Tetrahedron Letters No. 41, pp 3817 - 3820, 1971. Pergamon Press. Printed in Great Britain.

PERISPECIFICITY IN THE 1,3-DIPOLAR CYCLOADDITIONS OF BENZONITRILE OXIDE WITH FULVENES

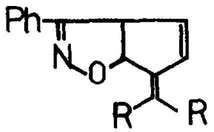
P.Caramella, P.Frattini and P.Grünanger
Istituto di Chimica Organica dell'Università, Pavia, Italy

(Received in UK 12 August 1971; accepted for publication 10 September 1971)

The competition between $[_{\pi}4_s+_{\pi}2_s]$ and $[_{\pi}6_s+_{\pi}4_s]$ cycloadditions, both symmetry allowed thermal processes, has recently aroused high interest, and several examples involving dienes are known.[1] Only two examples involving 1,3-dipoles as 4π components were hitherto described.[2,3] We have re-investigated the cycloaddition of benzonitrile oxide (BNO) to fulvenes and report here the first example of a $[6 + 4]$ cycloaddition involving nitrile oxides.[4] The reaction of BNO with some fulvenes was already known[5] to yield both 1:1 and 2:1 adducts, but the structural assignments were not unequivocal.

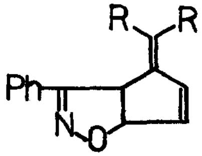
In our hands the reaction of 6,6-dimethylfulvene with BNO (2 equiv.) generated in situ in abs ether soln gave a mixture of at least five products in 71% total yield. Chromatographic separation on Kieselgel H, eluant cyclohexane:AcOEt 9:1, afforded the monoadducts I, m.p. 141-2° (34%; lit.[5] 142-3°), and II,[6] m.p. 81-2° (18%), and three bisadducts: III, m.p. 131-2° (4%), IV, m.p. 144-5° (5%) and V, m.p. 183-4° (10%; lit.[5] 183-4°).

The NMR spectra (see Table) of monoadducts I and II show non-equivalent ring protons and methyl peaks, ruling out a cycloaddition to the exocyclic C=C bond. The coupling constants between the two lower field (J=5.6 resp. 5.0 Hz) and between the two higher field (J=8.7 resp. 7.7 Hz) ring protons are in good agreement with the reported values for cyclopentene olefinic[7a] and 2-isoxazoline 4,5-protons.[8] The $[6 + 4]$ cycloadducts VIII and IX would require a completely different set of coupling constants.[9] Similar considerations exclude structures derived from VIII or IX through the easy $[1,5]$ sigmatropic shifts of cyclopentadiene derivatives.[10] The non-equivalent methyls of I resonate at 1.99 and 1.87 ppm, those of II at 1.75 and 1.47 ppm. Models inspection shows that one methyl of II lies in the shielding region of the phenyl ring. The UV spectra also support the proposed structures, the diene absorption of II (λ_{max} 236 nm) occuring at shorter wavelength than in I (λ_{max} 248 nm), where no steric overcrowding alters



