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Imidothiocarbonates. V.[1] Preparations and Properties of Novel Azomethine Ylides and Thiocarbonyl Ylides from Sulfur-contained Heterocycles

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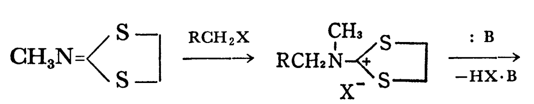
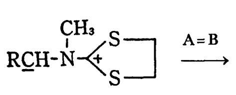
Preparations and properties of some novel azomethine ylides and thiocarbonyl ylides containing 1,3-dithiolanium moiety have been studied. Azomethine ylides, **3a**, **b**, and **c**, were prepared by deprotonation of 2-(*N*-methyl-*N*-phenacyl)amino-(**2a**)), 2-(*N*-*p*-nitrobenzyl-*N*-methyl)amino-(**2b**), and 2-(*N*-carbethoxymethyl-*N*-methyl)-amino-1,3-dithiolanium salt (**2c**), respectively. Azomethine ylides **3a**, **b** reacted with benzaldehydes to give 1,3-dipolar cycloadducts which are new class of spiro orthocarbonates, otherwise it is difficult to obtain. Elimination of ethylene sulfide from the spiro orthocarbonates easily occurred to give thiocarbonyl compounds. In the absence of dipolarophiles, **3a** cyclized intramolecularly to give 1,3-oxazoline-2-thione derivative. Formation of the thiocarbonyl ylides by deproptonation of 2-phenacylthio-1,3-oxazolium and 2-*p*-bromophenacylthio-1,3-dithiolanium salts, and their different cyclization to spiro compounds were also studied. Reaction of thiocarbonyl ylides **16** with *p*-nitrobenzaldehyde afforded *p*-nitrochalcone. Mechanisms of these interesting reactions and their synthetic utility were discussed.

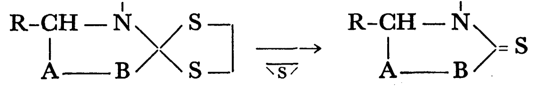
In continuation of our studies on iminodithiocarbonates, we have explored the formation of 2-(*N*,*N*-dialkylamino)-1,3-dithiolanium salts (**2**) from 2-methylimino-1,3-dithiolane (**1**) in high yield.[1] We consider here the possibility of the preparation of new azomethine ylides[2] (**3**) by deprotonation of the iminium salts **2**. It is expected that such an azomethine ylide may react with appropriate dipolarophiles (A=B) to yield spiro orthocarbonates. Moreover, such spiro orthocarbonates are expected to give heterocyclic thiocarbonyl compounds with a release of ethylene sulfide, because we have shown that spiro orthocarbonates containing 1,3-dithiolane or 1,3-oxathiolane ring, easily eliminate ethylene sulfide to produce thiocarbonyl or carbonyl compounds.[3,4)



1 **2a, b, c**



3a R=PhCO
b R=p-$NO_2C_6H_4$
c R=EtOCO



A compound in which the *N*-methyl group of ylide **3** is replaced by sulfur atom is also a new class of compounds named as thiocarbonyl ylide.[5]

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[1] Part III and Part IV of this series: Y. Ueno, T. Nakai, and M. Okawara, This Bulletin, **44**, 841, 1933 (1971).

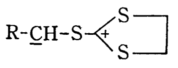
[2] The terms of azomethine ylide was used for the structure: $>\overset{+}{C}-\overset{|}{N}-\overset{-}{C}< \longleftrightarrow >C=\underset{|}{\overset{+}{N}}-\overset{-}{C}<$ R. Huisgen, *Angew. Chem. Internat. Edit.*, **2**, 565 (1963).

[3] Y. Ueno, T. Nakai, and M. Okawara, This Bulletin, **43**, 162 (1970).

[4] Y. Ueno, T. Nakai, and M. Okawata, *ibid.*, **43**, 168 (1970).

