Tetrahedron Letters,Vol.26,No.8,pp 1049-1052,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

ADAMANTANETHIONE AND DIAZOMETHANE; A RE-EXAMINATION

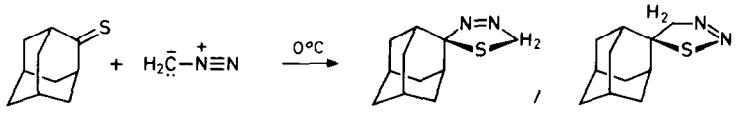
Rolf Huisgen* and Grzegorz Mloston

Institut für Organische Chemie der Universität München

Karlstr. 23, 8000 München 2, BRD

Summary The title reaction affords the two regioisomeric cycloadducts which were isolated and differ in their rates of nitrogen extrusion; the spiro-1,3,4-thiadiazoline furnishes the adamantanethione *S*-methylide which undergoes *in situ* cycloadditions to electron-deficient dipolarophiles.

According to Krapcho *et al.*,[1] adamantanethione (1)[2] combines with diazomethane at 0°C in the two conceivable addition directions to give the spiro-1,3,4-thiadiazoline 2 and the spiro-1,2,3-thiadiazoline 3. The claim was based only on ^{1}H NMR singlets at δ 5.82 and 5.0 (CH_2). The ratio of the integrals of the mentioned singlets exhibited a noteworthy dependence on solvent polarity, from 87:13 in petroleum ether to 22:78 in methanol.[3]

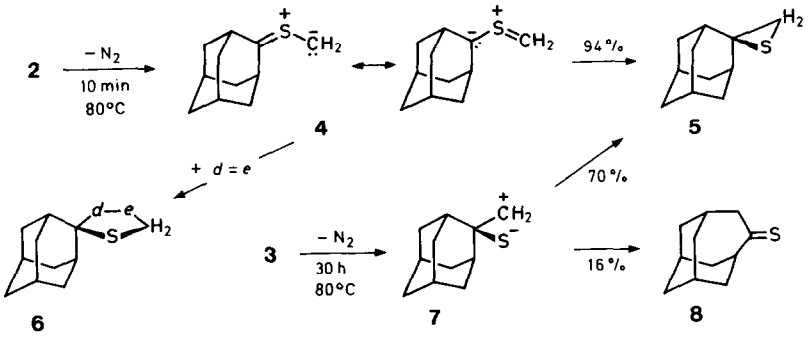


1 2 3

The experimental evidence may be meager, yet we can confirm the formation of 2 and 3. For the reaction of 1 with diazomethane, we observed a ratio of 91:9 in pentane at -20°C and of 10:90 in methanol at -30°C. This enrichment allowed the *crystallization* of the pure thiadiazolines: 2, mp 37.5-38.5°C, and 3, mp 64.5-65.5°C.[4] When separated by chromatography on silica gel, 2 moves faster than 3.

With CH_2 being the more nucleophilic of the termini of diazomethane, the additions to thiobenzophenone,[5] 2,2,4,4-tetramethylcyclobutane-1-one-3-thione,[6] thiofenchone, and thiocampher [7] exclusively follow the "thiophilic" direction providing the 1,3,4-thiadiazolines. In contrast, the high electrophilicity of the central C-atom of isothiocyanates favors the opposite direction yielding 5-amino-1,2,3-thiadiazoles.[8] Thioacetone + diazomethane use both regiochemical pathways, the preference for the 1,2,3-thiadiazoline being higher than for 1.[9]

Despite its lower bond energy, the 1,2,3-thiadiazoline 3 is - as was expected - more thermostable than the 1,3,4-isomer 2. The nitrogen extrusion of 2 has a half-reaction time of 58 sec at 80°C and 33 min at 45°C, whereas $t_{1/2}$ of 3 amounts to 4.6 min at 126°C, 25.6 min at 110°C, and ca. 9 h at 80°C in xylene. The N_2 elimination from 2 yields an attractive *all-octet intermediate*,



the resonance-stabilized thiocarbonyl ylide 4, which rests in a relatively deep energy well and is easily intercepted by dipolarophiles to furnish cycloadducts 6. In analogy to the thermolysis of 1-pyrazolines, the 1,2,3-thiadiazoline 3 gives rise to a *high-energy intermediate:* The thiatrimethylene species 7 can be described as a biradical or a carbonium zwitterion. Its flat hypersurface in the energy profile thwarted interception.

