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THE CHEMISTRY OF 1,3,4-THIADIAZOLINE-2-SPIRO-2'-FENCHANE

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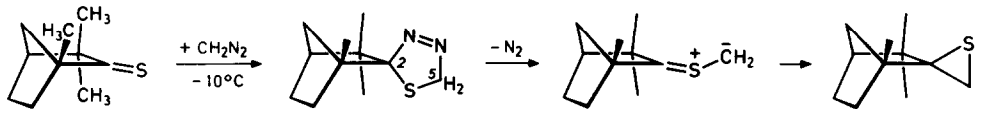
Summary Diazomethane adds to one of the two faces of the sterically hindered thiofenchone furnishing the title compound which extrudes N_2 at 46°C with $t_{1/2}$ = 22 min; the thiofenchone *S*-methylide is intercepted by dipolarophiles and acts as a base in reactions with methanol, thiophenol and acetic acid, in the latter case accompanied by skeletal rearrangement.

Thiofenchone (1), accessible from fenchone with H_2S + HCl,[1] is highly encumbered at the thione group and, therefore, stable in the monomeric state. Beiner et al.[2] reacted 1 with diazomethane at 0°C and obtained 50% of the spirothiiranes, *exo* (4) and *endo* 65:35, after gas chromatography.

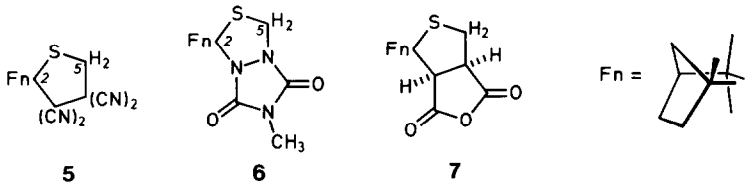


1 2 3 4

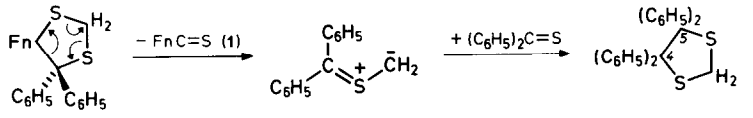
Diazomethane was passed into the orange etheral solution of 1 at -10°C until the color turned yellow. The ^{1}H NMR spectrum (C_6D_6) indicated a *single* spiro-1,3,4-thiadiazoline, probably the *exo*-adduct 2: δ = 0.45, 0.65, 0.70 (3s, 3 CH_3), 4.92 (s, 5-H_2). The colorless 2, mp 66-67°C (dec), crystallized from pentane or ether at -78°C.[3]

The N_2 extrusion from 2 - a 1,3-dipolar cycloreversion - followed the first order with $10^4 k_1$ = 5.2 s^{-1} at 46°C and 7.0 s^{-1} at 52°C (toluene, volumetry). ^{1}H NMR analysis with standard (Cl_2C=CHCl) showed 63% of the thiiranes (bp 55-60°C/0.001 torr), *exo* (4) and *endo*, the assignment in the 60:40 mixture remaining open.

The intermediacy of thiofenchone *S*-methylide (3) was established by trapping reactions. The solution of 2 and 1.2 equiv. of *tetracyanoethylene* in THF evolved 98% N_2 in 2 h at 45°C. ^{1}H NMR analysis revealed 88% of 5A + 5B in a 67:33 ratio. Thus, the dipolarophile approaches 3 from both faces, the attribution of the cycloadducts to *endo* and *exo* being uncertain. Separation furnished 5A, mp 166-167°C, and 5B, mp 165-166°C. The diastereotopic 5-H_2 appear at δ 2.45 and 2.65 with *J* = 13.5 Hz for 5A and at 2.41 and 2.67, *J* = 13.8 Hz, for 5B (C_6D_6), the δ(C-5) triplets were found at 39.0/41.5 and the singlets of δ(C-2) at 78.5/81.8 ($CDCl_3$).



