

Δ^2 -Isoxazoline Derivatives. Part 11.† Reactions of Nitrile Oxides, Diazoalkanes, and Dienes with 2-Oxa-3-azabicyclo[3.2.0]hepta-3,6-diene Derivatives

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Nitrile oxides and diazoalkanes with 4-phenyl-2-oxa-3-azabicyclo[3.2.0]hepta-3,6-diene yield new heterocyclic cyclobutane derivatives. The structures and stereochemistry of the cycloadducts are attributed on the basis of n.m.r., i.r., Raman, and dipole moment measurements. In all the reactions explored, the sterically favoured *anti*-adducts are formed in larger amounts than the *syn*-isomers. The observed regioisomer ratios agree with those predicted by perturbation theory. 4-Phenyl-2-oxa-3-azabicyclo[3.2.0]hepta-3,6-diene reacts as a dienophile with several dienes to give only *anti*-adducts.

THE present paper provides further data supporting the usefulness and validity of perturbation theory in predicting regioselectivity in 1,3-dipolar cycloadditions. The model considered takes into account only frontier orbital interactions. The cycloadditions studied are the LUMO-dipole controlled reactions of the nitrile oxides (1a and b) with the isoxazolines (2a and b) and the HOMO-dipole controlled reactions of the diazoalkanes (7) with (2b) (Schemes 1 and 2). Apart from their theoretical interests, these reactions make available compounds otherwise difficult to obtain.

The 2-oxa-3-azabicyclo[3.2.0]hepta-3,6-diene (2)¹ has a moderately perturbed carbon-carbon double bond and the *anti*-face of the cyclobutene region of the molecule appears particularly useful for studying the regiochemistry of 1,3-dipolar cycloadditions. Regioisomeric cycloadditions on the *anti*-face of the molecule (2) should be characterized by transition states with identical steric

requirements. Only a few dipolarophiles which can be compared with the model (2) have been studied previously from this point of view, namely some five-membered heterocycles,² tropone,³ 3-substituted cyclopentenes,⁴ and thiet S_S-dioxide.⁵ Compound (2) was found suitable for studying *syn-anti*-isomerism in both 1,3-dipolar and Diels-Alder cycloadditions. Diels-Alder reactions with (2) as a dienophile model also showed *endo-exo*-isomerism.

RESULTS

Nitrile oxides generated *in situ* from the corresponding chlorohydroxamic acid and triethylamine were treated with an equimolar quantity of the isoxazoline (2) in anhydrous benzene. Yields are reported in Table 1. Quantitative analysis of the components of the reaction mixtures was carried out by column chromatography. For the two nitrile oxides studied (1a and b), only three of the four possible isomeric adducts (3)–(6) were detected and separated. The large amount of furoxan isolated from the cycloaddition of (1a) with (2a) accounts for the low yield of cycloadducts.

³ C. De Micheli, R. Gandolfi, and P. Grünanger, *Tetrahedron*, 1974, **30**, 3765; M. Frank-Neumann and D. Martina, *Tetrahedron Letters*, 1975, 1755.

⁴ P. Caramella and G. Cellerino, *Tetrahedron Letters*, 1974, 229.

⁵ D. C. Dittmer and R. Glassman, *J. Org. Chem.*, 1970, **35**, 999.

† Part 10, G. Bianchi, C. De Micheli, and R. Gandolfi, *J.C.S. Perkin I*, 1976, 1518.

¹ G. Bianchi, R. Gandolfi, and P. Grünanger, *Tetrahedron*, 1970, **26**, 5113.

² P. Caramella, G. Cellerino, A. Corsico Coda, A. Gamba-Invernizzi, P. Grünanger, K. N. Houk, and F. M. Albini, *J. Org. Chem.*, 1976, **41**, 3349.

The adducts, however, were completely stable under the reaction conditions.

