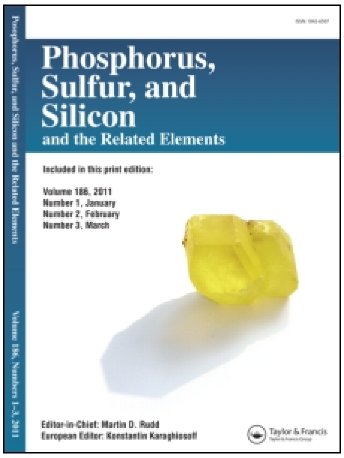

Phosphorus, Sulfur, and Silicon and the Related Elements

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Novel Reactions of Ambident Sulphur Compounds

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NOVEL REACTIONS OF AMBIDENT SULPHUR COMPOUNDS

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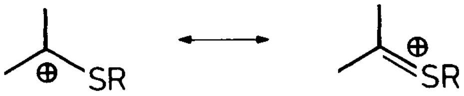
München

Abstract Regioselectivities in reactions of ambident ions depend on the electronic effects of substituents (allopolarization principle). New reactions of thioenolate anions, thioamide anions and 1-alkylthio-vinamidinium cations lead to 3,4-bis-dimethylamino-thieno(2,3-b) thiophene, diazaquinodimethanes, derivatives of 2,4-bis-methylthio-benzodiazepine, thiophenes, heterofulvalenes, heterosesquifulvalenes and heteroheptafulvalenes. Some of these electron-rich compounds form charge transfer-complexes and radical cation salts.

The objective of the work presented here is the synthesis of electron-rich π-systems and of formally antiaromatic compounds stabilized by donor and acceptor groups. The idea is to prepare new organic materials with interesting properties. Electron-rich π-systems, particularly such of the fulvalene series, are important compounds of charge-transfer complexes having high electrical conductivities[1], and stable crystalline salts containing antiaromatic ions, i.e., ions with triplet ground states, are promising candidates for ferromagnetic organic compounds[2]. For both classes of compounds, sulphur-containing substituents have some unique properties: Groups with bivalent sulphur, e.g. alkylthio groups, stabilize positive as well as negative charges (Scheme 1). Furthermore, groups with bivalent sulphur are powerful "soft" electron-donors and favor as such the formation of cation-radicals and CT-complexes.



Donor

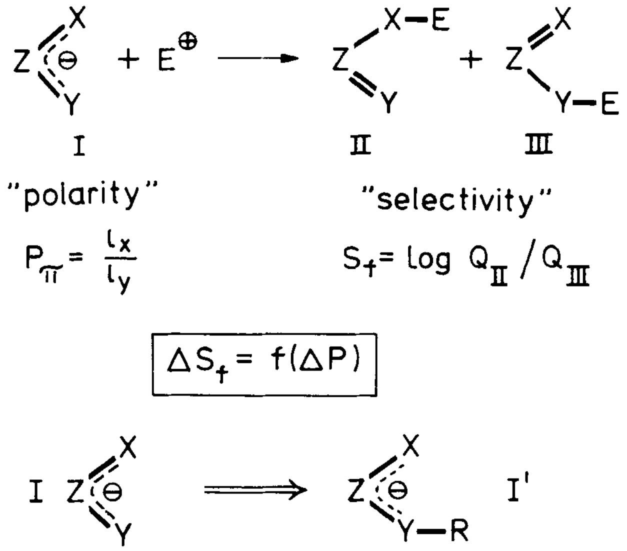
Acceptor

Scheme 1

Starting materials in our synthetic methodology are ambident compounds. In this report reactions based on thioenolate anions and thioamide anions on the one side and on alkylthiovinamidinium salts and dithiolium salts on the other side are discussed. It is meant as a survey of newer results rather than as a detailed description and it will cover 3 topics:

1) Synthesis of heterocyclic diamines as potential proton-sponges and as donors for charge-transfer complexes;
2) Syntheses and reactions of new benzodiazepine derivatives;
3) Syntheses and reactions of sulphur-containing quinodimethanes, fulvenes and fulvalenes.

At the outset the regioselectivity in reactions of ambident compounds [3] shall be briefly commented upon. This is a rather complex problem. Here only kinetically-controlled reactions of ions are considered. To rationalize regioselectivities in this field we put forward the allopolarization principle which is based on the idea that reactions of ions are charge-controlled and that there is a relationship between polarity and regioselectivity. Scheme 2 displays the general formula I of an ambident anion. Its reaction with an electrophile can lead to two products II and III, the yield ratio of which determines the selectivity factor (S_f). The polarity (P) of the ambident ion is defined as the relative charge density.

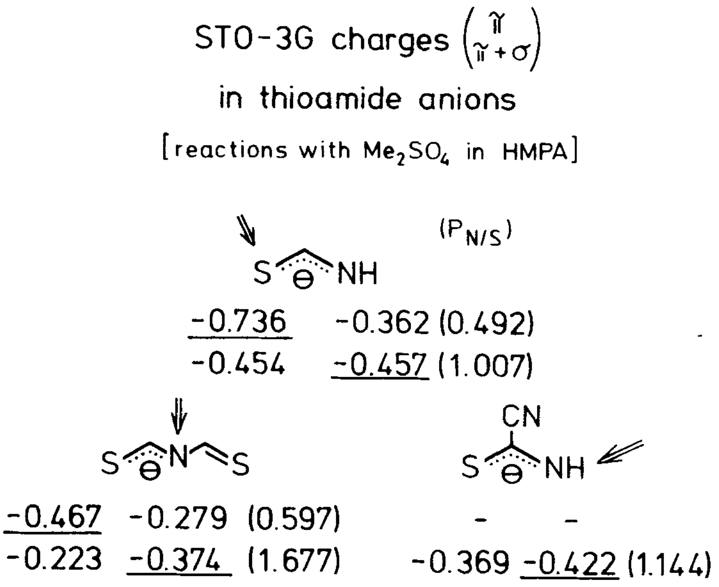


$P_{I'} > P_I$: An increase in polarity (polarity index P) causes an increase in charge control — favouring attack of the electrophile at the position with the highest charge density.

Scheme 2

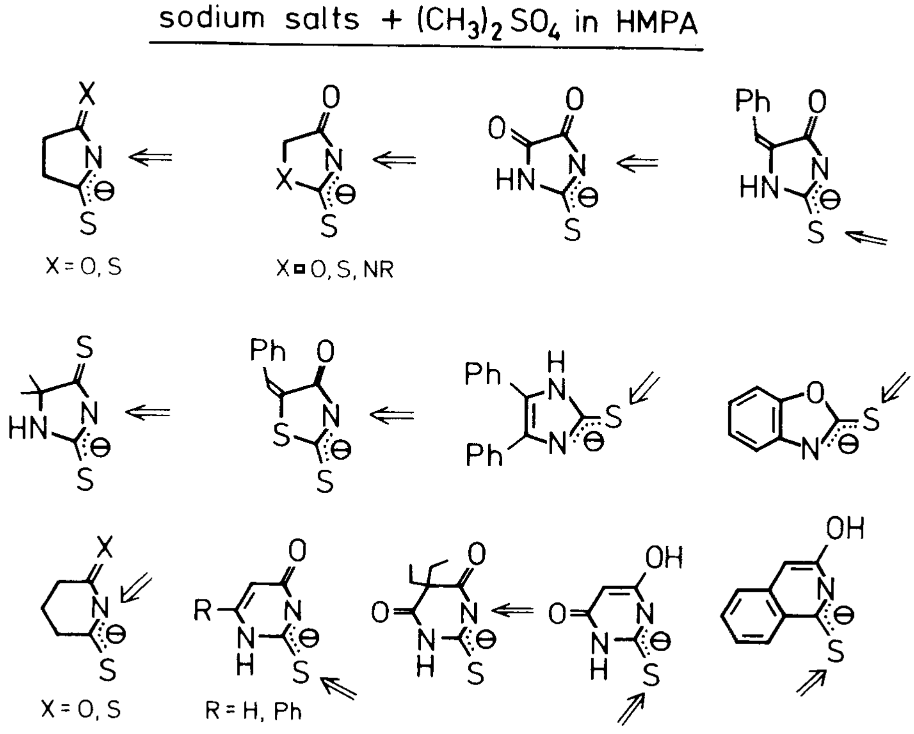
The allopolarization principle states that a change in selectivity is a function of a change in polarity of the ambident ion. To predict the selectivity of a new system, one simply has to compare its polarity index with the polarity index of a standard system whose selectivity is already known. An increase in polarity causes stronger charge-control and this in turn leads to a stronger tendency for the anion to be attacked at the position with the higher charge density. A decrease in polarity causes weaker charge-control and this brings about a higher reactivity of the centre with the lower negative charge density.

