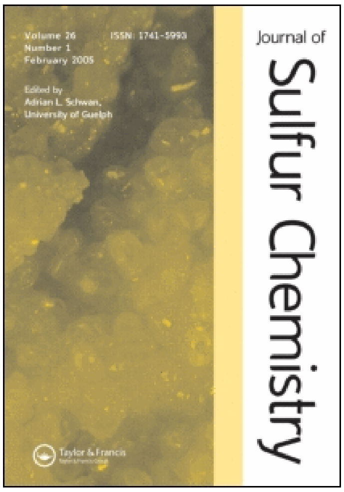

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Recent Studies on the Reactions of Thioaldehydes and Thioketones

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RECENT STUDIES ON THE REACTIONS OF THIOALDEHYDES AND THIOKETONES

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The present review deals with the recent reactions of thioaldehydes and thioketones. The references cover the reaction with dienes, dienophiles, 1,3-dipoles, and diplarophiles mainly from 1995.

Keywords: Thioaldehyde; Thioketone; Olefin; Diene; Benzyne; Alkene; Trithiolane; Benzothiete; Cycloaddition

CONTENTS

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1. INTRODUCTION

Since the beginning of the 19th century, the chemistry of aldehydes has been extensively explored. However, their thio analogs, thioaldehydes, have been thought of as intermediates. In 1960, Woodward and coworkers synthesized the first example of a stable thioaldehyde [1].

Generally, thioaldehydes are unstable due to the low polarization and can only be isolated under special conditions. For this reason, simple thioaldehydes are detected under low temperature or by their reaction products with alkenes. For example, thioaldehydes react with dienes to afford the corresponding [4 + 2] cycloadducts.

On the other hand, thioketones are relatively stable; first isolation of 4,4′-dimethoxythiobenzophenone was reported in 1895 by Gattermann [2]. Since the first isolation of thiobenzophenone, many reactions of thiobenzophenones with olefins were carried out. For example, the photochemical-promoted reaction of 1,3-dimethyl-2-thioparabate with dimethyl acetylenedicarboxylate provided the initial [2 + 2] adduct, which finally produced a 1 : 2 adduct *via* a [4 + 2] cycloaddition reaction.

In 1995, an excellent review of thiocarbonyl compounds were given by Whittingham [3]. This review summarizes the recent synthesis and reactions of thiocarbonyl compounds. For the purpose of this work, reactions of thiocarbonyl compounds with a range of dienes and dienophiles are treated along with brief introductions since 1995.

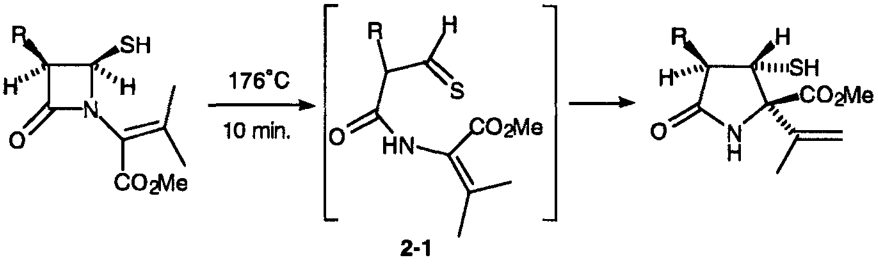
2. THIOALDEHYDES

2.1 Formation of Thioaldehydes

Until 1980, thioaldehydes were relatively unknown compounds. Duus describes two examples of stable thioaldehydes in his review, which were reported by Woodward *et al.* and Reid *et al.* [4,5].

The first convincing evidence for the formation of reactive thioaldehydes was reported in the 1980s. Baldwin and coworkers reported the synthesis of a γ-lactam from 4-mercaptoazetidin-2-one via a thioaldehyde intermediate (**2-1**) (Scheme 2-1-1) [6].

An application to natural product synthesis was performed by Vedejs and coworkers. They have developed the Norrish type II photolytic cleavage of phenacyl sulfides into a versatile method for the synthesis of thioaldehydes [7], which react with dienes to afford the corresponding [4 + 2] cycloadducts (Scheme 2-1-2) [8].



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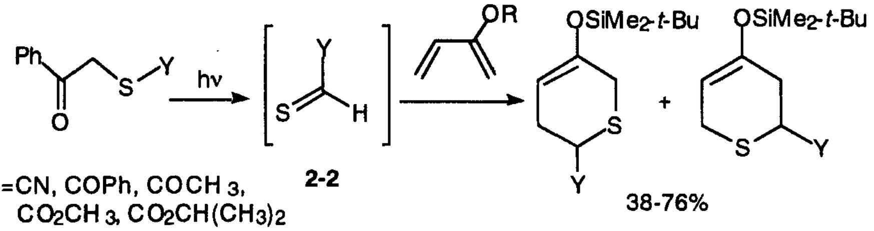

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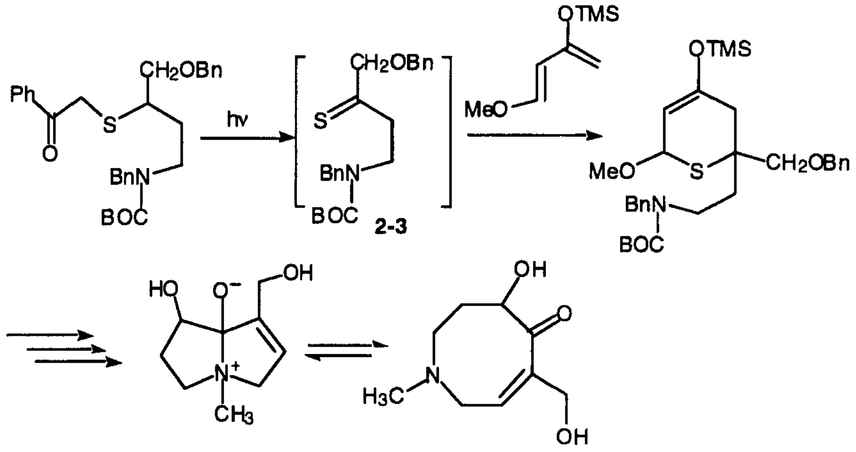


SCHEME 2-1-3

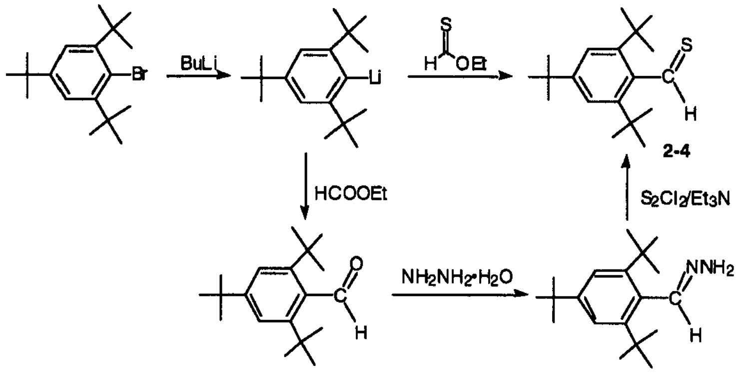
The total synthesis of cyctochalasans and zygosporin E was accomplished using this methodology [9]. More recently, Vedejs's group have reported the synthesis of Otonecine by a key step thio-Diels-Alder reaction of thioketone (**2-3**) derived from phenacyl sulfide with the Danishefsky diene (Scheme 2-1-3) [10].

The first kinetically stabilized aromatic thioaldehyde, 2,4,6-tri-*tert*-butylthiobenzaldehyde (**2-4**), was prepared by the reaction of 2,4,6,-tri-*tert*-butylphenyllithium with O-ethyl thioformate. This compound was also synthesized by the reaction of 2,4,6-tri-*tert*-butylbenzaldehyde hydrazone with disulfur dichloride in the presence of triethylamine (Scheme 2-1-4) [11].

This thioaldehyde is remarkably stable: it can be stored in the solid state at room temperature for several years. Upon heating at higher temperatures (*ca.* 200°C) in a degassed benzene solution, thioaldehyde **2-4** undergoes an intramolecular cyclization involving its thioformyl group to give a dehydrothiopyran almost quantitatively (Scheme 2-1-5).

Compound **2-4** undergoes [4 + 2] cycloaddition with 2,3-dimethyl-1,3-butadiene at 160°C and [3 + 2] cycloadditions with diphenylnitrilimine and mesitonitrile oxide at room temperature. Other reactions were also reported (Scheme 2-1-6) [12].

The synthesis of 2,4,6-tris[*bis*(trimethylsilyl)methyl]phenylthiobenzaldehyde (**2-5**) is based on desulfurization of two related cyclic polysulfides by triphenylphosphine.



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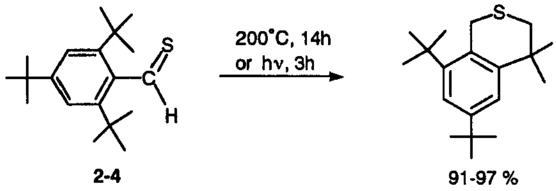

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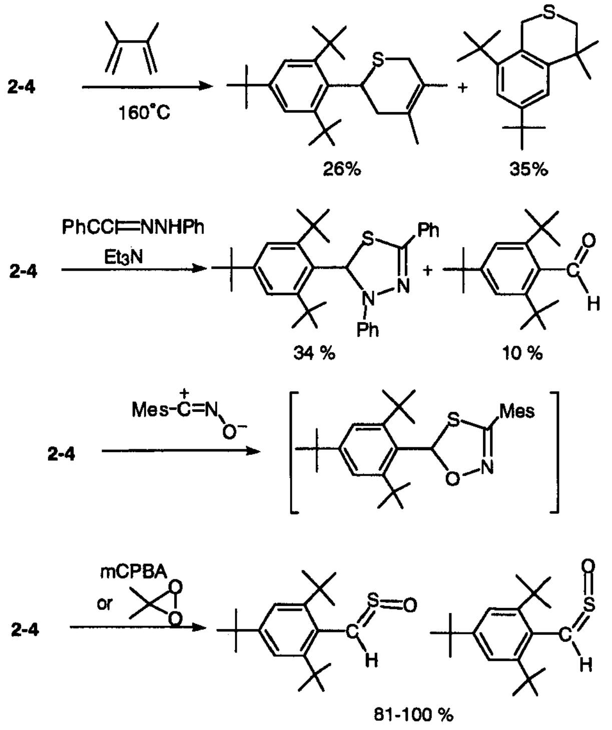
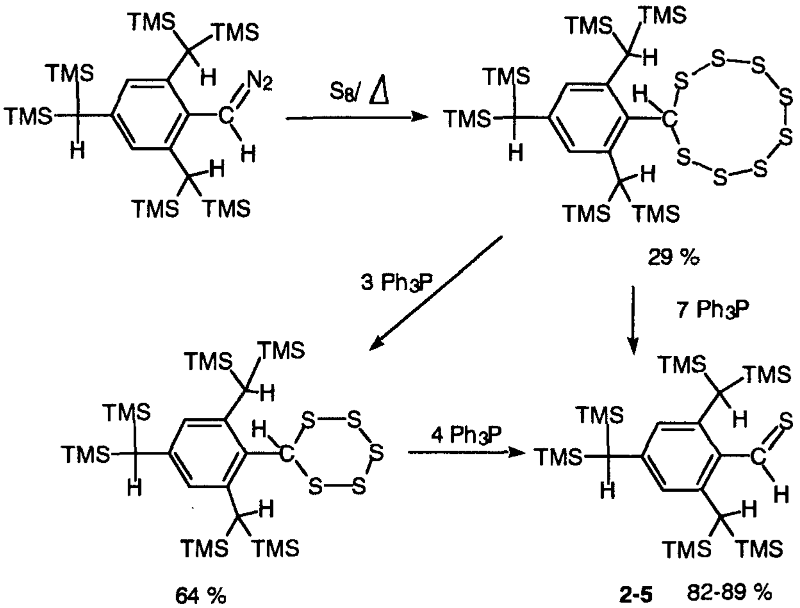


SCHEME 2-1-6

Interestingly, both cyclic polysulfides gave the two same stable rotational isomers (Scheme 2-1-7) [13].

These rotational isomers (**2-5**) reacted with hydrazine monohydrate in dichloromethane at 0°C to afford the corresponding hydrazone in almost quantitative yields. Treatment of **2-5** with mCPBA in dichloromethane at −78°C resulted in the formation of the corresponding (*E*)-sulfine in 89% yield (Scheme 2-1-8).