The structures of the cycloadducts were assigned on the basis of spectroscopic and dipole moment data. Although it was not possible to calculate the deceptively simple AA'BB' n.m.r. spectra of the adducts (3a)—(5a), the fact that the chemical shift values for (3a) [δ 3.90 (2 H, m, H-2

TABLE 1
Cycloadducts from nitrile oxides and isoxazolines (2)

	Ratios			Total yield (%)
	(3)	(4)	(5)	
a:	62	19	19	50
b:	66	19	15	88

a, R=Me b, R=Ph
SCHEME 1

and -4) and 4.91 (2 H, m, H-1 and -3); $N = J_{1,2} + J_{1,4} = 8.8$ Hz] and (4a) [δ 3.90 (2 H, d, H-2 and -3) and 4.91 (2 H, d, H-1 and -4); $N = J_{1,2} + J_{1,3} = 6.2$] were identical strongly favoured an *anti*-disposition of the isoxazoline rings.

The average (δ 4.64) of the chemical shifts of the cyclobutane protons of the isomer (5a) [δ 4.13 (2 H, t, H-2 and -4) and 5.12 (2 H, t, H-1 and -3); $N = J_{1,2} + J_{1,4} = 13.0$ Hz] differs from that of (3a) and (4a) (δ 4.40); thus a *syn*-structure is the most probable.⁶ X-Ray analysis of (5a) showed that the n.m.r. assignment was correct.⁷

Dipole moment measurements on the three isomers gave the values: (5a) 3.89, (4a) 4.98, (3a) 0.89 D.* As expected the lowest value was that of the centrosymmetric (3a). Five, fourteen, and eighteen coincidences (vibrations of the same frequency) in Raman and i.r. spectra were found for (3a), (4a), and (5a), respectively. The low number of coincidences for (3a) was considered proof of the presence of a C_i centre, as a consequence of the Rule of Mutual Exclusion.^{8,†}

For the adduct (4b) a complete and definitive analysis of its AA'BB' spectrum⁹ was possible; the following data were obtained: δ 5.18 (2 H, m, H-1 and -4, $J_{1,2}$ 7.25, $J_{1,4}$ 1.36, $J_{1,3}$ -0.83), 4.47 (2 H, m, H-2 and -3, $J_{2,3}$ 3.25 Hz). As already reported¹⁰ for cyclobutane rings, coupling constant values lower than 5 Hz cannot arise from *cis*-interactions of adjacent protons and the negative value must come from a 1,3-interaction (J) between two *trans*-protons,

* We thank Professor M. Sanesi, Institute of Physical Chemistry, University of Pavia, for the measurements. Experimental details and discussion of the dipole moment data will be reported in a forthcoming paper.

† A definitive proof for structures (3a) and (4a) is afforded by the preliminary results of an X-ray study (G. Bocelli, personal communication).

provided that the cyclobutane rings considered are planar or quasiplanar. The cyclobutane rings in the adducts (3)—(6) are expected to be planar because of the presence of the two rigid penta-atomic heterocycles; this was confirmed by the X-ray structure determination of (5a).⁷ Owing to the low solubilities of (5b) and (3b) in solvents suitable for n.m.r. measurements, their structures were attributed only tentatively, on the basis of their relative proportions in the reaction mixtures as compared with those of the 'a' series.

Reaction of diazoalkanes (in large excess) with the isoxazoline (2b) were carried out in ether at room temperature, in the case of dideuteriodiazomethane a slight excess of (2b) was used. The reactions proceeded smoothly and cycloadditions were complete in a few hours (<6 h) with high yields. Of the eight possible adducts from the reaction of diazoethane with (2b), only four [(8d)—(11d)] were fully characterized, and (8e) and (9e) were detected and estimated by n.m.r. in mixtures with (8d) and (9d). All the adducts were Δ^1 -pyrazolines, showing the characteristic i.r. band at *ca.* 1540 cm^{-1} . N.m.r. analysis¹¹ allowed the structures (8)—(11) to be assigned (Table 3).

The proton at position 5 of the pyrazoline ring (H-1) resonated at lower field than the other three cyclobutane ring protons. This assignment was demonstrated by the small coupling constant shown by the lowest field signal (which can only be due to the proton α either to nitrogen or to oxygen) in the case of compounds (8d)—(11d), due to

TABLE 2
Cycloadducts from diazoalkanes and the isoxazoline (2b)

	Ratios				Total yields (%)
	(8)	(9)	(10)	(11)	
a:	47.5	27	2.5	23	96
b:	47.5	26	3	23.5	97
c:	58	42			95
d:	31	20.5	3	17	98
e:	18	10.5			

coupling with the proton at position 3 ($R^1 = \text{H}$) of the pyrazoline.