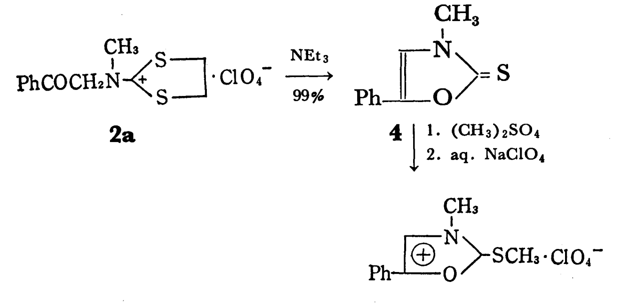
[5] The terms of thiocarbonyl ylide was used for the structure: $>\overset{+}{C}-S-\overset{-}{C}< \longleftrightarrow >C=\overset{+}{S}-\overset{-}{C}<$ R. M. Kellogg and S. Wassenaar, *Tetrahedron Lett.*, **1970**, 1987.

This paper describes the formation of novel azomethine ylides and thiocarbonyl ylides and their interesting reactions.



Results and Discussion

Formation of Azomethine Ylides and Their Properties. When 2-(*N*-methyl-*N*-phenacylamino)-1,3-dithiolanium perchlorate (**2a**) was treated with triethylamine in acetonitrile, 3-methyl-5-phenyl-1,3-oxazoline-2-thione (**4**) was obtained in quantitative yield. The infrared spectrum of **4** shows the characteristic bands at 3100 cm^{-1} (–CH=C<), at 1492, 1462 cm^{-1} (thioamide II), and at 1210, 1195 cm^{-1} (thioamide I). The structure of **4** was further characterized by the formation of the oxazolium salt **5**. Thus methylation of **4** with dimethyl sulfate afforded 2-methylthio-3-methyl-5-phenyl-1,3-oxazolium perchlorate (**5**).



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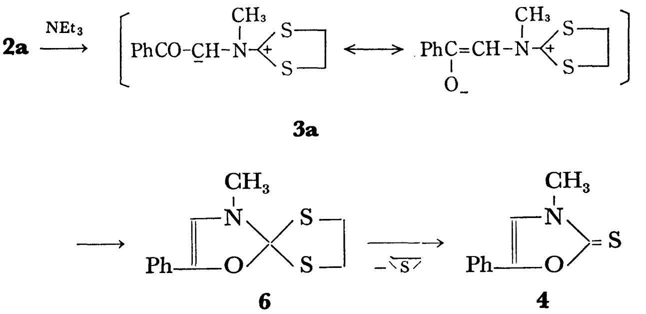
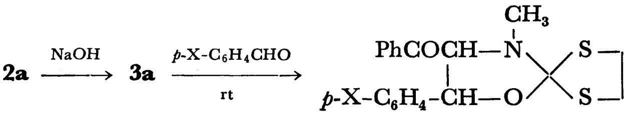
We postulate a mechanism involving prior formation of azomethine ylide **3a**, followed by intramolecular cyclization into spiro orthocarbonate **6**, and then elimination of ethylene sulfide, giving the final product **4** as formulated in Scheme 1.



Scheme 1.

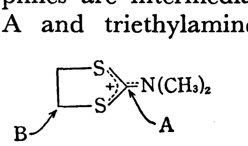
Attempts to trap the postulated intermediate, azomethine ylide **3a**, by 1,3-dipolar cycloaddition using phenyl isothiocyanate, carbon disulfide, or diethyl fumarate gave, instead, the intramolecular cyclization product **4** as the only isolated product. On the other hand, when *p*-nitrobenzaldehyde was employed as dipolarophile, 1,3-dipolar cycloaddition to the azomethine ylide **3a** occurred to give spiro orthocarbonate **7a** in 62% yield instead of **4**. Similarly benzaldehyde gave the cycloadduct **7b** in 55% yield.



7a, R=NO$_2$
b, R=H

The infrared spectrum of **7a** shows a carbonyl vibrations at 1670 cm^{-1} those of nitro at 1520 and 1350 cm^{-1} and reveals the absence of thiocarbonyl group observed in the compound **4**.