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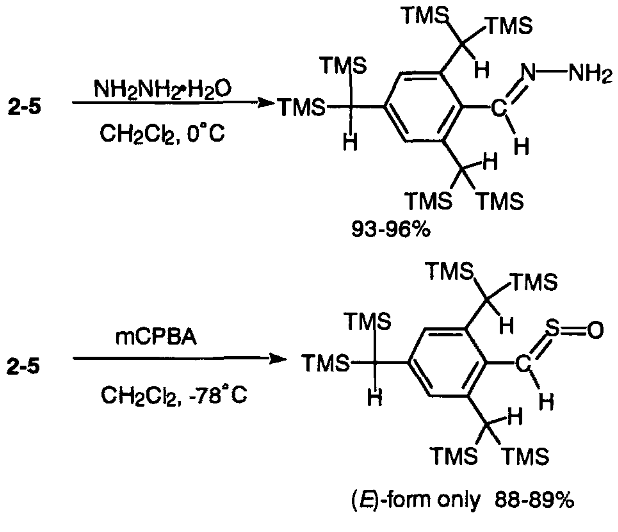


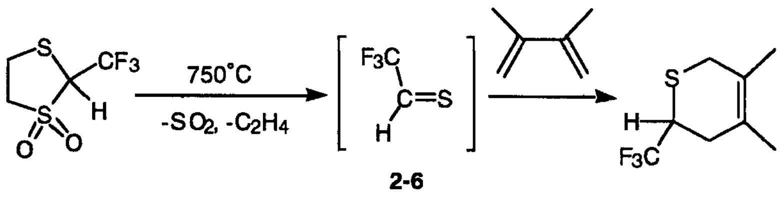
SCHEME 2-1-8

2.2 Reaction of Thioaldehydes with Dienes

The highly reactive trifluorothioacetoaldehyde (**2-6**) was synthesized by thermolysis of 2-(trifluoromethyl)-1,3-dithiolane 1,1-dioxide. The formation of **2-6** was confirmed by spectroscopy and by preparation of Diels-Alder adducts such as that with 2,3-dimethyl-1,3-butadiene (Scheme 2-2-1) [14].

The reaction of phosphorus ylides with thiopivaloaldehyde (**2-7**) gave the corresponding episulfide, which was finally converted to the olefin (**2-8**) by the reaction with butyllithium (Scheme 2-2-2) [15].

Thiophilic reaction of phosphorus ylides with thiiranes affords the corresponding thioaldehydes (**2-9**), which further react with ylides to give olefins (Scheme 2-2-3) [16]. The formation of **2-9** was confirmed by their reactions with dienes.



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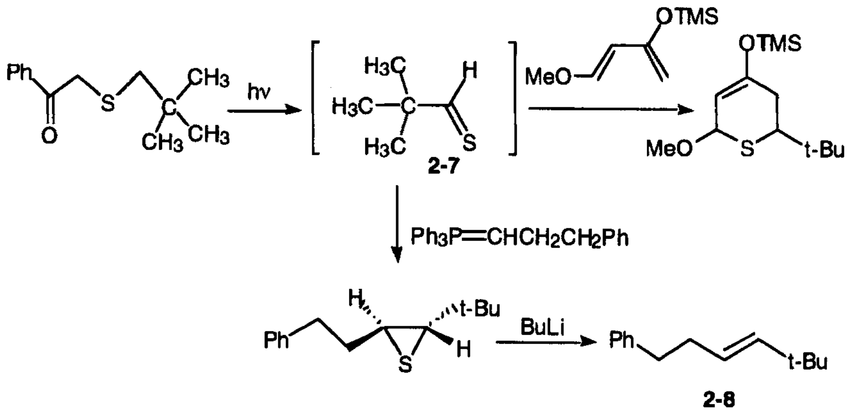

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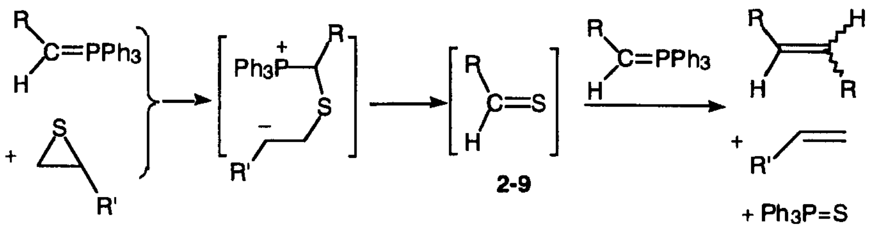


SCHEME 2-2-3

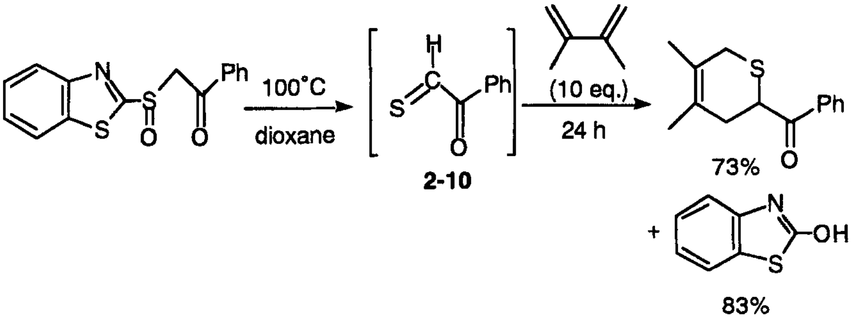
Thioaldehydes containing electron-withdrawing groups (**2-10**) were formed by thermolysis of benzothiazoyl sulfoxides. The yields of their adducts with 2,3-dimethyl-1,3-butadiene were in the range of 28–89% (Scheme 2-2-4) [17].

2.3 Other Reactions of Thioaldehydes

Stable 6-amino-5-thioformyluracils (**2-11**) were prepared starting from 6-amino-1,3-disubstituted uracils in 42–98% yields. These thioaldehydes are stable at room temperature. When hydrolysis of **2-11** was carried out in refluxing 50% EtOH, the corresponding aldehyde (70%) and isothiazolo[3,4-d]pyrimidines (17%) were obtained (Scheme 2-3-1) [18].

The reaction of thioaldehyde (**2-11**) with amines or phosphorus ylide afforded a new type of urasil compound (Scheme 2-3-2) [19].

Mloston *et al.* reported the ring-opening reaction of spirocyclic 2,5-dihydro-1,3,4-thiadiazoles. These compounds reacted with cyclic secondary amines at room temperature to give *N*-alkylidenehydrazones. They proposed the thioaldehyde intermediate (**2-12**) in this base-catalyzed transformation (Scheme 2-3-3) [20].



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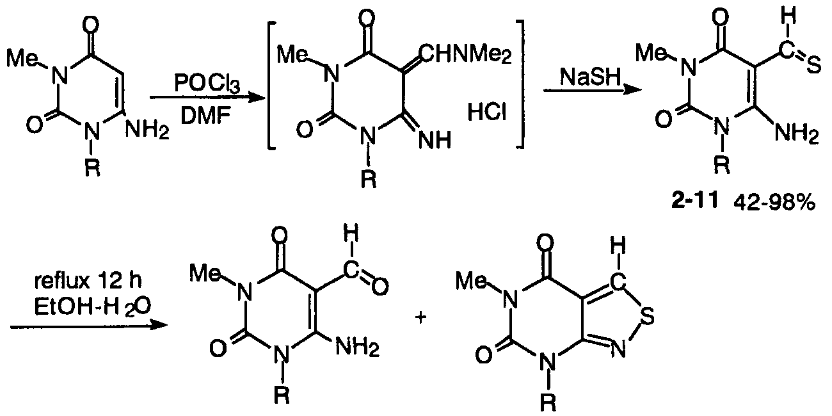

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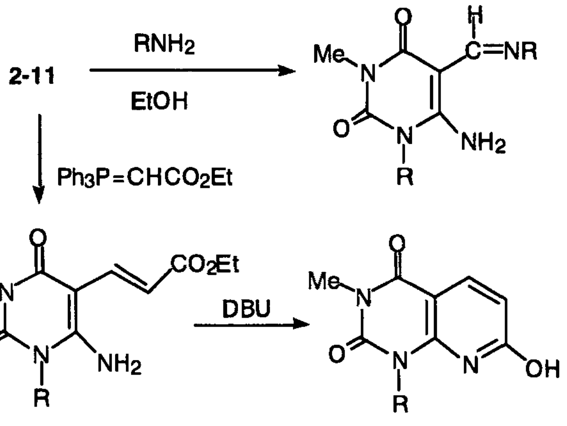

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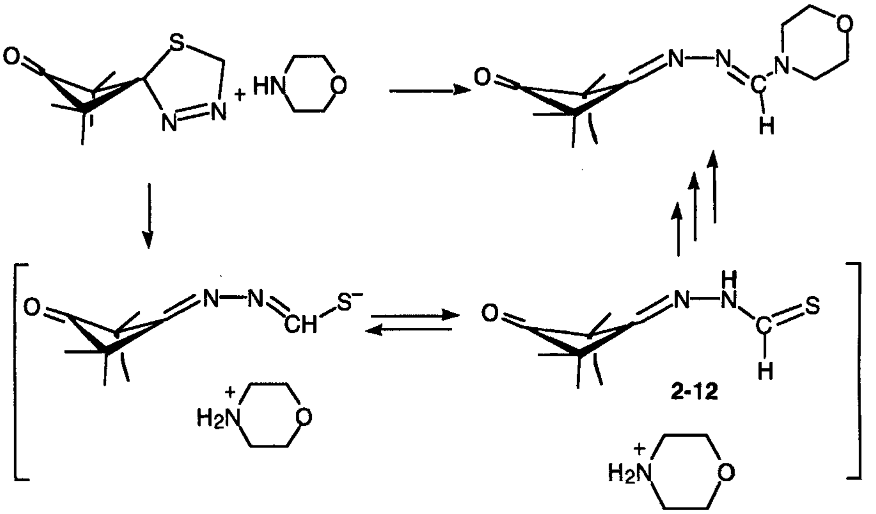


SCHEME 2-3-3

3. THIOKETONES

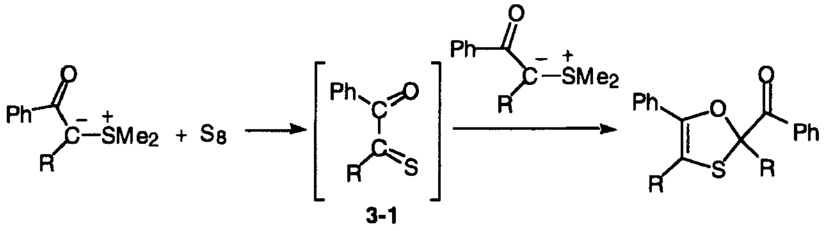
3.1 Synthesis of Thioketones from Ylides

Sulfonium ylides are well known methylene transfer reagents. Initial study includes the synthesis of epoxides by the reaction with carbonyl compounds (Corey and Chaykovsky reaction) [21]. Carbonyl-stabilized sulfonium ylides reacted with elemental sulfur to afford 1,3-oxathiols in good ylides. The intermediates should be the corresponding thioketones (**3-1**) (Scheme 3-1-1) [22].

It is widely known that Wittig reagents react with carbonyl compounds to produce the corresponding olefins. In 1953, Wittig and Geisler isolated methylenetriphenylphosphorane and found that this reagent reacted with benzophenone to give 1,1-diphenylethylene and triphenylphosphine oxide [23]. This reaction was applied to the industrial synthesis of Vitamin A. Surprisingly, the reaction of phosphorus ylides with elemental sulfur was already carried out by Staudinger and Meyer in 1919 (Scheme 3-1-2) [24]. The generality of this reaction to afford ArAr′C=S (**3-2**) was confirmed in 1972 [25].

By applying this method, trioaldehydes **2-9** were formed by the reaction of phosphorus ylides with elemental sulfur. This method provides a general method on the formation of thioaldehydes and thioketones (Scheme 3-1-3) [26].

The precise reaction mechanism for the reaction between thiobenzophenone (**3-2**) and methylenetriphenylphosphorane was carried out by Erker *et al.* [27].



