Purification for analysis was effected by vacuum sublimation.

*Anal.* Calcd. for  $C_7H_{17}OS$ : C, 58.29; H, 8.39. Found: C, 58.21; H, 8.36.

In a similar run, when the addition was completed in 25 hours, concentration of the ether extracts left an oil, from which 0.48 g. (2.2%) of 1-thiacyclooctan-5-one was obtained by vacuum distillation. The undistilled residue was subjected to vacuum sublimation for 24 hours at 0.3 mm. and 160–170°, yielding 0.61 g. (2.8%) of a pale yellow solid, m.p. 63.5–67°, recrystallized as colorless needles from ethyl acetate–pentane, m.p. 65–66°,  $\nu_{max}^{CCl_4}$  1715  $cm^{-1}$ , which was the dimer, 1,9-dithiacyclohexadecane-5,13-dione (V), m.p. depressed (liquid at 25°) on admixture with I.

*Anal.* Calcd. for  $C_{14}H_{24}O_2S_2$ : C, 58.29; H, 8.39; mol. wt., 288. Found: C, 58.64; H, 8.25; mol. wt. (Rast), 252.

**The 1-Thiacyclooctan-5-one-1,1-dioxide (VIII).**—1-Thiacyclooctan-5-one (0.5 g., 3.47 mmoles) was dissolved in 5 ml. of reagent grade acetone. An aqueous solution of hydrogen peroxide (0.7 g. of 30%  $H_2O_2$ ) was added, and the solution was warmed gently for a few minutes without boiling. The mixture was allowed to stand for 2 days at room temperature, the acetone was evaporated, and traces of water were removed from the sirupy residue under reduced pressure. The resulting solid was washed with pentane and recrystallized several times from absolute ethanol to give the pure sulfone, colorless needles, m.p. 124–127°, selected infrared maxima (5% in chloroform) at 1705 (C=O) and 1120 and 1318  $cm^{-1}$  ( $>SO_2$ ).

*Anal.* Calcd. for  $C_7H_{12}SO_3$ : C, 47.70; H, 6.87. Found: C, 47.73; H, 6.81.

When the oxidation was carried out at 0° for 1.5 hours using only one mole equivalent of peroxide, followed by standing at room temperature for 48 hours, the only product seemed to be a mixture of sulfone with starting material, as determined by m.p. (119–123°), infrared spectrum and analysis.

(39) H. S. Gutowsky, R. C. Rutledge, M. Tamres and S. Searles, *THIS JOURNAL*, **76**, 4242 (1954).

(40) T. F. Lavine, N. F. Floyd and M. S. Cammaroti, *J. Biol. Chem.*, **207**, 107 (1954).

(41) Melting points are corrected except where noted; boiling points are uncorrected. The authors are indebted to Mr. Josef Nemeth and his associates for the microanalyses, to Mr. Paul McMahon and his associates for the infrared spectra, and to Mr. Jen Chiu for the ultraviolet spectra.

(42) Prepared originally in this Laboratory, in 1954, by T. Hashizume; private communication.

(43) The method of G. R. Proctor and R. H. Thomson, *J. Chem. Soc.*, 2302 (1957), is now preferred for the preparation of this compound; cf. E. A. Prill and S. M. McElvain, *THIS JOURNAL*, **55**, 1233 (1933).

**1-Methylcyclooctan-5-one-1-thianium Iodide (XII).**—About 0.2 g. of the thiaketone was dissolved in excess methyl iodide. The original colorless solution became turbid in a few minutes, and a solid appeared in about 20 minutes. After standing for 10 hours, excess methyl iodide was evaporated and the solid was washed with dry ether. Considerable care was required to obtain reliable infrared and analytical data on the somewhat unstable salt. Success was finally achieved by recrystallization from methanol-ether, rapid drying, and analysis within 2 hours while protecting the sample from light. The colorless needles, m.p. 115–116° dec., had an infrared spectrum (Nujol) consistent with preservation of the 8-membered ring: selected maxima at 1683, 1405, 1380, 1340, 1180 and 890  $\text{cm}^{-1}$ , compared with 1685, 1410, 1380, 1335, 1178 and 891  $\text{cm}^{-1}$  for that of the starting material under the same conditions.

*Anal.* Calcd. for  $\text{C}_8\text{H}_{15}\text{IOS}$ : C, 33.57; H, 5.28. Found: C, 33.92; H, 5.20.