Of the two resonances of protons in isoxazoline ring that at lower field was attributed to the proton at position 5 of the heterocycle¹² [H-4 for compounds (8) and (10), and H-3 for (9) and (11)]. The negative $^4J_{1,3}$ and $^4J_{2,4}$ values and low $J_{2,3}$ and $J_{1,4}$ values for (8) and (9) (Table 3) indicate an *anti*-relationship, and the positive $^4J_{1,3}$ and $^4J_{2,4}$ values and high $J_{2,3}$ and $J_{1,4}$ values for (11) are consistent with a *syn*-disposition of the heterocycles.¹⁰ The n.m.r. data, considered in the light of the discussion on compound (4b), allow a choice between structure (8) and (9). The small positive coupling constants [$J_{1,4}$ (Table 3)] for the lower field protons, α to oxygen and nitrogen, of compound (8) indicate a vicinal *trans*-relationship of these protons

⁶ D. A. Ben-Efraim and B. S. Green, *Tetrahedron*, 1974, **30**, 2357.

⁷ G. D. Andreotti, G. Bocelli, and P. Sgarabotto, *Cryst. Struct. Comm.*, 1973, **2**, 115.

⁸ H. Ziffer and I. W. Levin, *J. Org. Chem.*, 1969, **34**, 4056.

⁹ B. Dischler and G. Englert, *Z. Naturforsch.*, 1961, **16a**, 1180.

¹⁰ R. Mondelli and A. Gamba, *Org. Magnetic Resonance*, 1973, **5**, 101; A. Gamba and R. Mondelli, *Tetrahedron Letters*, 1971, 2133; A. A. Formichov, I. A. Zon, I. M. Gella, R. G. Kostyanovsky, A. N. Soprin, and V. I. Markov, *Org. Magnetic Resonance*, 1973, **5**, 263.

¹¹ A. A. Bothner-By and S. Castellano, in 'Computer Programs for Chemistry,' ed. D. F. de Tar, Benjamin, New York, 1968, p. 10.

¹² G. Bianchi, C. D. Micheli, R. Gandolfi, P. Grünanger, P. Vita-Finzi, and O. V. de Pava, *J.C.S. Perkin I*, 1973, 1148.

and the two heteroatoms as in structure (8). On the other hand the protons α to oxygen and nitrogen of the adducts (9) show a small negative coupling constant ($J_{1,3}$), as expected for the *trans*-1,3-relationship in structure (9).

The regiochemistry of compounds (11) was attributed similarly, the low $J_{1,3}$ values for the two *cis*-protons rule out the possibility of two adjacent hydrogen atoms.

The pyrazoline protons at positions 3 ($R^1 = H$) and 4 (H-2) in compounds (8d), (9d), and (11d) are *trans* to each other as shown by the low coupling constants.

The adducts (10) had complex n.m.r. spectra and the

in 15 h, yielding a mixture of (12a) and (13a) (5.5 : 1) (Scheme 3).

Compound (2b) with tetraphenylcyclopentadienone gave only the adduct (12b). All the adducts (12) and (13) gave 3-phenylisoxazole, the corresponding tetrasubstituted benzene, and carbon monoxide on heating at their m.p.s.

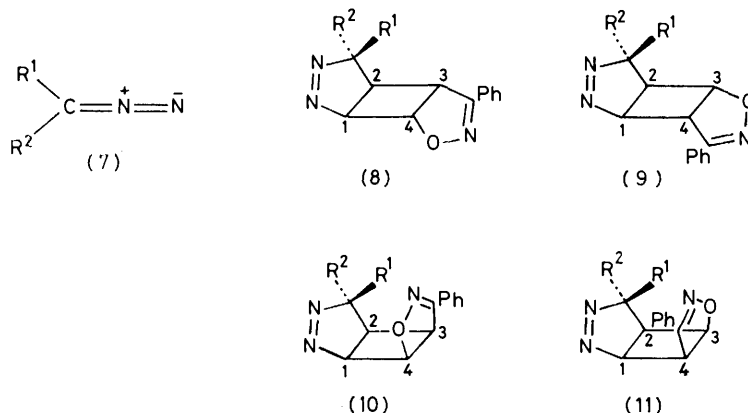
When compound (2b) was heated for 6 days with furan (as solvent and reagent) at 80 °C in a stainless steel bomb, the *anti*-adducts (12c) and (13c) were produced (93%); the *exo*-adduct was again dominant (2.0 : 1). Both the adducts were stable under the reaction conditions, but they underwent retro-cycloaddition at their m.p.s.

