Tetrahedron Letters,Vol.26,No.42,pp 5123-5126,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

1,3-DIPOLAR CYCLOADDITION OF PYRAZOLID-3-ONE AZOMETHINIMINES AND E-ß-NITROSTYRENE - ELUCIDATION OF THE GENERATION OF SEEMINGLY "NON CISOID" ADDUCTS

H e l m u t D o r n

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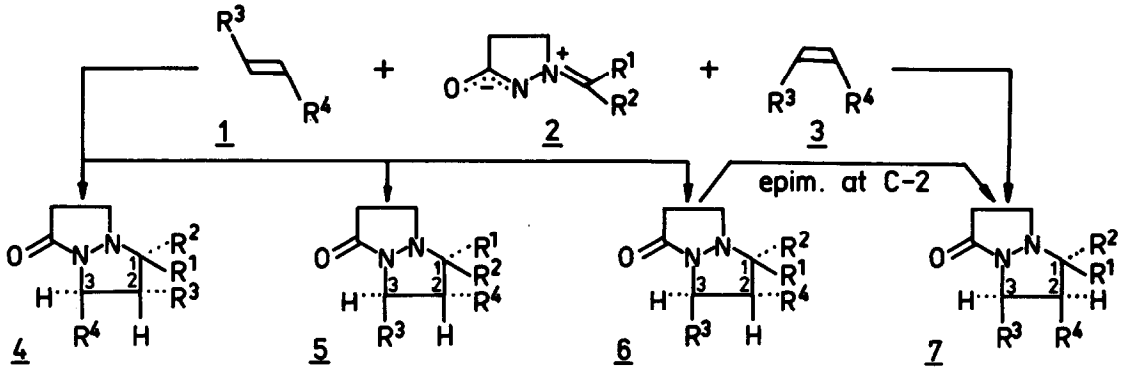
Abstract : Highly polar 1,3-dipoles like pyrazolid-3-one azomethinimines stereospecifically add polar dipolarophiles . A suggested "non cisoid" adduct of E-ß-nitrostyrene is generated by epimerization at C-2 , catalysed by Kieselgel 40 MERCK a n d small amounts of pyrazolid-3-one .

Are highly polar 1,3-dipoles like pyrazolid-3-one azomethinimines 2 [1] [μ(2a)=6.80 ±0.03 D , dioxane [2]] able to add polar dipolarophiles in polar solvents [E_T values (kcal/mole) given in ()] via zwitterions , leaving the concerted [$_{\pi}4_s + _{\pi}2_s$] [3] pathway ? As yet lack of stereospecificity is the only unequivocal proof of a two or more step mechanism . In a 1:1 molar ratio 2a , 2e or 2k , and pure E- resp. Z-olefins [dimethyl fumarate 1a or maleate 3a ($CHCl_3$, 39.1) [4] , methyl cinnamate 1b (chlorobenzene , 37.5) [5] , 4-nitrophenyl cinnamate 1c (toluene , 33.9) [5] , ß-nitrostyrene 1d (CH_2Cl_2 , 41.1)] only yielded the permitted stereoisomers of a concerted reaction . To elucidate the surprising lack of stereospecificity observed after the addition of 1d to 2a [we isolated formerly 6d and 7d [7]] meant to solve three problems : 1) Stereochemistry of further 1,3-dipolar cycloadditions using highly polar reactants ? 2) New non stereospecific pathways ? 3) Catalysed epimerisation at C-2 during work-up ?

1) The pyrazolid-3-one azomethinimines 2f , 2g [in CH_2Cl_2] and 2h [in chlorobenzene] with E-ß-nitrostyrene 1d [molar ratio 1:1] only yielded the "permitted" 6f , 6g and 6h [2] . 6g easily epimerized to 7g [CH_2Cl_2 , basic alumina , 20°C ; 60% 6g + 40% 7g] [2] . 1d added to HUISGEN's highly polar [μ(8h)=6.7 D , dioxane [8]] azomethinimines 8h and 9h [molar ratio 1:1 , 130h reflux , CH_2Cl_2] only to the "permitted" 2-cyano-3-phenyl-4ref,trans-nitro-pyrazolidin-5-spiro-9'-fluorenes 10h [m.p. 170-175°C , dec. , δ(H-3) =5.93 , δ(H-4)=5.95 , J_{34}=8.8 , 200 MHz ; proof by X ray analysis] and 11h [m.p. 177-183°C , dec. , δ(H-3)=5.94 , δ(H-4)=5.95 , J_{34}=9.0 , 200 MHz] [9].