**5-Methoxybicyclo[3.3.0]octane-1-thianium Iodide (XI. R =  $\text{CH}_3$ ).**—About 0.2 g. of 1-thiacyclooctan-5-one in ether was treated with a freshly prepared mixture of concentrated hydriodic acid and methanol. The resulting precipitate was washed with ether and recrystallized twice from methanol-ether as colorless needles, m.p. 129–130° dec. The product was unstable, turning yellow-brown on standing and generating a carbonyl compound, detected by infrared spectroscopy. The freshly prepared material had an infrared spectrum (Nujol) free of carbonyl absorption and identical with that of 5-methoxybicyclo[3.3.0]octane-1-thianium perchlorate (see below) except in the region masked by perchlorate anion, where the iodide reveals two doublets at 1108, 1098 and 1068, 1058  $\text{cm}^{-1}$  which we assign to the  $\text{RO}-\text{C}-\text{S}^+$  ketal moiety. A mixture melting point of this compound with the methyl iodide product (m.p. 115–116°) was depressed to 86–100°.

*Anal.* Calcd. for  $\text{C}_8\text{H}_{15}\text{IOS}$ : C, 33.57; H, 5.28. Found: C, 33.63; H, 5.36.

**5-Hydroxybicyclo[3.3.0]octane-1-thianium Perchlorate (IX).**—A sample of 1-thiacyclooctan-5-one (144 mg., 1 mmole) was dissolved in ether and treated with 70% perchloric acid until precipitation was complete. The crude salt (243 mg., 99%) was washed with ether and recrystallized from acetone-ether as fine colorless needles, m.p. 214–216° dec. Its infrared spectrum (Nujol) was free of absorption in the  $\mu$  region and had a band at 3340  $\text{cm}^{-1}$  (O—H).

*Anal.* Calcd. for  $\text{C}_8\text{H}_{15}\text{ClO}_5\text{S}$ : C, 34.36; H, 5.35. Found: C, 34.31; H, 5.13.

**Reaction of 5-Hydroxybicyclo[3.3.0]octane-1-thianium Perchlorate with Base.**—Fifty milligrams (0.2 mmole) of the hydroxy-perchlorate salt was dissolved in 5 ml. of 10% sodium hydroxide solution. The mixture was extracted with three 3-ml. portions of ether. The combined ether extracts were concentrated to yield 21 mg. (72%) of 1-thiacyclooctan-5-one, m.p. 51.2–54.5°; mixture m.p. with authentic material (I), 51.2–54.5°; identical infrared spectra.

**5-Methoxybicyclo[3.3.0]octane-1-thianium Perchlorate (X, R =  $\text{CH}_3$ ).**—To a solution of 1-thiacyclooctan-5-one in ether was added dropwise a solution of 1:1 70% perchloric acid in methanol until precipitation was complete. The crude product was washed with ether and recrystallized from methanol to give pure 5-methoxybicyclo[3.3.0]octane-1-thianium perchlorate, colorless needles, m.p. 147.5–149.5° dec. The infrared spectrum (Nujol) was free of C=O and O—H absorption.

*Anal.* Calcd. for  $\text{C}_8\text{H}_{15}\text{ClO}_5\text{S}$ : C, 37.14; H, 5.84; S, 12.39; OCH<sub>3</sub>, 11.99. Found: C, 37.34; H, 5.75; S, 12.81; OCH<sub>3</sub>, 11.50.

A similar reaction run in the presence of ethanolic acid gave 5-ethoxybicyclo[3.3.0]octane-1-thianium perchlorate (X, R =  $\text{C}_2\text{H}_5$ ), colorless needles from ethanol-ether, m.p. 95.4–96.1° dec., infrared spectrum devoid of C=O and O—H absorption.

*Anal.* Calcd. for  $\text{C}_9\text{H}_{17}\text{ClO}_5\text{S}$ : C, 39.63; H, 6.28. Found: C, 39.33; H, 6.29.

**Reaction of 5-Hydroxybicyclo[3.3.0]octane-1-thianium Perchlorate with Methanol.**—A sample of the bicyclic hydroxy-perchlorate (70 mg.) was dissolved in a minimal volume

of reagent grade methanol (ca. 0.2 ml.) at room temperature. On standing for about 2 minutes the solution solidified. The solid was recrystallized twice from methanol, affording colorless needles of 5-methoxybicyclo[3.3.0]octane-1-thianium perchlorate, m.p. 147–149° dec., identical with the material described above (X, R =  $\text{CH}_3$ ).