TABLE 3

^1H N.m.r. data [δ (CDCl_3)] for compounds (8)–(11) ^a

Compound	$J_{1,2}$	$J_{3,4}$	$J_{2,3}$	$J_{1,4}$	$^4J_{1,3}$	$^4J_{2,4}$	J_{1,R^1}	J_{2,R^1}	J_{R^1,R^2}	H-1	H-2	H-3	H-4	R^1	R^2	R.m.s. error
(8b) ^b	6.60	7.26	3.19	1.76	-1.32	-0.67				5.49	2.67	4.06	4.85			
(8d)	5.91	7.24	3.15	3.08	-1.33	-0.84	2.97	2.35	7.30	5.76	2.32	3.74	4.80	4.82	1.32	0.048
(9b)	6.16	6.93	2.10	2.20	0.00	-1.43				5.35	2.80	4.54	4.34			
(9d)	5.65	7.03	2.52	2.30	-0.09	-1.50	2.64	1.99	7.30	5.41	2.44	4.60	4.32	4.86	1.25	0.035
(11b) ^b	6.82	8.14	5.60	6.82	2.31	3.30				5.72	2.88	5.09	4.93			
(11d)	7.03	8.12	6.13	7.34	1.68	3.00	2.88	3.34	7.30	5.66	2.39	5.06	4.67	4.97	1.30	0.062
(8c)	6.10	7.21	3.55	1.44	-1.11	-0.67				5.50	2.48	3.97	4.92	1.75	1.18	
(9c)	5.77	7.10	2.77	2.11	0.00	-1.54				5.36	2.57	4.83	4.34	1.68	1.12	

^a The signs of the J values (Hz) were deduced by 'tickling' [adducts (8d), (9d), and (11d)] and selective decoupling [(8b), (9b), and (11b)]. ^b In $(\text{CD}_3)_2\text{SO}$.



a; $R^1=R^2=H$ b; $R^1=R^2=D$ c; $R^1=R^2=Me$ d; $R^1=H, R^2=Me$ e; $R^1=Me, R^2=H$

SCHEME 2

structural assignments are based on the following observations: structure (10d) is supported by the chemical shift values of the methyl group [δ 1.17 (d, J 7.30 Hz)] and of the pyrazoline proton at position 3 ($R^1 = H$) [δ 4.60 (m)], clearly shielded by the phenyl group [compare this value with the corresponding values of (8d), (9d), and (11d) (Table 3)]. Furthermore, as expected from structures with high dipole moments, the adducts (10) possessed the lowest R_F values of all the isomers, the order of decreasing R_F value being (9), (8), (11), (10).

Structures (8a)–(11a) were assigned by comparison (R_F values, m.p.s, and n.m.r. spectra) with compounds (8b)–(11b). Compounds (8d) and (9d) were obtained in a mixture with minor amounts of the epimers (8e) [δ 1.78 (d, J 7.3 Hz, Me)] and (9e) [δ 1.73 (d, J 7.3 Hz, Me)]. Compounds (8e) and (9e), however, were not isolated.

