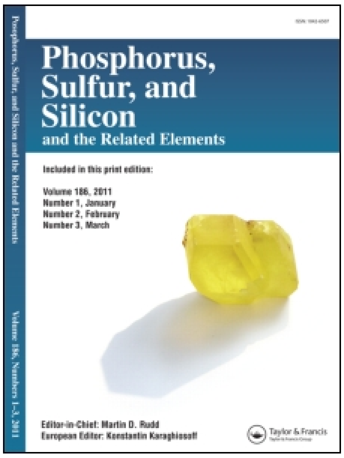

**Phosphorus, Sulfur, and Silicon and the Related Elements**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

# Aspects of Thioanhydhide Chemistry

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**To cite this Article** Cava, M. P. and Lakshmikantham, M. V.(1989) 'Aspects of Thioanhydhide Chemistry', Phosphorus, Sulfur, and Silicon and the Related Elements, 43: 1, 95 — 109

**To link to this Article: DOI:** 10.1080/10426508908040280

**URL:** http://dx.doi.org/10.1080/10426508908040280

*Phosphorus, Sulfur and Silica*, Vol. 43/1-2, pp. 95–109
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# ASPECTS OF THIOANHYDRIDE CHEMISTRY

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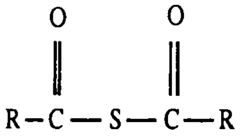
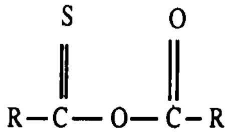
Abstract Cyclic anhydrides constitute one of the most thoroughly studied classes of organic compounds. In contrast, very little is as yet known concerning the thiocarbonyl analogs of cyclic anhydrides. In this lecture, the present status of thionoanhydride chemistry will be reviewed, with emphasis on studies from our laboratory.

The acid anhydrides are a very well known class of organic compounds. By analogy, one can expect two monosulfur substituted, two disulfur substituted, and one trithio anhydride **1**-**5** respectively; surprisingly, these functional types have been relatively little investigated.


$R-\overset{O}{\overset{\|}{C}}-S-\overset{O}{\overset{\|}{C}}-R$

**1**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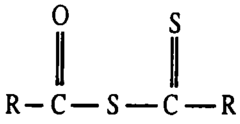
**2**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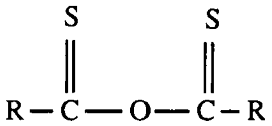
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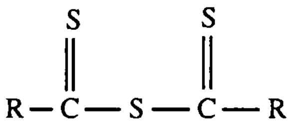
**4**


$R-\overset{S}{\overset{\|}{C}}-S-\overset{S}{\overset{\|}{C}}-R$

**5**

For convenience, we shall refer to **1** as a thioloanhydride, **2** as a thionoanhydride, **3** as a thionothioloanhydride, **4** as dithionoanhydride, and **5** as a trithioanhydride.

Whereas examples of **1** have long been known, the first reports of acyclic members of types **3** and **5** appeared in 1976 and 1977.[1,2] No acyclic members of type **2** and **4** appear to be known.

The methods of synthesis adopted for compounds **3** and **5** are limited by the availability of the required dithioacids and their salts. Acylation of a dithioacid anion at low temperatures produced **3**, while treatment of a free dithioacid with dicyclohexylcarbodimide led to **5**.

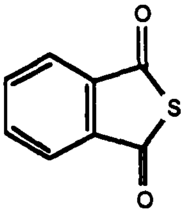
In 1983, addition of a dithioacid to ketene was reported to give a thiolothionoanhydride derived from acetic acid.[3]

All of the above acyclic thioanhydrides were found to be of limited stability, and were generally best stored at low temperature under an inert atmosphere.

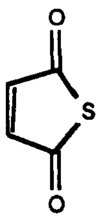
MINDO/3 calculations on trithioacetic anhydride and thiolothionoacetic anhydride were carried out. The central sulfur atom was predicted to carry a larger charge density than the C = S sulfur in the trithioanhydride and about the same in the latter case. The charge density on the carbonyl carbon of the unsymmetrical anhydride was found to be larger than that on the thiocarbonyl carbon. The dihedral angles between the -(CS)-S- and -(CS)-O- planes is 90° in the preferred conformation of both compounds.

