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(4+2)-CYCLOADDITION OF NITROALKENES WITH YNAMINES; FORMATION OF A 4*H*-1,2-OXAZINE 2-OXIDE DERIVATIVE

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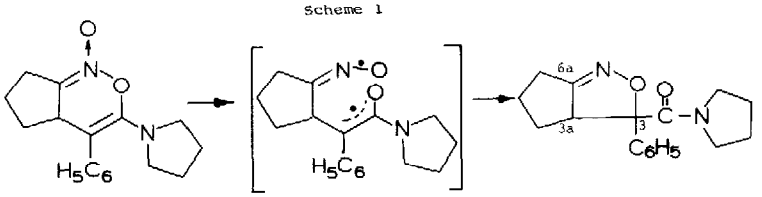
Abstract: The formation of a thermally unstable (4+2)-cycloadduct, a 4H-1,2-oxazine 2-oxide derivative (1), from the reaction of 1-nitrocyclopentene with 1-phenyl-2-(1-pyrrolidinyl)acetylene has been proven by the structure elucidation of isoxazole derivative 3 which results from thermal rearrangement and by the structure determination of the 1,3-dipolar adducts 5 of 1 with electron-deficient acetylenes.

Although the formation of 4*H*-1,2-oxazine 2-oxides has been reported by Stetter and Hoehne[1], the proposed structure was after a period of confusion[2,3] proven to be incorrect by an X-ray analysis[4]. The only six-membered cyclic nitronic esters that are known are 5,6-dihydro-4*H*-1,2-oxazine 2-oxides[5,6]. In this paper we describe such a hitherto unknown 4*H*-1,2-oxazine 2-oxide derivative from the reaction of 1-nitrocyclopentene with 1-phenyl-2-(1-pyrrolidinyl)acetylene. Contrary to Nielsen and Archibald[5] who have stated that an ynamine failed to react with 1-phenyl-2-nitropropene, we have recently found that nitroalkenes undergo a facile reaction with ynamines to yield both 3-nitrocyclobutenes and nitrones[7,8]. The formation of the nitrones was accounted for by a two-step process: (4+2)-cycloaddition to yield a 4*H*-1,2-oxazine 2-oxide and subsequent ring contraction[9].

1-Nitrocyclopentene and 1-phenyl-2-(1-pyrrolidinyl)acetylene react in light petroleum at room temperature to yield in addition to a nitrobicyclo[3.2.0]hept-6-ene another 1:1 reaction product (35%, MS: M^+ 284.15 ($C_{17}H_{20}N_2O_2$). IR(KBr): 1640 cm^{-1} (C=N and C=C). UV: λ_{max} 230 nm)[10]. Attempts to purify the crude product failed because of its thermal instability. Even in the crystalline state or in chloroform solution at room temperature it isomerises almost quantitatively to 3-phenyl-3-(1-pyrrolidinylcarbonyl)-3a,4,5,6-tetrahydro-3*H*-cyclopent[*c*]isoxazole 3 (scheme 1),

Scheme 1



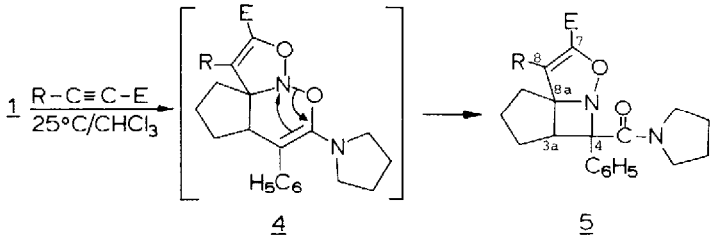
1 2 3

m.p. 109.5-110.5°C (white crystals from light petroleum). MS: M^+ 284.15 ($C_{17}H_{20}N_2O_2$). IR(KBr): 1640 cm^{-1} (C=N and C=0). ^1H NMR δ($CDCl_3$): 2.6-2.9 and 3.2-3.6 (m,4H,CH_2-N), 4.91 (dd,J_1 11Hz,J_2 8Hz,1H,H-3a), 7.2-7.5 (m,5H,H_{arom}) ppm. ^{13}C NMR data of 3 were compared with those of N,N-diethyl-3,3a-dihydro-3-methylbenzofuro [3,2-*e*]isoxazole-3-carboxamide 8, which was obtained from the reaction of 3-nitrobenzo[*b*]furan with 1-diethylaminopropyne (see table); the structure of 8 was elucidated by X-ray analysis[11].

The formation of 3 can be explained, assuming the initial product of the reaction between 1-nitrocyclopentene and 1-phenyl-2-(1-pyrrolidinyl)acetylene is the 4*H*-1,2-oxazine 2-oxide derivative 1. Homolytic cleavage of the weak N-O bond in 1 gives the diradical 2. Similar diradicals react further by the formation of a C-N bond to give 2,3-dihydro-azete 1-oxides like 6a[7]. However in the case of the fused 4*H*-1,2-oxazine 2-oxide derivative 1, this would lead to the nitrone 6b which has a bridgehead sp^2-hybridized carbon atom in a four-membered ring. Consequently 2 reacts by formation of a C-O bond to yield the isoxazole derivative 3 (see also ref. 11).

Further support for structure 1 has been obtained from the identification of the reaction products of the 1,3-dipolar additions[12] of 1 with electron-deficient acetylenes. Reaction of 1 with dimethyl acetylenedicarboxylate or methyl propiolate in chloroform solution at room temperature afforded the cycloadducts 5 (scheme 2)[13].