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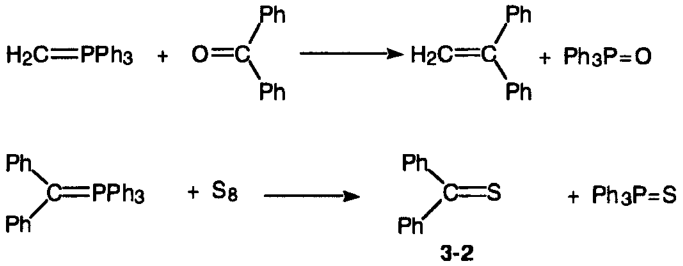

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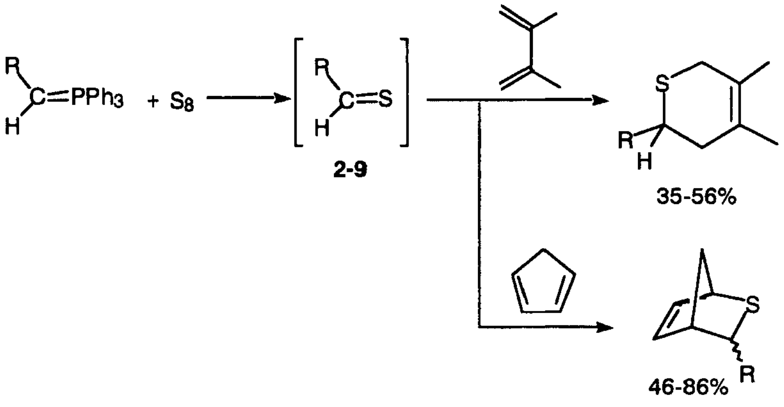


SCHEME 3-1-3

They observed a thiaphosphetane intermediate at – 20°C, which equilibrated to styrene sulfide and triphenylphosphine at 0°C. The final products were diphenylethylene and triphenylphosphine sulfide (Scheme 3-1-4) [27].

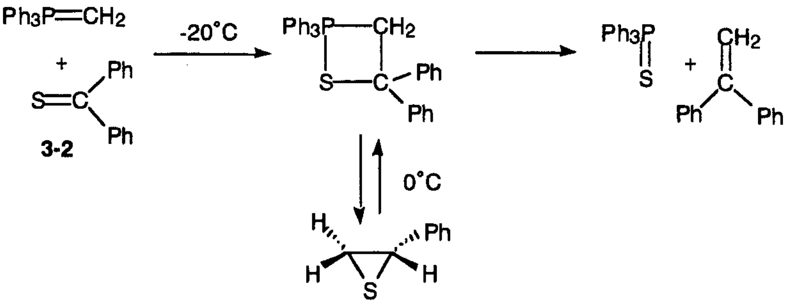
3.2 Synthesis of Thioketones from Lawesson's Reagent

Lawesson's reagent is still a good choice to convert ketones into thioketones. Montenegro and coworkers reported the synthesis of 10-methylthiocamphorthione (**3-3**) by the reaction of 10-methylthiocamphor with Lawesson's reagent. They prepared (2*R*-exo)-2,10-*bis*(methylthio)bornane from thione **3-3** followed by additional two-step reactions [28]. This compound would be expected to be useful as a chiral ligand in enantioselective catalysis (Scheme 3-2-1).

3.3 Other Synthetic Methods of Thioketones

A new type of the synthesis of thioacylsilanes was provided by Degl'Innocenti *et al.* [29]. Silylated thiocarbonyl compounds (**3-4**) were prepared by the reaction of hexamethyldisilathiane with trimethylsilyl acetals derived from 1-(benzotriazol-1-yl)-1-phenoxy alkanes (Scheme 3-3-1) [29].

Thionation of ketones by hexamethyldisilathiane is a well known, simple and direct route on the synthesis of thioketones [30]. Acetylenic thioketones (**3-5**) and thioaldehydes were synthesized by reaction of *β*-silyl acetylenic ketones with hexamethyldisilathiane in the presence of trimethylsilyl triflate. The obtained thiocarbonyl compounds were trapped by reaction with 2,3-dimethyl-1,3-butadiene (Scheme 3-3-2) [31].



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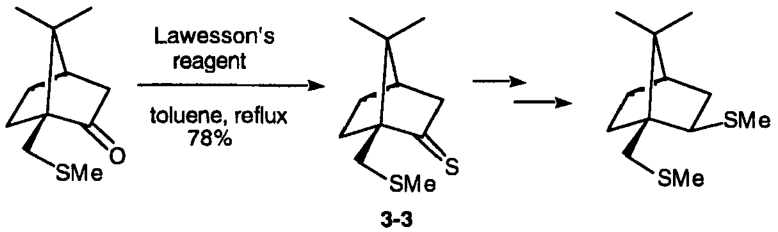

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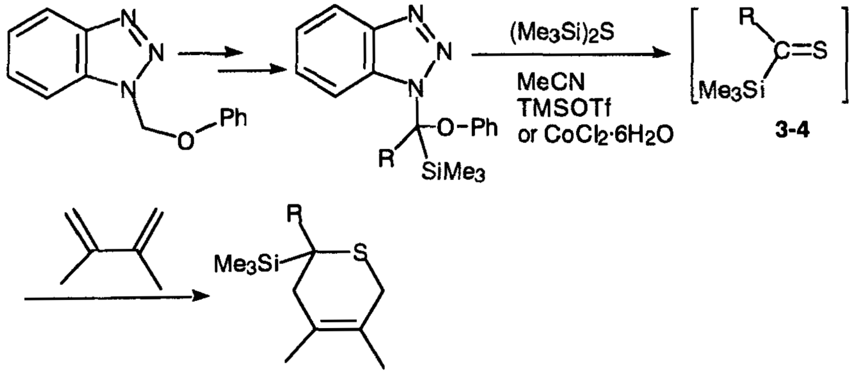

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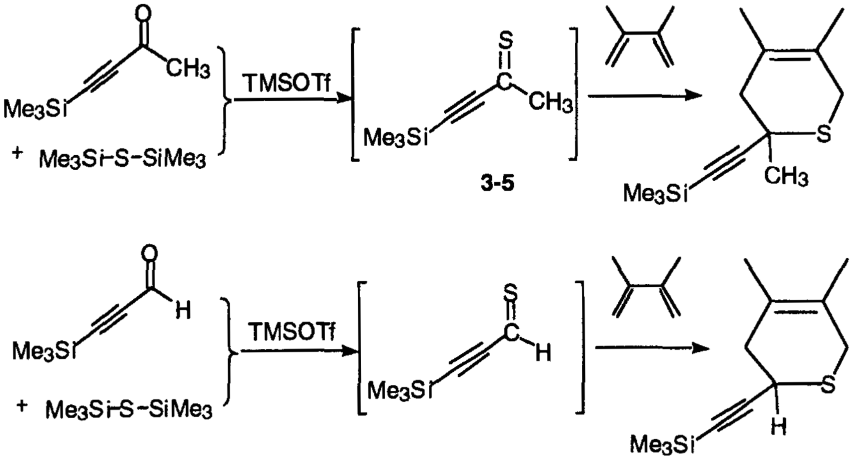


SCHEME 3-3-2

3.4 Generation of α,β-Unsaturated Thioketones

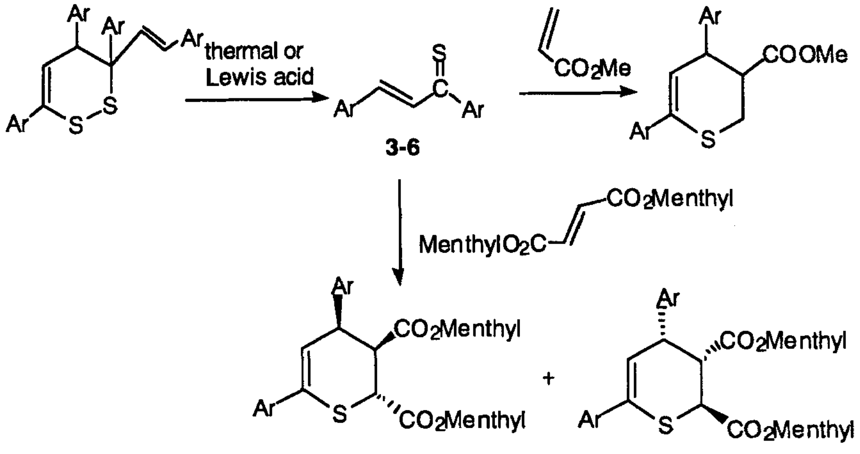
Unsaturated thioketones are generally obtained by thionation of the corresponding unsaturated ketones, and are trapped *in situ* with suitable dienophiles. Thermal and Lewis acid-promoted reaction of thiochalcones (**3-6**) with dimethyl or dimenthyl fumarate gave two 3,4-*cis*-cycloadducts in good ylides. However, their diastereoselectivities were moderate (Scheme 3-4-1) [32].

Enantiomerically pure diols were obtained by reduction of dihydrothiopyrans (Scheme 3-4-2) [33].

The hetero-Diels-Alder reactions of **3-6** with dienophiles using homochiral copper, nickel, and ytterbium triflate *bis*(imine)complex catalysts afforded enantiomerically pure dihydrothiopyrans (Scheme 3-4-3) [34].

Six ring-fused heterocycles were prepared by the sequential hetero-Diels-Alder and Diels-Alder reactions from divinyl thioketones (**3-7**) (Scheme 3-4-4) [35].

α,β-Unsaturated thioaldehydes and thioketones (**3-8**) were also synthesized *in situ* by the reaction of unsaturated carbonyl compounds with *bis*(dimethylaluminum) sulfide.



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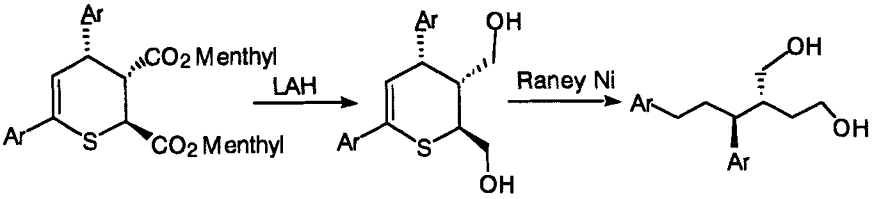

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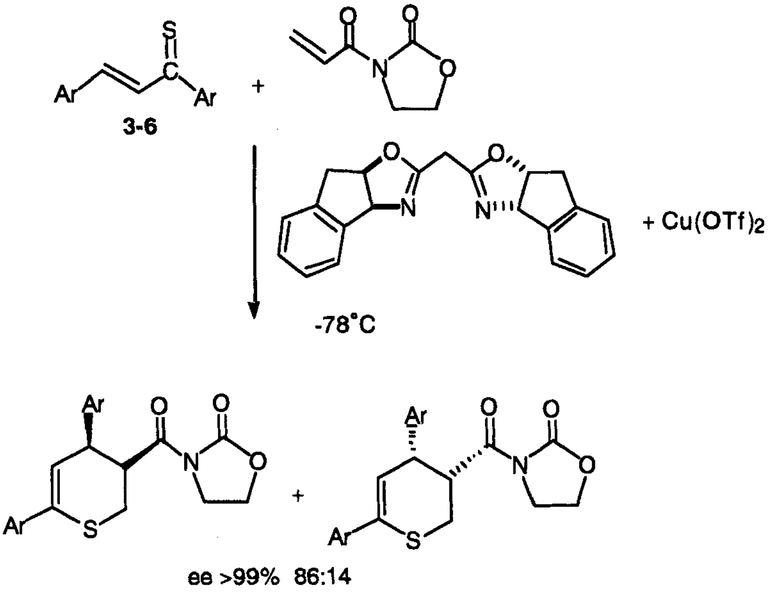

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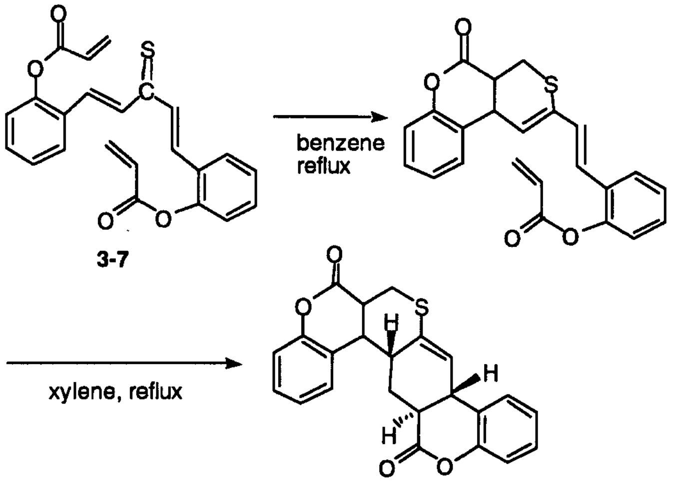