	R^1	R^2	R^3	R^4	from 1	μ [D] of 1
a	H	Ph	CO_2Me	CO_2Me	5 + 6[a]	2.25 , CCl_4
b	H	Ph	Ph	CO_2Me	5 + 6	1.93 , diox.
c	H	Ph	Ph	CO_2-C_6H_4-NO_2-4	4[b] + 5 + 6	6.0 , diox.
d	H	Ph	Ph	NO_2	5[c] + 6	4.27 , diox.
e	H	C_6H_4-Cl-4	C_6H_4-Cl-4	NO_2	6	
f	Me	Me	Ph	NO_2	5 = 6	
g	cyclohexylidene		Ph	NO_2	5 = 6	
h	fluorenylidene		Ph	NO_2	5 = 6	
i	H	Ph	C_6H_4-OMe-4	NO_2	6[d]	
k	H	C_6H_4-OMe-4	Ph	NO_2	6[e]	

All ^1H nmr data : if not given otherwise , 100 MHz , $CDCl_3$, TMS int. , δ [ppm] , J [Hz] , calc. ABC systems . i.r. : [cm^{-1}] in KBr .

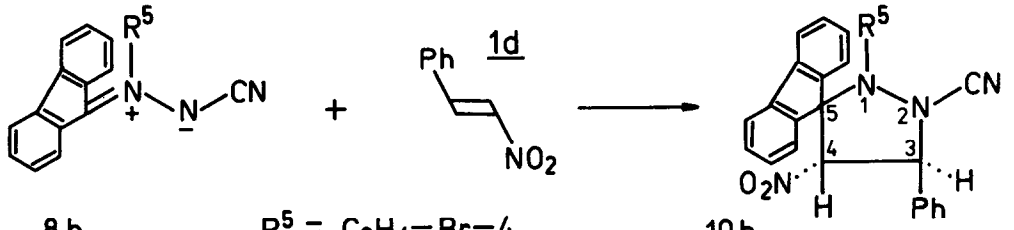
a) Numbering at poss. 1 and 3 of 5a , 6a and 7a must be exchanged [4] ; 2a and dimethyl maleate (3a , R^3=R^4=CO_2Me ; μ=2.48 D , CCl_4) only yield 7 (R^1=H , R^2=Ph) and 7 (R^1=Ph , R^2=H) [4].

b) 4c : c. 5% of yield , m.p. 178-181°C ; δ(H-1)=3.65 , δ(H-2)=3.93 , δ(H-3)=5.10 , J_{12}=10.0 , J_{13}=0.0 , J_{23}=7.5 .

c) We detected 5d in a new type of reaction [2a + $MeNO_2$ [6]] , then after addition of 1d to 2a [less than 1% 5d] : m.p. 105-108°C ; δ(H-1)=4.18 , δ(H-2)=5.01 , δ(H-3)=5.60 , J_{12}=8.0 , J_{13}=0.0 , J_{23}=4.5 ; ν(C=O) = 1707 .

d) 6i : m.p. 166-172°C (dec.=retro rc.) ; δ(H-1)=4.29 , δ(H-2)=5.22 , δ(H-3)=5.53 , J_{12}=6.8 , J_{13}=0.0 , J_{23}=2.5 .

