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CYCLOADDITIONS OF DIALKYL THIOKETONE-*S*-METHYLIDES [1]

Rolf Huisgen* and Grzegorz Mloston [2]

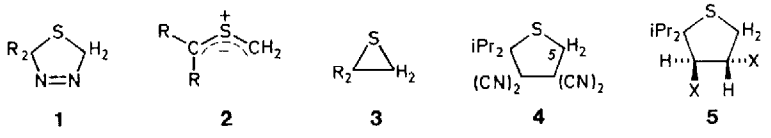
Institut für Organische Chemie der Universität München
Karlstr. 23, D-8000 München 2, Federal Republic of Germany

Summary Various mechanistic criteria were employed in the effort to establish the borderline between one-step and two-step pathways in the reactions of two thiocarbonyl ylides, diisopropyl, and di-*tert*-butyl thioketone-*S*-methylide, with electron-deficient alkenes and thiones.

What is required for the two-step mechanism of 1,3-cycloaddition to predominate over the concerted pathway ? Theory and experiment suggest that a great difference of the π-MO energies of a nucleophilic 1,3-dipole and an electrophilic dipolarophile coupled with steric hindrance are necessary.[3] Exploring the *borderline between one-step and two-step processes* requires careful structural variation. Amongst the known 1,3-dipoles, thiocarbonyl ylides probably have the highest π-MO energies. Comparison of thione-*S*-methylides 2 with isopropyl and *tert*-butyl in the role of R has proved informative.

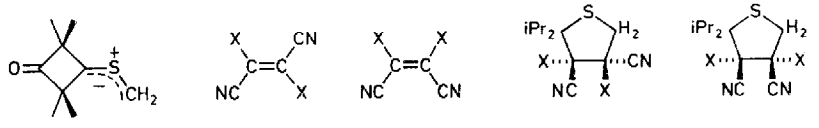
Diisopropyl thioketone-*S*-methylide (2a) was generated from the thiadiazoline 1a [4] by N_2 extrusion in the presence of 1.1 equiv of dipolarophile at 65°C (THF, 6 h). Quantitative ^{1}H NMR analysis ($CDCl_3$) with weighed standard was followed by isolation and characterization; 2a resembles adamantanethione-*S*-methylide [6] in its reactivity (Table 1). The ^{1}H NMR signals of the isopropyl groups in thiolanes and 1,3-dithiolanes [5] reflect symmetry: diastereotopic pairs of methyls, *e.g.*, in 4, versus four CH_3 doublets in 5, 12-14.

Thione-*S*-methylide 6 reacts *nonstereospecifically* with dimethyl 2,3-dicy-



1 **2** **3** **4** **5**

a: R = $CH(CH_3)_2$ b: R = $C(CH_3)_3$



6 R = H **8** X = CO_2CH_3 **9** **12** X = CO_2CH_3 **13**
7 R = CH_3 **10** X = CF_3 **11** **14** X = CF_3

anofumarate (8) and the cis-isomer 9.[7,8] The test failed here because catalysis of the cis,trans isomerization, 8 ⇌ 9 (equil. 91:9) by the thiadiazoline 1a could not be suppressed. Trans- and cis-adduct, 12 and 13, resulted in 67:33 ratio, but it is not clear whether or not rotation in a zwitterionic intermediate 15 is partly responsible. The alternative concerted pathway is supported by the formation of only one adduct, 14, with 2,3-bis(trifluoromethyl)fumaronitrile (10).

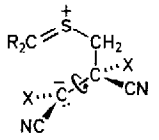
Table 1. Cycloadditions of diisopropyl thioketone-*S*-methylide in THF at 65°C

Dipolarophile	% Yield	mp(bp)	Formula
Tetracyanoethylene	82	79-80.5°C	4
Dimethyl fumarate	90	(70°C/0.2)	5, X = CO_2CH_3
Fumaronitrile	79	114-115°C	5, X = CN
N-Phenylmaleimide	70	80-82°C	
Dimethyl 2,3-dicyano-fumarate	60	116-117°C	12
	29	117-119°C	13
2,3-Bis(trifluoromethyl)fumaronitrile	98	(90°C/0.2)	14
Benzylidene malononitrile	90	98-99°C	22
Methyl α-cyanocinnamate	96	106-108°C	24
Thiobenzophenone	67	138-140°C	25
	22	93-96°C	28
Diisopropyl thioketone	39	oil	31

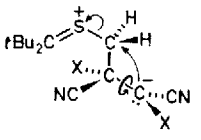
How different behaves di-*tert*-butyl thioketone-*S*-methylide (2b) generated from 1b at 100°C.[4] Ylide 2b is no longer planar and was not intercepted by dimethyl acetylenedicarboxylate or azodicarboxylate; thiirane 3b (73 and 80%) was obtained instead.