Compound (2b) readily underwent the Diels–Alder reaction. With 2,5-dimethyl-3,4-diphenylcyclopentadienone in boiling chloroform quantitative reaction was achieved

Compound (2b) with anthracene under reflux in xylene (48 h) gave the adduct (14) (53%); with 1,3-diphenylisobenzofuran at room temperature (48 h) it gave the adduct (15) in quantitative yield. The latter adduct underwent aromatization to (16) on brief refluxing in methanolic hydrogen chloride. The structures of the Diels–Alder adducts were deduced from their n.m.r. data. The coupling constants for the adducts (12)–(15) were those expected for an *anti*-configuration of the cyclobutane ring. In fact H-1 and -2 gave rise to a four-line signal with $J_{1,2}$ ca. 7 Hz, and the $J_{1,3} + J_{1,4}$ or $J_{2,3} + J_{2,4}$ values were < 2.5 Hz. Experiments with the shift reagent $\text{Eu}(\text{dpm})_3$ allowed us to distinguish between structures (12) and (13). Addition of the reagent caused linear shifts (Δ) to lower fields for H-1 and -2; these were larger for (12a) (e.g. for $[\text{Eu}(\text{dpm})_3]/[\text{substrate}] = 0.5$, $\Delta_1 = 8.70$, $\Delta_2 = 7.25$) than for (13a) ($\Delta_1 = 4.40$ and $\Delta_2 = 3.50$) as expected for an *exo*-structure (from models). Similarly the *endo*-structure of (13c) was indicated by the shifts to lower field of the H-3

and -4 signals, which were greater for (13c) ($\Delta_3 = \Delta_4 = 6.25$) than for (12c) ($\Delta_3 = \Delta_4 = 4.55$).

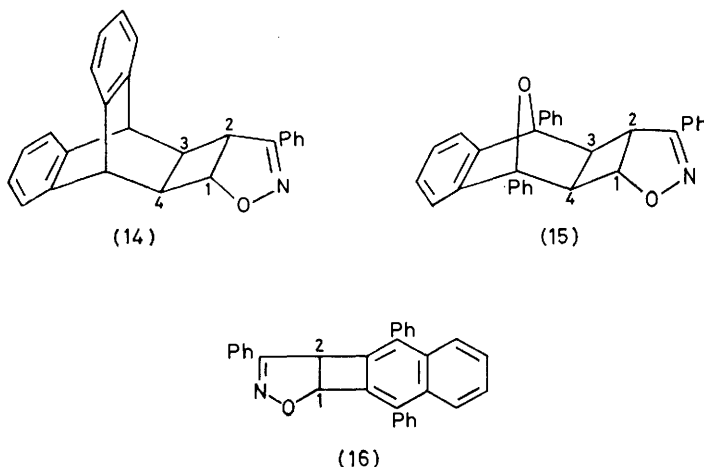
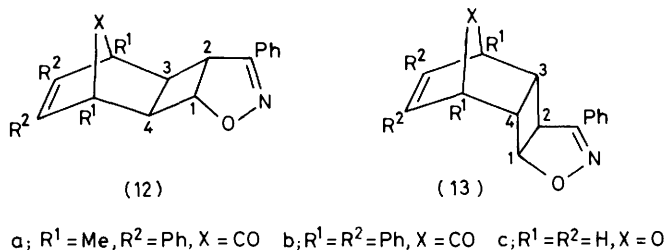
The formation of a single isomer in the reactions leading to (12b) and (15) did not allow the attribution of definitive structures; they were tentatively assigned as *exo*.

DISCUSSION

In our opinion, the dominant factors governing the regiochemistry of the *anti*-adducts formed in the 1,3-dipolar cycloadditions studied here are frontier orbital

assumption that the oxygen atom is more electronegative than the C=N group.

The cycloadditions of diazoalkanes, in which the strongest interaction is HOMO(dipole)-LUMO(dipolarophile)¹⁷ (except for reactions with very electron-rich dipolarophiles), should be governed by the perturbation (a) (Scheme 4). Of the two possible orientations, the products of the coefficients indicate that the more favoured is the case where C-6 of compound (2) and the



SCHEME 3

perturbations. Dipole-dipole interactions are expected to intervene appreciably only in the cycloadditions with nitrile oxides, which possess high dipole moments (*e.g.* benzonitrile oxide has $\mu = 4.00$ D¹³), and to be unimportant with diazoalkanes, which have low dipole moments (*e.g.* diazomethane has $\mu = 1.50$ D¹⁴). On the other hand the dipolarophile (2) should have a fairly high dipole moment (*cf.* 3.40 D for 3-phenyl- Δ^2 -isoxazoline¹⁵).