**5-Acetoxybicyclo[3.3.0]octane-1-thianium Perchlorate (XIII).**—A portion of 5-hydroxybicyclo[3.3.0]octane-1-thianium perchlorate (100 mg., 0.4 mmole) was dissolved in 1 ml. of acetic anhydride. In about one minute crystals of the acetate appeared. The mixture was allowed to stand for 30 minutes and was then diluted with 10 ml. of ether. The liquid was decanted and the precipitate was washed with ether, leaving 90 mg. (77%) of the acetate, which was purified for analysis by recrystallization from acetic anhydride; fine colorless needles, m.p. 162–163° dec. (tube inserted in bath at 140°; m.p. depends on rate of heating),  $n_{\text{D}}^{25}$  1.377 as well as 1270(w), 1250(m) and 1227(s),  $\text{cm}^{-1}$ , consistent with the acetate ester function.

*Anal.* Calcd. for  $\text{C}_9\text{H}_{15}\text{ClO}_6\text{S}$ : C, 37.70; H, 5.27. Found: C, 37.82; H, 5.15.

**Reaction of 5-Acetoxybicyclo[3.3.0]octane-1-thianium Perchlorate with Potassium *t*-Butoxide.**—A solution of potassium *t*-butoxide (115 mg., 2.94 mg.-atom of potassium) in 5 ml. of dry *t*-butyl alcohol was mixed with a suspension of the acetate (0.78 g., 2.72 mmoles) in 10 ml. of *t*-butyl alcohol. The mixture was boiled for 3 hours on the steam-bath, the solvent was evaporated, and the pasty residue was partially dissolved in ether. The ether solution was filtered to give 0.38 g. (100%) of potassium perchlorate, and the filtrate was concentrated to leave an oil which was partially crystallized from ether-pentane. It was identified by its infrared spectrum as crude 1-thiacyclooctan-5-one, m.p. 45–49.5°, yield 80 mg. (44%).

**5-Methoxybicyclo[3.3.0]octane-1-thianium Fluoborate.**—A 350-mg. portion (2.43 mmoles) of 1-thiacyclooctan-5-one was dissolved in the minimal volume of 48% aqueous fluoboric acid. Benzene was added and the water was removed by azeotropic distillation from the mixture. The residual oil was crystallized from methanol to furnish 323 mg. (54%) of crude product, which was brought to analytical purity by repeated recrystallization from methanol; colorless hygroscopic needles, m.p. 119.5–120°. The infrared spectrum (Nujol) was free of C=O and O—H absorption.

*Anal.* Calcd. for  $\text{C}_8\text{H}_{15}\text{BF}_4\text{OS}$ : C, 39.04; H, 6.14. Found: C, 39.32; H, 6.04.

**Dimethyl  $\gamma,\gamma'$ -Oxa-bis-butyrate.**<sup>42</sup>—A mixture of 172 g. (0.91 mole) of  $\gamma,\gamma'$ -oxa-bis-butyric acid, m.p. 77–79°,<sup>44</sup> and 300 ml. (2.4 moles) of acetone dimethyl ketal (Dow Chemical Co.) with 75 ml. of methanol and 1 g. of *p*-toluenesulfonic acid was stirred at 25° for 35 hours. Anhydrous potassium carbonate (10 g.) was then added, and stirring was continued for 1 hour. The mixture was filtered, the excess solvents were removed, and the product was distilled through a 30-cm. Vigreux column. After a 20-ml. forerun, b.p. 54–91° (0.8 mm.), the dimethyl ester was obtained as a colorless oil (135.1 g., 69%), b.p. 92–97° (0.8 mm.),  $n_{\text{D}}^{25}$  1.4329 (reported<sup>44</sup> 154–155° (12 mm.)).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_{18}\text{O}_5$ : C, 55.03; H, 8.31. Found: C, 55.05; H, 8.54.