Our interest in these compounds has focused on the cyclic members of the series **1** - **5** where the atoms of the thioanhydride functionality are forced to be in a single plane. Thiolophthalic anhydride (**6**) and thiolomaleic anhydride (**7**) are known compounds and are examples of type **1**. Thionophthalic anhydride (**8**) was described only once, in 1967.[6] In addition to these, a monosulfur analog of 1,8-naphthalic anhydride of unspecified constitution was reported.[7] Attempts to prepare a perthiomaleic anhydride led to a tetramer.[8]

The remainder of this lecture will consist of results from our laboratory on the synthesis and properties of the sulfur analogs of naphthalic anhydrides, and attempts to prepare trithiophthalic anhydride.



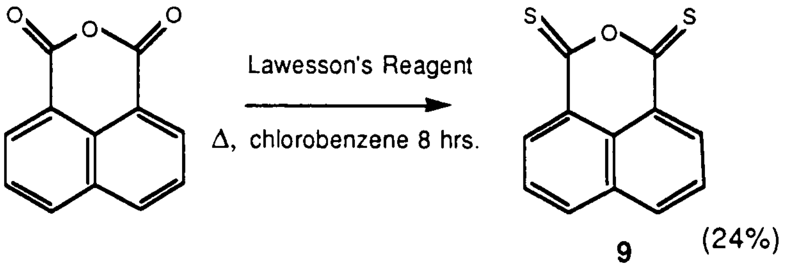
**6**



**7**

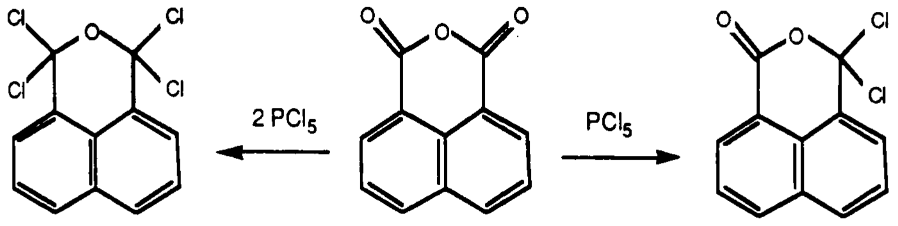
The literature procedures, starting from the dithioacids, are inapplicable in the case of phthalic anhydride and naphthalic anhydride.

The simplest approach seemed to be direct thionation of the anhydrides. It was found after considerable experimentation that the use of Lawesson's reagent in boiling chlorobenzene does indeed thionate 1,8-naphthalic anhydride. A mixture of products is formed from which, fortunately, the dithiono 1,8-naphthalic anhydride **9** crystallized out in >95% purity and in about 24% yield. Prolonged boiling over days did lead to the isolation of small quantities of the trithio anhydride **13**, but this procedure was impractical from a synthetic point of view.



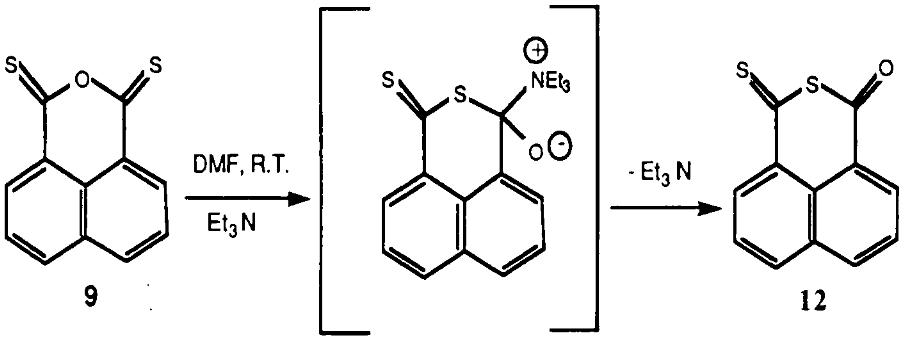
The FT nmr spectrum of this material consisted of two 2 H doublets at δ 8·83, 8·28, and J = 8·0 and J - 7·5 Hz, respectively, and a 2 H unsymetrical triplet at δ 7·8, J = 8·0, and 7·5 Hz. The mass spectrum showed m/e 230 (100%), in accord with its structure.