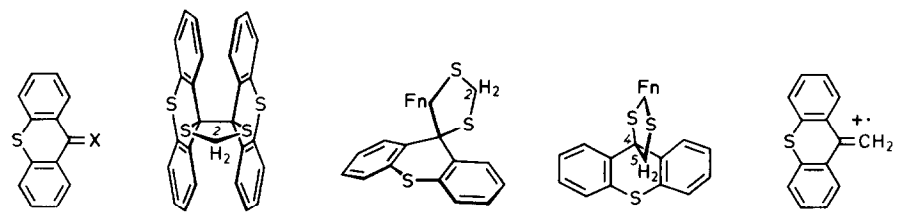
5 6 7



8 9 10

Diastereomeric cycloadducts 6 were likewise observed with *4-methyl-1,2,4-triazoline-3,5-dione*; the rate of N_2 evolution from 2 was independent of the dipolarophile. ^{1}H NMR analysis resulted in 54% of 6A + 6B (55:45); only the major isomer was obtained pure, mp 166-167°C (dec). AB spectra of 5-H_2 occur at δ 4.44 and 4.58 (J = 8.0 Hz) for 6A and at 4.48 and 4.84 (J = 9.2 Hz) for 6B ($CDCl_3$). Thiofenchone radical cation is the base peak in the MS of 6A. The reaction of 2 with *maleic anhydride* was less productive: 22% of crystalline 7, mp 185-186°C. Distillation of the mother liquor afforded 38% of a product isomeric with the 1,3-dipole 3 (see below).

The interaction of 2 with 2 equiv. of *thiobenzophenone* took an unusual course. ^{1}H NMR analysis with standard disclosed the presence of 88% of both thiofenchone (1, CH at δ 2.29) and 4,4,5,5-tetraphenyl-1,3-dithiolane (10, 5-H_2 at δ 3.72); 10, 206-208°C ($CHCl_3$/pentane), was identified with the product from thiobenzophenone and diazomethane.[4,5] Probably the cycloaddition of the thiocarbonyl ylide 3 to thiobenzophenone renders the very crowded 1,3-dithiolane 8 which *in situ* breaks down in a 1,3-dipolar cycloreversion yielding 1 and thiobenzophenone *S*-methylide (9). The latter is intercepted by the second molecule of thiobenzophenone affording 10.

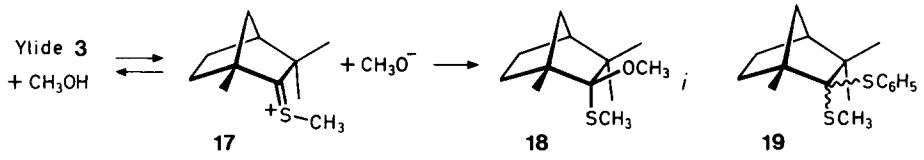


11 X = S
12 X = $\overset{+}{S}-\overset{-}{C}H_2$
13 14 15 16

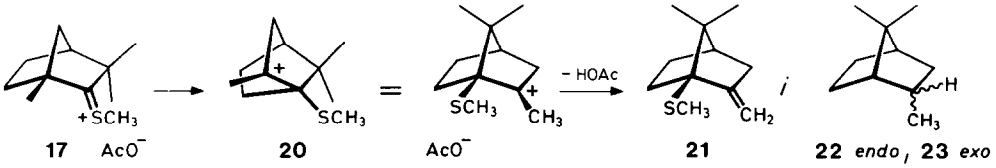
The steric requirements of the rigid *thioxanthione* (11) exceed those of thiobenzophenone. The solution of 2.0 mmol 2 was stirred with 2.2 mmol 11 in 4 ml THF for 8 h at 40°C (98% N_2). After removal of the solvent, trituration with $CDCl_3$ left 0.60 mmol of 13 undissolved, mp 169-170°C, identical with the

product from 11 and diazomethane.[6] From the ^{1}H NMR spectrum of the $CDCl_3$ solution (Cl_2CH-$CHCl_2$, standard) 49% of the dithiolanes 15 (*exo* and *endo*) were analyzed by their 5-H_2 signals. Tlc on silicagel yielded thiofenchone and the *exo,endo* mixture of 15 (colorless crystals, mp 168-175°C) which we could not separate; comparison of the ^{13}C NMR signals provided the ratio 85:15. The 5-H_2 of the major isomer appeared at δ_H 3.44 and 3.73 (AB, J = 12.3 Hz) whereas the singlet at δ 3.52 was assigned to the minor isomer (C_6D_6). CS hydrogenolysis of 15 with Raney-Ni (W-2)[7] in refluxing ethanol furnished 60% 1,3,3-trimethylnorbornane (δ_H 0.95 for 2 CH_3, 1.05 for CH_3) and 79% 1,1-diphenylethane (δ_H 1.52 and 3.99, d and q, J = 8.0 Hz). The occurrence of the base peak at m/e = 210 - $C_{14}H_{10}S$ is the radical cation 16 - in the MS of 15 accords with the fragmentation of *type B* dithiolanes.[8]