The application of the allopolarization principle is demonstrated here with thioamide anions. Charge densities of 3 typical thioamide anions are shown in Scheme 3. The



Scheme 3

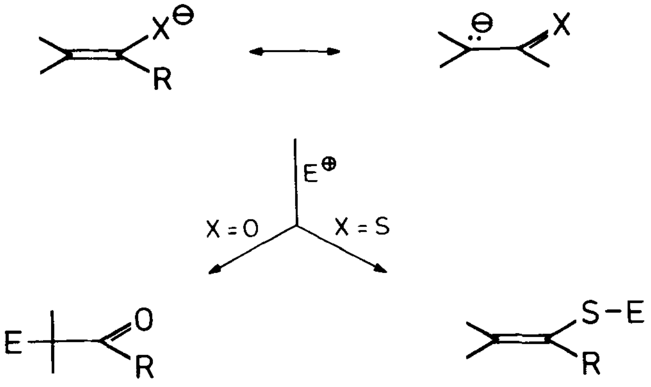
STO-3G method gives sulphur and nitrogen in the thioformamide anion roughly the same charge density. Simple thioamide anions are S-alkylated to form thioimidates. That is the standard selectivity connected with $P_{S/N} \approx 1$. An electron-withdrawing substituent on nitrogen such as the thioformyl group brings about a shift of negative charge towards the nitrogen and the polarity index increases from 1 to 1.7. The increase in polarity should induce stronger charge-control and more N-alkylation at the expense of S-alkylation is to be expected. A cyano group in position 2 exerts a similar however smaller effect. These predictions are confirmed by the experiments [5]



Scheme 4

summarized in Scheme 4. Like simple aliphatic thioamide or thiourea anions, heterocyclic derivatives are normally S-alkylated. Compounds of the succinimide or phthalimide type, however, are prone to N-alkylation. In this series of thioamides, S-alkylation occurs only when the acceptor effect is offset by a donor-group.

In enolate anions (Scheme 5) C-alkylation predominates.

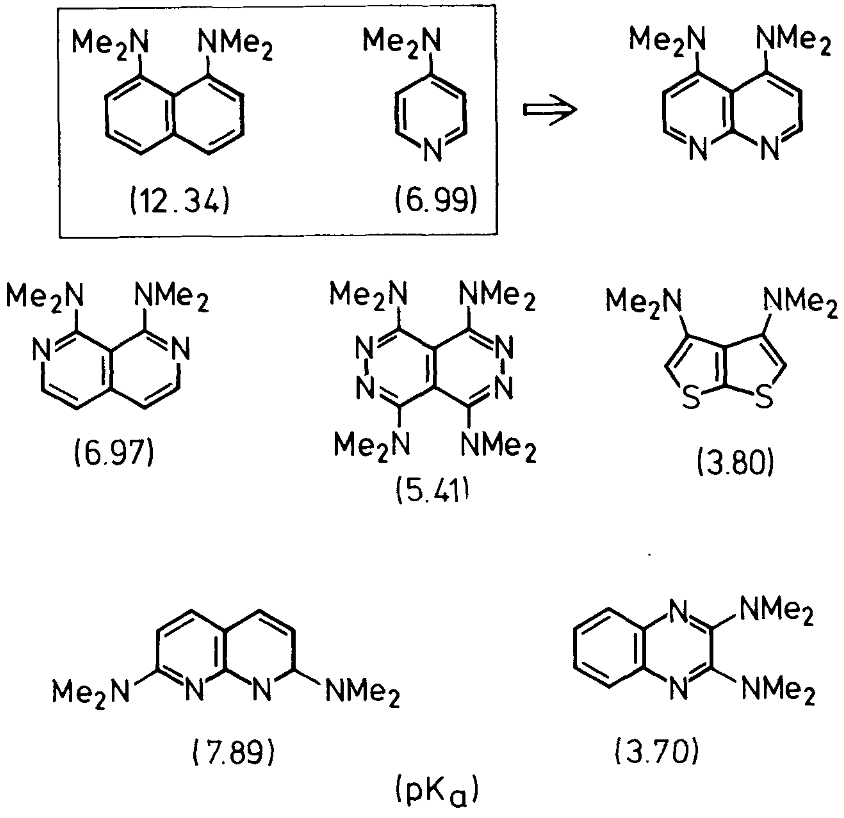


Scheme 5

In thioenolate anions, however, S-alkylation is preferred and thioenolethers and ketene mercaptals are formed. We used this type of reaction when we studied new peridiamines[6] (Scheme 6).

Bis-dimethylamino-naphthalene is known as proton-sponge[7] but it has found only little if any preparative use. 4-Dimethylaminopyridine is a very effective acylation catalyst[8]. We set out to synthesize a combination of these two compounds to get information about the influence of ring-N-atoms on proton-sponge properties.

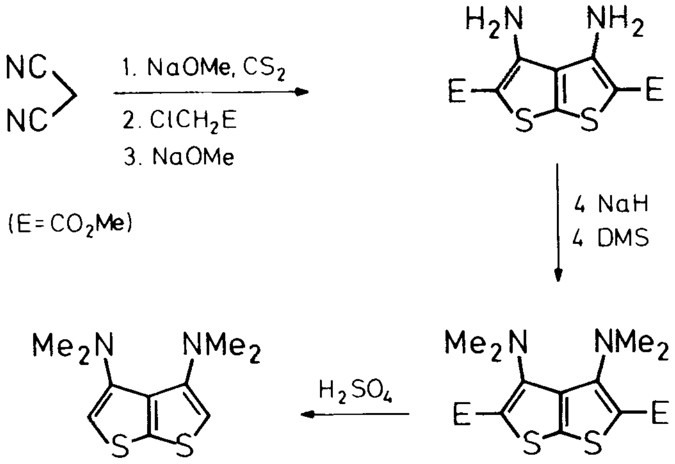
A sulphur analogue of the proton-sponge is the thieno-



Scheme 6

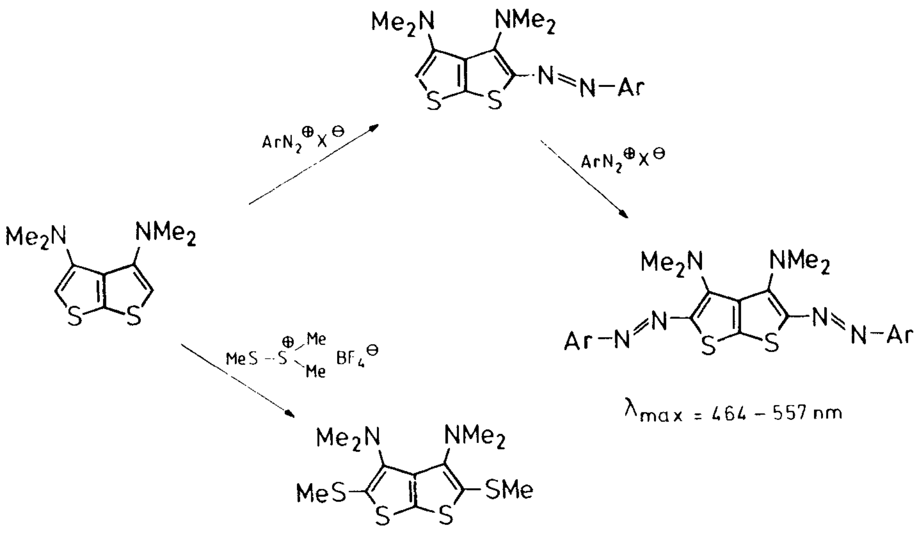
thiophene shown in Scheme 6. It can be prepared in the following way (Scheme 7).