A more practical route to **9** involved the thionation of the acid chloride derived from 1,8-naphthalic anhydride. Previous investigations had recognized the ambiguity of the structure of the acid chloride derived by treating 1,8-naphthalic anhydride with 1 equivalent of $PCl_5$. We have shown conclusively (from its unsymmetrical nmr spectrum) that it is the pseudo acid chloride **10**. We have also found that 1,8-naphthalic anhydride reacts with 2 equivalents of $PCl_5$ to give the previously unknown tetrachloride **11**.



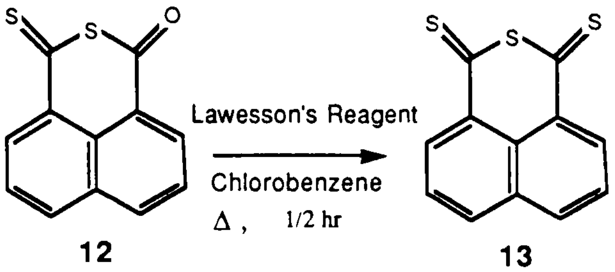
**11** **10**

Pseudochloride **10** reacts with Lawesson's Reagent in boiling chlorobenzene to give a 40% yield of dithionoanhydride **9**. In contrast, the tetrachloride **11** does not undergo thionation. Dithionoanhydride **9** is quantitatively isomerized to the thiolothione anhydride **12** by treatment with a trace of triethylamine in DMF. The unsymmetrical pattern in the nmr spectrum of **10**, and the appearance of a $>$CO band in its ir spectrum is in accord with the assigned structure.



**9** **12**

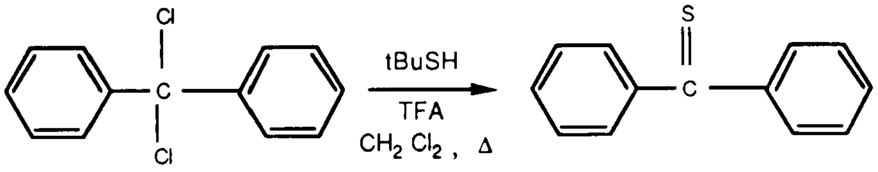
In contrast to **9**, anhydride **12** undergoes rapid thionation to the trithioanhydride **13** within an half hour. Trithioanhydride **13** forms black irridescent needles and its nmr spectrum is symmetrical, like that of **9**.

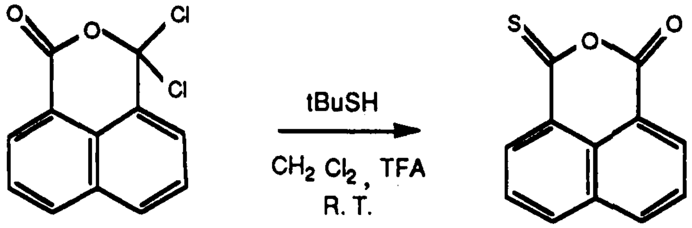


An X-ray structure determination was carried out.[9]

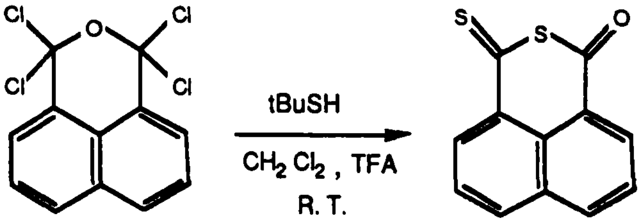
In contrast to the acyclic trithioanhydrides reported in the literature, 1,8-naphthalic trithioanhydride is extremely stable and can be stored under ambient laboratory conditions indefinitely. The black color of the crystals in the solid state can be ascribed to the nature of the packing in the crystal which could lead to internal charge-transfer.

In 1978, Pedersen et al. reported the synthesis of thiobenzophenone by heating diphenyldichloromethane with t-butyl mercaptan in the presence of trifluoracetic acid in methylene chloride solution.[10] In view of the ready accessibility of the pseudo acid chloride **10** and the tetrachloride **11**, the Pedersen reaction was attempted with these substrates. Pseudochloride **10**, upon treatment with tBuSH and TFA in methylene chloride at room temperature, furnished a highly crystalline red anhydride which was identified as the unknown thionoanhydride **14**. On the other hand, the tetrachloride **11** furnished the green thiolothiononaphthalic anhydride **12**, instead of the expected dithiononaphthalic anhydride **9**.