In order to demonstrate the role played by frontier orbitals in these cycloadditions we show in Scheme 4 the HOMO's and LUMO's with their coefficients (calculated by the CNDO/2 method) of nitrile oxides, diazoalkanes,¹⁶ and a model for the carbon-carbon double bond of the isoxazolines (2). The different sizes of the orbital lobes of (2) were based on the reasonable

carbon atom of the diazoalkane interact, so that the final product should be (8) or (10). The experimental results of the 1,3-dipolar cycloadditions on the *anti*-face of (2b) conform with this theory.

Addition on the *syn*-face of the cyclobutane ring with respect to the isoxazoline ring showed inverse regiochemistry, the adduct (11) being dominant over (10). Repulsive steric interactions in the transition state leading to (10) in which the bulky ends of both diazoalkane (R_2C) and isoxazoline (2b) (PhC) are facing each other, explain the results. Particularly significant are the high yields of *syn*-adducts (11) in the reactions of diazoalkanes with (2): the ratios of the *syn*-adducts (11) to the *anti*-adducts (9) were *ca.* 1:1. These results confirm the peculiarity of diazoalkanes, which give high

¹⁵ M. Sanesi, personal communication.

¹³ Ch. Grundmann and P. Grünanger, 'The Nitrile Oxides,' Springer-Verlag, Berlin, 1971.

¹⁴ J. Sheridan, 'Advances in Molecular Spectroscopy,' Pergamon, New York, 1962, p. 139.

¹⁶ K. N. Houk, J. Sims, R. E. Duke, jun., R. W. Strozier, and J. K. George, *J. Amer. Chem. Soc.*, 1973, **95**, 7287.

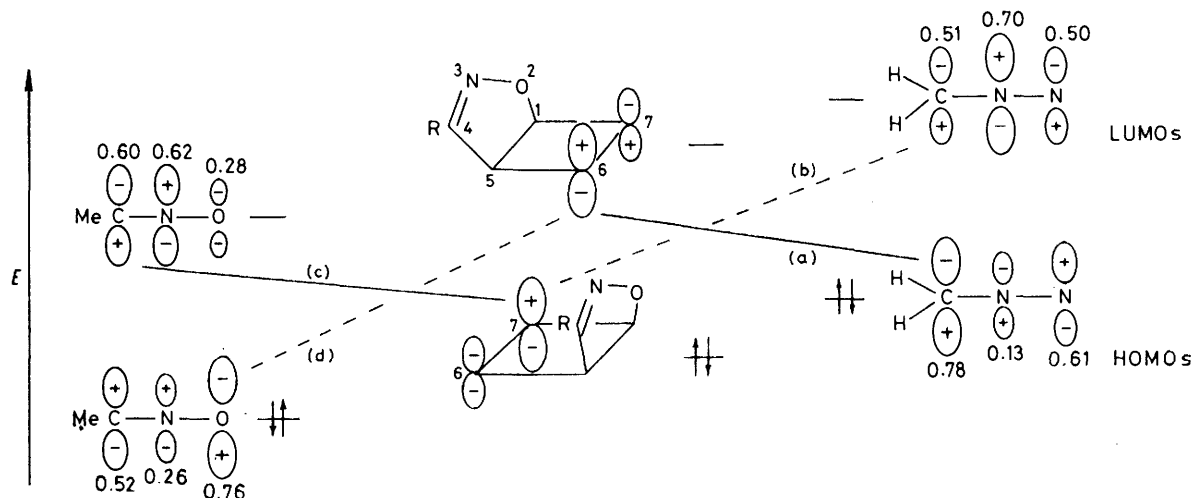
¹⁷ K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Amer. Chem. Soc.*, 1973, **95**, 7301.

proportions of *syn*-adducts in their reactions with *cis*-3,4-disubstituted cyclobutenes.¹⁸ A satisfactory explanation for such behaviour has still to be found.

The regiochemistry of the adducts (3)—(5) of the nitrile oxides agrees with the theoretical predictions. As

hindrance whereas (6) and (4) are less favoured than (5) and (3) because of dipole-dipole interactions.