**Dieckmann Cyclization of Dimethyl  $\gamma,\gamma'$ -Oxa-bis-butyrate.**—In a 5-l. indented flask fitted with a high-speed stirrer and dilution cycle as previously described was placed 1 l. of dry xylene. About 150 ml. was distilled under a nitrogen stream to ensure dryness of the apparatus, freshly cut potassium (9.75 g., 0.25 g.-atom) was added, followed by 100 ml. of anhydrous *t*-butyl alcohol. When most of the metal had reacted to form a slush, 1.8 l. of xylene was added and the mixture was heated and stirred until all the potassium was consumed. Excess *t*-butyl alcohol was removed by distillation until the temperature of the distillate reached 133°. A solution of dimethyl  $\gamma,\gamma'$ -oxa-bis-butyrate (21.8 g., 0.1 mole) in 400 ml. of xylene was then added dropwise to the refluxing mixture through a controlled rate dropping funnel<sup>45</sup> over a period of 63 hours with occasional removal of a xylene-methanol mixture by distillation. Heating and stirring were continued for 1 hour after the addition was complete. The reaction mixture was cooled and neutralized with 18 g.

(44) W. Reppe, *Ann.*, **596**, 158 (1955); see p. 169.

(45) Funnel with ground glass micrometer valves obtained from Normag Glass Co., Hochheim am Taunus, Germany.



of glacial acetic acid, followed by the addition of 100 ml. of water. The layers were separated, and the xylene layer was washed with two 200-ml. portions of water and partially dried with magnesium sulfate. After removal of the solvent under reduced pressure the residue was fractionated through a Holzman column. The colorless distillate, b.p. 78–100° (1.2–1.5 mm.), had an anomalous refractive index behavior, the middle fraction having  $n_{24.5}^{24.5D}$  1.4850, while the others had  $n_{24.5}^{24.5D}$  1.4768–1.4783. After standing for 24 hours, however, the main fraction had  $n_{24.5}^{24.5D}$  1.4767. Evidently there was partial separation of the enol and keto forms on distillation. This conclusion was supported by the fact that the infrared spectrum of the freshly distilled material (liquid film) had bands at 1740, 1700, 1640 and 1610  $\text{cm}^{-1}$ , characteristic of some enolized form,<sup>46</sup> whereas after standing for 24 hours, cooling to  $-78^\circ$ , and slowly warming to room temperature, the compound crystallized in the keto form, a colorless, waxy solid, m.p. 41–46.5°,  $\nu_{\text{max}}^{\text{Nujol}}$  only at 1743 and 1698  $\text{cm}^{-1}$  in the  $6\mu$  region. The total yield of crystalline material, presumably methyl 1-oxacyclooctan-5-one-4-carboxylate (VI, R = CH<sub>3</sub>), was 3.56 g. (19%). It was converted directly to the benzyl  $\beta$ -ketoester for analysis.

**Benzyl 1-Oxacyclooctan-5-one-4-carboxylate (VI, R = C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>).**—The methyl  $\beta$ -ketoester (3.25 g., 17.5 mmoles) was heated with 2.1 ml. of benzyl alcohol (2.16 g., 20 mmoles) in a side-arm test-tube for 1.7 hours at 153–157° while a slow nitrogen stream was passed through the mixture from a capillary bubbler.<sup>47,48</sup> The entrained methanol was collected in a Dry-Ice cooled trap connected to the side arm. The residue crystallized on cooling. The crude product was triturated with cold ether and washed with pentane containing a little ether, leaving 3.0 g. (65.5%) of a white powder, m.p. 40–57°. Two recrystallizations from 1:5 ether-pentane afforded pure benzyl 1-oxacyclooctan-5-one-4-carboxylate as short, thick colorless rods, m.p. 71–73.5°;  $\nu_{\text{max}}^{\text{CCl}_4}$  1740, 1167 (benzyl ester), 1707 (ketone) and 1097  $\text{cm}^{-1}$  (ether).

*Anal.* Calcd. for C<sub>15</sub>H<sub>18</sub>O<sub>4</sub>: C, 68.68; H, 6.82. Found: C, 68.81; H, 6.79.