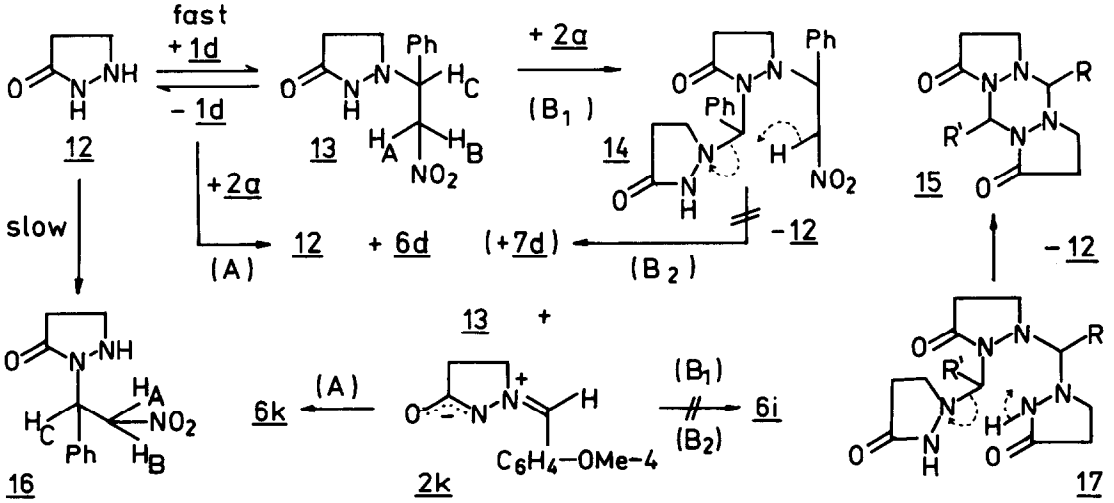
e) 6k : m.p. 171-177°C (dec.=retro rc.) ; δ(H-1)=4.28 , δ(H-2)=5.22 , δ(H-3)=5.62 , J_{12}=6.5 , J_{13}=0.0 , J_{23}=2.9 ; for assignment use δ(H-3) !



8h $R^5 = C_6H_4-Br-4$ 10h

9h $R^5 = C_6H_4-Cl-4$ 11h

2) We found 13 [m.p. 99-104°C (dec.=retro rc.), δ_A=4.63 , δ_B=4.92 , δ_C= 4.52 , J_{AB}=-13.0 , J_{AC}=6.0 , J_{BC}=8.5] as kinetically controlled MICHAEL adduct of E-ß-nitrostyrene 1d to pyrazolid-3-one 12 . 13 via 1d and 12 slowly rearranges to the thermodynamically controlled 16 [m.p. 87-88°C , δ_A=4.94 , δ_B=5.30 , δ_C=5.91 , J_{AB}=-13.0 , J_{AC}=4.5 , J_{BC}=10.5 , CD_3OD] . Pyrazolid-3-one azomethinimines 2 mostly contain more or less traces of pyrazolid-3-one 12 ! We excluded the non stereospecific pathway B_1/B_2 via a MANNICH-like addition of 2 to 13 (B_1) and elimination of pyrazolid-3-one 12 from 14 (B_2) : 13 with 1-(4-methoxy-benzylidene)pyrazolid-3-one-azomethinimine 2k yielded 12 , and 6k (path A) , i.e. the 1,3-dipolar cycloadduct of E-ß-nitrostyrene 1d to 2k [10] , whereas via B_1/B_2 the isomer 6i should have been formed . As by-products we isolated "thermal dimers" 15 of



pyrazolid-3-one azomethinimines 2 , above all a m i x e d 15 with R=C_6H_4-OMe-4 and R'=Ph , formed via the MANNICH-like adduct 17 according to our mechanism of the thermal 1,3-dipole dimerisation [11].

Results 1) + 2) , and later on valuable discussions with Prof. Rolf Huisgen forced us into further studies on epimerisation at C-2 , especially of 6d , which formerly was isolated after elution from Kieselgel (KG) 40 MERCK (0.06-0.2 mm) with CH_2Cl_2 [7] . After pouring 1.00 g of 6d in 10 ml CH_2Cl_2 on a column with 40 g KG 40 , followed by elution with CH_2Cl_2 or CH_2Cl_2 and MeOH at 20°C no 7d was detected by ^1H nmr . If 7 mg of pyrazolid-3-one 12 [purified by Kugelrohr distillation at 175-200°C , 1 - 0.5 Pa] were added , similar elution gave 91% 6d and 9% 7d (by ^1H nmr). 1d and 2a , which can be purified by trituration with MeOH , according to [7] but without passing a KG 40 column only gave 6d (^1H nmr control). Thus , a combination of surprisingly small amounts of pyrazolid-3-one 12 , sparingly soluble in CH_2Cl_2 , a n d KG 40 catalyses epimerisation at C-2 of 6d , generating 7d under very mild conditions as an artefact .

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(Received in Germany 12 August 1985)