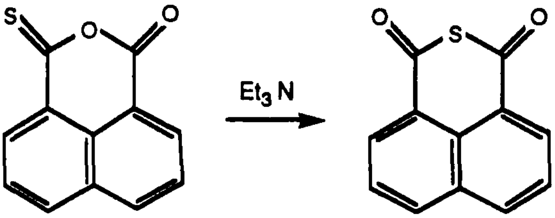
**10** **14**



**11** **12**

Anhydride **12** had been made previously by the base-catalyzed rearrangement of **9**. Treatment of **9** with tBuSH in $CH_2Cl_2$ containing TFA, did not convert it into the green isomer **12**, eliminating the possibility of an acid-catalyzed isomerization of **9**.

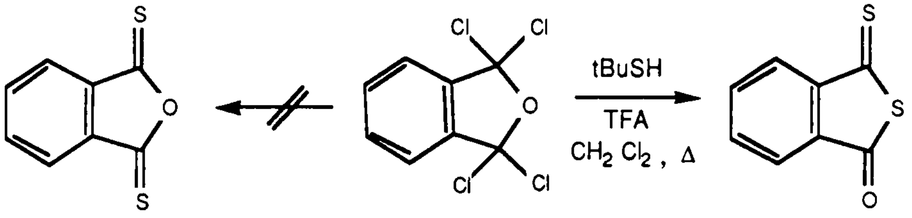
The thionoanhydride **14** underwent base catalyzed rearrangement to the yellow thiolonaphthalic anhydride **15**, as expected. We now feel that the orange thioanhydride, reported in the literature,[7] by treatment of the acid chloride (which we now know to be the pseudochloride) with $H_2S$ in boiling xylene is indeed the thiono isomer **14**. We have not yet confirmed this experimentally and plan to do so.



**14** **15**

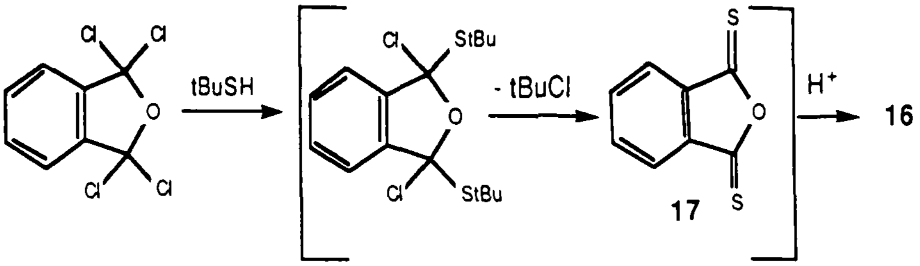
Having synthesized all the five sulfur analogs of naphthalic anhydride, we turned our attention to the problem of the sulfur analogs of phthalic anhydride. At the beginning of our investigation, the only well-known sulfur analog was the thioloanhydride **6**, made by treatment of phthalic anhydride with sodium sulfide and reacidification.[11] We have now found that this reaction is best done under phase transfer conditions to obtain **6** in reproducible yields. Sharts and Fong reported the formation of the thiono isomer **8** by treatment of phthaloyl chloride with hydrogen disulfide in the presence of $ZnCl_2$. They also reported that **8** appeared to be unstable and isomerized to **6** during attempted purification.[6] This is in marked contrast to the situation in the 1,8-naphthalic anhydride series, where the monothiono analog is very stable.

Since tetrachlorophthalan **15** is easily prepared from phthalide and $PCl_5$, we were interested in carrying out the Pedersen reaction with it. The reaction yielded, after 15 h reflux, a 47% yield of the green thiothionophthalic anhydride **16**, and not the dithiono isomer **17**.[12]