Malononitrile reacts with carbon disulfide in the presence of sodium methoxide to the disodium salt of a dithiocarboxylic acid which on treatment with methyl chloroacetate gives rise to a ketene mercaptal and this can be cyclized to a diaminothienothiophene [9]. This compound can be methylated to give its bis-dimethylamino derivative and this in turn yields 3,4-bis-dimethylamino-

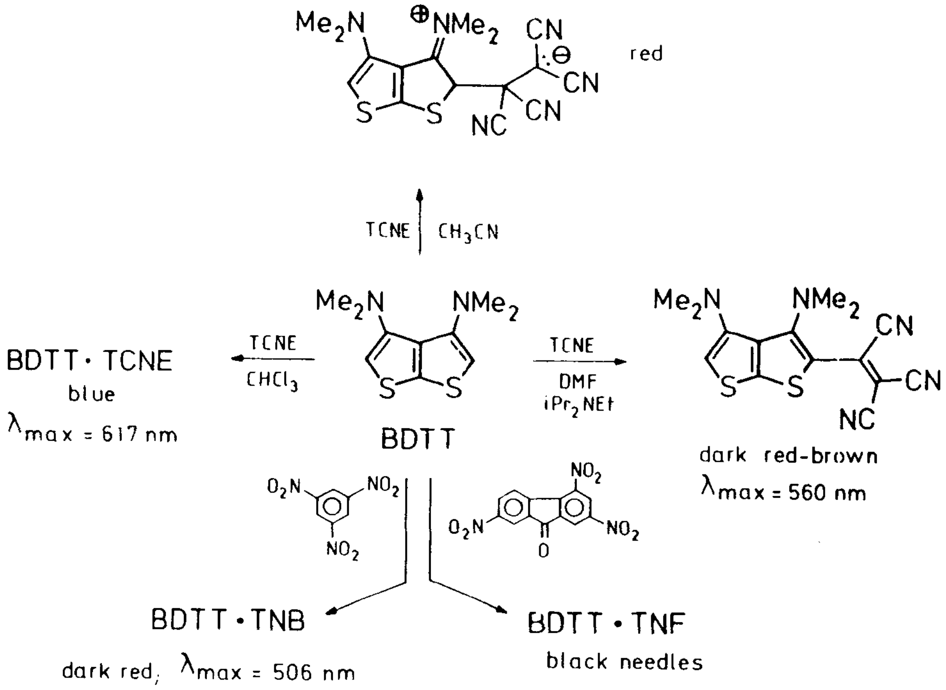


Scheme 7

thieno(2,3-b)thiophene [6]. Some typical electrophilic substitution reactions of this thienothiophene are depicted in Scheme 8 (only reactions that are of relevance to ambident reactivity and to electron-transfer properties of our new compounds are mentioned in this report). Coupling with diazonium salts leads to azo dyestuffs. Reaction with Smallcomb's salt [10] gives rise to a thienothiophene with four donor-groups. TCNE forms different products depending on the solvent used (Scheme 9). In Chloroform, a deep blue charge-transfer complex is observed. In acetonitrile, a red 1,4-dipole can be detected and in DMF tricyanovinylation takes place. Charge-transfer complexes are also obtained with trinitrobenzene and with trinitrofluorenone. It is remarkable that the black complex in the latter case is even formed in a solid state reaction when a mixture of both compounds is pulverized.

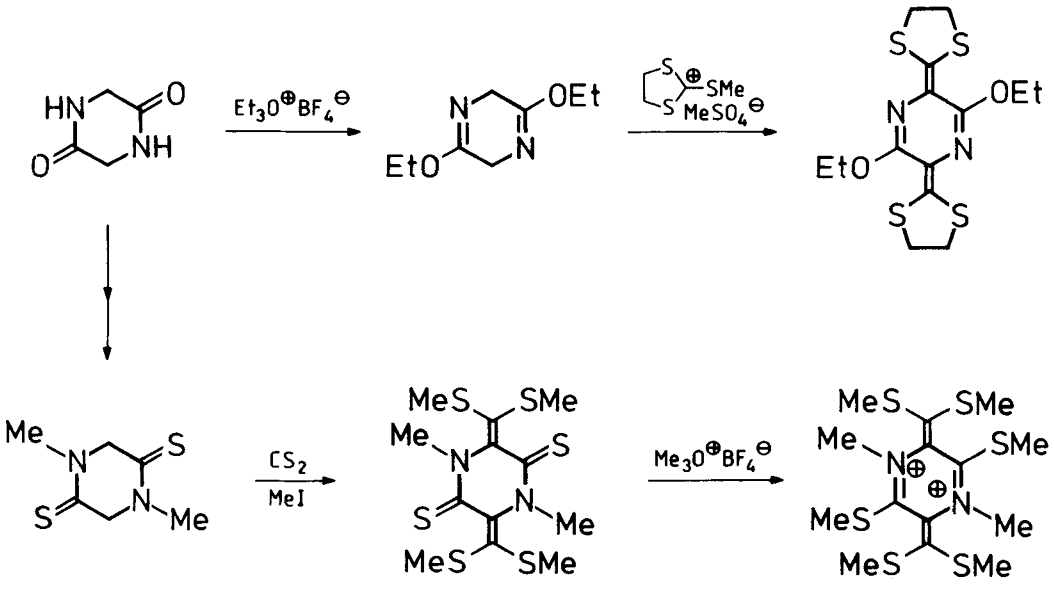


Scheme 8



Scheme 9

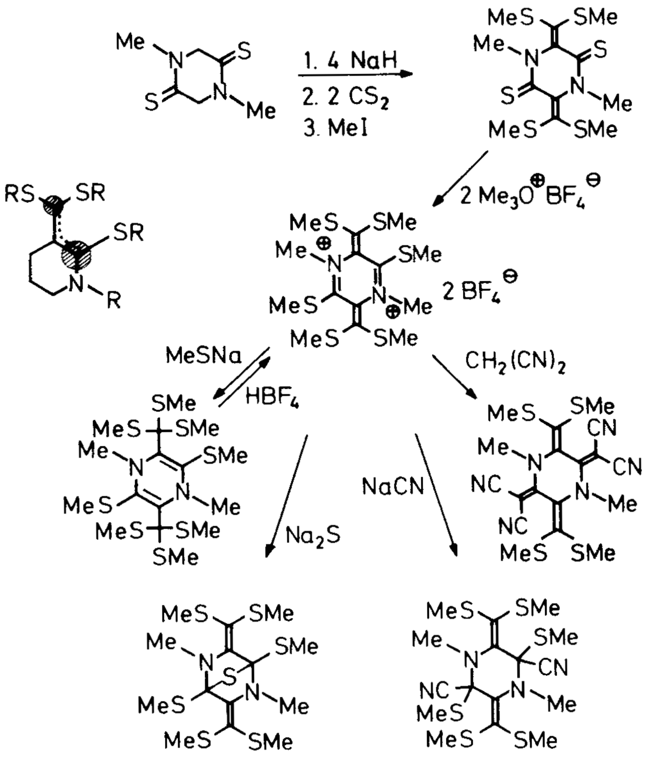
Another example of ketene mercaptal chemistry is shown in Scheme 1o [11]. Dimethyldithiodiketopiperazine reacts with carbon disulfide and sodium hydride followed by methyliodide under standard conditions to a twofold ketenemercaptal. As a thioamide this can be S-alkylated and, in this way, a diquaternary salt of a diazaquinodimethane is formed in high yield. Another diazaquinodimethane [11] can be obtained on heating of the bisimidate



Scheme 1o

of diketopiperazine with methylthio-dithiolanylium methylsulfate.