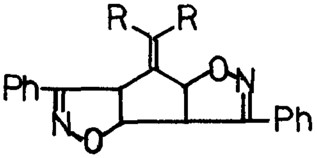
I , R=Me

X , R=Ph



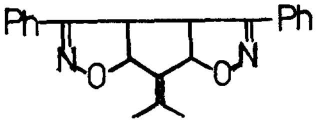
II , R=Me

XI , R=Ph

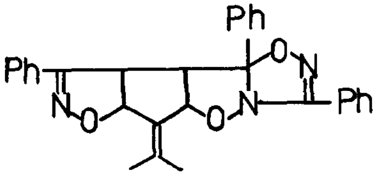


III,V , R=Me

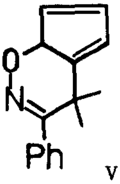
XII , R=Ph



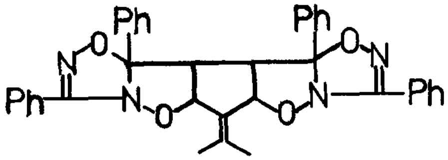
IV



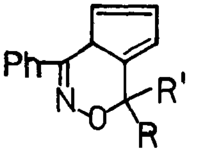
VI



VIII

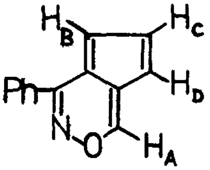


VII



IX , R=R'=Me

XIII , R=H,R'=NMe_2



XIV

TABLE. Chemical shifts (coupling constants) of cycloadducts

(i) Monoadducts:	I	II	X	XI
Olefinic	6.47q(5.6;2) 5.99q(5.6;2)	6.62d(5.0) 5.95d(5.0)	6.39q(5.3;2) 6.06q(5.3;2)	6.58d(5.6) 6.12q(5.6;2)
H-5*	5.80d(8.7)	5.82d(7.7)	5.34d(8)	5.90q(8;2)
H-4*	4.72sx(8.7;2;2)	4.65d(7.7)	4.57sx(8;2;2)	5.38d(8)
Methyls	1.99s 1.87s	1.75s 1.47s	--	--

(ii) Adducts:	III	IV	V	XII	VI	VII
H-5*	5.63d(10.4) 5.06q(8.3;3.9)	5.73d(7.8)	5.63d(8.3) 5.47t(8.3)	5.62t(8) 5.34d(8)	5.70d(9.3) 5.28d(5.3)	5.28m
H-4*	4.70d(8.3) 4.14q(10.4;3.9)	4.12d(7.8)	4.85d(8.3) 4.09t(8.3)	5.22d(8) 4.14t(8)	3.98q(9.3;6.3) 3.55q(5.3;6.3)	3.80m
Methyls	1.92s 1.56s	2.02s	1.88s 1.70s	--	1.94s 1.75s	1.66s

* Numbering refers to isoxazoline ring.

the planarity of the diene system.

Although sluggishly, I reacted further with BNO to yield the bisadduct IV, whereas II gave a mixture of the bisadducts III (11%) and V (41%), in full agreement with the well-established regiospecificity of the cycloadditions to dienes.[4] The symmetrical structure of IV is evidenced by NMR (see Table). IV itself sluggishly added BNO, affording VI, m.p. 141-2°, whose structure was deduced from the presence of two non-equivalent allylic methyls and from the further reaction to give a symmetrical tetraadduct VII, m.p. 170-1°dec. Similar cycloadducts on the C=N bond of condensed 2-isoxazolines have been recently demonstrated.[11] The isolation of VI and VII strongly supports the *anti* structure of the bisadduct IV for steric considerations. The NMR spectra of both bisadducts III and V do not show the cyclopentene olefinic protons, as evidenced by coupling constants and chemical shifts, but non-equivalent cyclopentane protons and methyls.[12] The higher field shift of the shielded methyl of II in comparison with III and V may be ascribed to the larger flexibility of the cyclopentane ring of the bisadducts.

6,6-Diphenylfulvene and BNO (2 equiv.) similarly afforded the monoadducts X, m.p. 161-3° (51%; lit.[5] 162-3°), and XI, m.p. 138-140° (8%), as well as the bisadduct XII, m.p. 248-9° (17%; lit.[5] 244-5.5°). Whereas the monoadduct X reacted further with BNO only very sluggishly, from XI the bisadduct XII was readily attained in good yields. Structural assignments are based on the striking similarities of the NMR pattern with the adducts from dimethylfulvene.

Therefore, the $[4 + 2]$ process prevails in the cycloaddition of BNO with 6,6-dimethyl- and with 6,6-diphenylfulvene.