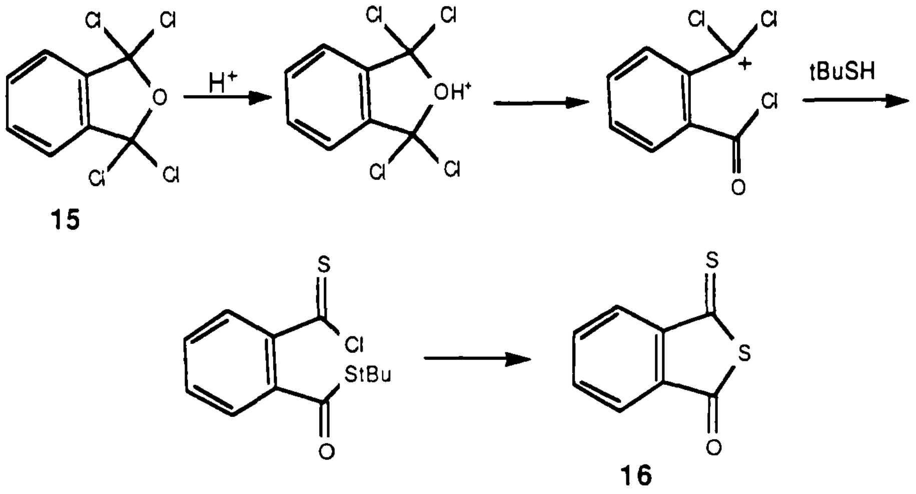


**17** **15** **16**

This result is entirely analogous to that observed in the naphthalene series. Originally we had assumed that **17** was formed and rearranged to **16** under the reaction conditions.

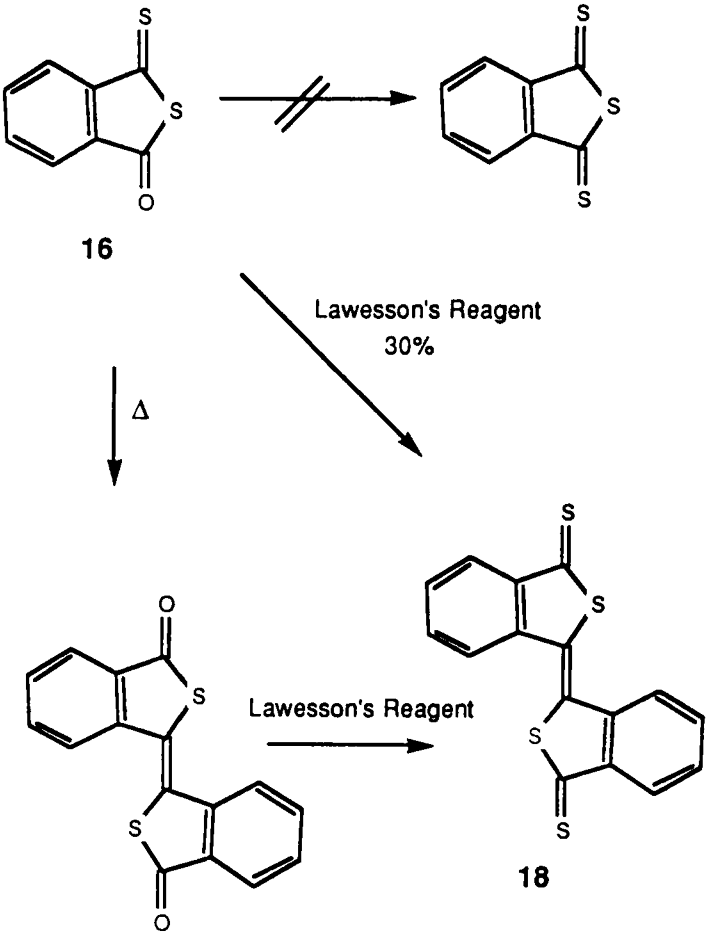


In view of the fact, that the dithiono anhydride **9** does not rearrange to the isomer **12**, we feel there must be an unifying mechanism explaining these results. We now propose an alternate mechanism for the formation of **16**, proceeding via the thionoacid chloride.

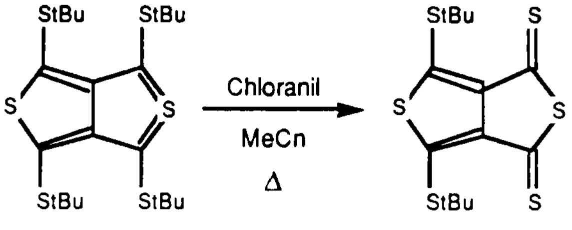


Such a mechanism will be equally applicable to the naphthalic anhydride series.