**1-Oxacyclooctan-5-one (II).**—A solution of benzyl 1-oxacyclooctan-5-one-4-carboxylate (2.0 g., 7.63 mmoles) in a mixture of 20 ml. of ethyl acetate and 5 ml. of ethanol was hydrogenated in the presence of 0.4 g. of 5% palladium-on-carbon catalyst.<sup>49,50</sup> The catalyst was removed by filtration, the solvents were removed under reduced pressure, and the residue was distilled to yield 0.67 g. (69%) of colorless oil, b.p. 112–119° (22 mm.),  $n_{25}^{25D}$  1.4710–1.4727. This material was contaminated by traces of water and ethanol as indicated by analysis and gas chromatography on a Carbowax column at 130°. The product was brought to analytical purity by azeotropic removal of the impurities with benzene followed by distillation in a Hickman still;  $n_{25}^{25D}$  1.4746;  $\nu_{\text{max}}^{\text{film}}$  1696(s), 1475, 1452, 1437, 1414 and 1095(s)  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}^{\text{EtOH}}$  272  $\mu\text{m}$ ,  $\epsilon$  16.4 (for cyclooctanone: 283  $\mu\text{m}$ ,  $\epsilon$  13.7).

*Anal.* Calcd. for C<sub>7</sub>H<sub>12</sub>O<sub>2</sub>: C, 65.59; H, 9.44. Found: C, 65.40; H, 9.45.

When the same series of benzylation-hydrogenation reactions was repeated without purification of the benzyl ester and using no ethanol in the hydrogenation solvent, a 58% over-all yield of crude oxaketone was obtained, b.p. 110–115° (14 mm.),  $n_{25}^{25D}$  1.4782–1.4813. Vapor phase chromatography indicated the presence of 5–8% of benzyl alcohol, which could not easily be removed by distillation. An ether solution was therefore chromatographed on a short column of alumina in a sintered glass funnel, and distillation afforded pure ketone in 20% yield, b.p. 114° (15 mm.)  $n_{25}^{25D}$  1.4746.

A similar Dieckmann reaction was run on diethyl  $\gamma,\gamma'$ -oxa-bis-butyrates with an addition period of 136 hours. The crude  $\beta$ -ketoester was refluxed with 6 N hydrochloric acid in the standard hydrolysis-decarboxylation conditions used on the analogous sulfur compounds, the solution was made

strongly basic and extracted with ether, but the product isolated by distillation in 27% yield was 1,7-dichloro-4-heptanone (III), b.p. 72–85° (0.2 mm.),  $n_{25}^{25D}$  1.4733; reported<sup>51</sup> 106–110° (4.0 mm.),  $n_{25}^{25D}$  1.4713. The somewhat unstable ketone was identified by a comparison of its infrared spectrum (5% CCl<sub>4</sub>) and the melting point (70–71.5°) of its 2,4-dinitrophenylhydrazone with those of an authentic sample (m.p. of 2,4-dinitrophenylhydrazone 71–72°, mixture m.p. 70–71°; reported<sup>52</sup> 74–75°).

**5-Methylmercapto-2-pentanone (XVI)** was synthesized from 5-bromo-2-pentanone<sup>53,54</sup> and sodium methylmercaptide by the method of Bacchetti and Fiechi.<sup>55</sup> The yield of colorless liquid, b.p. 95.5–98° (16 mm.),  $n_{25}^{25D}$  1.4718, was 59%; 2,4-dinitrophenylhydrazone, orange needles from methanol-acetone, m.p. 100–101°; reported<sup>55</sup> b.p. 90–92° (18 mm.), 2,4-dinitrophenylhydrazone, m.p. 99–100°. The infrared spectrum of 5-methylmercapto-2-pentanone (5% in CCl<sub>4</sub>) had maxima at 1720 (C=O) and 1360  $\text{cm}^{-1}$  (–COCH<sub>3</sub>).

**5-Dimethylsulfonium-2-pentanone *p*-Toluenesulfonate.**—A solution of 5-methylmercapto-2-pentanone (2.64 g., 0.02 mole) and methyl *p*-toluenesulfonate (7.43 g., 0.04 mole) in 15 ml. of reagent grade acetone was refluxed for 9 hours. The colorless solution was cooled under a running tap and crystallized to a white slush. Excess methyl *p*-toluenesulfonate was removed by washing twice with ether. The product was air-dried (6.34 g., 99%) and recrystallized from pure acetone as matted fine needles, m.p. 94.4–95°,  $\nu_{\text{max}}^{\text{Nujol}}$  1723  $\text{cm}^{-1}$  (C=O).

*Anal.* Calcd. for C<sub>14</sub>H<sub>22</sub>O<sub>4</sub>S<sub>2</sub>: C, 52.80; H, 6.97. Found: C, 53.10; H, 7.00.