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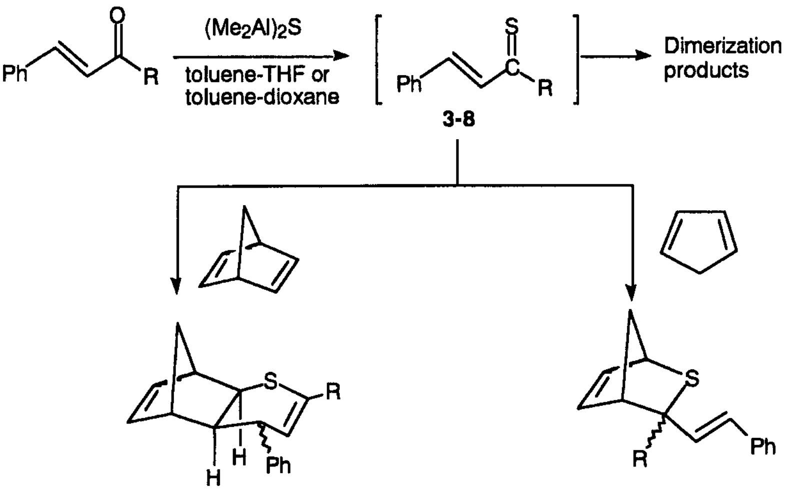
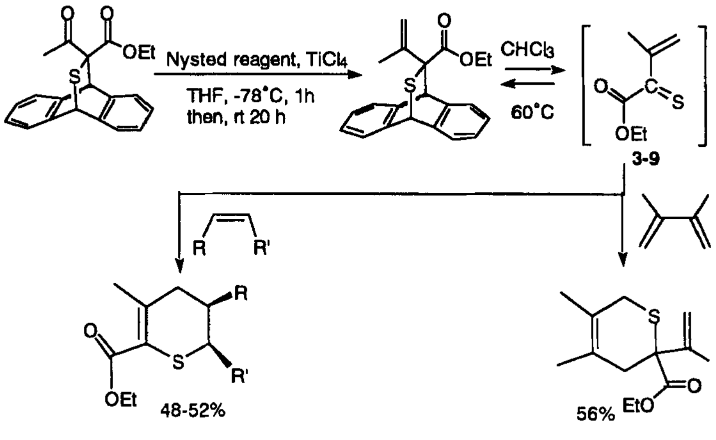


SCHEME 3-4-5

These thiones undergo [4 + 2] self-dimerization reactions in which one molecule serves as the heterodiene component and the other serves as the dienophile to afford different types of dimeric products. These differences in selectivity were explained on the basis of the relative energies evaluated by molecular orbital calculations (Scheme 3-4-5) [36].

Sometimes, direct thionation of the corresponding unsaturated ketones was unsuccessful due to a sterically hindered moiety or the tendency of self-condensation. Capozzi *et al.* [37] found a useful method for the generation of α,β-unsaturated thiones (**3-9**) by transformation of the ketone group of thione-cycloadducts into the corresponding methylenic group, which was thermally decomposed to α,β-unsaturated thioketones (Scheme 3-4-6) [37].



SCHEME 3-4-6

3.5 Reaction of Thioketones with Alkenes

In 1971, Ohno and coworkers reported the photoaddition of thiobenzophenones (**3-2**) with dimethyl acetylenedicarboxylate (Scheme 3-5-1) [38].

While a systematic survey of this reaction was only done recently, Breu *et al.* [39] have reported the reaction of **3-2** and thiofluorenones (**3-10**) with cyclic and open-chain dienes [39]. In the reaction of **3-2** with butadienes, ylides were around 25–60% at 20°C. By using **3-10**, much higher ylides were obtained (Scheme 3-5-2).

The reactivity of **3-10** toward 4π systems was so high that the cycloadducts were obtained in the reaction with electron-deficient 5,5-substituted 1,2,3,4-tetrachloro-1,3-cyclopentadienes (Scheme 3-5-3).

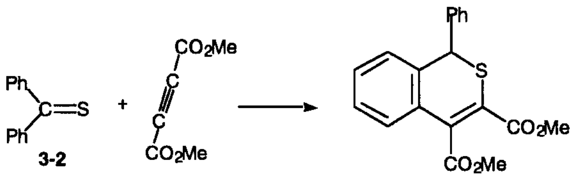
Ohmura and Motoki reported that the reaction of **3-2** with norbornene or maleic anhydride gave the corresponding [4 + 2] cycloadduct [40]. They applied this method to the synthesis of heterocycle-fused 2H-thiopyrans by using other aromatic thiones (**3-11**) (Scheme 3-5-4) [40].

Rapp and Huisgen reported the reaction of **3-2** with dienophiles (dimethylacetylenedicarboxylate, methyl propiolate, cyanoacetylene, and cyclooctene) [41]. The obtained products were 1H-2-benzothiopyrans (Scheme 3-5-5).

We have also reported the reaction of **3-2** with norbornadiene, which resulted in the formation of unusual products [42]. First, we thought that the obtained products were dihydrobenzothiepines. However, by analogy with selenobenzophenones, the products were found to be benzothiopyrans (Scheme 3-5-6) [42].

Tetracyanoethylene (TCNE) has played an important role in extensive applications in organic synthesis owing to its anomalous reactivity [43]. Previously Machiguchi *et al.* [44a] reported the reaction of tropothione (**3-12**) with TCNE to afford 8,8-dicyanoheptafulvene via a [2 + 2]-type cycloaddition [2]. Huisgen *et al.* [44b] reported that thiobenzophenone (**3-2**) reacted with TCNE to give 2 : 1 adducts of thiophene derivatives and six-membered dithiins in moderate ylides (Scheme 3-5-7) [44a–c].

Interestingly, 4,4′-dimethoxythiobenzophenone (**3-2b**) reacts with tetracyanoethylene to give different types of 2 : 1 adducts. The electron-donating group may cause the different reactivity. Actually, 4,4′-difluorothiobenzophenone (**3-2c**) reacted with TCNE to afford the normal type of 2:1 adduct (Scheme 3-5-8) [45].



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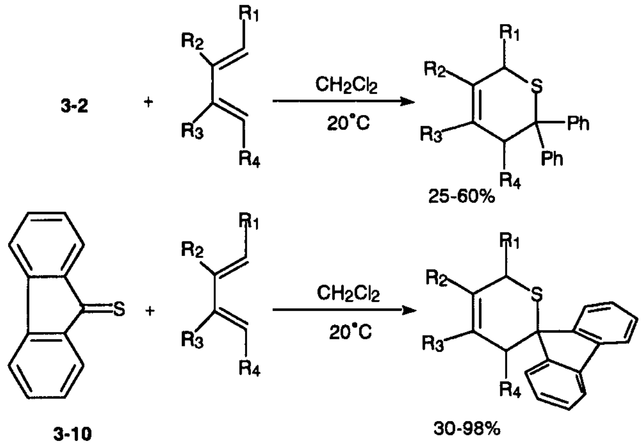

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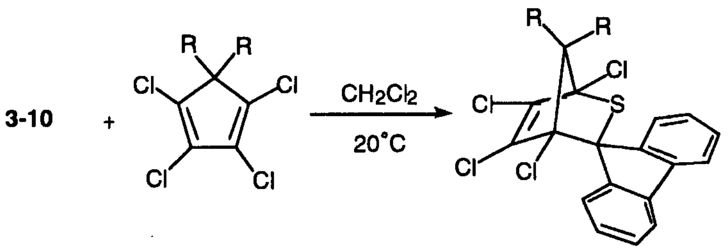

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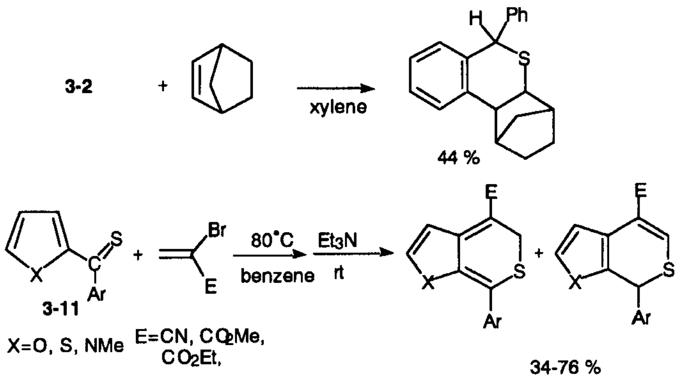

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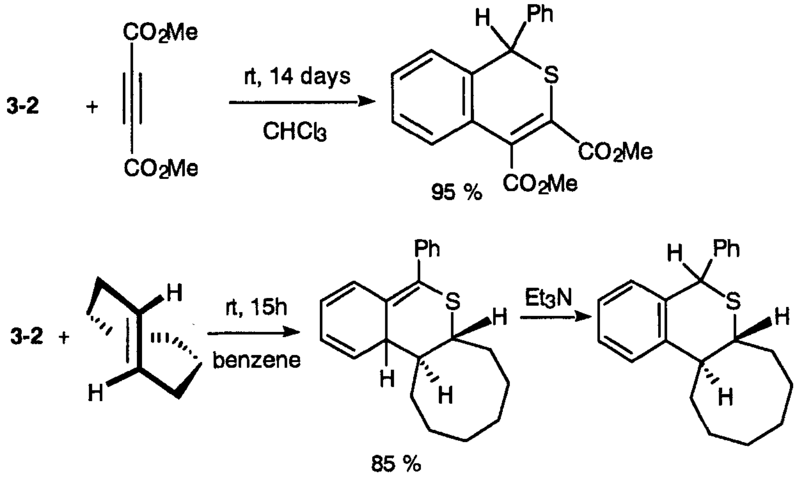
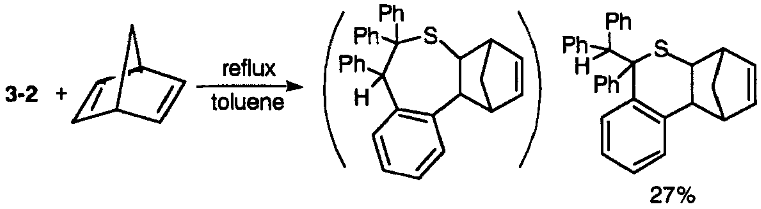
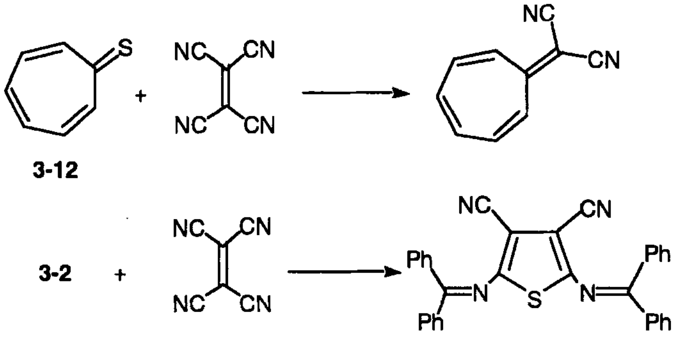


