Tetrahedron Letters,Vol.29,No.24,pp 2939-2942,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

ADDITION-ADDITION-ELIMINATION MECHANISM OF 1,3-DIPOLE "DIMERIZATION"

H e l m u t D o r n [x] and T h o m a s K r e h e r

Zentralinstitut für Organische Chemie , Akademie der Wissenschaften der DDR

Rudower Chaussee 5 , DDR-1199 Berlin-Adlershof , DDR

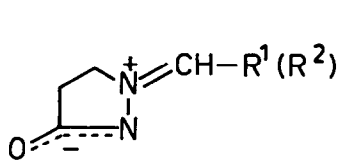
Abstract : Proof is presented for the three step ADD-ADD-EL pathway to thermal "dimers" of pyrazolidin-3-one-azomethinimines without a centre of symmetry, pyrazolidin-3-one acting as a special type of nucleophilic catalyst .

Thermal dimerizations of azomethinimines, for example of N-amino-(3,4-dihydroisoquinolines), are well known, often spontaneous reactions, previously formulated as equilibria between two 1,3-dipolar monomers and the dimer [1,2]. Although from such dimers with dipolarophiles 1,3-dipolar cycloaddition products of the monomers are easily obtained, the thermal dimerization of 1,3-dipoles obviously is no simple head-to-tail process or vice versa. Concerted thermal dimerizations as for example [π4s + π4s]-reactions are symmetry forbidden. They are only permitted, if a 1,3-dipole may react as a 4π- , and as a 2π- or 6π-species as well, for example a 3-hydroxy-pyridinium-betaine [3], or a nitrile oxide [4]. A two step dimerization (via zwitterions) is preferred for thiocarbonyl ylides [5], but in this case the general addition(ADD)-addition(ADD)-elimination(EL) mechanism discussed and proposed below also is conceivable, the starting 1,3,4-thiadiazoline playing the part of the nucleophilic catalyst Nu^- .

In general the dimer's structure, often with a centre of symmetry, doesn't reveal wether it was formed via the thermally forbidden or via an ADD(1,3-dipole + Nu^-)-ADD(+ 1,3-dipole)-EL(- Nu^-) process. There are as yet 2 exceptions : a) a centrosymmetric dimer demonstrably is formed, only if Nu^- is present (1,4,2,5-dioxadiazines from nitrile oxides + pyridine) [6], b) Nu^- is part a-b of a dimerizing 1,3-dipolar system a-b-c , causing a formal "dimer" a-b-c-b-a-c without a centre of symmetry. As a first case of b) we found a formal "dimerization" of pyrazolidin-3-one-azomethinimines and gave indirect proof of the ADD-ADD-EL mechanism [7], which we now are able to confirm .

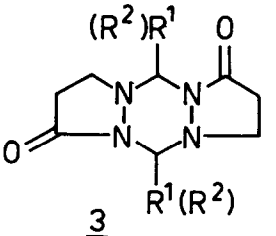
While pyrazolidin-3-one-azomethinimines (1 , 2) via a concerted [π4s + π4s]-

pathway A (i.e. photochemically) yield small amounts of centrosymmetric dimers 3 (which also could be formed by a two step process via zwitterions), they thermally "dimerize" to 7 - 10 without a centre of symmetry. First step (ADD B_1) is the addition of the nucleophilic catalyst pyrazolidin-3-one 4. Similar additions of nucleophiles to azomethinimines are known and may result in stable products, i.e. with alcohols [8] or with Grignard reagents [9], while on heating with alkoxide in alcohol 1-substituted 3-hydroxy-pyrazoles are formed [(pyrazolidin-3-one-azomethinimine)-(3-hydroxy-pyrazole)-transformation, mech. cf. [10]]. The second step (ADD B_2) resembles

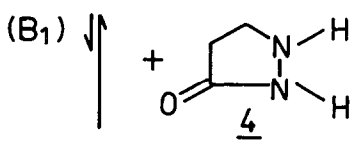


1 : R^1 = Ph

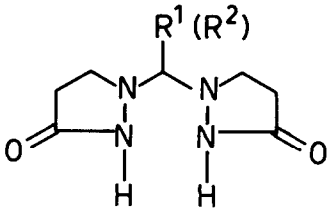
2 : R^2 = C_6H_4–OMe–4



3

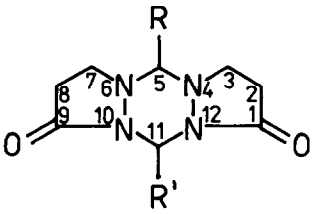


4

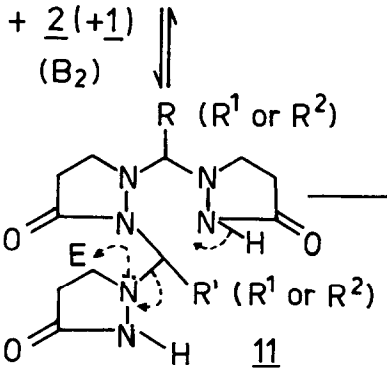


5 : R^1 = Ph

6 : R^2 = C_6H_4–OMe–4



	R	R'
7	Ph	Ph
8	C_6H_4–OMe–4	C_6H_4–OMe–4
9	Ph	C_6H_4–OMe–4
10	C_6H_4–OMe–4	Ph



11

4 combinations in steps (B_2) / (B_3) :

5 + 1 ⟶ 7 + 4

6 + 2 ⟶ 8 + 4

5 + 2 ⟶ 9 + 4

6 + 1 ⟶ 10 + 4

the Mannich reaction, which works well at (N-2) of (N-1)-substituted pyrazolidin-3-ones [11]. The carbonium-immonium species adding to 5 resp. 6 is a second molecule of the azomethinimine 1 resp. 2 . The proof for ADD B_2 is the isolation of mixed "dimers" (9 and 10) after "codimerization" of equimolar amounts of 1-benzylidene 1 , and 1-(4-methoxy-benzylidene)pyrazolidin-3-one-azomethinimine 2 in boiling chloroform with catalytic amounts of pure (Kugelrohr distilled) pyrazolidin-3-one 4 (0.01 mol 4 per 1 mol 1). Chloroform (like H^+ , acetonitrile or other C-H acidic solvents) is efficient as a promoting electron acceptor catalyst (E) in the cyclisation step (EL of 4 , B_3) to the stable bis-aminals 7-10 . Practically EL B_3 is irreversible, if the "dimer" is precipitated as a stable product .