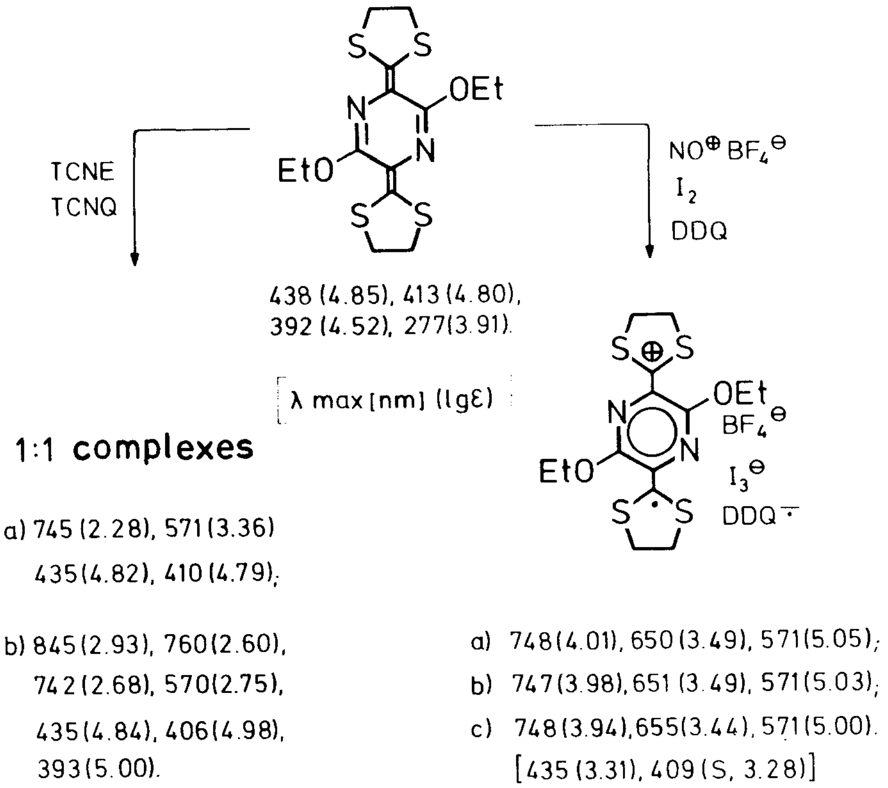
Both quinone derivatives show some interesting reactions (Scheme 11). The bis-quaternary salt contains two allyl cation moieties. Since the amino group is a stronger donor than an alkylthio group, a charge distribution results as is shown schematically in Scheme 11. The allopolarization principle predicts the α-position between



Scheme 11

N and S to have the highest reactivity toward charged nucleophiles. In fact, reactions with malononitrile, sodium cyanide and sodium sulfide proceed as expected and yield new methylene piperazine derivatives.

The only exception is the reaction with sodium methanethiolate which produces a new dihydropyrazine derivative. The high stability of this compound is remarkable with regard to its formal antiaromatic nature. The deviant course of the thiolate addition might be a consequence

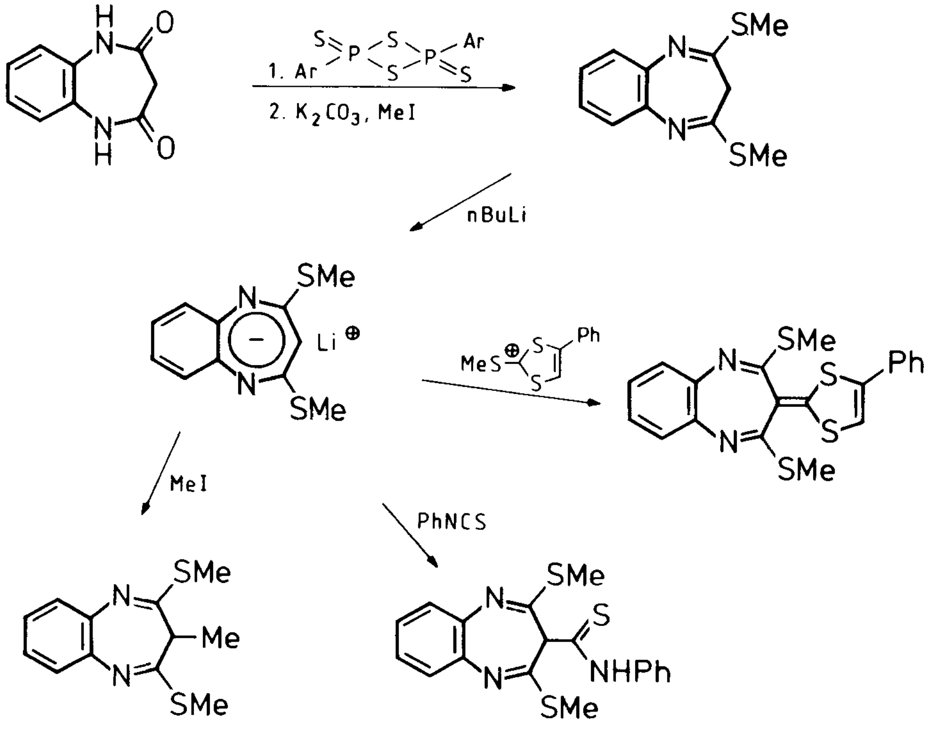


Scheme 12

of the lower polarity of the thiolate anion.

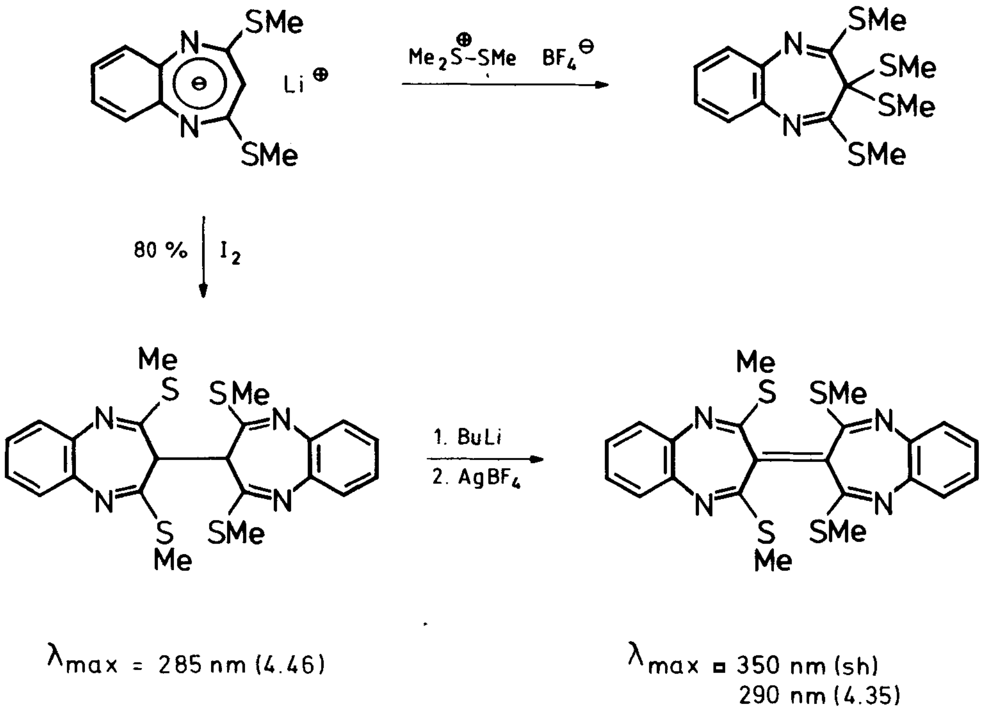
The neutral diazaquinodimethane mentioned in Scheme 1o is a good electron-donor (Scheme 12). With iodine, nitrosyl tetra-fluoroborate or DDQ it forms stable, dark green cation radical salts, with TCNE or TCNQ dark green and bluish-black charge-transfer complexes.

As emphasized in the beginning one of the objectives of our work is to synthesize stabilized formally antiaromatic species. The example discussed next is based again on thioamide anion and thioenolate chemistry (Scheme 13). 1,2,4,5-Tetrahydro-1,5-benzodiazepin-2,4-dione, on treatment with Lawesson reagent and subsequently with methyliodide and potassium carbonate yields 2,4-bis-methylthiobenzodiaazepine [12]. With butyl-Li the latter forms a deep red anion which is formally antiaromatic. It readily reacts with methyl iodide and phenylisothiocyanate and yields a new type of diazasesquifulvalene on reaction with 2-methylthio-4-phenyl-1,3-dithiolium-tetrafluoroborate.