SCHEME 3-5-5



SCHEME 3-5-6

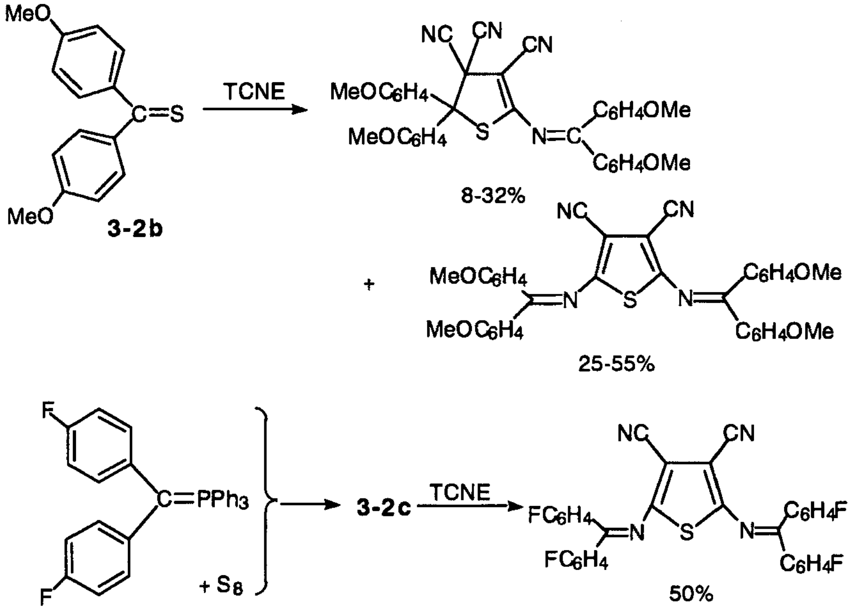


SCHEME 3-5-7

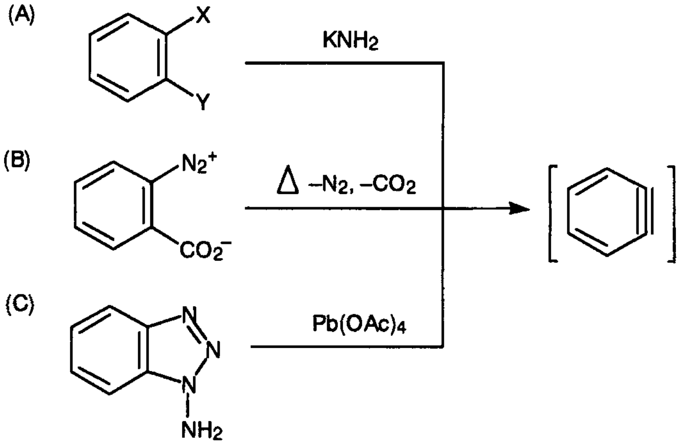
Selenobenzophenones also reacted with TCNE to give exclusively unsymmetrical 2 : 1 adducts [46].

3.6 Reaction of Thiocarbonyl Compounds with Benzyne

Benzyne is a reactive intermediate and reacts with many dienes to afford the corresponding cycloadducts [47]. Three major methods are commonly used to generate



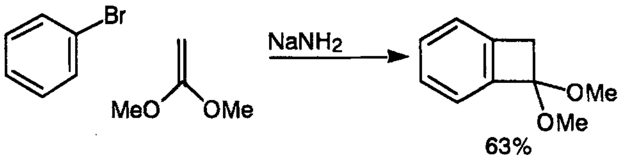
SCHEME 3-5-8



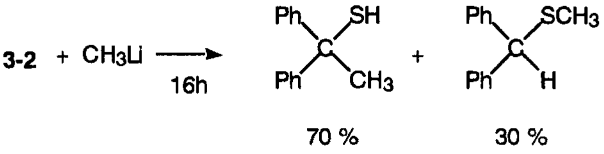
SCHEME 3-6-1

benzyne. These methods include: (A) base-induced reaction of dihalobenzene; (B) thermolysis of benzenediazonium or related carboxylates; and (C) oxidation of benzotriazoles or photolysis of heterocyclic systems (Scheme 3-6-1).

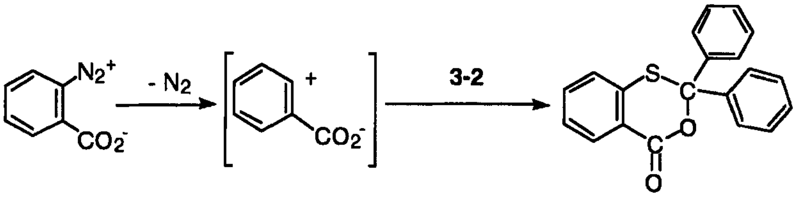
Generally, benzyne reacts with simple alkenes to give benzocyclobutenes in only moderate to low ylides in a [2 + 2] manner. Because of the electrophilic nature of benzyne, the reactions proceed best with alkenes bearing electron-donating substituents. Despite these limitations, the reaction sometimes offers a simple, direct and one-step route to useful synthetic intermediates (Scheme 3-6-2) [48].



SCHEME 3-6-2



SCHEME 3-6-3



SCHEME 3-6-4

However, these methods are not adequate to react with thiocarbonyl compounds: basic conditions, strong nucleophiles, photoreaction, or oxidizing reagents should be avoided. For example, reaction of **3-2** with alkyllithium led to the thiophilic and carbophilic adducts (Scheme 3-6-3) [49].

The only reported example was the reaction of **3-2** with benzenediazonium 2-carboxylate. In this case, the zwitter ionic intermediate reacted with **3-2** to give the corresponding adducts (Scheme 3-6-4) [50].

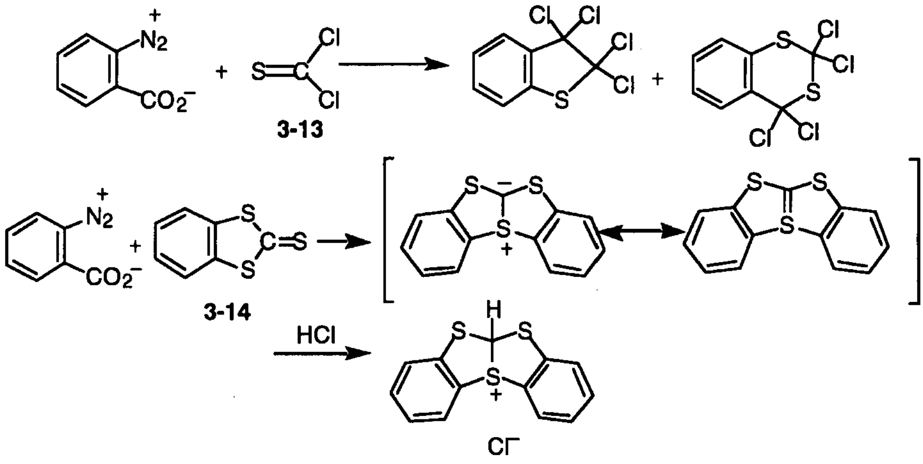
Related examples include the reaction of benzyne with thiosphosgene (**3-13**) and the formation of dibenzotrithiocin derivatives from the reaction of 1,3-benzodithiole-2-thione (**3-14**) with benzyne (Scheme 3-6-5) [51].

Benzyne is a necessary intermediate in the diazotization of 2-[(2-acetoxyethyl)sulfinyl-anilines. Aprotic diazotization of anilines afforded biphenylene and dibenzo-1, 4-thiooxin. Formation of oxin required cleavage of the SO bond, most probably via benzooxathiete or thione (**3-15**) as shown in Scheme 3-6-6 [52].

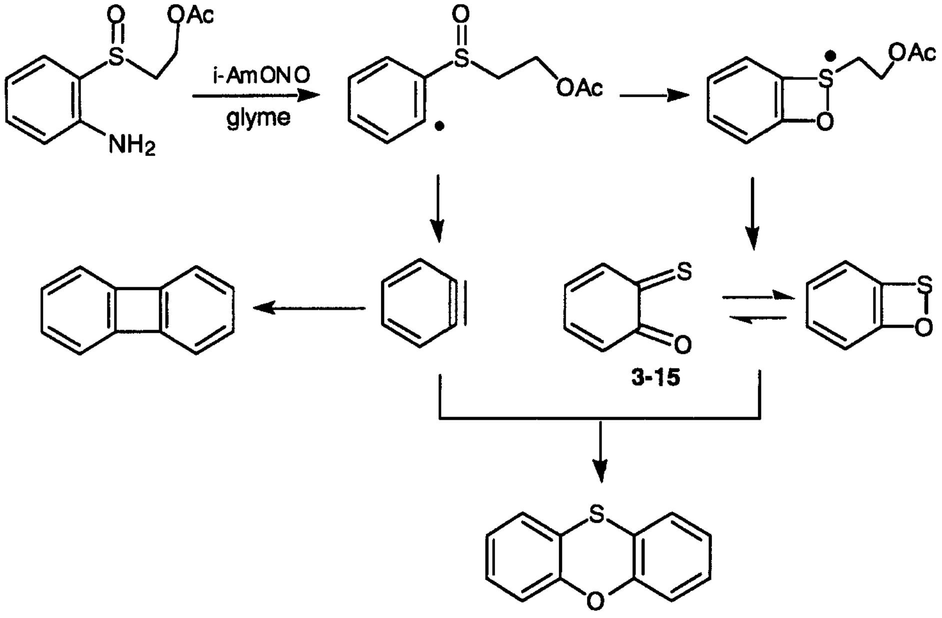
In 1995, Kitamura and Yamane introduced a new type of benzyne precursor, phenyl[2-(trimethylsilyl)phenyl]iodonium trifluoromethanesulfonate (**3-16**), which was found to produce benzyne under very mild conditions (Scheme 3-6-7) [53].

The reaction **3-16** with furan, 2-methylfuran, anthracene, and tetraphenylcyclopentadienone afforded the corresponding benzyne adducts in quantitative ylides (Scheme 3-6-8) [54].

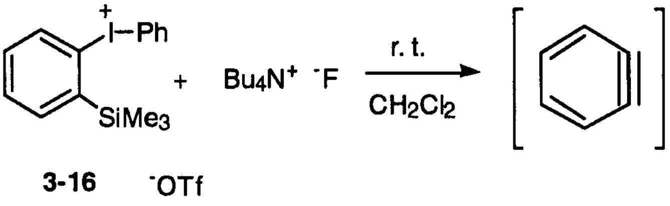
Compound **3-16** provides the possibility of a new type of thione–benzyne addition. The reaction of **3-2** with **3-16** gave the corresponding [4+2] benzyne adducts in good ylides (Scheme 3-6-9) [55].



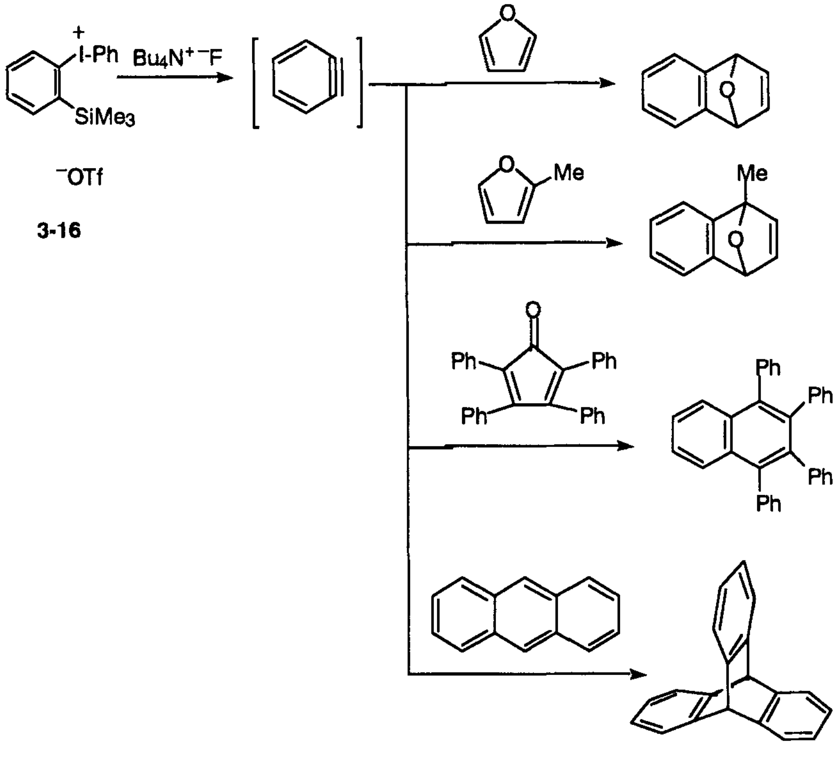
SCHEME 3-6-5



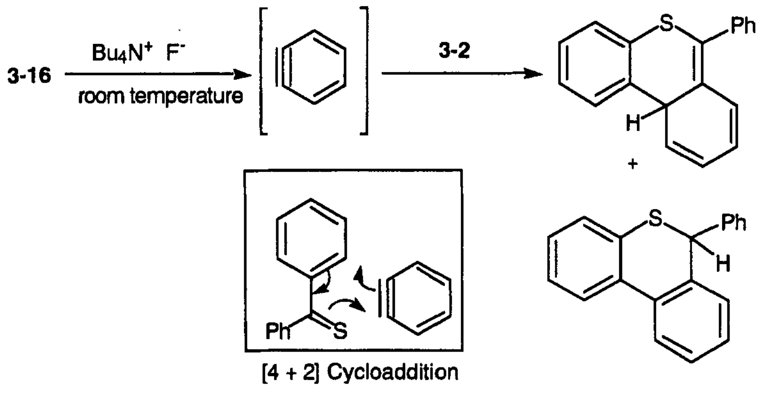
SCHEME 3-6-6



SCHEME 3-6-7



SCHEME 3-6-8

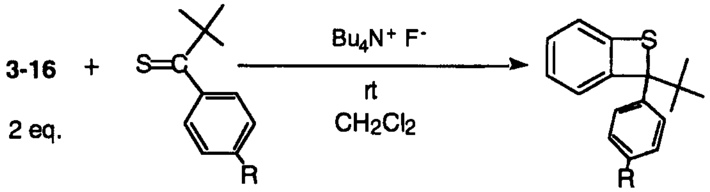


SCHEME 3-6-9

Since iodonium salts are found to be a good benzyne precursor, their reactions with thiopivalophenones (**3-17**) were carried out. When the reaction was carried out at room temperature, the corresponding [2 + 2] adducts were obtained (Scheme 3-6-10).

