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NEW REACTIONS OF THIOBENZOPHENONE S-METHYLIDE

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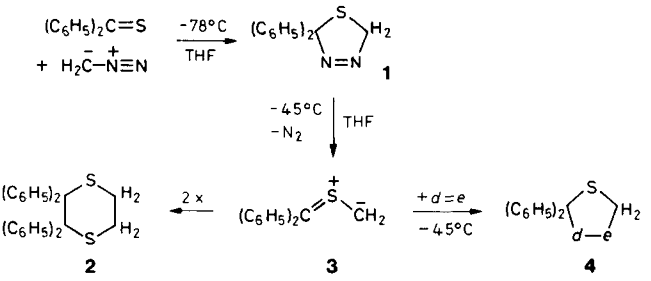
Summary 2,2-Diphenyl-1,3,4-thiadiazoline, prepared from thiobenzophenone and diazomethane at -78°C, extrudes N_2 at -45°C and allows to study in situ 1,3-cycloadditions of thiobenzophenone S-methylide (3) with electrophilic C=S, C=C, C≡C, and N=N bonds.

We reported recently that thiobenzophenone combines with one equiv. of diazomethane at -78°C in THF to furnish quantitatively 2,2-diphenyl-1,3,4-thiadiazoline (1), which eliminates nitrogen at -45°C with a half-life of 55 min.[1] The intermediate thiobenzophenone S-methylide (3) undergoes head-head dimerization to give the 1,4-dithiane derivative 2.



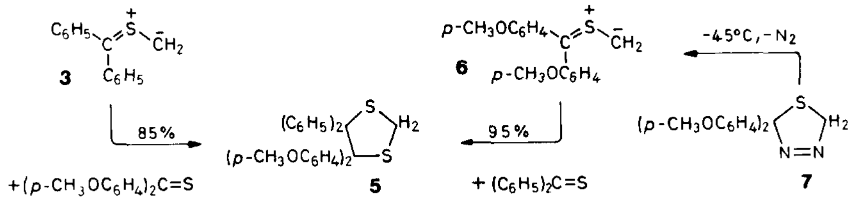
When a dipolarophile *d=e* was added at -78°C to the solution of 1, the thiocarbonyl ylide 3, generated on warming to -30°C, furnished the cycloadduct 4.[1] Thiobenzophenone or xanthione as dipolarophiles gave 1,3-dithiolanes whereas tetracyanoethylene, maleic anhydride and N-methylmaleimide afforded tetrahydrothiophenes. Also dimethyl acetylenedicarboxylate and azodicarboxylic ester were suitable dipolarophiles; in contrast, dimethyl fumarate and methyl propiolate failed to react.[1]

The scale of applicable dipolarophiles can be substantially extended by the simple trick of carrying out the in situ cycloadditions at -45°C. The stationary concentration of thiobenzophenone S-methylide (3) is smaller at -45°C than at -30°C so that many further dipolarophiles (usually 1.1 equiv.) win in the competition for 3 over the dimerization. Thus, the adducts of Table 1 were prepared.[2]

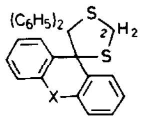
Amongst the two conceivable directions of addition to aromatic thioketones, the thiocarbonyl ylide 3 chooses the "thiophilic" one, i.e., its nucleophilic CH_2 group (vide infra) becomes bonded to the thioketone sulfur as testified by the reductive hydrogenolysis of the 1,3-dithiolanes.[1,3,4] The struc-

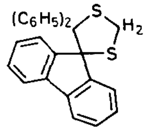
Table 1. 1,3-Dipolar cycloadditions of thiobenzophenone S-methylide to various dipolarophiles in tetrahydrofuran at -45°C