Scheme 13

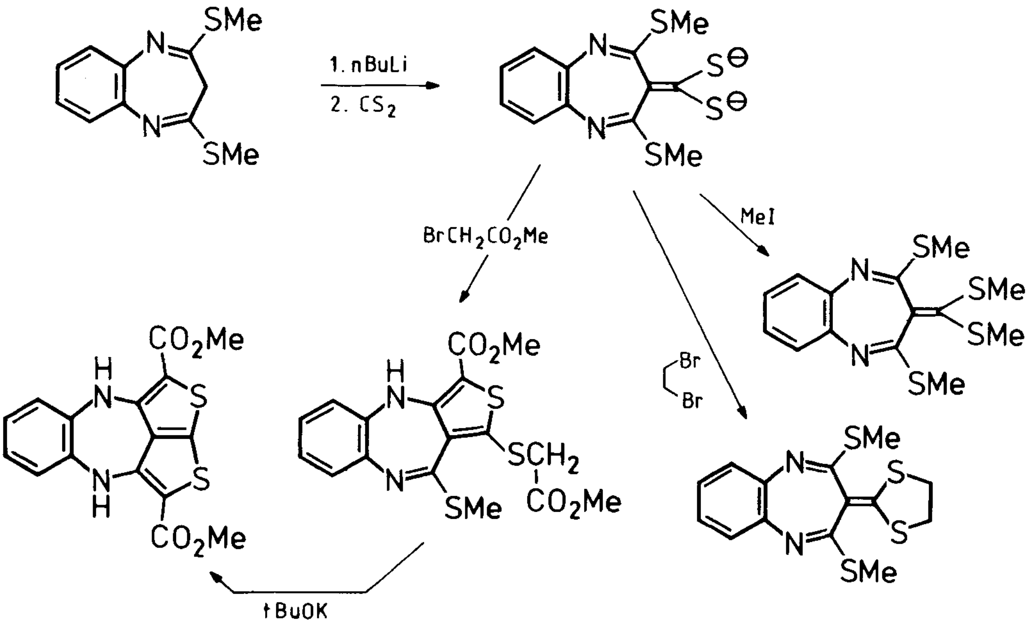
Heptafulvalene derivatives can be obtained as well (Scheme 14).



Scheme 14

Under the influence of iodine, the benzodiazepine anion dimerizes to a dihydrodibenzotetraazaheptafulvalene. Its further oxidation then gives rise to a new dibenzotetraazaheptafulvalene.

2,4-Bis-methylthio-1,5-benzodiazepine can also be used as a starting material for the preparation of new ketene mercaptals (Scheme 15). Treatment of the Li-salt with carbon disulfide yields a dianion of a dithiocarboxylic acid and this can be alkylated to form diazaheptafulvenes. With methyl bromoacetate, a ring closure takes place after the alkylation step and a thienobenzodiazepine is formed in high yield. A second ring closure can be carried

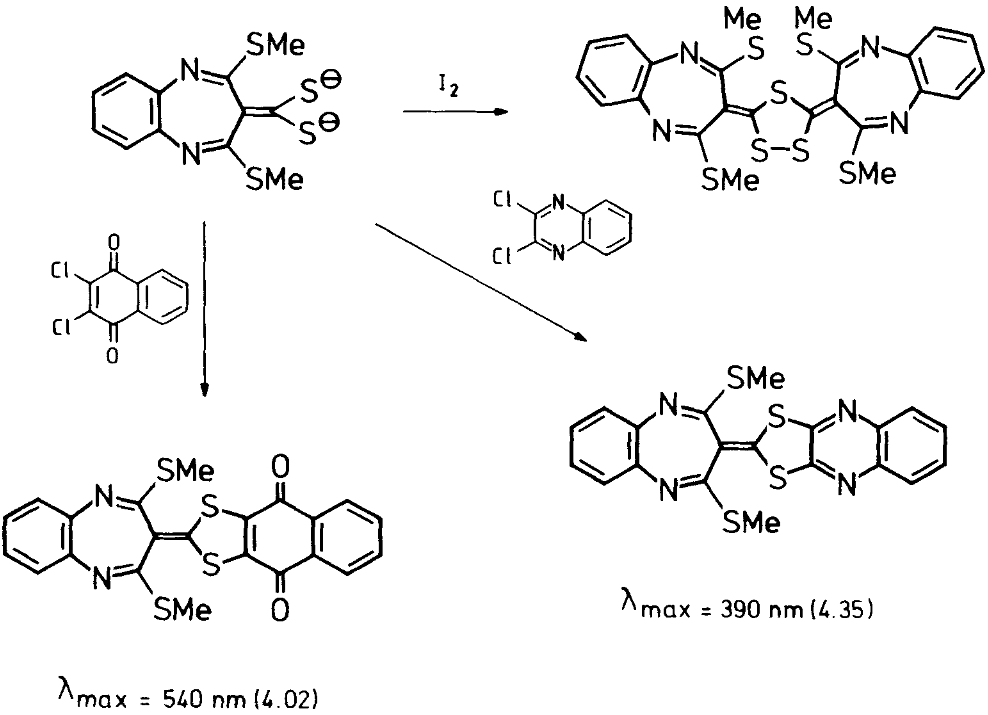


Scheme 15

out with potassium t-butoxide.

Further reactions of the benzodiazepin dithiocarboxylic acid are shown in Scheme 16. A trithiole derivative is obtained upon treatment with iodine. Sesquifulvalene derivatives are formed with dichloronaphthoquinone and dichloroquinoxaline.

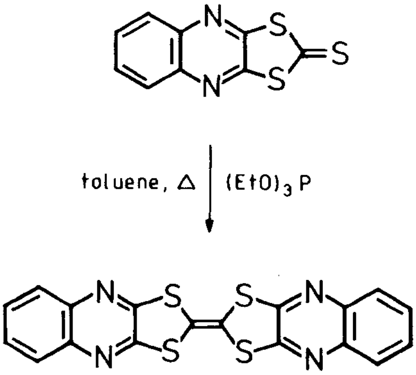
The "dimer" of the left hand part of the benzo-quinoxalinodiazadithiosesquifulvalene is listed in Scheme 14. The synthesis [13] of the corresponding "dimer" of the right hand part of this molecule is depicted in Scheme 17. Bis-quinoxalino-tetrathiafulvalene is virtually insoluble in most solvents.



λ_{max} = 540 nm (4.02)

λ_{max} = 390 nm (4.35)

Scheme 16



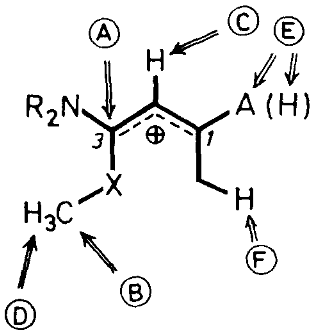
Scheme 17

Having described reactions of ambident anions leading to electron-rich thienothiophenes, to quinodimethanes and to fulvenes and fulvalenes of the benzodiazepine series, some reactions of sulphur-containing ambident cations and related compounds shall be discussed now. Target molecules are again electron-rich π-systems, particularly thiophenes, thiazoles and dithiafulvalenes.

As mentioned before, the APP is applicable also to ambident cations. Very useful compounds in this field are vinamidinium salts which can be looked at as allyl cations stabilized by two amino groups in 1,3-positions.

Reactions that are relevant in the context of applications of the allopolarization principle are summarized in Scheme 18. Electron-withdrawing substituents direct additions (A) to position 3[14], electron-releasing groups to position 1. Dealkylations (B) are normally unwanted. Deprotonation (C) at position 2 gives rise to electron-rich allenes[15].