**Reaction of 5-Methylmercapto-2-pentanone with Methanol and Perchloric Acid.**—The ketone XVI did not react with methanolic perchloric acid at room temperature. A mixture of the ketone (2.64 g., 0.02 mole) and 70% perchloric acid (2.87 g., 0.02 mole) was refluxed for 3.5 hours in 5 ml. of reagent grade methanol. The mixture was cooled and diluted with ether. The resulting oil was washed repeatedly with dry ether and cooled in Dry Ice, when it crystallized as a soft colorless mass, m.p. 28.5–30.5° (uncor.) yield 3.00 g. (65%). The product had selected infrared maxima at 1708 (C=O) and 3038  $\text{cm}^{-1}$  (CH<sub>3</sub>S<sup>+</sup> (?); (CH<sub>3</sub>)<sub>2</sub>S<sup>+</sup> Br<sup>–</sup> has a Raman line at 3018  $\text{cm}^{-1}$ )<sup>56</sup> as a crystal melt, a Nujol null or a mull in hexachlorobutadiene. It gave a strong positive iodoform test and formed a 2,4-dinitrophenylhydrazone, m.p. 212–223° dec., yellow-orange needles from acetonitrile, whose empirical formulas as determined from analysis corresponded to C<sub>13</sub>H<sub>19</sub>ClN<sub>4</sub>O<sub>6</sub>S.

*Anal.* Calcd. for C<sub>13</sub>H<sub>19</sub>ClN<sub>4</sub>O<sub>6</sub>S: C, 36.58; H, 4.49; N, 13.13. Found: C, 36.87; H, 4.65; N, 13.14.

This led to a proposed structure for the primary product of 5-dimethylsulfonium-2-pentanone perchlorate (XVII). Unfortunately several attempts to convert it to the known *p*-toluenesulfonate salt by ion exchange techniques were not successful.

**4-Oxothiepane.**—1-Thiacycloheptan-4-one was synthesized by the method of Overberger and Katchman<sup>18</sup>;  $\nu_{\text{max}}^{\text{CCl}_4}$  1707  $\text{cm}^{-1}$  (5%), 1711  $\text{cm}^{-1}$  (10<sup>–2</sup>M).

**1,7-Dichloro-4-ethylenedioxyheptane (IV).**—A solution of 22.5 g. (0.123 mole) of 1,7-dichloro-4-heptanone,<sup>51,52</sup> 7.62 g. (0.123 mole) of ethylene glycol and 0.1 g. of *p*-toluenesulfonic acid in 100 ml. of benzene was refluxed under a Dean-Stark continuous water separator for 13.5 hours. The benzene was removed under reduced pressure, and the residue was fractionally distilled, b.p. 81–83° (0.25 mm.),  $n_{20}^{20D}$  1.4774,  $\nu_{\text{max}}^{\text{CCl}_4}$  1115 and 1055  $\text{cm}^{-1}$ ,  $\nu_{\text{max}}^{\text{film}}$  1115 and 1050  $\text{cm}^{-1}$ ; yield 16.76 g. (60%).

*Anal.* Calcd. for C<sub>9</sub>H<sub>16</sub>Cl<sub>2</sub>O<sub>2</sub>: C, 47.59; H, 7.10. Found: C, 47.73; H, 6.90.

**1,5-Dithiacyclooctane (XV).**—The method of Meadow and Reid<sup>35</sup> was modified to make use of the simultaneous

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(47) H. R. Snyder and D. S. Matteson, *ibid.*, **79**, 2217 (1957).

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(49) D. E. Ames and R. E. Bowman, *J. Chem. Soc.*, 1079 (1951), and following papers.

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(51) O. E. Curtis, Jr., J. M. Sandri, R. E. Crocker and H. Hart, *Org. Syntheses*, **38**, 19 (1958).

(52) H. Hart and O. E. Curtis, Jr., *THIS JOURNAL*, **78**, 112 (1956).

(53) W. R. Boon, U. S. Patent 2,370,392, February 27, 1945; C. A., **39**, 4090 (1945).

(54) G. W. Cannon, R. C. Ellis and J. R. Leal, *Org. Syntheses*, **31**, 74 (1951).

(55) T. Bacchetti and A. Fiechi, *Gazz. chim. ital.*, **83**, 1037 (1953).