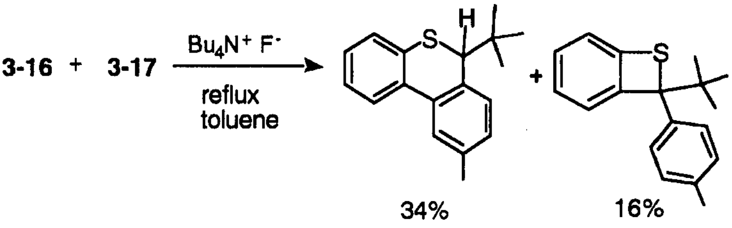
On the other hand, when the reaction was carried out in refluxing benzene or toluene, [4 + 2] adducts were obtained along with the [2 + 2] adducts (Scheme 3-6-11).

In 1983, Sonoda and coworkers developed another type of benzyne precursor, *o*-trimethylsilylphenyl trifluoromethanesulfonate (**3-18**), which was also found to be a good



3-17 R	Yield/%
H	51
Me	49
MeO	44
PhO	38

SCHEME 3-6-10



SCHEME 3-6-11

benzyne precursor [56]. The reaction of this reagent with **3-17** followed by the addition of tetrabutylammonium fluoride at room temperature afforded the corresponding [4 + 2] cycloadducts (Scheme 3-6-12) [56].

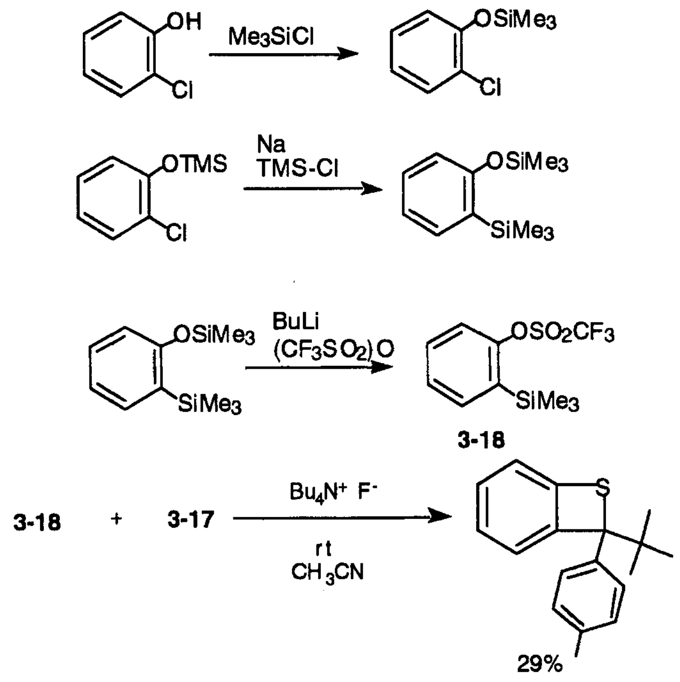
When benzenediazonium 2-carboxylate was used as a benzyne precursor, benzyne adducts and the corresponding oxathian-4-one was obtained. Thus, this reagent was not a useful benzyne precursor (Scheme 3-6-13).

In the case of thiocamphor (**3-19**), a quite different result was observed. The main product obtained was an ene reaction product (**3-20**) (Scheme 3-6-14).

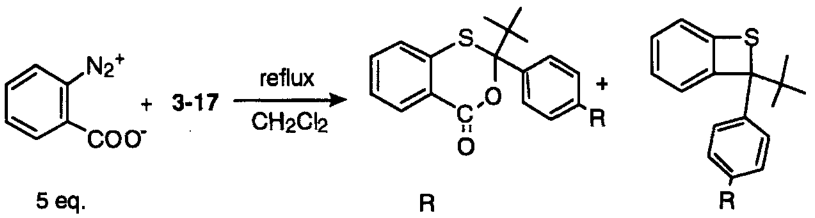
Thus, the reaction of thioketones with benzyne afforded the corresponding [2 + 2] adducts, [4 + 2] adducts, and ene reaction products.

Thioaldehydes generally oligomerize to give the corresponding trimers or polymers. There is no report on the reaction of thioaldehydes with benzyne. Thus the reaction of sterically congested thioaldehyde with benzyne was carried out. Reaction of 2,4,6-tri-*tert*-butylthiobenzaldehyde (**2-4**) with benzyne prepared from **3-16** and tetrabutylammonium fluoride afforded 5,7-di-*tert*-butyl-3,3-dimethyl-1-indanyl phenyl sulfide (**3-21**) in 92% yield. When *o*-trimethylsilylphenyl trifluoromethanesulfonate was used as a benzyne precursor, the yield of **3-21** decreased to 86%. In both cases, the corresponding [2 + 2] adduct (**3-22**) was not detected (Scheme 3-6-15).

This result is quite different from that of thiopivalophenone **3-17**, which gave [4 + 2] or [2 + 2] cycloaddition products. The thioaldehyde **2-4** is too sterically congested, thus, the reaction would proceed via a radical intermediate [57].



SCHEME 3-6-12

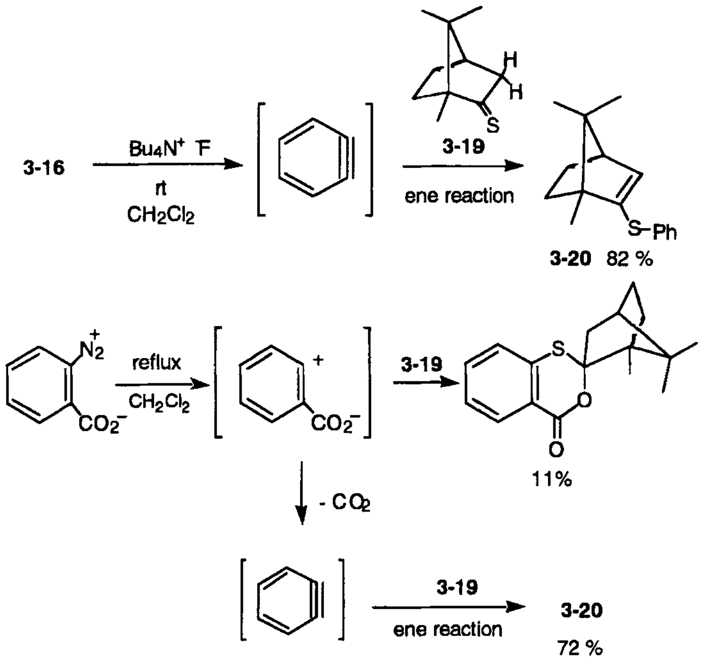


R		
H	15%	41%
Me	82%	8%

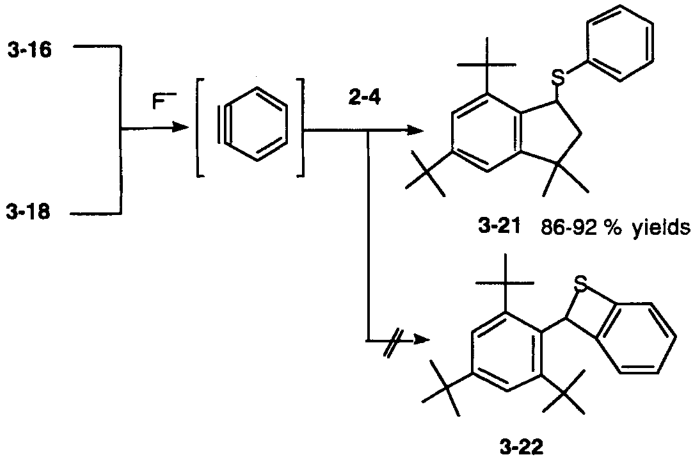
SCHEME 3-6-13

3.7 Synthesis of 1,2,4-Trithiolane from Thioketone

In 1928, Staudinger and Freudenbergar reported the synthesis of 3,3,5,5-tetraphenyl-1,2,4-trithiolane (**3-23**) by oxidation of **3-2** for 6 days at room temperature [56]. In 1972, *cis*- and *trans*-3,5-dimethyl-1,2,4-trithiolanes (**3-24**) were isolated from the headspace of beef broth. Adesogan isolated *cis*-3,5-diphenyl-1,2,4-trithiolane (**3-25**) from the chloroform extract of the wet root of *P. allicia* [59]. After these findings, the chemistry of 1,2,4-trithiolanes has been studied extensively because of their unique and interesting properties (Scheme 3-7-1).



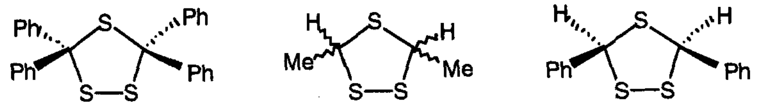
SCHEME 3-6-14



SCHEME 3-6-15

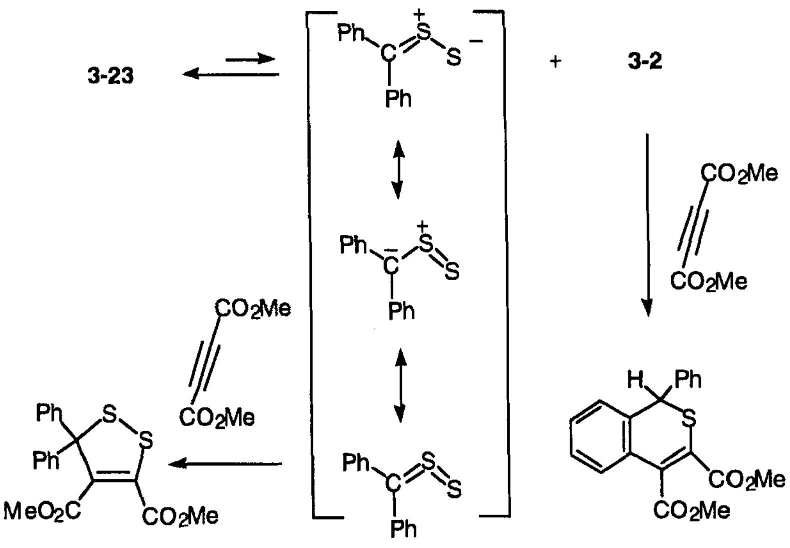
In 1987, Huisgen and Rapp reported the reaction of **3-23** with dimethyl acetylenedicarboxylate, which afforded the corresponding 1,2-dithiolane and 1H-2-dihydrobenzothiopyran in 59% and 94% ylides, respectively. Dicyanoacetylene and cyclooctyne also work as trapping reagents for thione-*S*-sulfide (Scheme 3-7-2) [60].

When this trithiolane **3-23** was refluxed with 1.4 molar equiv. of adamantanethione (**3-26**) in chloroform, the corresponding adamantine-spiro-1,2,4-trithiolane (**3-27**) was isolated in 81% yield (Scheme 3-7-3) [60].