Dipolarophile	% Yield	m.p. (°C)	Formula
Thiobenzophenone	95	202 - 203	
4,4'-Dimethoxythiobenzophenon	85	181 - 183	5
Xanthione [1]	84	158 - 160	8
Thioxanthione [1]	95	149 - 151	9
Thiofluorenone	82	236° (dec)	10
4,5-Dioxo-1,3-dithiolane-2-thione	75	198 - 199	11
Methyl dithio-1-naphthoate	87	151 - 153	12
Diphenyl trithiocarbonate	85	162 - 163	
Methyl acrylate	80	78.5 - 79.5	16
Dimethyl fumarate	80	146.5 - 148	13
Dimethyl maleate	65	120 - 122	15
Tetramethyl ethylenetetracarboxylate	28	129 - 131	18
Maleic anhydride [1]	96	126 - 128	
N-Methylmaleimide [1]	80	174 - 176	
N-Phenylmaleimide [1]	79	208 - 209	
Acrylonitrile	76	141 - 143	17
Fumaronitrile	92	198 - 200	14
Tetracyanoethylene [1]	89	177 - 178.5	
Dimethyl 2,3-dicyanofumarate	82	196 - 197	
Dimethyl acetylenedicarboxylate [1]	70	140 - 142	19
Methyl propiolate	19	101.5 - 102.5	20
Dimethyl azodicarboxylate [1]	72	98 - 100	
4-Phenyl-1,2,4-triazoline-3,5-dione	87	160 - 162	



tures of "mixed" 1,3-dithiolanes are firmly established by their formation from two reactant pairs; e.g., only 5 fulfils the structural requirements imposed by the formation from 3 + p,p'-dimethoxythiobenzophenone and from the S-methylide 6 + thiobenzophenone. p,p'-Dimethoxythiobenzophenone is converted by diazomethane at -78°C to the crystalline thiodiazoline 7 which extrudes nitrogen in THF solution at -45°C with a half-life of 37 min giving rise to the ylide 6.


8 X = O
9 X = S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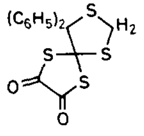
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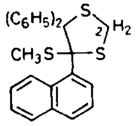
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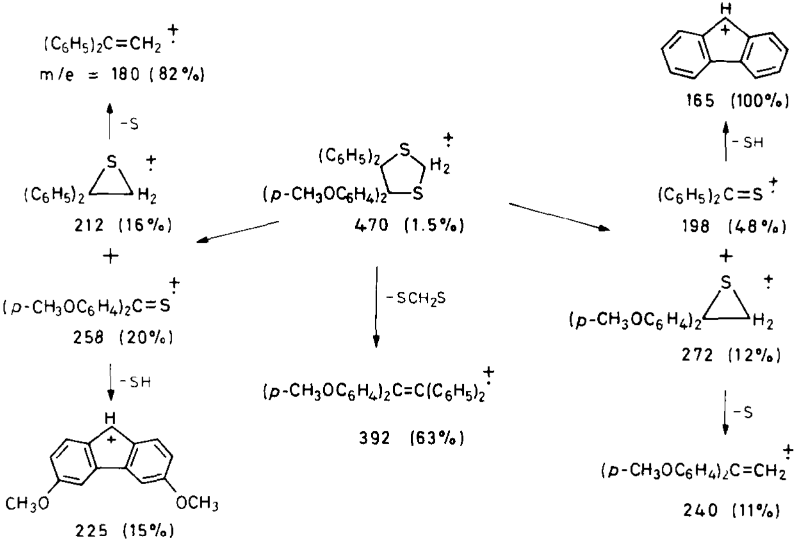
Analogously, the dithiolanes 9 and 10 were synthesized by the two independent pathways. Whereas 2-H_2 appeared as a singlet in the ^{1}H-NMR spectra of 5 (δ 3.66) and the spiro compounds 8 - 11 (4.11, 4.08, 4.28, 3.88), the expected AB spectrum at δ 3.25 and 3.81 with J = 9.3 Hz was observed for 12. The ^{13}C-NMR data confirmed that the CH_2 group is the 2-position in all 1,3-dithiolanes of Table 1.

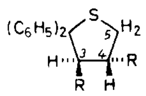
SCHEME 1



The noteworthy MS fragmentation pattern of the mixed 1,3-dithiolanes is illustrated in Scheme 1 by the radical cation of 5. In addition to the two splitting modes which mirror the dichotomy of formation, the occurrence of the tetraarylethylene radical cation indicates the loss of CH_2S_2. Both 1,1-diarylethylene radical cations are formed from ring carbon atoms which are non-bonded in 5. The radical cation species of the two thioketones lose SH as confirmed by the MS of the pure thioketones; the fluorenylium cation is an attractive structure and constitutes the base peak in Scheme 1.