The reaction with 1.1 equiv of 8 (4 h toluene, 100°C) afforded 41% each of the trans- and cis-cyclopropane derivatives 17 and 18 which were identified with authentic specimens;[9] the red solution showed the ^1H singlet of di-*tert*-butyl thioketone. Zwitterion 16 is the logical precursor; *intramolecular nucleophilic substitution* with the thione as leaving group gives rise to 17 and 18. Recently we observed this reaction type in the system 7 + 8,[10] but the loss of stereochemical integrity was moderate there. Here 2b combined with dimethyl dicyanomaleate (9) furnishing the same 1:1-mixture of 17 and 18. It remains open whether rotational equilibrium of 16 or a thiadiazoline-catalyzed equilibration, 8 ⇌ 9, is responsible.

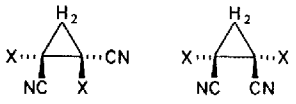
In the gauche zwitterion 15, R = $C(CH_3)_3$, the bulky *tert*-butyl groups prevent *1,5 combination*, i.e., thiolane formation. However, *1,? recombination* was observed when the acceptor olefins 10 and 11 were used as dipolarophiles. Heating of 1b with 1.15 equiv of 10 in $CDCl_3$ to 110°C for 30 min (81% conver-



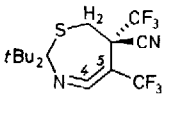
15 *gauche*



16 *anti*



17 X = CO_2CH_3 **18**
19 X = CF_3



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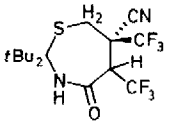

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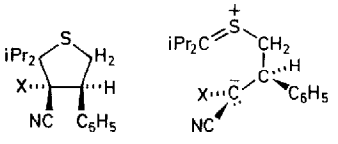
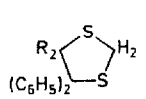


22 X = CN **23**
24 X = CO_2CH_3

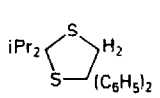
sion of 1b) afforded the *7-membered cyclic ketene imine* 20 and the trans-cyclopropane 19 in 78:22 ratio. The pale-yellow crystals of 20 (mp 81-82°C), stabilized by the CF_3 groups, showed the strong IR absorption of C=C=N at 2039 cm^{-1}. C-4 appears at δ_C 181.8 and C-5 at 60.1, both as quartets with C-F coupling (J = 3.6 and 41 Hz). Aqueous THF converted 20 to the lactam 21 (mp 147-148°C). The cis acceptor olefin 11 produced 20 and 19 in the same ratio as 10 on heating with 1b.

In the reaction of 6 with 10 the corresponding ketene imine was likewise the major product as recently reported;[11] in solution it slowly rearranged to the thiolane. Ketene imine 20 is likewise thermolabile; via 15 and 16 it is converted to trans-cyclopropane 19 + thione (20/19 = 38:62 after 50 min at 110°C).

In contrast to 2b, the question "concerted or nonconcerted cycloadditon" is still open for 2a. The latter combined with benzylidene malononitrile and methyl α-cyanocinnamate furnishing *regioselectively* 22 and 24 in high yields (Table 1); the orientation was established by the ABX pattern of the ring protons. AMPAC calculation[12] of thioacetone-*S*-methylide provided nearly identical AO coefficients for the C termini of the π-HO,[13] *i.e.*, comparable nucleophilicities are expected for the π termini of 2 within the concerted mechanism. The intermediacy of zwitterion 23 would offer a way out, but we regard the evidence as inconclusive.



25 R = $CH(CH_3)_2$
26 R = C_6H_5
27 R = $C(CH_3)_3$



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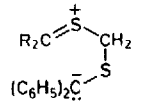
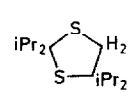


29 R = $CH(CH_3)_2$
30 R = $C(CH_3)_3$



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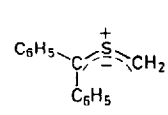

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Interaction of 2a with thiobenzophenone provided 89% of the regioisomeric 1,3-dithiolanes 25 and 28 (75:25); $\delta_C(CH_2)$ allowed structural assignment on the basis of earlier experience.[14] Conspicuously, the sterically burdened 25 is the major product. In the framework of an uncertain two-step mechanism, a zwitterionic (or biradical) intermediate 29 is conceivable. Diisopropyl thioketone accepted 2a only affording the sterically preferred dithiolane 31; the yield was only 39% and ∿30% thiirane 3a testified to a low cycloaddition rate.

The di-*tert*-butyl compound 2b reacted with 2 equiv of thiobenzophenone (4 h 100°C, toluene) yielding 67% of 26 and 75% of di-*tert*-butyl thioketone besides 13% 3b. 4,4,5,5-Tetraphenyl-1,3-dithiolane (26) is the product of the Schönberg reaction of thiobenzophenone and diazomethane.[15] Here, 26 must come from a 1,3-dipole metathesis furnishing thiobenzophenone-*S*-methylide (32) and the aliphatic thione; 32, in turn, combines with thiobenzophenone. Of the two conceivable intermediates, 27 or 30, we slightly prefer the open-chain 30 to the sterically congested cycloadduct 27. Does 26 originate from a *one-step* or *two-step* cycloaddition of 32 + $(C_6H_5)_2C{=}S$?

REFERENCES

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