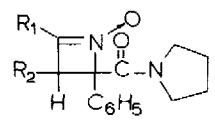
Scheme 2



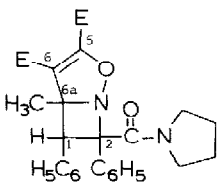
E = $COOCH_3$ a R = E b. R = H

Since the bridgehead carbon atom in the intermediates 4 is no longer sp^2-hybridized, ring contraction to 5 no longer leads to the formation of an anti-Bredt type of compound like 6b. The tricyclic products 5a and 5b were obtained as white solids in 83 and 85% yield respectively; 5a: m.p. 140-142°C (from benzene/hexane). MS: M^+ 426.18 ($C_{23}H_{26}N_2O_6$). IR(KBr): 1755 and 1715 cm^{-1} ($COOCH_3$), 1640 and 1660 cm^{-1} (C=C and C=0). ^1H NMR δ($CDCl_3$): 3.1-3.6 (m,4H,CH_2-N), 3.76 and 3.88 (s,3H, O-CH_3), 4,66 (dd,J_1 8Hz,J_2 1Hz,1H,H-3a), 6.7-7.0 (m,1H,*o*-H_{arom}), 7.1-7.5 (m,3H, H_{arom}), 7.8-8.1 (m,1H,*o*-H_{arom})ppm. 5b: m.p. 124-126°C (from light petroleum). MS: M^+ 368.17 ($C_{21}H_{24}N_2O_4$). IR(KBr): 1730 cm^{-1} ($COOCH_3$) and 1630 cm^{-1} (C=C and C=0). ^1H NMR δ($CDCl_3$): 3.2-3.6 (m,4H,CH_2-N), 3.80 (s,3H,O-CH_3), 6.00 (s,1H,H-8), 6.7-7.0 (m,1H,*o*-H_{arom}), 7.1-7.6 (m,3H,H_{arom}), 7.9-8.2 (m,1H,*o*-H_{arom})ppm. The formation

of 5a and 5b occurs stereospecifically and from the nonequivalence of the ortho-phenyl protons in the ^1H NMR spectra can be concluded, that the phenyl ring and the cyclopentane ring are on the same side of the azetidine ring. A molecular model shows that in this configuration of 5 the rotation around the C_6H_5-C-4 bond is restricted. The structures of 5a and 5b were also confirmed by comparison of the ^{13}C NMR data of 5a and 5b with those of dimethyl 1,6a-dihydro-1,2-diphenyl-6a-methyl-2-(1-pyrrolidinylcarbonyl)-2*H*-azeto[1,2-*b*]isoxazole-5,6-dicarboxylate 7 (see table). For this purpose compound 7 has been prepared by 1,3-dipolar addition of dimethyl acetylenedicarboxylate with the cyclic nitrone 6a[7]. After 18 hours stirring in chloroform solution at room temperature, 7 was isolated as a white solid, m.p. 142-144°C. MS: M^+ 476.19 ($C_{27}H_{28}N_2O_6$). IR(KBr): 1755 and 1715 cm^{-1} ($COOCH_3$), 1650 cm^{-1} (C=O and C=C). ^1H NMR $\delta(CDCl_3)$: 1.25 (s,3H,CH_3), 3,58 and 3.79 (s,3H,O-CH_3), 5.19 (s,1H,H-1), 7.1-7.9 (m,10H,H_{arom}) ppm.



6 a $R_1 = CH_3$, $R_2 = C_6H_5$
b $R_1R_2 = -(CH_2)_3-$



7 E = $COOCH_3$

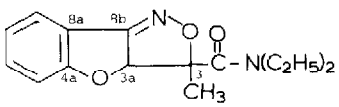


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Table

Characteristic ^{13}C NMR absorptions of compounds 3, 5a, 5b, 7 and 8

3		8		5a	5b		7	
94.4	C-3	94.6	C-3	153.3	147.1	C-7	152.9	C-5
63.2	C-3a	96.6	C-3a	110.1	112.4	C-8	115.4	C-6
167.4	C-6a	167.3	C-8b	82.1	81.4	C-8a	76.5	C-6a
171.2	C=O	169.8	C=O	50.9	51.9	C-3a	51.6	C-1
				84.7	85.1	C-4	82.6	C-2
				165.5	166.5	>N-C=O	167.7	>N-C=O
				161.8	158.6	-O-C=O	162.1	-O-C=O
				159.1		-O-C=O	158.1	-O-C=O

All chemical shifts were recorded in deuteriochloroform with TMS as internal standard (δ in ppm)

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References and notes

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9. In our first paper[8] the formation of N-heteroaryl-C-carbamoyl nitrones was attributed to a two-step process involving a (2+2)-cycloaddition of the ynamine to the N=O bond of the nitro group.
10. Dilute solutions of this product were studied by ^{1}H and ^{13}C NMR spectroscopy, but the presence of radical species made this impossible. In the case of ^{13}C NMR only minor amounts of rearranged product 3 could be traced.
11. See preceeding paper.
12. A.T. Nielsen in 'The Chemistry of the nitro and nitroso groups', ed. H. Feuer, J. Wiley & Sons, New York, 1969; part I, p. 349.
13. The isoxazole derivative 3 failed to react with dimethyl acetylenedicarboxylate under the same reaction conditions.

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