Thus, thione 11 accepts the 1,3-dipole 3 in the two addition directions. The electronically favored one produces the highly crowded 14 which undergoes cycloreversion to 1 and thioxanthione *S*-methylide (12) which captures a second molecule of 11 forming 13. Dithiolane 15 constitutes the sterically favored orientation and is stable; the *exo,endo* assignment is unknown.



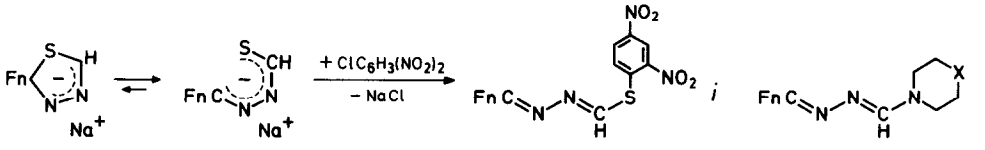
Thiofenchone *S*-methylide (3) is a base. Extrusion of N_2 from 2 in *methanol* (8 h, 40°C) produced 96% fenchone *O,S*-dimethylacetal (18), mp 126-128°C; ^{1}H NMR ($CDCl_3$): δ = 1.10, 1.13, 1.16 (3s, 3 CH_3), 1.93 (s, SCH_3), 3.42 (s, OCH_3). Without evidence for another diastereomer, we assume a proton transfer to 3 and an *exo* attack of the nucleophile on the sulfonium ion 17. The interaction of 3 with 1.1 equiv of *thiophenol* in THF furnished 94% of two dithioacetals 19; $\delta(SCH_3)$ 2.12 and 2.15 ($CDCl_3$). The ratio of diastereomers - originally 7:3 - was reversed to 1:9 on contact with silica gel; 1:9 probably refers to the equilibrium. The conversion of 18 and 19 to fenchone 2,4-dinitrophenylhydrazone, mp 159-161°C, confirmed the unchanged carbon skeleton.



Elimination of N_2 from 2 in THF at 40°C in the presence of 1 equiv *acetic acid* yielded 52% $C_{11}H_{18}S$, mp ∿20°C, *i.e.*, an isomer of thiofenchone *S*-methylide (3). ^{1}H NMR singlets at δ 0.78 and 1.05 (2 CH_3), 2.07 (SCH_3), as well as at

4.83 and 5.12 (broad, $=CH_2$) revealed the conversion of C-CH_3 to S-CH_3. The structure of 1-methylthio-α-fenchene (21) found support in the reduction to 2,7,7-trimethylnorbornane (22 and 23, 32:68) by Ni/ethanol. The same 19 (instead of 20) ^{13}C NMR signals of 22 + 23 occurred in the reduction product of α-fenchene with Ni/ethanol in a 39:61 ratio whereas H_2/Pd converted α-fenchene to a 71:29 mixture of 22 + 23. A careful comparison of the ^{13}C NMR spectra led to the assignment, and a statistical analysis gave the *endo/exo* ratios.

Structure 21 indicates a Wagner-Meerwein rearrangement of cation 17 yielding the *tert*-carbocation 20 which transfers a proton to the acetate anion. The pathway to a by-product, 45% fenchone dimethyldithioacetal (mp 117-119°C, δ_H 2.05, 2.11 for 2 SCH_3), is still to be clarified.



24 **25** **26** X = CH_2; **27** X = O

The acidity of a 1,3,4-thiadiazoline and the electrocyclic ring opening of its anion were demonstrated previously.[9] The solution of 2 and 1 equiv sodium methoxide did not lose N_2 at 45°C; the sodium salt of the ring-opened anion 24 reacted with 2,4-dinitrochlorobenzene furnishing 25: yellow needles (56%), mp 72-73°C, δ_H 7.80 (s, HC=N). The reactions of 2 with piperidine or morpholine likewise proceeded as described for the adamantane derivative.[9] The formamidrazones 26 and 27 were isolated in 48% and 42% yield after chromatography.

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