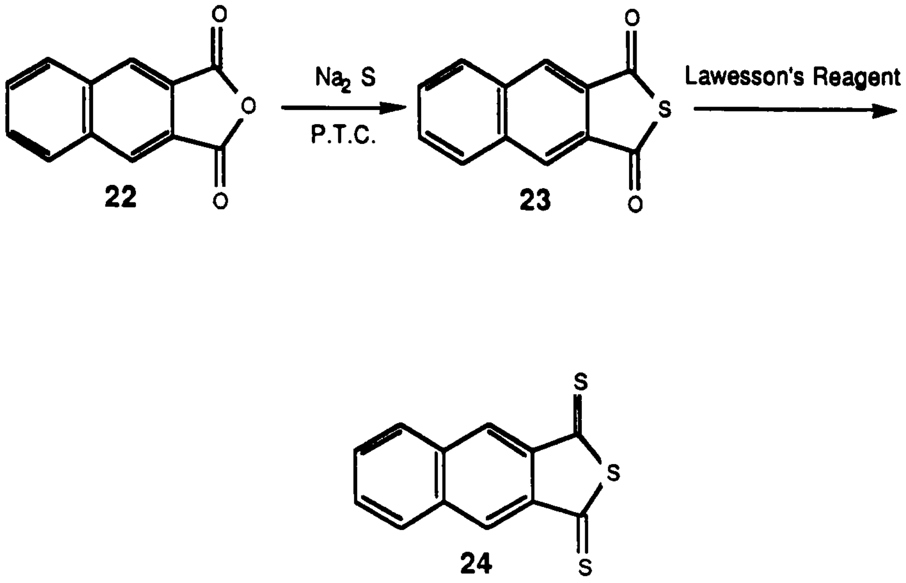
Having obtained **16** in reasonable yield, its further thionation to trithiophthalic anhydride **17** was attempted. In contrast to the 1,8-naphthalic series, thiolothionophthalic anhydride, upon thionation with Lawesson's Reagent, gave rise to a black polymeric material from which tetrathiobiphthalide **18** was isolated in 30% yield as black needles. Its structure was confirmed by independent synthesis from **16** via **19** as follows:



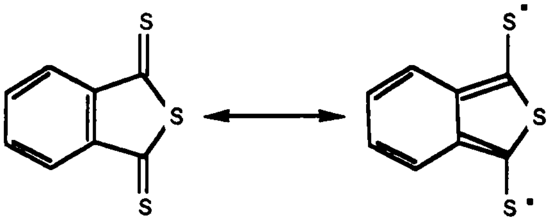
During the time of this study, Yoneda et al. reported the synthesis of the first stable five-membered trithioanhydride **21** by an unusual reaction, namely the oxidation of a stable nonclassical thienothiophene **20** using chloranil.[13]



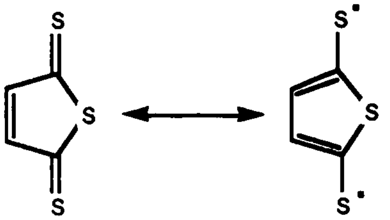
Having failed to prepare **17**, we extended our investigation to the 2,3-naphthalic anhydride series. The 2,3-naphthalic anhydride **22** was readily converted to the thioloanhydride **23** by treatment with $Na_2S$ under phase-transfer conditions. The thioloanhydride could be thionated, albeit in low yield, to the trithioanhydride **24**, which forms long black needles and is very stable under laboratory conditions.

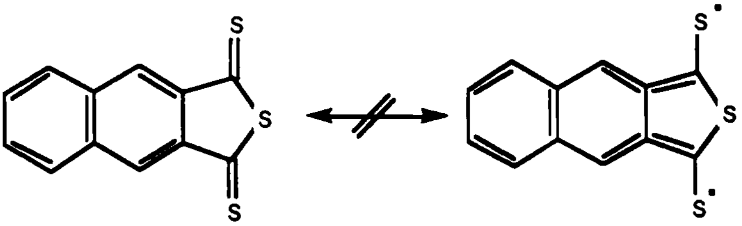


We can now explain the inherent instability of trithiomaleic anhydride and of trithiophthalic anhydride as a result of the increased contribution from diradical structures. Such diradical structures are not of great importance in the case of **21** or **24**, thereby making these accessible. Work is in progress to modify the trithiophthalic anhydride structure in such a way as to destablize the diradical contributor, which should lead to the isolation of substituted trithiophthalic anhydrides.