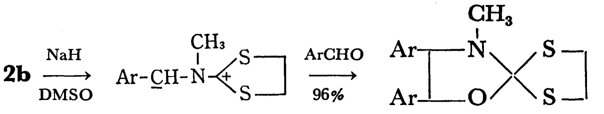
Reactivities of the azomethine ylide **3a** towards dipolarophiles seem to be dependent upon that of the cationic part of **3a**. Thus we have explored that tri(hetero)substituted carbonium ions are greatly stabilized by nitrogen or sulfur atoms and that they have more than two reaction sites.[6] For example, it was shown that 2-(*N*,*N*-dimethylamino)-1,3-dithiolanium salt **8** reacts with various nucleophiles at two sites, A or B, and that whether the reactions take place at A or B, chiefly depends upon the nature of nucleophiles. In general, hard-nucleophiles (HO$^-$, RO$^-$) are most powerful to attack at A, whereas soft-nucleophiles (RS$^-$, R$_2$NC(=S)S$^-$) at B. Nitrogen-containing nucleophiles are intermediate between the two (aniline at A and triethylamine at B).



8

These facts are consistent with the observation that benzaldehydes (hard nucleophile) react with ylide **3a** to give 1,3-dipolar cycloaddition product **7**, and that the other dipolarophiles such as phenyl isothiocyanate, carbon disulfide, and diethyl fumarate (soft-nucleophiles) do not react.

When **2b** was treated with sodium hydride or potassium *t*-butoxide in dimethyl sulfoxide (DMSO) or acetonitrile, the reaction mixture turned to deep violet and returned to colorless by the addition of hydrochloric acid. This deep colored material seems to be the azomethine ylide **3b**. This was confirmed by 1,3-dipolar cycloaddition of *p*-nitrobenzaldehyde to the deep colored material. Thus a mixture of **2b** and *p*-nitrobenzaldehyde in DMSO was treated with sodium hydride at room temperature to produce the spiro orthocarbonate **9** in almost quantitative yield.



3b **9**
(Ar=*p*-NO$_2$C$_6$H$_4$)

The infrared spectrum of **9** reveals the presence of a nitro group (1530, 1350 cm^{-1}) and an etheral group (1062 cm^{-1}). The NMR spectrum in (CD$_3$)$_2$SO exibits singlet peak at τ 7.70 (*N*-CH$_3$, 3H), triplet peaks at τ 7.60 (CH$_2$CH$_2$, 4H), a singlet peak at τ 7.06 (>CH–

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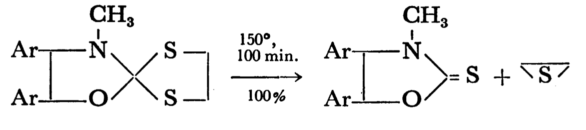
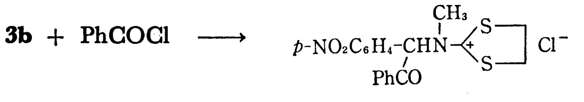
[6] T. Nakai, Y. Ueno, and M. Okawara, This Bulletin, **43**, 3175 (1970).

CH⟨, 2H), and two multiplet peaks centered at 2.45 and 1.75 (aromatic protons, each 4H). It was found that, as expected, the spiro orthocarbonate **9** afforded 1,3-oxazolidine-2-thione derivative **10** at the temperature above its melting point with a release of ethylene sulfide in quantitative yield.



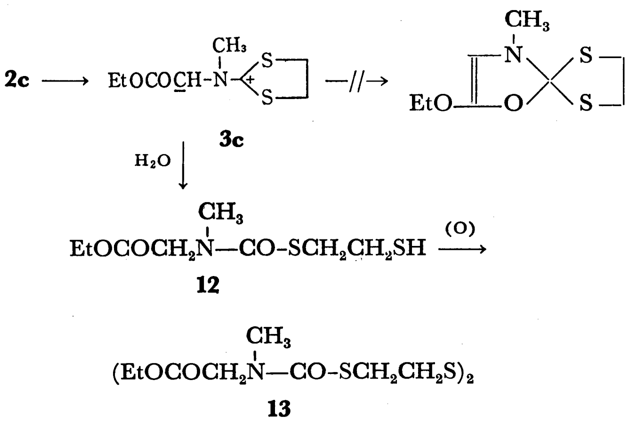
9 **10**

Acylation of the azomethine ylide **3b** with benzoyl chloride gave *C*-benzoylated product **11**, of which infrared spectrum shows the presence of a carbonyl group (1660 cm^{-1}). **11** was stable salt and recovered unchanged on heating at 180°C for 30 min.