The fact that the *anti*-cycloaddition is only regioselective and not regiospecific [substantial amount of the adducts (4) are formed together with the dominant



SCHEME 4

TABLE 4

Physical and analytical data for compounds (3)—(16)

Compound	Cryst. solvent	M.p. (<i>T</i> /°C)	Found %			Formula	Required %		
			C	H	N		C	H	N
(3a)	EtOAc ^a	247—248	58.0	6.5	17.1	C ₈ H ₁₀ N ₂ O	57.8	6.1	16.9
(4a)	EtOH ^b	146—147	57.9	6.2	17.0				
(5a)	EtOH ^b	139—140	58.1	6.2	16.9				
(3b)	Dioxan ^b	286 (decomp.)	74.3	4.9	9.5	C ₁₄ H ₁₄ N ₂ O ₂	74.5	4.9	9.7
(4b)	EtOH ^b	172—173	74.4	5.0	9.5				
(5b)	Dioxan ^b	300 (decomp.)	74.1	4.8	9.6				
(8a)	Benzene ^b	217—218	68.0	5.3	20.1	C ₁₂ H ₁₁ N ₃ O	67.6	5.2	19.8
(9a)	EtOH ^b	163	68.0	5.4	20.1				
(10a)	EtOH ^b	134—135	67.8	5.4	19.8				
(11a)	Benzene ^b	172	67.9	5.3	29.9	C ₁₂ H ₉ D ₂ N ₃ O	67.0	6.1	19.5
(8b)	Benzene ^b	213—214	67.1	6.1	19.9				
(9b)	EtOH ^b	162—163	67.3	6.0	19.4				
(10b)	EtOH ^b	133—134	67.2	6.0	19.6	C ₁₄ H ₁₅ N ₃ O	69.7	6.3	17.4
(11b)	Benzene ^b	171—172	67.3	6.1	19.3				
(8c)	Cyclohexane ^b	146—148	69.8	6.3	17.6				
(9c)	Cyclohexane ^b	128—129	69.9	6.1	17.4	C ₁₃ H ₁₃ N ₃ O	68.7	5.8	18.5
(8d)	EtOH ^b	123—126 ^c	68.6	6.1	18.3				
(9d)	EtOH ^b	151—152	68.5	6.0	18.1				
(10d)	EtOH ^b	157—158	68.7	6.1	18.4	C ₃₀ H ₂₅ NO ₂	83.5	5.8	3.3
(11d)	EtOH ^b	146—148	68.9	5.9	18.5				
(12a)	Benzene-MeOH ^b	243—244 (decomp.)	83.5	6.1	3.1				
(13a)	Benzene-MeOH ^a	178—180 (decomp.)	83.8	5.7	3.0	C ₄₀ H ₂₉ NO ₂	86.5	5.3	2.5
(12b)	CHCl ₃ -EtOH ^b	231 (decomp.)	86.6	5.4	2.5				
(12c)	EtOH ^b	168	75.3	5.7	5.9				
(13c)	EtOH ^a	163—164	75.0	5.5	6.0	C ₂₅ H ₁₉ NO	85.9	5.5	4.0
(14)	MeOH ^b	222—223	86.3	5.7	3.8				
(15)	Benzene-MeOH ^b	191—193	84.4	4.9	3.3				
(16)	Benzene-MeOH ^b	188—190	87.8	5.4	3.1	C ₃₁ H ₂₁ NO	87.9	5.4	3.1

^a As prisms. ^b As needles. ^c Even after several recrystallisations the product still contained some (8e).

depicted in Scheme 4, both the interactions LUMO-(nitrile oxide)-HOMO(cyclobutene) (c) (dominant)¹⁷ and HOMO(nitrile oxide)-LUMO(cyclobutene) (d) make the adducts (3) and (5) more favoured than (4) and (6). Furthermore (6) is less favoured than (5) because of steric

(3)] can be explained in terms of a small difference between the coefficients of the frontier orbitals of the dipolarophile.

The marked reactivity of (2b) in the Diels-Alder reactions confirms that cyclobutenes are very reactive dienophiles.

Our results show once more that the preferred orient-

¹⁸ M. Frank-Neumann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 210; C. De Micheli and R. Gandolfi, unpublished results.

ations in Diels–Alder reactions are those which give rise to the sterically favoured *exo*-adducts, unless strong secondary orbital interactions are working in the opposite direction. The exclusive *anti*-stereochemistry of the adducts is considered to be due to repulsive steric interactions between the reactants.

