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SYN-ANTI SELECTIVITY OF CIS-3,4-DISUBSTITUTED CYCLOBUTENES

Part 3: Chloro-thio- and Dithio-substituted Cyclobutenes [1]

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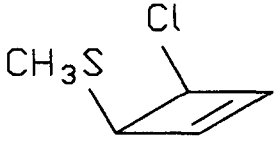
Summary: Cycloadditions of the 3.4-substituted cyclobutenes L, M with diazoalkanes RR'CN$_2$, R = H und R' = H, alkyl, aryl or alkoxycarbonyl exclusively yield syn-adducts. Diphenylnitrilimine and mesitonitrile oxide mainly undergo anti-addition.

The remarkable contra-sterical syn-addition of diazoalkanes to cis-3,4-dichlorocyclobutene [2] has led to the following interpretations:

a) lone pair interactions,
b) out-of-plane distortions of the olefinic hydrogen atoms, and
c) interaction with low-lying σ^* (C-Cl) orbitals [3].

Torsional effects in transition structures have also been considered [2].

In order to investigate particularly the influence of the contributions a) and c) the cyclobutenes L und M were synthesized [4] and their stereo- and regioselectivity in reactions with dipoles was studied. Sulphur atoms have lone pair orbitals which are more easily to be ionized than those of chlorine atoms whereas the electron affinity of the C-S bond is comparable to that of the C-Cl bond.



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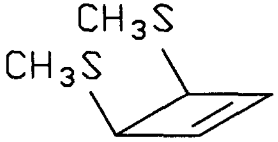
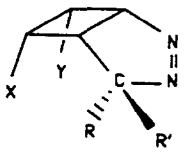


M

To be able to carry out comparative studies, we used almost the same dipoles for our investigation as for the additions to 3,4-dichlorocyclobutene [2].

The experiments yielded the following types of compounds:



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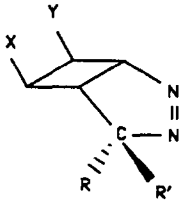

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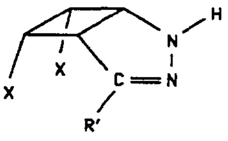

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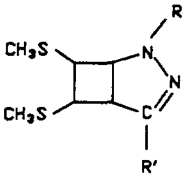

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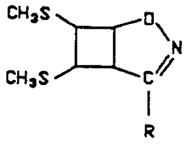

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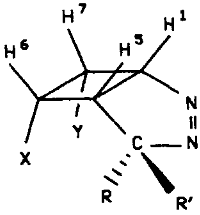
Exclusively syn-adduct (type 1) was formed with R = H and:
R': = H (11), = CH_3 (12), = CO_2-tert-butyl (13), = C_6H_5 (14), = (C_6H_4-4-NO_2) (15), = (C_6H_4-3-NO_2) (16), = (C_6H_4-2-NO_2) (17), = (C_6H_4-4-Cl) (18), = (C_6H_4-2-Cl) (19), = (C_6H_4-4-CH_3) (20), = (C_6H_4-4-OCH_3) (21), = (C_6H_4-4-CN) (22).
Exclusively anti-adduct (type 2) was formed with: R,R' = -C_6H_5 (23).
The Δ^2-pyrazoline (type 3) was obtained in one case (compound M17 with R'= -(C_6H_4-2-NO_2)).
The reactions of compound M with diphenylnitrilimine and mesitonitrile oxide leading to type 4 and 5 gave the compounds M24 und M25 (each syn and anti).

The experimental results are summarized in the following table.

Compound	R	R'	Yield [%]	Melting point [°C]	Addition	Remarks
L 11	-H	-H	87	yellow Oil	syn	8:9 = 1:2
L 12	-H	-CH_3	72	47/84	syn	8:9 = 1:2
L 13	-H	-CO_2-tert-butyl	18	90-96	syn	8:9 = 4:1
L 14A	-H	-C_6H_5	17	127-128	syn	8:9 = 1:3
L 14B	-H	-C_6H_5	51	83-85	syn	
L 15	-H	-(C_6H_4-4-NO_2)	60	128-131	syn	8:9 = 1:2.5
L 16	-H	-(C_6H_4-3-NO_2)	49	99/111	syn	8:9 = 1:1.8
L 17	-H	-(C_6H_4-2-NO_2)	55	140-141	syn	only 8
L 18	-H	-(C_6H_4-4-Cl)	65	107-110	syn	8:9 = 1:1.5
L 19	-H	-(C_6H_4-2-Cl)	52	134.5-135	syn	only 8
L 20	-H	-(C_6H_4-4-CH_3)	67	115/135	syn	8:9 = 1:1.5
L 21	-H	-(C_6H_4-4-OCH_3)	62	98/110	syn	8:9 = 1:1.2
L 22	-H	-(C_6H_4-4-CN)	67	99/118	syn	8:9 = 1:1.77
L 23	-C_6H_5	-C_6H_5	21	120-121	anti	8:9 = 1:7