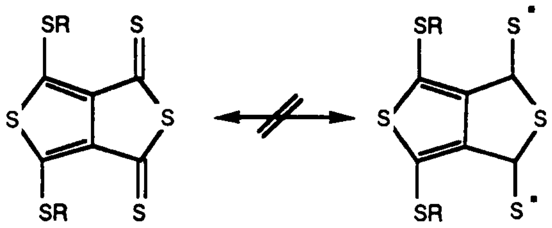


**17**



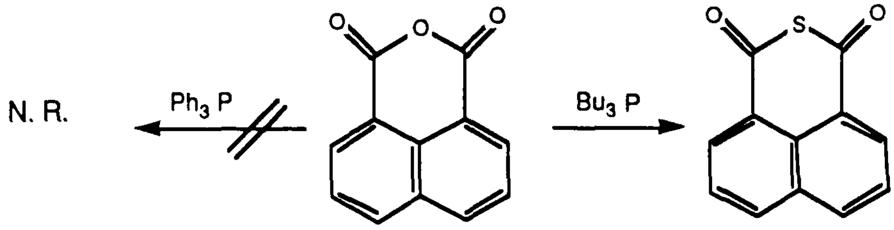


**24**



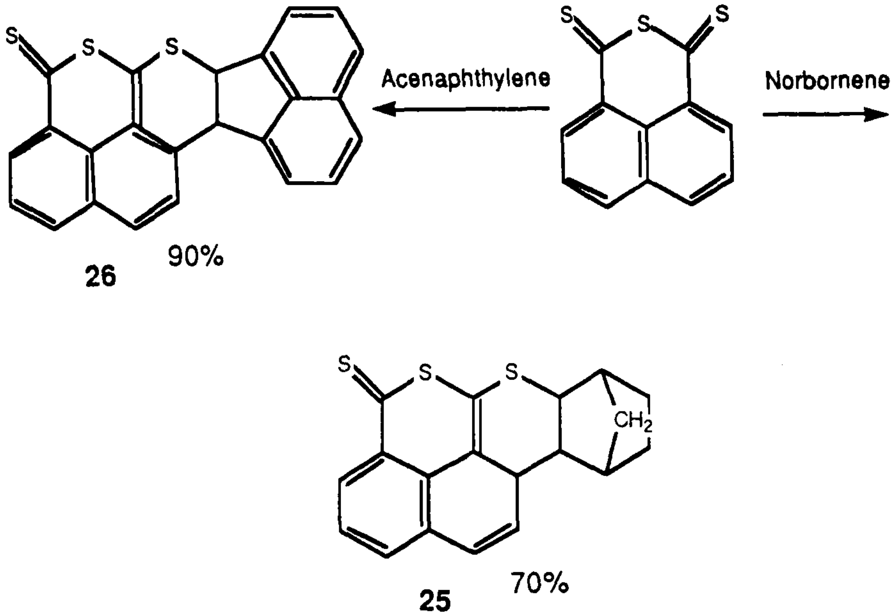
**21**

The remainder of the lecture will describe some unusual reactions of several thionaphthalic anhydrides. Desulfurization of thionoanhydride **14** was attempted using $Ph_3P$ leading to the recovery of starting material. On the other hand, the use of $Bu_3P$ led to the isolation of the thiolo isomer **15**.

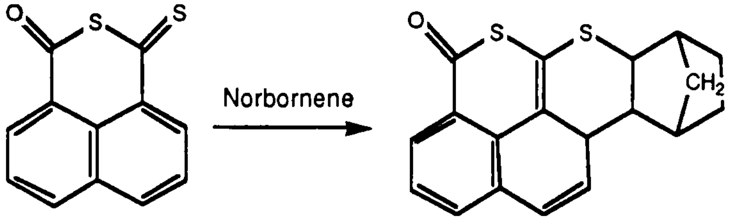


**14** **15**

1,8-Trithionaphthalic anhydride undergoes an inverse demand cycloaddition with electron-rich strained olefins such as norbornene and acenaphthylene, to give adducts **25** and **26**.