11

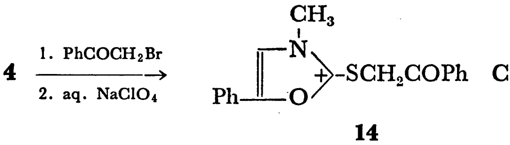
An attempt to cyclize the azomethine ylide **3c**, derived from the iminium salt **2c**, into spiro orthocarbonate in a similar manner as in the case of azomethine ylide **3a** failed. It was observed that only the hydrolysis of the salt **2c** by the water added after the reaction, and subsequent air-oxidation of the resulting mercaptan derivative **12** to disulfide **13**. The infrared spectrum of **13** reveals the presence of ester group (1750, 1200 cm^{-1}), and the amide carbonyl (1660 cm^{-1}), and the absence of thiol group. Similar hydrolysis of the iminium salt **8** into mercaptan or disulfide derivative has been reported.[7] No formation of spiro orthocarbonate from **3c** may be explained by the less reactivity of ester carbonyl towards carbonium ion in comparison with ketonic carbonyl of **3a**.



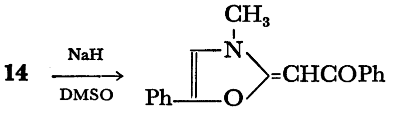
$EtOCOCH_2\overset{CH_3}{N}\text{—}CO\text{-}SCH_2CH_2SH \xrightarrow{(O)}$

$(EtOCOCH_2\overset{CH_3}{N}\text{—}CO\text{-}SCH_2CH_2S)_2$

Formation of Thiocarbonyl Ylides and Their Properties. As described above, 1,3-oxazoline-2-thione **4** was easily alkylated to 2-methylthio-1,3-oxazolium salt **5** with deimethyl sulfate. When phenacyl bromide was employed in place of dimethyl sulfate, 2-phenacylthio-1,3-oxazolium salt **14** was obtained in 68% yield. Oxazolium salt **14** was expected to produce a new interesting thiocarbonyl ylide by deprotonation with base. Upon treatment of **14** with sodium hydride in DMSO at room temperature afforded 2-phenacylidene-3-methyl-5-phenyl-1,3-oxazoline **15** in 75% yield.



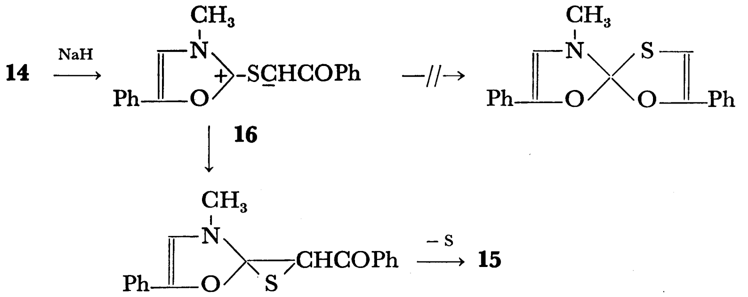
14



15

A possible reaction sequence for the formation of **15** was indicated in Scheme 2. Thus the thiocarbonyl ylide **16** derived from **14** cyclized into the thiirane derivative[8] **17**, instead to the five-membered ring as observed in azomethine ylide **3a**. The thiirane **17** afforded **15** with liberation of elemental sulfur.

On the other hand, it was found that the thiocarbonyl ylide **19**, derived from 2-(*p*-bromophenacylthio)-1,3-dithiolanium bromide,[9] cyclized into spiro orthocarbonate **20** instead to the thiirane derivative



Scheme 2.