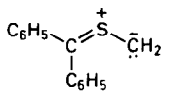
In xylene at 80°C in the absence of trapping reagents, the *S*-methylide 4 underwent *electrocyclization* yielding the thiirane 5, mp 135-137°C; ^{1}H NMR analysis of the CH_2 singlet at δ 2.37 indicated 94% 5. By the same method, 5 was shown to be the main product of thermolysis of 3 *via* 7, here accompanied by homoadamantane-2-thione (8, δ 3.27, 3-H_2) and 3% of methyleneadamantane (s, 4.50, 2 vinyl-H). The thiirane-2-spiro-2'-adamantane (5) was identified with an authentic specimen [10] and 8 was compared with the product from homoadamantanone [11] + H_2S + HCl, mp 122-123°C.

Adamantanethione *S*-methylide (4) is an *active 1,3-dipole*. Its *in situ* cycloadditions were carried out by warming the 1,3,4-thiadiazoline 2 with 1.1 equiv of dipolarophile in THF at 40°C for 8 h; in the case of less active partners, the excess of dipolarophile served as solvent. Most of the yields of Table 1 are based on the ^{1}H NMR analysis, the standard usually being 1,1,1,2-tetrachloroethane. Purification was achieved by recrystallization or chromatography.

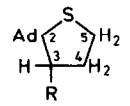
Thiocarbonyl ylides are *nucleophilic* 1,3-dipoles which preferably combine with electron-deficient dipolarophiles as previously demonstrated for thiobenzophenone *S*-methylide (9).[12,13] In spite of the steric hindrance by the adamantylidene residue, the *S*-methylide 4 appears to surpass 9 in 1,3-dipolar activity. Ethylenetetracarboxylic ester, maleic ester and propiolic ester combined with 9 in poor yields due to the competing dimerization;[12] the additions of 4 are more productive (Table 1). The *S*-methylides 4 and 9 did not react with enol ethers or common alkenes, not even with norbornene which adds diazomethane 5 000 times faster than cyclohexene.[14] The twisted double bond of *trans*-cyclooctene, however, accepts the *S*-methylide 4.

TABLE 1. Cycloadducts 6 of Adamantanethione *S*-methylide (4) [4]

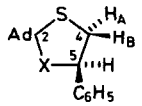
Dipolarophile	% yield	mp (°C)	Formula
Acrylonitrile	82	71-72	10
Methyl acrylate	89	101-102	11
Fumaronitrile	87	159-160	
Dimethyl fumarate	90	76-78	
Dimethyl maleate	92	131-132	
Maleic anhydride	95	142-143	16
N-Phenylmaleimide	92	167-168	
Tetracyanoethylene	94	181-182	17
Tetramethyl ethylenetetracarboxylate	84	122-123	
Dimethyl 2,3-dicyanofumarate	95	178-179	
trans-Cyclooctene	48	83-85	
Methyl propiolate	38	123-124	14
" "	27	oil	15
Dimethyl acetylenedicarboxylate	87	119-120	
Benzaldehyde	82	oil	12
Chloral	81	oil	
Butyl glyoxalate	98	35-37	
Diethyl mesoxalate	87	oil	
N-Benzylidenemethylamine	13	97-99	13
Dimethyl azodicarboxylate	90	112-113	18
N-Phenyl-1,2,4-triazoline-3,5-dione	55	156-158	