Reactions with Bases / Nucleophiles



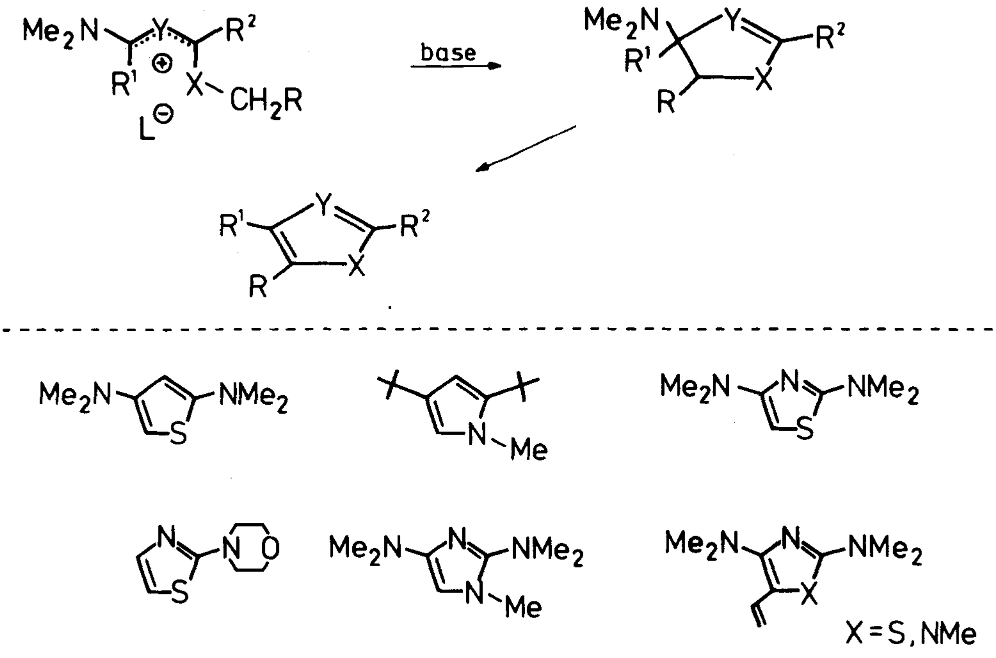
Ⓐ addition to C-3/C-1
Ⓑ dealkylation
Ⓒ → allenes
Ⓓ → 1,5-dipoles (1,5-dipolar cyclization)
Ⓔ → vinyl carbenes
Ⓕ → butadienes

Scheme 18

Deprotonation (D) leads to 1,5-dipoles which in turn undergo 1,5-dipolar cyclization [16,17]. If one includes 2-aza-vinamidinium salts in this kind of reaction, electron-rich thiophenes and thiazoles, pyrroles and imidazoles can readily be obtained in high yield. Removal (E) of the acceptor-group yields a nucleophilic vinyl carbene [18]. Deprotonation (F) of a methyl group at C-1 is a efficient synthesis of electron-rich butadienes [19,20].

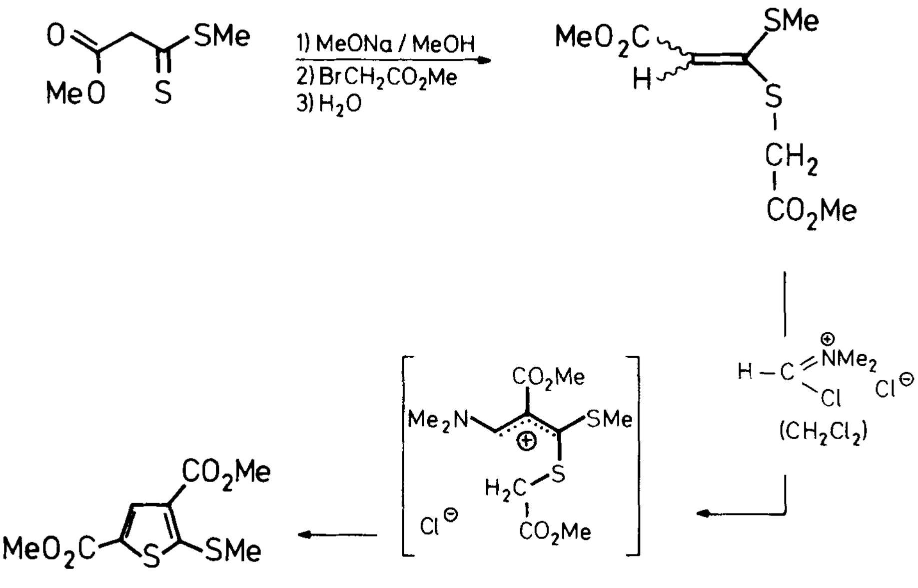
In this report only 1,5-dipolar cyclizations are considered.

Some typical electron-rich 5-membered heterocycles are presented in Scheme 19. Thiazoles and imidazoles are formed in excellent yields.



Scheme 19

An extension of this synthetic procedure is shown in Scheme 2o[21].

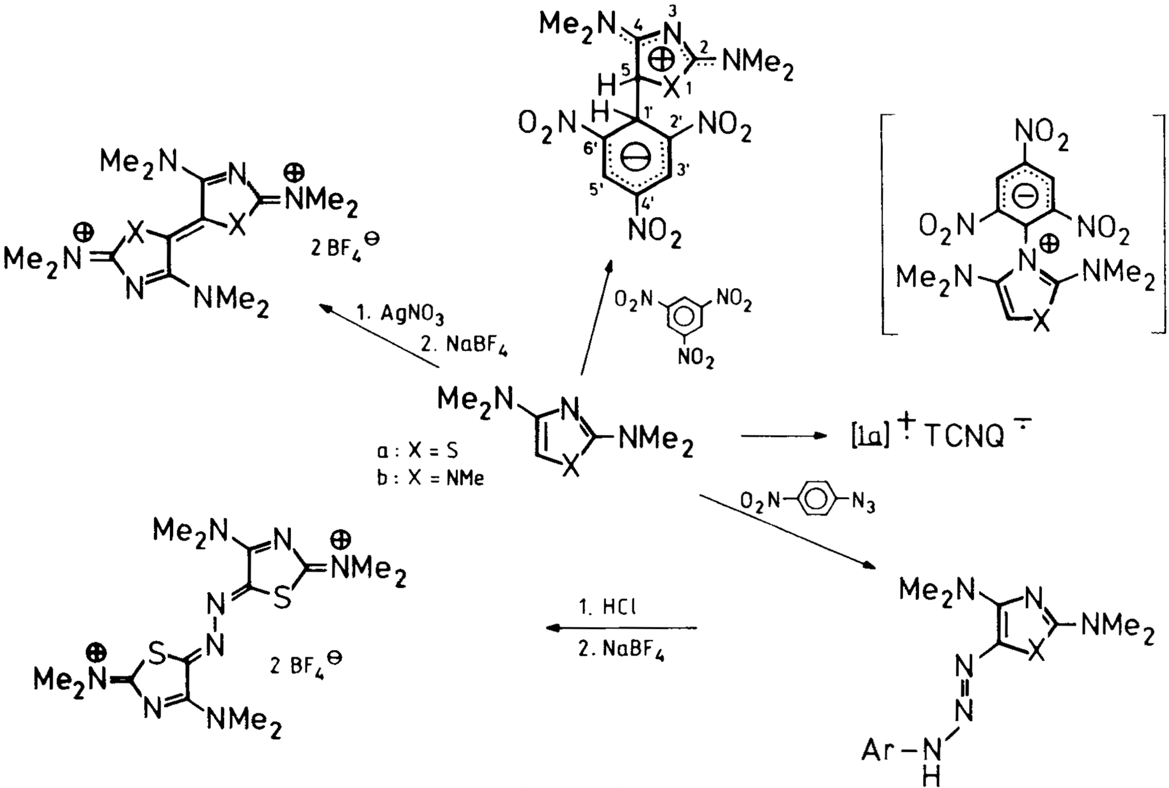


Scheme 2o

Dimethyl dithiomalonate reacts with methyl bromoacetate to a ketene mercaptal. One expects this compound to be transformed into a propeniminium salt on treatment with dimethylformamidechloride. Instead, dimethyl 5-methylthio-thiophene-2,4-dicarboxylate is obtained in high yield. This is the first case where a 1,5-dipolar cyclization takes place in the absence of a base.

Some reactions of electron-rich thiazoles and imidazoles are summarized in Scheme 21[22].