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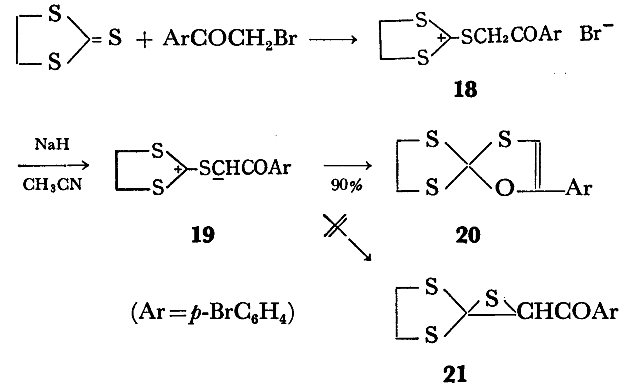
[7] T. Nakai and M. Okawara, *ibid.*, **43**, 1864 (1970).

[8] Takaku *et al.* reported the following reaction, in which thiirane derivative was postulated as intermediate to the isomerized product: $(Me_2N)_2\overset{+}{C}\text{-}SCH_2R\ X^- \xrightarrow{:B} \underset{\mathbf{25}}{(Me_2N)_2\overset{+}{C}\text{-}S\text{-}\overset{-}{C}HR} \longrightarrow (Me_2N)_2\underset{\diagdown S \diagup}{C\text{—}CHR} \xrightarrow{O} (Me_2N)_2C{=}C(SH)R$, M. Takaku, S, Mitamura, and H. Nozaki, *Tetrahedron Lett.*, **1969**, 3651.

[9] R. Mayer and K. Schafer, *J. Prakt. Chem.*, (4) **26**, 279 (1964).

21. The IR spectrum of **20** shows no absorption bands in carbonyl region. The NMR spectrum in CCl_4 exhibits a singlet peak at τ 6.46 (SCH_2-CH_2S, 4H), a singlet peak at τ 3.97 (CH=, 1H), and multiplet peaks centered at τ 2.65 (aromatic protons, 4H).



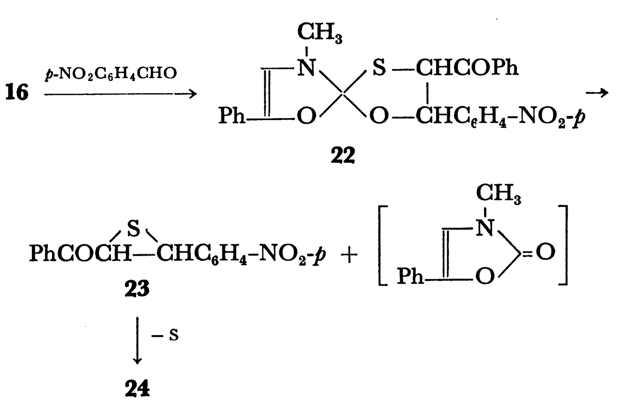
Finally, 1,3-dipolar cycloaddition of thiocarbonyl ylide **16** was undertaken. Thus **14** was treated with sodium hydroxide in the presence of *p*-nitrobenzaldehyde at room temperature to give *p*-nitrochalcone **24** in 85% yield.

$$\mathbf{14} + p\text{-}NO_2C_6H_4CHO \xrightarrow[EtOH\text{-}H_2O]{NaOH}$$

$$PhCOCH{=}CHC_6H_4\text{-}NO_2\text{-}p$$

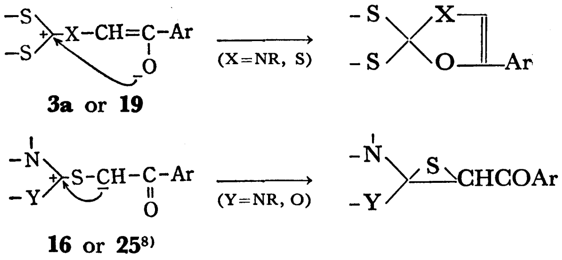
24

Facile elimination of thiirane from spiro orthocarbonates seems to be a general property of these types of compounds as observed above or as reported previously.[3,4] Moreover, it is well known that some kinds of thiiranes are quite readily decomposed to olefins with liberation of elemental sulfur. On the basis of these facts, a possible reaction mechanism may be illustrated in Scheme 3. Although the fate of the fragmented oxazolone group has not been established, the reaction seems to proceed *via* 1,3-dipolar cycloaddition of *p*-nitrobenzaldehyde to the thiocarbonyl ylide **16**, giving the spiro orthocarbonate **22**, which readily decomposes to the thiirane **23** and, possibly, the oxazolone derivative. The thiirane **23** finally decomposes to *p*-nitrochalcone **24** with liberation of elemental sulfur.