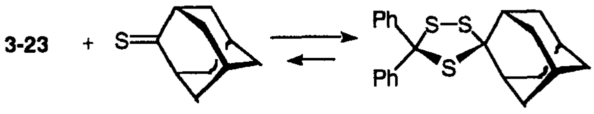


3-23 **3-24** **3-25**

SCHEME 3-7-1



SCHEME 3-7-2



3-26 **3-27**

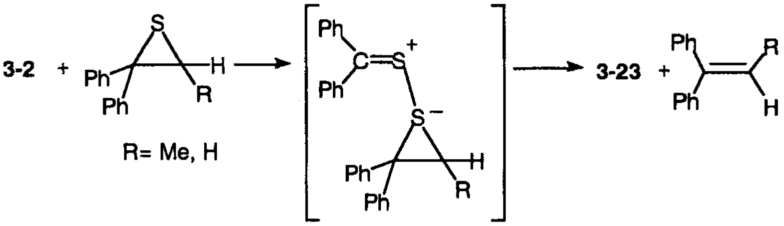
SCHEME 3-7-3

These workers also reported the reaction of **3-2** with thiiranes to afford the 1,2,4-trithiolane (**3-23**) in 84% yield (Scheme 3-7-4).

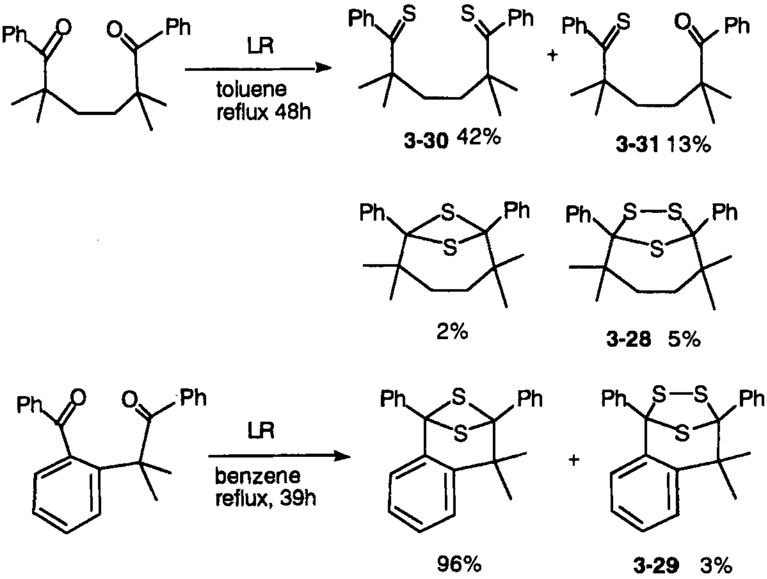
Nakayama and coworkers synthesized 1,2,4-trithiolanes (**3-28**) by intramolecular cycloaddition of thione and thione-*S*-sulfide. They also prepared unsymmetrical bicyclic 1,3-dithietanes and bicyclic 1,2,4-trithiolanes (**3-28** and **3-29**) along with thiones (**3-30**, **3-31**) by the reaction of dicarbonyl compounds with Lawesson's reagent (LR) in refluxing benzene (Scheme 3-7-5) [61].

In 1981, Okazaki *et al.* reported the synthesis of thioketones by the reaction of hydrazones with disulfur dichloride in the presence of triethylamine (Scheme 3-7-6) [62].

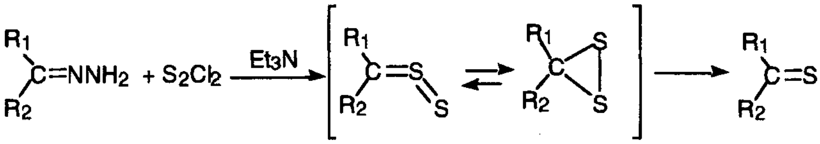
Nakayama and coworkers reinvestigated this reaction in the hope of obtaining a dithiirane-intermediate [63]. The isolated products were not the corresponding dithiiranes but thiones, ketones, and cyclic polysulfides (Scheme 3-7-7).



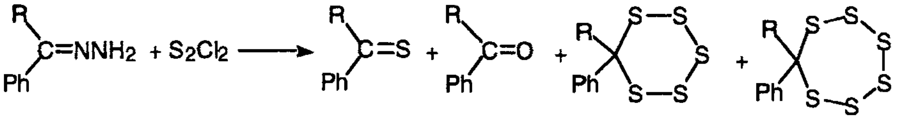
SCHEME 3-7-4



SCHEME 3-7-5



SCHEME 3-7-6



R=1-Ad	**3-32**	50%	15%	11%	6%
R=t-Bu	**3-33**	10%	63%	7%	3%
R=Ph	**3-2**	17%	47%	4%	7%

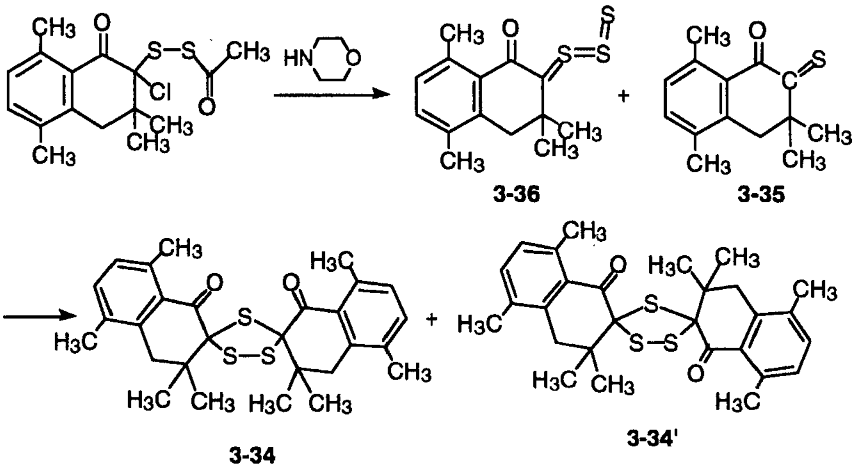
SCHEME 3-7-7

Senning and coworkers reported the synthesis of trithiolanes (**3-34** and **3-34′**) from the reaction α-chlorosulfenyl disulfide with triethylamine [64]. The obtained thiosulfine may undergo a disproportionation reaction to give thione (**3-35**) and thione-disulfide (**3-36**), which combine to afford trithiolanes **3-34** and **3-34′** (Scheme 3-7-8).

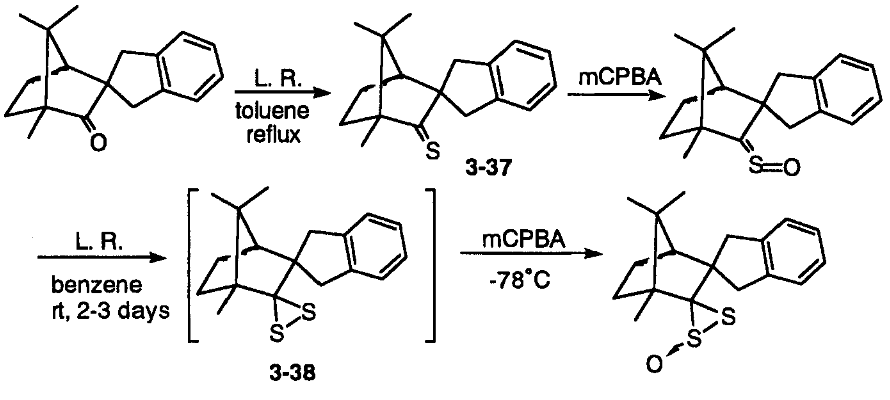
Shimada *et al.* reported the synthesis of new type of sterically crowded thiones (**3-37**) derived from d-camphor [65]. Oxidation of **3-37** afforded the corresponding sulfines, which further reacted with Lawesson's reagent (LR) to give the corresponding dithiiranes (**3-38**). Since the isolation of **3-38** was unsuccessful due to instability, the structure of dithiirane was confirmed by X-ray crustallographic analysis of its dithiirane *S*-oxide (Scheme 3-7-9) [65].

We have also reported the reaction of **3-2** with elemental sulfur and maleic anhydride in refluxing xylene. The product was the corresponding [3 + 2] adducts (**3-39**) (Scheme 3-7-10) [66].

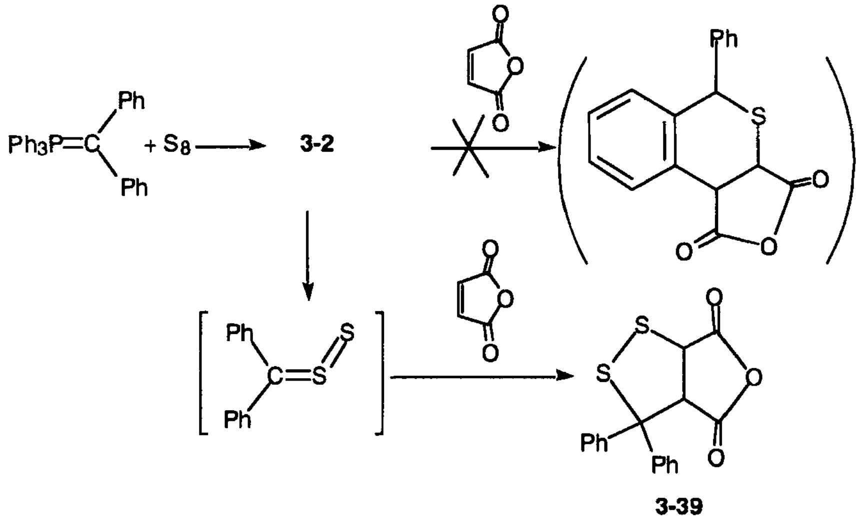
Thiopivalophenone (**3-16**) was generally synthesized by the reaction of pivalophenones with tetraphosphorus decasulfide. Careful investigation of this reaction



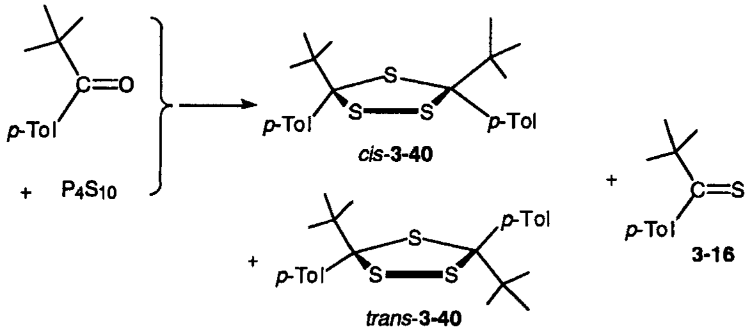
SCHEME 3-7-8



SCHEME 3-7-9



SCHEME 3-7-10



SCHEME 3-7-11

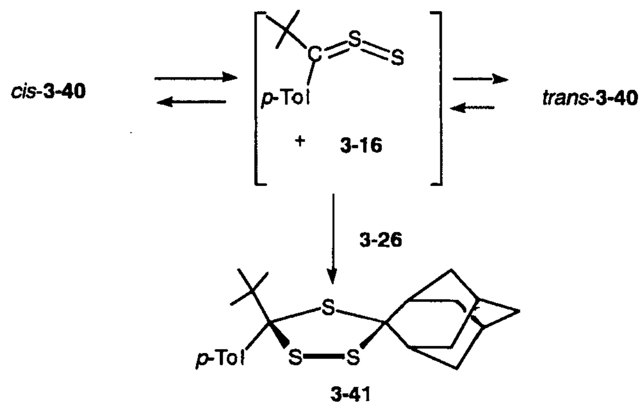
suggested the formation of *cis*- and *trans*-1,2,4-trithiolanes (**3-40**). Prolonged heating resulted in the formation of *trans*-**3-40** as the major product. Both isomers interconvert in refluxing toluene via a thione *S*-sulfide intermediate (Scheme 3-7-11) [67].

The reaction of *cis*-**3-40** with adamantine-2-thione **3-26** in refluxing toluene gave the corresponding [3 + 2] adduct **3-41** (67%) (Scheme 3-7-12).