(56) H. Siebert, *Z. anorg. u. allgem. Chem.*, **271**, 65 (1953).

addition of the reagents, 1,3-dibromopropane and disodium 1,3-propanedimercaptide, as alcoholic solutions (0.05 mole in 300 ml. of absolute ethanol) to a large volume of refluxing ethanol through the usual high dilution cycle during 69 hours. The main fraction, 0.504 g. (6.8%), b.p. 46–55° (0.1 mm.), obtained by distillation of the crude product, was redistilled from sodium for analysis; b.p. 43–46° (0.1 mm.),  $n_D^{25}$  1.5770 (reported<sup>35</sup> b.p. 245–246°,  $n_D^{20}$  1.5747;  $\nu_{\max}^{\text{film}}$  at 1445, 1412, 1272, 925 and 690  $\text{cm}^{-1}$ ).

*Anal.* Calcd. for  $\text{C}_6\text{H}_{12}\text{S}_2$ : C, 48.64; H, 8.16. Found: C, 48.76; H, 8.26.

That this was actually the desired 8-membered ring compound was confirmed by the oxidation of a small sample with hydrogen peroxide in acetone to the known 1,5-dithiacyclooctane-1,1,5,5-tetroxide, m.p. 257.5–259°; reported 257.5–258°,<sup>35</sup> 258–259°.<sup>36</sup>

**Physical Measurements. Infrared Spectra.**—All measurements were made on a Perkin-Elmer model 21 spectrometer using matched sodium chloride cells with pure solvent in the reference beam. Solvents were reagent grade commercially available samples except where noted; acetonitrile and trichloroacetonitrile were distilled from phosphorus pentoxide prior to use. The instrument was calibrated with the vibrational bands of water vapor and/or polystyrene.

When the spectral intensities were being measured quantitatively, a fixed slit width of 25  $\mu$  was used, the scale was greatly expanded by adjustment of the instrument gear ratio, and a pure solvent base line was inscribed on the graph over the region examined. The region of 1750–1660  $\text{cm}^{-1}$  was then scanned at a slow speed with zero suppression. Under these conditions the integrated areas of bands could be measured accurately, but band shapes were not clearly defined. For a better, if qualitative, picture of the effect of solvent on band shapes and frequencies the same region was scanned at moderate speeds and suppression with a normal scale and programmed slit.

The spectra of 5-hydroxy- and 5-methoxybicyclo[3.3.0]octane-1-thianium perchlorates in  $\text{D}_2\text{O}$  solutions were kindly run by Dr. Harold Boaz at the Lilly Research Laboratories using a calcium fluoride cell. Both exhibited a strong carbonyl band at 1667  $\text{cm}^{-1}$ .

It was decided that the infrared maximum corresponding to  $\text{C}=\text{O}$  stretching in the  $\text{RC} \begin{array}{l} \diagup \text{O} \\ \diagdown \text{SR} \end{array}$  group is centered at 1694  $\text{cm}^{-1}$  (10% in carbon tetrachloride solution) by examination of the following compounds, all of which were generously provided by Dr. Robert H. Levin of The Upjohn Co., Kalamazoo, Mich.: benzyl 3 $\alpha$ ,12 $\alpha$ -diacetoxy-nor-thiolcholanate, ethyl 3 $\alpha$ ,12 $\alpha$ -diformoxy-thiolcholanate and ethyl 3 $\beta$ -acetoxy- $\Delta^8$ -thiolcholanate.<sup>57</sup>

The spectrum of 1,5-dithiacyclooctane ( $\lambda_{\max}$  202  $\mu$ ) was examined down to 190  $\mu$  by opening the slit width to a maximum (50) and using a high amplification (position 5). The resultant "noisy" curve was corrected for solvent absorption by point by point subtraction of a base line. Intensity measurements are not very meaningful in this region.

The spectrum of 5-hydroxybicyclo[3.3.0]octane-1-thianium perchlorate in water and the related  $pK_a'$  measurements were recorded at the Lilly Research Laboratories through the cooperation of Dr. Harold Boaz, the  $pK_a'$  value being obtained from the equation

$$pK_a = pH + \log \frac{\epsilon_B - \epsilon_A}{\epsilon_A}$$

where  $\epsilon_A$  was measured in 1.84  $M$  hydrochloric acid and  $\epsilon_B$  was measured after the  $pH$  was raised to 3.0 with potassium hydroxide. Ionic strength effects on the hydrogen ion activity were neglected.