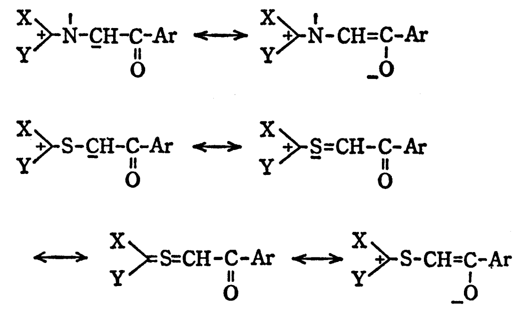


Scheme 3

Differences in the Intramolecular Cyclization Mode between Azomethine Ylides and Thiocarbonyl Ylides. It is quite interesting that two kinds of intramolecular cyclization modes of the azomethine and thiocarbonyl ylides were found. Thus the azomethine ylide **3a** and thiocarbonyl ylide **19** cyclized to five-membered ring at oxygen anion, whereas the thiocarbonyl ylide **16** cyclized to three-membered ring at carbanion as illustrated below.



These differences can not be clearly explained at the present stage. However we assume that the formation of thiirane derivatives, which are sterically unfavorable because of their subsequent facile occurrence of elimination or isomerization[8] of sulfur atom, is related to the stabilization or carbanion by sulfur atom in thiocarbonyl ylides. Thus in contrast to the azomethine ylides, the larger contribution of the carbanion-structure is postulated in thiocarbonyl ylides, if in which the carbanion can be stabilized by vacant *d*-orbitals of bivalent sulfur atom. The cyclization at the carbanion to the thiirane derivatives seems to become feasible only in such a case.



In thiocarbonyl ylide **19**, however, other factors seem to be operative for the cyclization.

Experimental

All the melting points were uncorrected. The IR spectra were recorded on Japan Optics JNL 4H-100 spectrometer using tetramethylsilane (TMS) as an internal standard. All experiments on ylides were carried out under nitrogen atmosphere.

Materials. 2-(*N*-Methyl-*N*-phenacyl)amino-(**2a**), 2-(*N*-*p*-nitrobenzyl-*N*-methyl)amino-(**2b**), and 2-(*N*-carbethoxymethyl-*N*-methyl)amino-1,3-dithiolanium salt (**2c**) were prepared from 2-methylimino-1,3-dithiolane (**1**) and corresponding alkyl bromides, respectively, as previously reported.[1]

*Intramolecular Cyclization of Azomethine Ylide **3a**.* A mixture of 1.7 g (4.8 mmol) of 2-(*N*-methyl-*N*-phenacyl)-amino-1,3-dithiolanium perchlorate (**2a**) and 1 m*l* of triethylamine in 20 m*l* of acetonitrile was heated at 60°C for 5 hr. Addition of water, extraction with ether, drying with sodium sulfate, and then concentrating the ethereal solution afforded 0.9 g (99%) of 3-methyl-5-phenyl-1,3-oxazoline-2-thione (4) : mp 140—141°C (recrystallized from acetonitrile ether)

Found: C, 62.41; H, 4.63; N, 7.32%. Calcd for $C_{10}H_9NOS$: C. 62.82; H, 4.75; N, 7.33%.

The compound **4** was also formed in quantitative yield when the salt **2a** was treated with sodium hydride in dioxane at room temperature for 0.5 hr. Under similar conditions **4** was obtained in almost the same yield even in the presence of the dipolarophiles such as phenyl isothiocyanate, carbon disulfide, or diethyl fumarate.