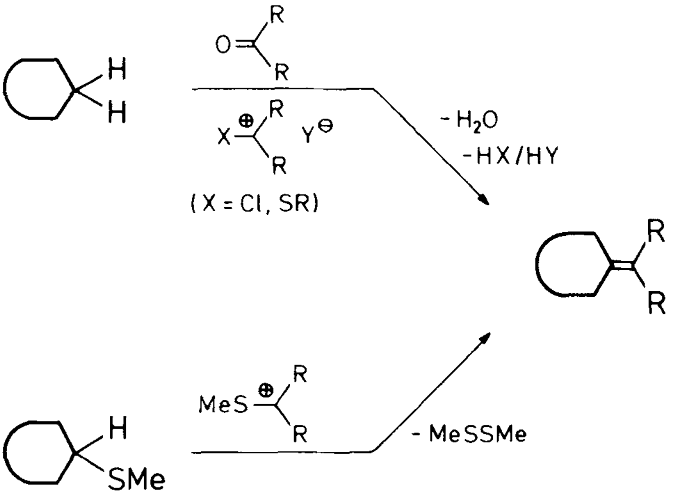
With TCNQ, black crystals of a radical cation salt are formed. With trinitrobenzene, a Meisenheimer complex is produced. With silver nitrate, the radical cations formed



Scheme 21

in the first step dimerize and further oxidation eventually gives rise to fulvalene derivatives.

As sulphur-containing fulvalenes are of paramount importance for the preparation of "organic metals" [1], this report shall be concluded with some more remarks on novel heterofulvalenes. Traditionally, fulvenes as well as fulvalenes are prepared from cyclopentadienes and carbonyl compounds (Scheme 22). An alternative used for the synthesis of fulvenes with electron releasing groups at C-6 and for fulvalenes is the condensation of cyclopentadienes with stabilized carbenium salts and their precursors such as amide chlorides and amide acetals or dithiolium salts.

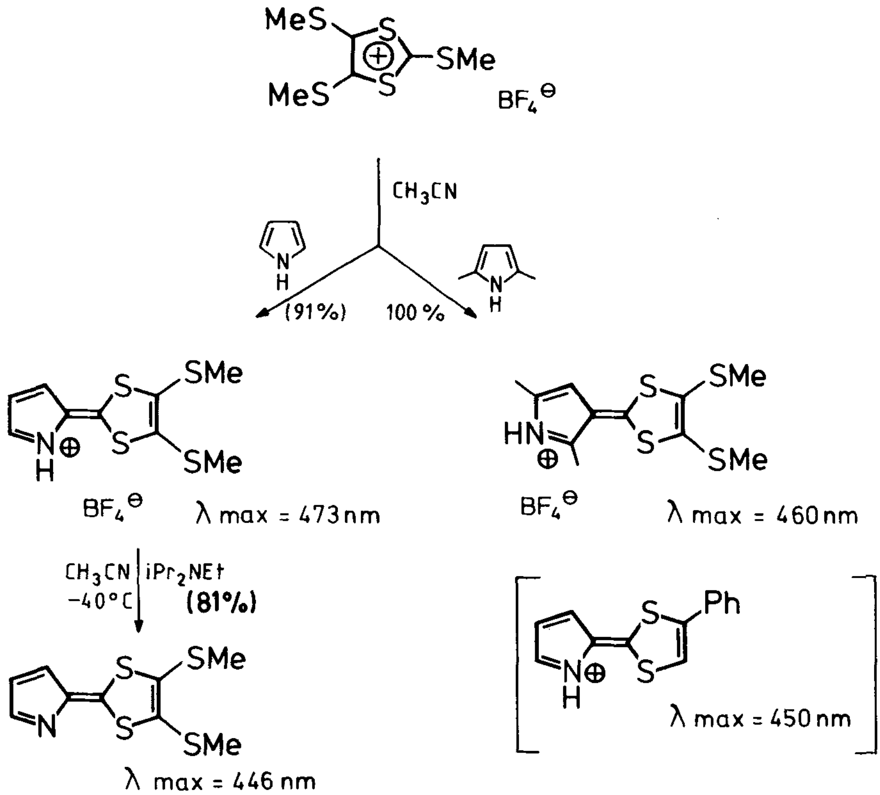


Fulven/Fulvalen - Syntheses

Scheme 22

A useful extension of these methods has now been found in the condensation of methylthio-cyclopentadienes and related compounds with methylthiosubstituted carbenium salts. The driving force of this condensation is the elimination of dimethyldisulfide in the second step (cf. ref. 23,24).

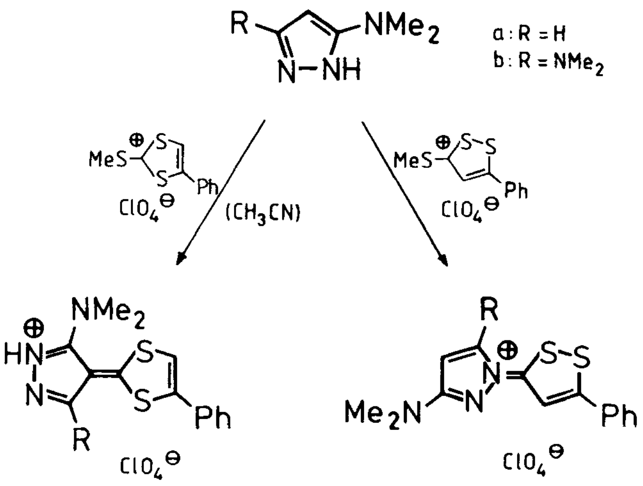
An example for a conventional fulvalene synthesis aimed on new fulvalenes with electron-releasing substituents is shown in Scheme 23. Tris-methylthio-1,3-dithiolium-fluoroborate [25] reacts, like other dithiolium salts, with pyrroles to azadithiofulvalenes. Indoles behave accordingly. Electron-rich pyrazoles, however, are an exception (Scheme 24). Dimethylaminopyrazole and Bis-dimethylaminopyrazole react with 1,3-dithiolium salts in the normal fashion and diazadithiafulvalenes are obtained. 1,2-Dithiolium salts, however, attack the nitrogen



Scheme 23

of the pyrazole ring and azoniafulvalenes are formed. Interestingly enough, they show a longer-wave-length absorption than normal fulvalenes.

The novel type of fulvalenes synthesis is depicted in Scheme 25. The sodium salt of pentakis-methylthio-cyclopentadiene has been prepared by Wudl [26]. On acidification of the sodium salt, we obtained pentakis-methylthio-cyclopentadiene [27]. When this compound is warmed up with 3-methylthio-5-phenyl-1,2-dithiolium-perchlorate in acetonitrile solution in the presence of Hünig's base, a pentakis-methylthio-dithiafulvalene is produced in fair yield [28].



λmax (lgε)	a	b
	440 (4.25)	405 (4.39)

λmax (lgε)	a	b
	486 (4.41)	492 (4.21)

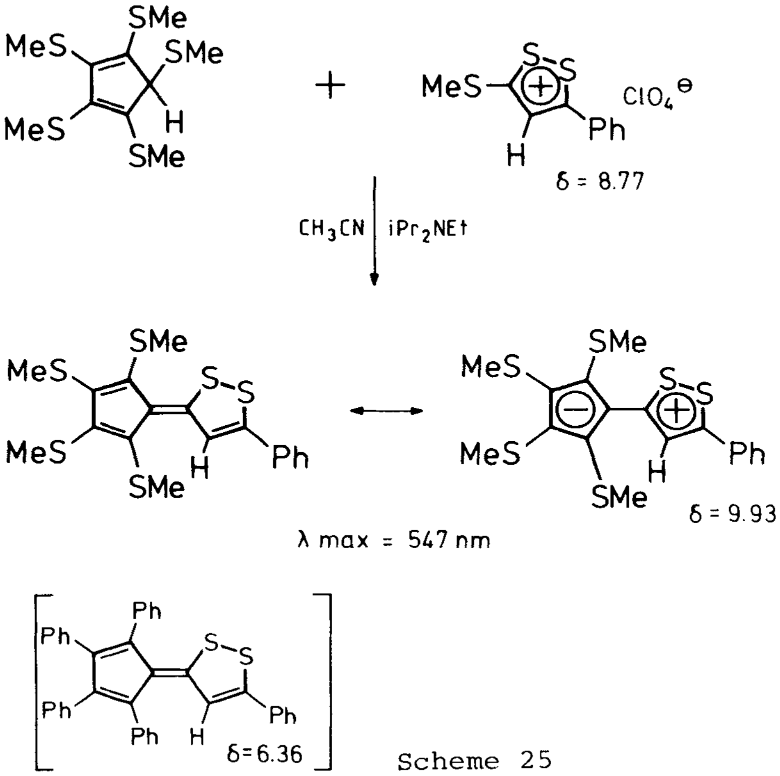
Scheme 24

1,3-Dithiolium salts react accordingly. These dithiafulvalenes are highly polar compounds as can be derived from their NMR spectra.