	$\delta^{13}C$ ($CDCl_3$, TMS int.) [ppm]				$\delta^{1}H$ ($CDCl_3$, TMS int.) [ppm]		
	(C-5)	(C-11)	(C-4'/R)	(C-4"/R')	(H-5)	(H-11)	OMe
7	91.2	62.2	129.4	128.3 lit.[7]			
8	91.2	62.1	160.9	159.5 lit.[7]			
9	92.2	62.6		159.7	3.97 s	7.17 s	3.81 s (3H)
10	91.4	62.5	161.1		3.94 s	7.14 s	3.81 s (3H)

^1H , and ^{13}C nmr data of 5,11-bis-phenyl- (7) [7], 5,11-bis-(4-methoxy-phenyl)-(8) [7], 11-(4-methoxy-phenyl)-5-phenyl- (9) , and 5-(4-methoxy-phenyl)-11-phenyl-perhydro-dipyrazolo[1,2-a;1',2'-d][1,2,4,5]tetrazine-dione-(1,9) (10)

After elution with CH_2Cl_2 from a kiesel gel 40 (Merck) column we obtained a crystalline mixture of the "dimers" 7, 8, 9, and 10 (overall yield 57%) . Unreacted 1 and 2 were then eluted with methanol. The pure mixed "dimers" 9 (m.p. 225-245°C, dec., m/e 378), and 10 (m.p. 187-191°C,dec., m/e 378) were isolated by fractional crystallisation from either ethanol, propanol, 2-butanone or ethyl acetate .

Carbon atoms C-5 and C-11 of the mixed "dimers" 9 and 10 are not equivalent, which is demonstrated by the ^{13}C and ^{1}H nmr data. From Dreiding models we suggested, that a chair conformation with equatorial R at C-5 and axial R' at C-11 to be one of the least sterically hindered [7], which was meanwhile confirmed by X-ray analysis [12] of 9 and 10. The rotation of the eq R at C-5 is significantly more hindered by the H atoms at C-3 and at C-7 than the ro-

tation of the ax R' at C-11 . Thus the mixed "dimer" structures 9 resp. 10 can be assigned : While the ^{1}H nmr of 9 shows a sharp AA'BB' system (δ_A = 6.89 ppm , δ_B = 7.68 ppm , J_{AB} = 9.0 Hz ; in $CDCl_3$, 100 MHz , TMS int.) at 25°C for the m,m';o,o' H atoms of R' = 4-MeO-C_6H_4 , the corresponding AA'BB' system for R = 4-MeO-C_6H_4 of 10 is only sharp above 83°C (δ_A = 6.88 ppm , δ_B = 7.35 ppm , J_{AB} = 8.0 Hz ; in $CDBr_3$) .

We believe that most 1,3-dipole dimerizations under mild conditions follow the ADD-ADD-EL pathway, as outlined above for a special case, leading to non centrosymmetric "dimers" , whereby in general even a protic solvent or an aprotic electron donor centre can act as the nucleophilic catalyst Nu^- .

REFERENCES

1 C.G. Stuckwisch , Synthesis 1973 , 469 especially 471.

2 R. Huisgen, R. Grashey, and R. Krischke , Liebigs Ann.Chem. 1977 , 506.

3 N. Dennis, A.R. Katritzky, and Y. Takeuchi , Angew.Chem. 88 , 41 especially 47 (1976) ; Angew.Chem.Int.Ed.Engl. 15 , 1 (1976).

4 R. Huisgen , Angew.Chem. 75 , 604 especially 612 (1963) ; Angew.Chem.Int. Ed.Engl. 2 , 565 (1963).

5 I. Kalwinsch , Li Xingya , J. Gottstein, and R. Huisgen , J.Am.Chem.Soc. 103 , 7032 (1981).

6 A. Corsaro, G. Perrini, P. Caramella , F.M. Albini, and T. Bandiera , Tetrahedron Lett. 27 , 1517 (1986).

7 H. Dorn, R. Ozegowski, and R. Radeglia , J.Prakt.Chem. 319 , 177 (1977).

8 K. Burger, W. Thenn, H. Schikaneder, and H. Peuker , Angew.Chem. 86 , 483 (1974); Angew.Chem.Int.Ed.Engl. 13 , 476 (1974) ; W. Theis, W. Bethäuser, and M. Regitz , Tetrahedron 41 , 1965 (1985).

9 H. Dorn, and H. Graubaum , J.Prakt.Chem. 318 , 253 (1976).

10 H. Dorn , Khim.Geterotsikl.Soed. 1981 , 1 especially 10 ; Chem.Heterocycl.Compd. USSR (Engl.Transl.) 1981 , 1 especially 6 ; Z.Chem. 14 , 231 (1974).

11 H. Dorn , and H. Dilcher , J.Prakt.Chem. 313 , 229 (1971).

12 I. Seidel, P. Leibnitz, L. Kutschabsky, and Th. Kreher , prepared for print.

(Received in Germany 18 August 1987)