Methylation of 3-Methyl-5-phenyl-1,3-oxazoline-2-thione ***4***. A mixture of equimolar amount of **4** and dimethyl sulfate was heated at 60°C for 1 hr, followed by treatment with aqueous sodium perchlorate, afforded 2-methylthio-3-methyl-5-phenyl-1,3-oxazolium perchlorate (**5**) in 70% yield: mp 189—190°. IR 1080 cm^{-1} (ClO_4^-).

Found: C, 43.01; H, 3.75; N, 4.47%. Calcd for $C_{11}H_{12}NO_5SCl$: C, 43.22; H, 3.96; N, 4.58%.

Reaction of Azomethine Ylide ***3a*** *with Benzaldehydes.*

A. p-*Nitrobenzaldehyde*: To a mixture of 1.3 g (3.7 mmol) of the 1,3-dithiolanium salt **2a** and 1 g (6.6 mmol) of *p*-nitrobenzaldehyde in 80 m*l* of ethanol and 40 m*l* of water, was added with stirring 0.36 m*l* of 10 N aqueous sodium hydroxide solution. After about 30 min, white solid precipitated out was collected by filtration. Recrystallization from ethanol-acetone solution afforded 0.9 g (62%) of the spiro orthocarbonate **7a** : mp 132—133°C; IR, 1670 cm^{-1} (C=O), 1520, 1350 cm^{-1} (NO_2).

Found: C, 56.44; H, 4.43; N, 6.61%. Calcd for $C_{19}H_{18}N_2O_4S_2$: C, 56.71; H, 4.51; N, 6.96%.

B. *Benzaldehyde*: Similarly, **3a** reacted with benzaldehyde to give the spiro orthocarbonate **7b** in 54% yield: mp 84—85°C (recrystallized from ether): IR 1690 cm^{-1} (C=O).

Found: N, 3.96%. Calcd for $C_{19}H_{19}NO_2S_2$: N, 3.92%.

Reaction of the Azomethine Ylide ***3b*** *with* p-*Nitrobenzaldehyde.* To a mixture of 0.7 g (2 mmol) of 1,3-dithiolanium bromide **2b** and 0.3 g (2 mmol) of *p*-nitrobenzaldehyde in 10 m*l* of DMSO was added 0.1 g of 50% sodium hydride at room temperature. The reaction mixture turned to deep violet with evolution of hydrogen. The reaction mixture was stirred at room temperature for 2 hr and then poured into 50 m*l* of water to give 0.8 g (96%) of the cycloadduct **9** : mp 142—143°C (recrystallized from ethyl acetate); IR 1530, 1350 cm^{-1} (NO_2).

Found: C, 51.17; H, 3.99; N, 9.64%. Calcd for $C_{16}H_{13}N_3O_5S$: C, 51.15; H, 4.09; N, 10.02%.

Pyrolysis of the Spiro Orthocarbonate ***9***. Pyrolysis of **9** (1 g) at 150—160°C for 15 min. gave 0.85 g (100%) of 3-methyl-4,5-di(*p*-nitrophenyl)-1,3-oxazolidine-2-thione (10): mp 198—199°C (recrystallized from boiling acetone); IR 1505 (thioamide), 1530, 1350 cm^{-1} (NO_2).

Found: C, 53.80; H, 3.48; N, 11.43%. Calcd for $C_{16}H_{13}N_3O_5S$: C, 53.48; H, 3.65; N, 11.70%.

Reaction of the Azomethine Ylide ***3b*** *with Benzoyl Chloride.* *C*-Benzoylated product **11** was isolated in 21% yield in the reaction of the ylide **3b** with benzoyl choride in acetonitrile at room temperature for 3 hr: mp 80—81°C (recrystallized from methanol); IR 1660 cm^{-1} (C=O).

Found: C, 54.94; H, 4.62; N, 6.94; S, 16.59%. Calcd for $C_{18}H_{17}ClN_2O_3S_2$: C, 55.04; H, 4.36; N, 7.13; S, 16.29%.