Compound	R	R'	Yield [%]	Melting point [°C]	Addition	Remarks
M 11	-H	-H	83	37-37.5	syn	
M 12	-H	$-CH_3$	74	61	syn	
M 13	-H	$-CO_2$-tert-butyl	7	83-84	syn	
M 14	-H	$-C_6H_5$	59	127-128	syn	
M 15	-H	$-(C_6H_4$-4-$NO_2)$	55	139-141	syn	
M 16	-H	$-(C_6H_4$-3-$NO_2)$	38	128-130	syn	
M 17	-H	$-(C_6H_4$-2-$NO_2)$	48	123-124	syn	^{2}-pyrazoline (type 3)
M 18	-H	$-(C_6H_4$-4-Cl)	55	125-126	syn	
M 19	-H	$-(C_6H_4$-2-Cl)	53	77	syn	
M 20	-H	$-(C_6H_4$-4-$CH_3)$	56	102-103	syn	
M 21	-H	$-(C_6H_4$-4-$OCH_3)$	44	124-125	syn	
M 22	-H	$-(C_6H_4$-4-CN)	52	161-163	syn	
M 23	$-C_6H_5$	$-C_6H_5$	21	93-94	anti	
M 24A	$-C_6H_5$	$-C_6H_5$	74	128-129	anti	syn:anti = 1:24 (type 4)
M 24B	$-C_6H_5$	$-C_6H_5$	3	179-180	syn	
M 25A	Mesityl		69	136	anti	syn:anti = 1:10 (type 5)
M 25B	Mesityl		7	137-138	syn	

^1H-NMR spectra were measured for all compounds listed in the table. The stereo- und regioisomers formed in these reactions were definitely characterized.



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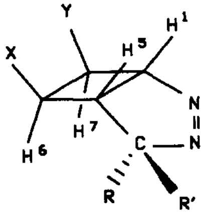

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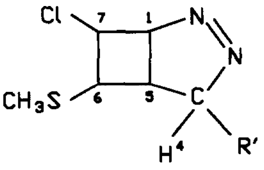

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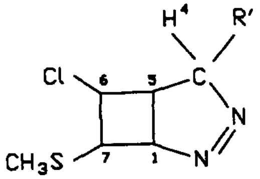

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Only a few representative compounds will be discussed spectroscopically. As a criterion of assignment for the stereoisomers 6 and 7 the corresponding $^3J_{5,6}$ und $^3J_{1,7}$ coupling constants were used, which are higher for the <u>syn</u>-adduct.

	syn-Addition			anti-Addition
	L14A (8)	**L14B (9)**	**M14**	**M23**
${}^3J_{5,6}$	8.1 Hz	8.2 Hz	8.0 Hz	7.2 Hz
${}^3J_{1,7}$	7.9 Hz	8.2 Hz	8.0 Hz	2.2 Hz

As example for the chemical shifts of the possible regioisomers 8 and 9 compound L14 with R = -H and R' = $-C_6H_5$ was chosen.

L14	H^1	H^4	H^5	H^6	H^7
Isomer 8	5.8 ppm	6.1 ppm	2.8 ppm	4.1 ppm	5.2 ppm
Isomer 9	5.7 ppm	6.1 ppm	2.9 ppm	5.0 ppm	4.4 ppm

The experimental results obtained for the compounds L and M show clearly for the diazoalkane series that in the case of R = H exclusively syn-addition takes place independent of the substituent R' in the dipole, as has already been described for the additions to 3,4-dichlorocyclobutene [2]. It must be remarked that in the case of compound L with the exceptions of L13, L17 and L19 the regioisomer 9 is preferantially formed. However, with few exceptions (L13, L17, L19, L23) the regioselectivity is low. The listed melting points of cycloaddition products of compound L represent melting intervals of mixtures of regioisomers. By repeated fractional cristallization an enrichment of the isomers 8 and 9 can be achieved. Isomer 9 is less polar and has a lower melting point. The regioisomer ratios of the adducts of compound L were determined ^1H-NMR spectroscopically [6].

These investigations show that similar to chlorine atoms alkylthio substituents act in a syn-directing way. Although the sulphur lone pair is by 2 eV more easily ionized than the chlorine lone pair (see Part 4) its influence on the regioselectivity is usually low in the L series. This may be due to the small significance of a lone pair effect, a conformational inefficiency of the lone pairs, the dominant σ^* interaction or a combination of these and other effects. Electron transmission and photoelectron spectra have been recorded and are discussed in Part 4.

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References and Notes

1) Part 2: H. Landen, B. Margraf, H. D. Martin, preceding communication. This is also Part 71 of Small and Medium Rings.

2) see Part 2, preceding communication.

3) see Ref. 2-10 in Part 2.

4) Synthesis of L and M has been achieved by treatment of cis-3,4-dichlorocyclobutene with equimolar or excess sodiummethanethiolate in THF and carefully repeated distillation.

5) R. Modelli and A. Gamba, *Org. Magn. Res.* 5 (1973) 101.

6) All adducts gave satisfactory elemental analyses.

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