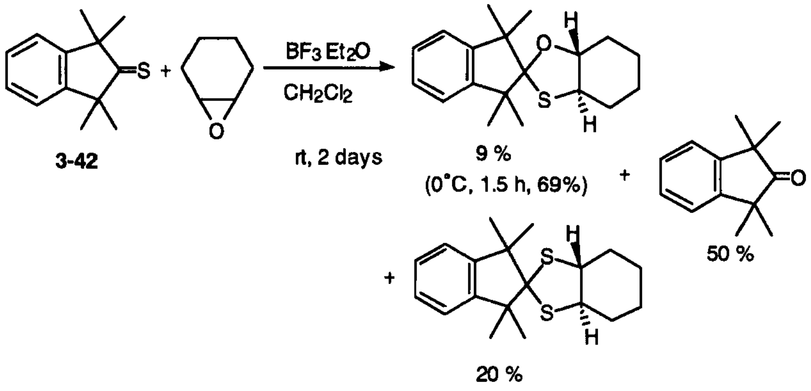
3.8 Other Reactions

Lewis acid catalyzed the reaction of thioketones (**3-42**) with 1,2-epoxycycloalkanes afforded 1,3-oxathiolannes, 1,3-dithiolanes, and ketones. Generally, the ylides were low (Scheme 3-8-1) [68].

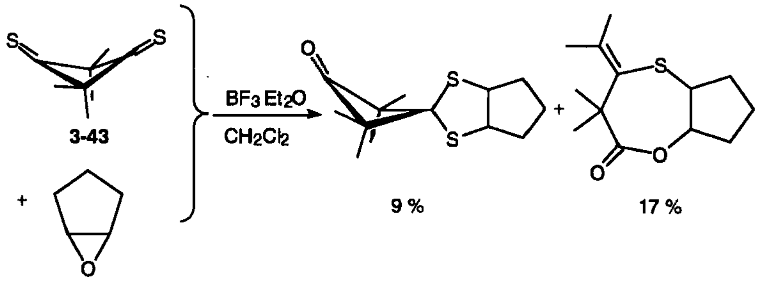
In the case of tetramethylcyclobutanedithione (**3-43**), the result was quite different. Fused 1,4-oxathiepane and 1,3-dithiolane were the main products (Scheme 3-8-2).



SCHEME 3-7-12



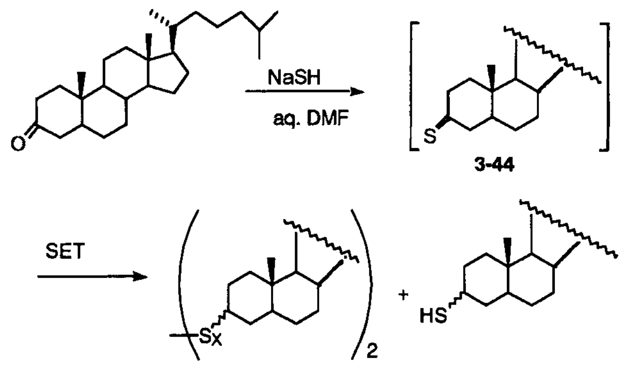
SCHEME 3-8-1



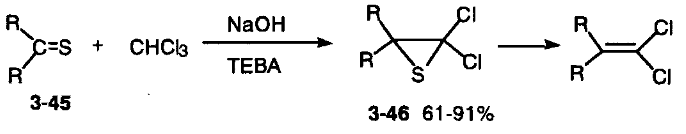
SCHEME 3-8-2

Cholestan-3-one was reduced by sodium hydrogen sulfide in water or aqueous DMF to give the corresponding dimer and thiol of the intermediate thione (**3-44**). The reaction proceeds by a thiophilic addition of HS^- on the thioketone **3-44** via a single electron transfer mechanism (Scheme 3-8-3) [69].

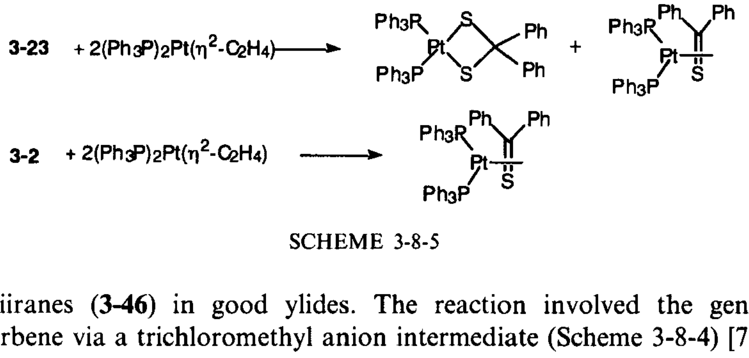
The reaction of sterically crowded thiones (**3-45**) with $CHCl_3$/NaOH under phase-transfer catalysis with benzyltriethylammonium chloride afforded the corresponding



SCHEME 3-8-3



SCHEME 3-8-4



SCHEME 3-8-5

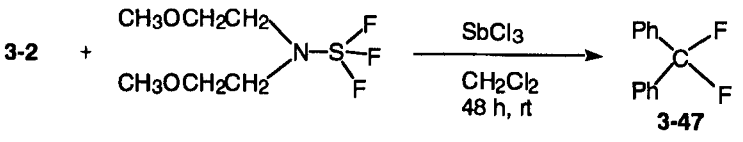
dichlorothiiranes (**3-46**) in good ylides. The reaction involved the generation of dichlorocarbene via a trichloromethyl anion intermediate (Scheme 3-8-4) [70].

3,3,5,5-Tetraphenyl-1,2,4-trithiolane **3-23** reacts with 2 molar equiv. of $(Ph_3P)_2Pt(\eta^2\text{-}C_2H_4)$ to afford a 1 : 1 mixture of the complexes $(Ph_3P)_2Pt(SCPh_2S)$ and $(Ph_3P)_2\eta^2\text{-}Ph_2C{=}S$. The latter complex was also obtained from an analogous reaction of **3-2** in 89% yield (Scheme 3-8-5) [71].

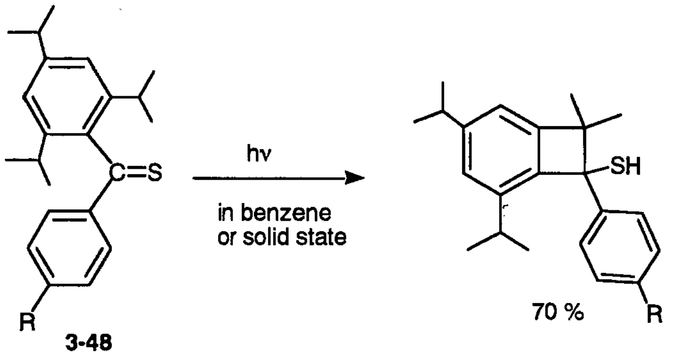
Thione **3-2** was converted to difluorodiphenylmethane (**3-47**) in 89% yield on reaction with *bis*(2-methoxyethyl)aminosulfur trichloride in the presence of $SbCl_3$ [72]. Generally, the direct conversion of benzophenone to the *gem*-difluoride is known to be difficult. This is an alternative method to produce the *gem*-difluoride from benzophenone via thiobenzophenone (Scheme 3-8-6).

Internal photocyclization was observed by using 2,4,6-trisopropylthiobenzophenones (**3-48**). Photolysis of a degassed benzene solution of **3-48** through Pyrex gave the corresponding benzocyclobutenethiols in *ca.* 70% ylides. Interestingly, the same photoreaction was carried out in the crystalline state (Scheme 3-8-7) [73].

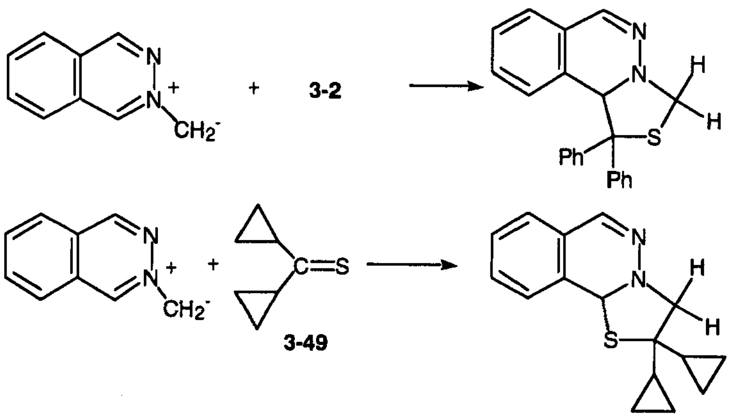
Butler and coworkers reported the 1,3-dipolar reactions of thioketones with phthalazinium-2-methanide. With **3-2**, the regiochemistry was such that the nucleophilic methanide terminus of the dipole bonded to the sulfur atom. With dicyclopropyl



SCHEME 3-8-6



SCHEME 3-8-7

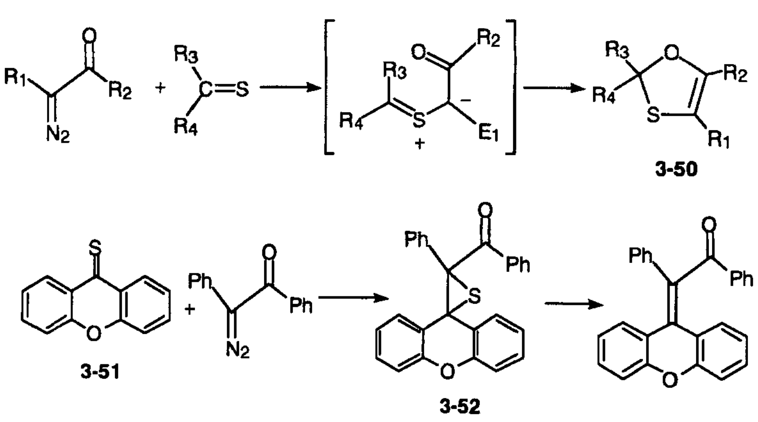


SCHEME 3-8-8

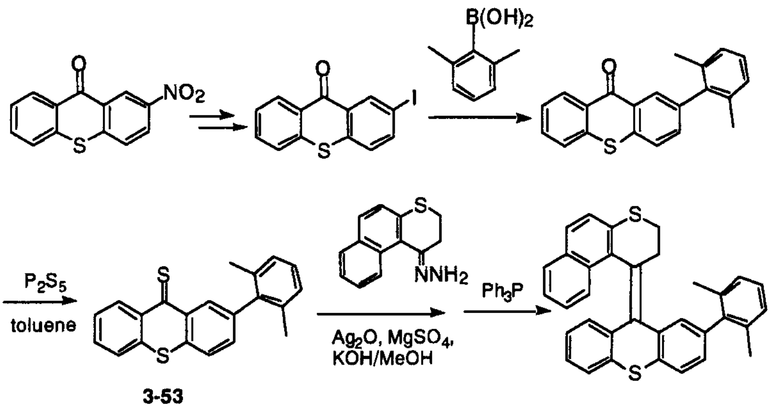
thioketone (**3-49**) and admantanethione, steric effects caused a gradual reversal of the regiochemistry (Scheme 3-8-8) [74].

The reaction of α-diazocarbonyl compounds with thioketones generally afforded 1,3-oxathiols (**3-50**). When 9H-xanthene-9-thione (**3-51**) was used as a substrate, a thiirane (**3-52**) was isolated instead of a 1,3-oxathiol (Scheme 3-8-9) [75].

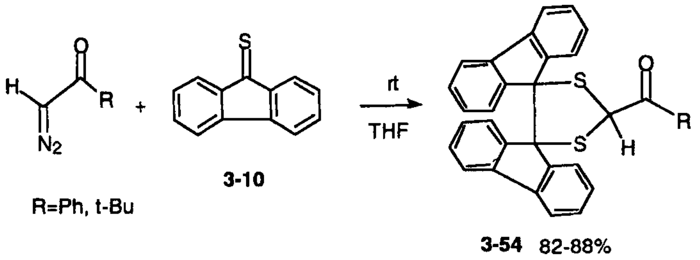
A similar reaction was reported by Schoevaars *et al.* [76]. A photochemically bistable molecular rotor, 2-(2,6-dimethylphenyl)-9-(2′,3′-dihydro-1′H-naphtho[2,1-b]thiopyran-1′-ylidene)-9H-thioxanthene was prepared starting from 2-nitrothioxanthone via a 7-step reaction sequence. Key steps in the synthesis were the Suzuki coupling to attach



SCHEME 3-8-9



SCHEME 3-8-10



SCHEME 3-8-11

the xylyl rotor to the thioxanthone and the coupling of the upper and lower half of the helical alkene using a diazo-thioketone (**3-53**) method (Scheme 3-8-10) [76].

Kagi *et al.* further investigated this type of reaction [77]. The reaction of 9H-fluorene-9-thione (**3-10**) with α-diazoketones gave 1,3-dithiolanes (**3-54**) in 82–88% ylides (Scheme 3-8-11).

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