EXPERIMENTAL

N.m.r. spectra were recorded at 36 °C for solutions in CDCl₃ with a Perkin-Elmer R 12 A (60 MHz) spectrometer (Me₄Si as internal standard). The protons are numbered as shown in the Schemes. N.m.r. measurements with Eu(dpm)₃ were run in 0.2M-solutions, with maximum [Eu(dpm)₃]/[substrate] values of 0.5 and 0.8 for (12a) and (13a), and (12c) and (13c), respectively. I.r. spectra were examined for KBr discs with a Perkin-Elmer 125 spectrophotometer. Raman spectra (of solids) were recorded with a Cary 81 spectrometer. Reaction mixtures were analysed by t.l.c. on silica gel GF 254 (Merck); spots were detected under u.v. light (254 nm). Compounds (3a)–(5a) could be detected on t.l.c. plates only by spraying with 3% chromic oxide in sulphuric acid (50%) followed by heating at 120 °C. Column chromatographic separations were carried out on Kieselgel H (Merck), with cyclohexane–ethyl acetate and benzene–ethyl acetate as eluants. Physical and analytical data of new compounds are given in Table 4.

As regards reaction procedures and isolation and separ-

ation of compounds, the work-up procedure was as reported in previous papers (*e.g.* see ref. 12). Compounds (12a) [ν_{\max} 1 775 cm⁻¹ (C=O)] and (13a) [ν_{\max} 1 785 cm⁻¹ (C=O)] were separated by fractional crystallisation (from benzene–methanol).

N.m.r. data of compounds (12)–(16) were as follows: (12a) δ 2.82 (2 H, m, H-3 and -4), 3.95 (1 H, q, H-2, $J_{1.2}$ 7.30, $J_{2.3} + J_{2.4}$ 2.22 Hz), 4.86 (1 H, q, H-1, $J_{1.3} + J_{1.4}$ 1.55 Hz), and 1.42 and 1.51 (s, Me); (13a) δ 3.00 (2 H, m, H-3 and -4), 4.08 (1 H, q, H-2, $J_{1.2}$ 7.30 and $J_{2.3} + J_{2.4}$ 2.22 Hz), 5.09 (1 H, q, H-1, $J_{1.3} + J_{1.4}$ 1.55 Hz), and 1.40 and 1.47 (s, Me); (12c) δ 2.27 (2 H, m, H-3 and -4), 3.82 (1 H, q, H-2, $J_{1.2}$ 7.05, $J_{2.3} + J_{2.4}$ 1.40 Hz), 4.71 (1 H, q, H-1, $J_{1.3} + J_{1.4}$ 1.40 Hz); (13c) δ 2.94 (2 H, m, H-3 and -4), 3.38 (1 H, q, H-2, $J_{1.2}$ 7.0, $J_{2.3} + J_{2.4}$ 2.20 Hz), 4.36 (1 H, q, H-1, $J_{1.3} + J_{1.4}$ 1.80 Hz); (14) δ 2.76 (2 H, m, H-3 and -4), 3.30 (1 H, q, H-2, $J_{1.2}$ 7.34, $J_{2.3} + J_{2.4}$ 2.66 Hz), and 4.20 (1 H, q, H-1, $J_{1.3} + J_{1.4}$ 2.00 Hz); (15) δ 2.99 (1 H, m, H-3, $J_{3.4}$ 5.99, $J_{2.3}$ 2.75, $J_{1.3} - 0.20$ Hz), 3.17 (1 H, m, H-4, $J_{1.4}$ 1.67, $J_{2.4} - 1.09$ Hz), 3.66 (1 H, m, H-2, $J_{1.2}$ 7.34 Hz), and 4.79 (1 H, m, H-1); (16) δ [(CD₃)₂SO] 5.77 (1 H, d, H-2, $J_{1.2}$ 5.3 Hz) and 6.27 (1 H, d, H-1).

Owing to the low solubility of compound (13b) [ν_{\max} 1778 cm⁻¹ (C=O)], no n.m.r. spectrum was obtained.

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