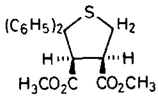
Thiobenzophenone S-methylide (3) refuses to accept p,p'-bis(dimethylamino)thiobenzophenone - more nucleophilic than the p,p'-dimethoxy compound - as a dipolarophile; 87% 1,4-dithiane 2 was isolated. Also O-methyl thiobenzoate and thiobenzamide were unreactive. Here resonance provides the CS bond with a higher single bond character than in the dithioester or trithiocarbonates of Table 1.

The cycloadditions of 3 with dimethyl fumarate and dimethyl maleate proceed stereospecifically. The adducts 13 and 15 were isolated with yields of 80% and 65%; the NMR spectra of the mother



13 R = CO_2CH_3

14 R = CN



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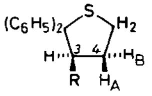
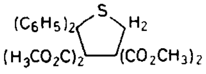


16 R = CO_2CH_3

17 R = CN



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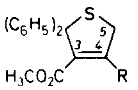
liquors did not reveal any mutual admixture. Due to the lower dipolarophilic activity of the cis-1,2-disubstituted ethylene, the maleate adduct 15 was accompanied by some dimer 2. Fumaronitrile gave rise to 92% of the tetrahydrothiophene 14, but in the presence of maleonitrile only the dimer 2 was obtained.

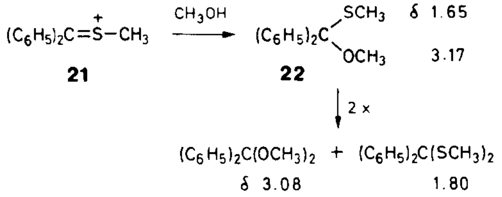
The formation of the 3-carboxylic ester 16 from 3 + methyl acrylate is suggested by the high-field methylester singlet at δ 3.31 and by the doublet of doublets for 3-H at 4.03. The 360 MHz ^{1}H-NMR spectrum of the acrylonitrile adduct[5] is fully resolved and only compatible with structure 17; the 3H-signal is quoted here: δ 3.95 (dd, $J_{3,4A}$ = 5.6 Hz, $J_{3,4B}$ = 9.0 Hz).

In contrast to tetracyanoethylene which is a top-notch dipolarophile, tetramethyl ethylenetetracarboxylate is a border line case as disclosed by 28% 18 besides 33% dimer 2. The 82% yield of the adduct from dimethyl 2,3-dicyanofumarate gave no indication of steric hindrance.



19 R = CO_2CH_3

20 R = H



21 **22**

Whereas dimethyl acetylenedicarboxylate furnished 70% 19, methyl propiolate is a limiting case. It required 4M methyl propiolate in THF to obtain 19% of adduct 20 besides 74% of the dithiane 2 at -45°C. Propiolic ester is usually regarded as an active electrophile; obviously, the thiocarbonyl ylide 3 is very selective and prefers to dimerize despite its low stationary concentration at -45°C. The 3-CO_2CH_3 and 4-CO_2CH_3 of 19 give rise to δ_H 3.40 and 3.73. The intermediate δ 3.53 of 20 forbids conclusions. The 5-H_2 in 20 couples with 3.0 Hz which is in accordance with $J_{2,3}$ of cyclopentene (2.1 Hz) and is too large for an allylic coupling; also the analogy with the acrylic ester adduct 16 supports 20.

The nucleophilic thiocarbonyl ylide 3 does not interact with nucleophilic solvents like methanol, piperidine or aniline. Therefore, decomposition of 1 at -40°C afforded only the dithiane 2, e.g., 84% in methanol. However, a few drops of trifluoroacetic acid changed the reaction course dramatically: 83% of benzophenone O,S-dimethylacetal (22) was formed which disproportionates in $CDCl_3$ within several weeks at 25°C. Protonation of 3 at the methylene C-atom leads to the supposed sulfonium ion intermediate 21. Thus, the charge distribution chosen in resonance structure 3 symbolizes the behavior of the 1,3-dipole on protonation and in its cycloaddition to electrophilic π-systems.

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5. The authors thank Professor M. Schlosser, Université de Lausanne, for the 360 MHz spectrum.

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