Hydrolysis of the Azomethine Ylide ***3c***. A solution of 2.8 g (9.9 mmol) of the 1,3-dithiolanium perchlorate **2c** in 10 m*l* of acetonitrile was treated with 4 m*l* of triethylamine at 60°C for 4 hr. Water was added to the reaction mixture and extracted with ether, drying with sodium sulfate and evaporation of the solvent and trituration of the residue with a small amount of ether - *n*-hexane afforded 1 g (43%) of disulfide **13**: mp 75—76°C (recrystallized from ether); IR 1750 (ester C=O), 1660 (amide C=O), and 1200 cm^{-1} (C–O–C).

Found; C, 41.25; H, 6.08; N, 5.87%. Calcd for $C_{16}H_{28}N_2O_6S_4$: C, 40.67; H, 5.95; N, 5.95%.

Alkylation of 3-Methyl-5-phenyl-1,3-oxazoline-2-thione ***4*** *with Phenacyl Bromide.* A mixture of 2.9 g (15 mmol) of **4** and 3 g (15 mmol) of phenacyl bromide in 30 m*l* of tetrahydrofuran (THF) was allowed to stand at room temperature for 2 days. Treatment of the reaction mixture with aqueous sodium perchlorate solution gave 4.26 g (68%) of 2-phenacylthio-3-methyl-5-phenyl-1,3-oxazolium perchlorate **14**: mp 208—209°C (d.) (recrystallized from acetonitrile); IR 1680 cm^{-1} (C=O).

Found; C, 53.39; H, 3.90; N, 3.58%. Calcd for $C_{18}H_{16}ClNO_6S$: C, 52.76; H, 3.94; N, 3.42%.

Formation of 2-Phenacylidene-1,3-oxazoline ***15***. A solution of 1.0 g (2.5 mmol) of oxazolium salt **14** in 10 m*l* of DMSO was treated with 0.12 g of 50% sodium hydride at room temperature. The reaction mixture turned to red with evolution of hydrogen. After standing at room temperature over one night, the mixture was poured into excess water to give 0.5 g (75%) of 2-phenacylidene-3-methyl-5-phenyl-1,3-oxazoline **15**: mp 196—197°C (d). (recrystallized from acetone); IR 1530 cm^{-1} (C=O); NMR ($CDCl_3$) τ 6.65 (s, 3H, *N*-CH_3), τ 4.55 (s, 1H, –CH=), τ 3.21 (s, 1H, –CH=), and τ 2.4 (m, 10H, phenyl protons).

Found: C, 76.95; H, 5.10; N, 4.78%. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05%.

Intramolecular Cyclization of the Thiocarbonyl Ylide ***19***. To a suspension of 1.24 g (3 mmol) of 2-(*p*-bromophenacylthio)-1,3-dithiolanium bromide (prepared by the method of Mayer[9]) in 40 m*l* of acetonitrile, was added 0.2 g of 50% sodium hydride. The reaction mixture turned to reddish-brown, was stirred at room temperature for 3 hr and then was poured into water (*ca*. 500 m*l*) with stirring to give 0.9 g (90%) of spiro orthocarbonate **20**; mp 85—86°C (d.) (recrystallized from n-hexane–ether).

Found: C, 39.84; H, 2.87%. Calcd for $C_{11}H_9BrOS_3$: C, 39.66; H, 2.72%.

The NMR spectral data of **20** was described in the text.

Reaction of Thiocarbonyl Ylide **16** *with p-Nitrobenzaldehyde.* To a suspension of 0.8 g (2 mmol) of 14 and 0.4 g (2.6 mmol) of *p*-nitrobenzaldehyde in 70 m*l* of water and 50 m*l* of ethanol, was added 0.2 m*l* of aqueous solution of 10 N sodium hydroxide. The reaction mixture turned to orange-brown and deposited the brown precipitates, which were collected by filtration after 2 hr. Recrystallization from ether - ethyl acetate afforded yellowish-brown solid **24** (85): mp 162.0—162.5°C (lit,[10] 162.5°); IR 1655 cm^{-1} (C=O).

Found: C, 70.85; H, 4.14; N, 5.33%. Calcd for $C_{15}H_{11}NO_3$: C, 71.14; H, 4.37; N, 5.53%.

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[10] H. Wieland, *Ber*., **37**, 1149 (1904).