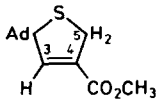
9



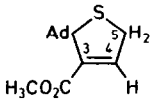
10 R = CN
11 R = CO_2CH_3



12 X = O
13 X = NCH_3



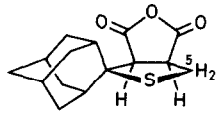
14



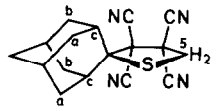
15

Thiocarbonyl ylides are ambident nucleophiles. The formation of 10 and 11 with acrylonitrile and methyl acrylate suggests that the *terminal* CH_2 of 4 is the more nucleophilic center. The low-field 3-H of 10 occurs as dd at δ 3.60 with $J_{3,4}$ = 5.0 and $J_{3,4'}$ = 1.3 Hz ($CDCl_3$). The addition to aldehydes obeyed the same regiochemistry. Benzaldehyde which did not combine with 9, afforded here 90% of the 1,3-oxathiolane 12; the fully resolved ABX spectrum ($CDCl_3$) established the structure: δ 5.13 (5-H), 3.22 (4-H_A), 2.90 (4-H_B) with $J_{4A,5}$ = 4.5 Hz, $J_{4B,5}$ = 9.8 Hz, $J_{4A,4B}$ = 10.0 Hz. *N*-Benzylidenemethylamine - likewise inert towards 9 - is border-line here, too; the yield fell to 13% and the ABX spectrum of the thiazolidine protons confirms structure 13. If the azomethine contained a few % of benzaldehyde, more 12 than 13 is observed.

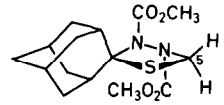
In contrast, methyl propiolate furnished the regioisomers 14 and 15 in comparable yields. Both the vicinal coupling in 15 and the allylic one in 14 showed $J \sim 2$ Hz. We assign the structures on the basis of the vinyl-H, δ 7.27 in 14 and 6.07 in 15, assuming steric hindrance of resonance between ester group and CC double bond in 15.



16



17



18

The configuration of *cis,trans isomeric* ethylene derivatives is retained in the cycloadducts of 4. ^{1}H and ^{13}C NMR spectra reflect the *symmetry properties* of the spiro-thiolanes. Whereas, *e.g.*, 15 δ_C values for the maleic anhydride adduct 16 confirm the non-equivalence of all C-atoms, the tetracyanoethylene adduct 17 reveals the symmetry plane with the singlet for 5-H_2 as well as a reduction of δ_C values for the adamantane skeleton: 4 of the 5 CH_2 and 2 of the 4 CH are pairwise equivalent. Exceptional is the adduct 18 of dimethyl azodicarboxylate; with two AB spectra for 5-H_2, the ^{1}H NMR spectrum unveils a 3:1 equilibrium of diastereomeric conformations. Many adducts display cycloreversion in their mass spectra by the occurrence of m/e = 180 for the radical cation of 4, sometimes as the base peak.

ACKNOWLEDGMENT

We express our thanks to the "Fonds der Chemischen Industrie" for the support of this work. G.M. is grateful to the Alexander von Humboldt Foundation for a fellowship.

REFERENCES

1. A.P. Krapcho, D.R. Rao, M.P. Silvon, and B. Abegaz, *J.Org.Chem.*, 36, 3885 (1971).
2. J.W. Greidanus, *Canad.J.Chem.*, 48, 3530 (1970).
3. A.P. Krapcho, M.P. Silvon, I. Goldberg, and E.G.E. Jahngen, Jr., *J.Org. Chem.*, 39, 860 (1974).
4. Satisfactory elemental analysis and spectra were obtained for all new compounds described.
5. I. Kalwinsch, Li X., J. Gottstein, and R. Huisgen, *J.Am.Chem.Soc.*, 103, 7032 (1981).
6. C. Fulka, Diploma Thesis, University of Munich, 1982.
7. A. Pröbstl, Diploma Thesis, University of Munich, 1983; G. Mloston, University of Munich, unpublished experiments.
8. H. von Pechmann and A. Nold, *Ber.Dtsch.Chem.Ges.*, 29, 2588 (1896).
9. A. Zilko, University of Munich, unpublished experiments, 1984.
10. A.P. Krapcho, M.P. Silvon, and S.D. Flanders, *Tetrahedron Lett.*, 1974, 3817.
11. R.M. Black and G.B. Gill, *J.Chem.Soc. (C)*, 1970, 671.
12. Li X. and R. Huisgen, *Tetrahedron Lett.*, 1983, 4181.
13. R. Huisgen and Li X., *Tetrahedron Lett.*, 1983, 4185.
14. R. Huisgen, P.H.J. Ooms, M. Mingin, and N.L. Allinger, *J.Am.Chem.Soc.*, 102, 3951 (1980).

(Received in Germany 30 November 1984)