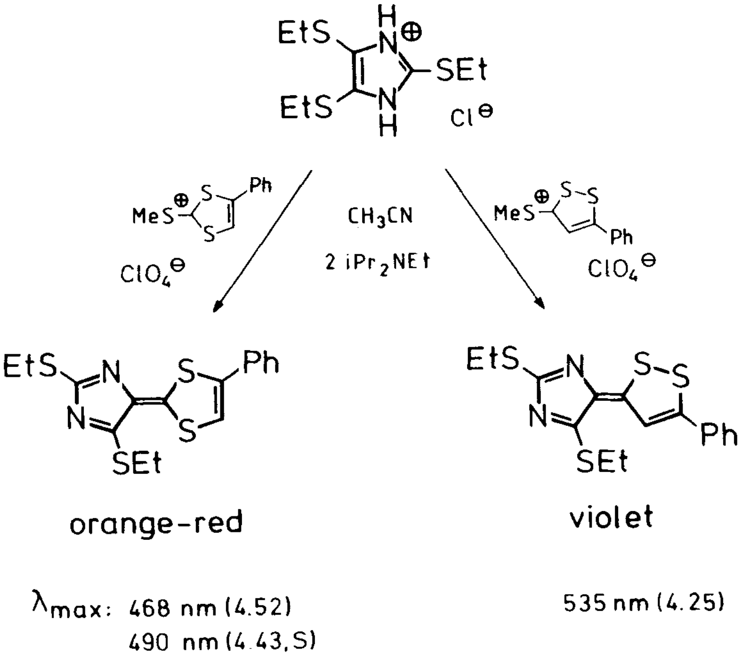
Tris-ethylthio-imidazole (Scheme 26) shows the same type of reaction with dithiolium salts. The electrophilic attack on the imidazole ring takes place exclusively at position 4.

Tris-ethylthio-imidazole is also the starting material for the preparation of tetraazafulvalenes (Scheme 27). The idea was to prepare a tris-ethylthioimidazolylium salt (cf. Ref. 29).

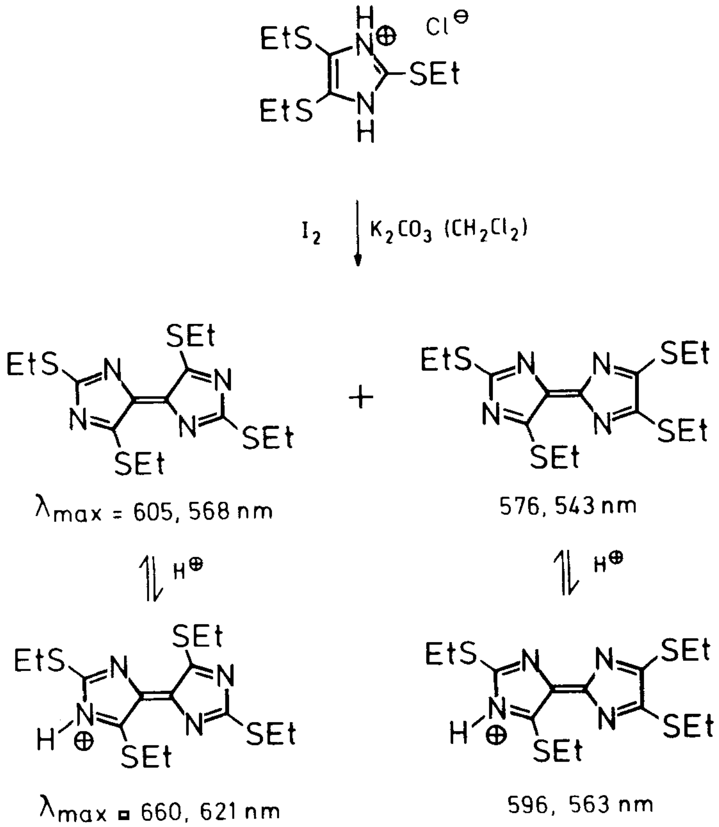
Instead, the intermediate imidazolyl radical dimerized and after spontaneous elimination of diethyldisulfide two isomeric tetraazafulvalenes were obtained in good yield.



Scheme 25

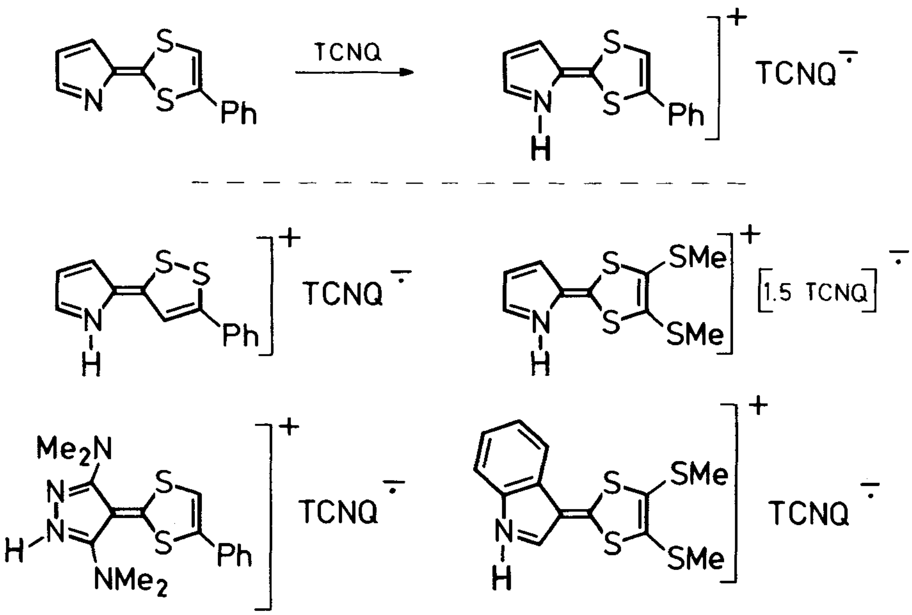


Scheme 26



Scheme 27

In contrast to the condensation shown in Scheme 26, coupling takes place here in position 4,4' and 2,4'. Like tetrathiafulvalene (TTF), the new azadithiofulvalenes are expected to form charge-transfer complexes with TCNQ and other electron acceptors. In most cases (Scheme 28), however, at least with TCNQ, fulvalenium salts are formed. Some of these salts are good electrical conductors [30] (Table 1).



Scheme 28

Electrical conductivity

(2-point probe, 1800 Kp/cm^2)

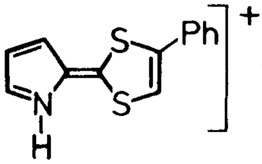
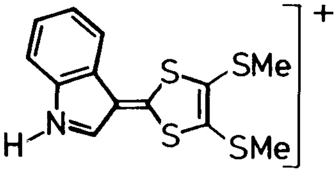
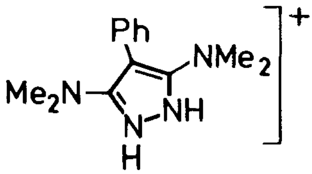
		σ (S/cm)
	$TCNQ^{\cdot -}$	5.6×10^{-12}
	$TCNQ^{\cdot -}$	8.3×10^{-3}
	$[1.5\ TCNQ]^{\cdot -}$	6.1×10^{-3}

Table 1

These results and results of work that is under progress demonstrate that the new diazaquinodimethanes, fulvalenes and electron-rich aromatic systems presented here are promising models for further studies in the field of organic metals.

Acknowledgement

Our work on ambident compounds and donor-acceptor-substituted aromatic, quinoid and fulvenoid compounds has been funded and continues to be funded by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. I am grateful to Dr. J. Hocker , Bayer AG, Leverkusen, for carrying out the conductivity measurements.

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