Starting from 6-dimethylaminofulvene on the contrary only the $[6 + 4]$ pathway could be observed. Admixture of BNO and 6-dimethylaminofulvene in 2:1 molar ratio in ether soln gave a reaction mixture, from which three products were isolated: XIV, m.p. 53-5° (60%), N,N-dimethylbenzamide oxime (40%) and 3,5-diphenyl-1,2,4-oxadiazole 4-oxide (3%). The UV spectrum of XIV shows typical fulvene bands at 237 nm (lg ε 4.28), 275 sh (lg ε 3.92) and 326 nm (lg ε 3.55).[13] Its NMR spectrum (in CCl_4, δ values) shows, besides five phenyl protons, signals at 8.90 (1H, d, J=1.2 Hz), 7.23 (1H, q, J=2.9 and 4.6 Hz) and 6.8-7.0 (2H, m). In CCl_4/acetone-d_6 the multiplet was separated into a quartet (J=1.2 and 4.6 Hz) and a multiplet. Upon irradiation at 8.90 this latter signal collapsed to a quartet (J=1.2 and 2.9 Hz). The following parameters have been deduced: δ_A 8.90 d, δ_B 6.8-7.0 m, δ_C 7.23 q, δ_D 6.91 q; $J_{AB}= J_{BD}=$ 1.2 Hz, $J_{BC}=$ 2.9 Hz, $J_{CD}=$ 4.6 Hz. The J_{AB} coupling agrees with the reported value of long-range coupling in butadiene derivatives.[7b] The low field position of H_A, compatible only with an adjacent oxygen atom, rules out the regioisomeric structure.

The isolation of XIV and of its accompanying products can be rationalized as follows. The initial $[6 + 4]$ 1,3-dipolar adduct XIII eliminates dimethylamine, which adds BNO to give the N,N-dimethylbenzamide oxime. This latter compound in turn reacts further to yield the 3,5-diphenyl-1,2,4-oxadiazole 4-oxide. The dipolarophilic reactivity of amidoximes toward nitrile oxides has been recently demonstrated.[14]

The different behaviour of dimethylfulvene toward diazomethane[3] and BNO should be ascribed to the different steric and electronic requirements of the two 1,3-dipoles, BNO being generally more sensitive to steric factors.

The strong directing effect of the enamino moiety on the regiospecificity of 1,3-dipolar cycloadditions with nitrile oxides is well-known. Our results with 6-dimethylaminofulvene emphasizes that the amino group, if proper located, also controls the perispecificity of the reaction. Further work is in progress in order to test the concertedness of this latter cycloaddition.

Acknowledgement. This work has been supported by C.N.R., Rome.

References and Footnotes

1. K.N.Houk and R.B.Woodward, J.Am.Chem.Soc., 92, 4143, 4145 (1970) and references therein.
2. K.N.Houk and C.R.Watts, Tetrahedron Letters 4025 (1970).
3. K.N.Houk and L.J.Luskus, Tetrahedron Letters 4029 (1970).
4. For a recent review on nitrile oxides cycloadditions, see Ch.Grundmann and P. Grünanger, The Nitrile Oxides, Chap.V, pp.85-139. Springer-Verlag, 1971.
5. A.Quilico, P.Grünanger and R.Mazzini, Gazz.Chim.Ital., 82, 349 (1952).
6. All new compounds gave satisfactory elemental analyses. UV spectra were run in EtOH soln, NMR at 60 MHz in $CDCl_3$ soln; chemical shifts are expressed in ppm (δ) from internal TMS and coupling constants (J) in Hz.
7. L.M.Jackman and S.Sternhell, Application of NMR Spectroscopy in Organic Chemistry, 2nd Ed. Pergamon Press, 1969: (a) p.303; (b) p.341; (c) p.287.
8. R.Sustmann, R.Huisgen and H.Huber, Chem.Ber., 100, 1802 (1967).
9. W.Brügel, NMR Spectra and Chemical Structure, p.63. Academic Press, 1967.
10. W.R.Roth, Tetrahedron Letters 1009 (1964).
11. G.F.Bettinetti and A.Gamba, Gazz.Chim.Ital., 100, 1144 (1970).
12. The NMR data of the bisadducts III and V do not allow to assign with certainty the syn and anti structure, owing to the unreliability of coupling constants in flexible rings.[7c]
13. P.Yates, in Adv.Alicyclic Chem., vol.II (ed. by H.Hart and G.J.Karabatsos), p.103. Academic Press, 1968.
14. P.Caramella and E.Cereda, unpublished results.