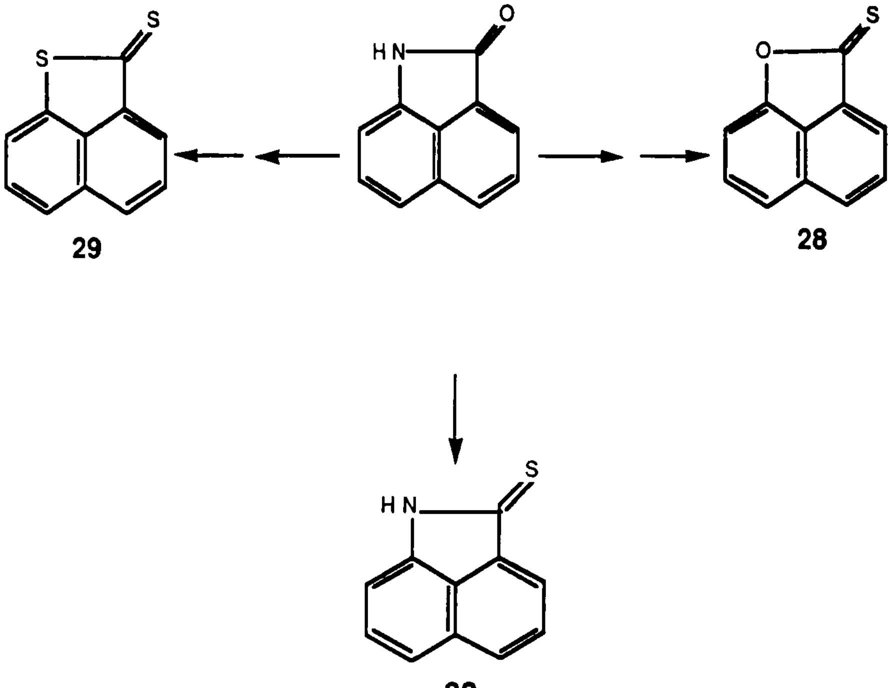


Likewise, the green anhydride **12** reacts with norbornene to give **27**.



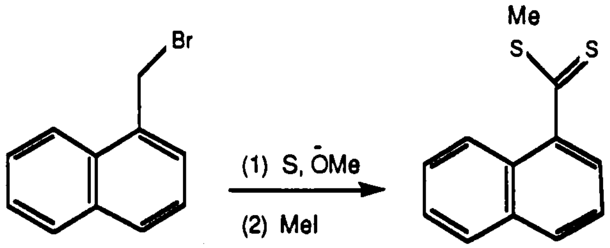
**12** **27**

This result led us to investigate the propensity of other thiocarbonyl substituted naphthalenes to undergo such inverse demand cycloaddition. Substrates **28** - **31** were synthesized as shown below.



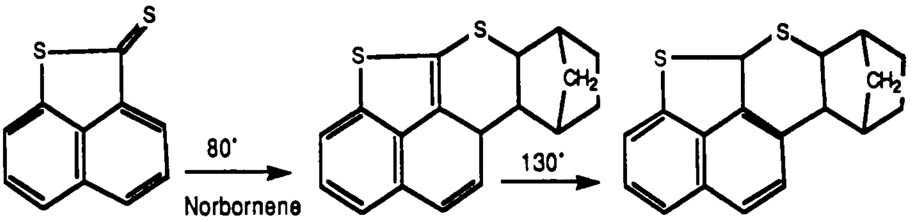
**29** **28**

**30**



**31**

Substrates **28**, **30**, and **31** failed to react with norbornene. The dithiolactone **29**, however, added norbornene to give adduct **32** at 80°. Prolonged heating at 130° led to a 1,3-hydrogen shift leading to aromatization of the naphthalene moiety in **32**, giving adduct **33**.



**29** **32** **33**

Further studies on cyclic thioanhydrides is in progress in our laboratories. Most of our efforts until now have focused on a search for practical methods of synthesis, but future investigations will undoubtedly uncover many new and unusual chemical transformations of these compounds.

## Acknowledgement

We wish to acknowledge the collaboration of Drs. M. S. Raasch, N. Z. Huang, and Mr. W. Chen in this project. Financial support from the National Science Foundation, which made this work possible, is hereby gratefully acknowledged.

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