The transition energies for the thiaetone (the concentration of perchloric acid,  $ca. 3 \times 10^{-4} M$ , released by ionization is so small as to be neglectable<sup>26</sup> in the dilute solutions used for spectral measurements) in various solvents were calculated from the equation  $E_T = 2.859 \times 10^{-3}\nu$ , where  $E_T$  is in kcal. mole<sup>-1</sup> and  $\nu$  is the frequency in  $\text{cm}^{-1}$ . These points were plotted against  $Z$ ,<sup>26</sup> and the best straight line was calculated by the method of least squares.

**Nuclear Magnetic Resonance Spectra.**—The n.m.r. spectra of these compounds were obtained on a Varian Associates model 4300-2 instrument operated in conjunction with a V-K3506 super stabilizer using methylene chloride in an annular cell as an external reference, the curves being calibrated by the usual sideband technique. The concentrations ranged from 35 to 50 mg. in 0.2 ml. of solvent. A 40-megacycle probe was used.

**Mass Spectrum.**—The mass spectrum of 1-thiacyclooctan-5-one was measured on a Consolidated Electrodynamics Corp. model 103 Mass spectrometer by Dr. Al Struck at the Stamford, Conn., laboratories of the American Cyanamid Co. through the good offices of Dr. Everett J. Frazza. The instrument was operated at an inlet temperature of 150° and a pressure of 32.6  $\mu$ . The parent peak at 144 (intensity 100) furnished an accurate molecular weight. The other major peaks and their relative intensities appeared at 116(20), 102(80), 96(10), 74(60), 60(60) and 55(100).

**Dipole Moments.**—The electric moments of 1-thiacyclooctan-5-one, 1-oxacyclooctan-5-one, 4-oxothiepane and tetrahydro-4H-thiapyran-4-one were measured in benzene solution. In one case (1-thiacyclooctan-5-one) the measurement was repeated in carbon tetrachloride and found to be within 0.01 D. of the value in benzene. The dielectric

TABLE IV

EMPIRICAL CONSTANTS AND DIPOLE MOMENTS IN BENZENE SOLUTION AT 24°

Compound	$\epsilon$	$\alpha$	$\nu_1$	$\beta$	$P_2$	$MR_D$	$\mu_{\text{obsd}}$
1-Thiacyclooctan-5-one	2.2745	11.2	1.1435	-0.318	339	40.4	3.81
1-Thiacyclooctan-5-one in $\text{CCl}_4$ sol.	2.226	19.6	0.63027	0.244	336	40.4	3.80
Tetrahydro-4H-thiapyran-4-one	2.2745	2.96	1.1434	-0.328	92.9	31.1	1.73
4-Oxothiepane	2.2745	7.95	1.1434	-0.310	226	35.8	3.04
1-Oxacyclooctan-5-one	2.2745	14.1	1.1434	-0.120	377	34.3	4.09

**Ultraviolet Spectra.**—The electronic absorption spectra were obtained on a Cary model 14 recording spectrophotometer, and maxima were considered accurate to  $\pm 1 m\mu$ . Cyclohexane was freed from benzene by stirring with powdered silica gel. Very dry methanol was prepared from reagent grade methanol by distillation from Drierite, passage through type 4A molecular sieve, shaking with fresh Drierite, and filtration under nitrogen pressure into a dried bottle. Absolute ethanol was reagent grade, used without further purification. Acetonitrile was distilled from phosphorus pentoxide.

(57) R. H. Levin, A. V. McIntosh, Jr., G. B. Spero, D. E. Rayman and E. M. Meinzer, *THIS JOURNAL*, **70**, 511 (1948).

constants and densities of several solutions, ranging in concentration from 0.001 to 0.008 in weight fraction of solute, were measured at 24°. The constants  $\epsilon$ ,  $\alpha$ ,  $\nu_1$ ,  $\beta$  of the Halverstadt-Kunler equation are shown in Table IV for each compound along with the derived value of the molar polarization of solute at infinite dilution,  $P_2$ . The sum of the electronic and atomic polarizations was taken to be equal to the molecular refraction  $MR_D$ , calculated from empirical constants. The observed values of the electric moments are shown in Table IV; the probable error in each is about  $\pm 0.1$  D.

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