Tetrahedron, Vol. 37, pp. 1349 to 1357, 1981
Printed in Great Britain.

0040-4020/81/071349-09$02.00/0
Pergamon Press Ltd.

SITE SELECTIVITY IN THE REACTIONS OF 1,3-DIPOLES WITH NORBORNADIENE DERIVATIVES

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(*Received in U.K. 4 August* 1980)

Abstract—The cycloadditions of arylazides, benzonitrile oxides and diphenylnitrile imine to norbornadiene derivatives **1a–c** showed varying degree of site- and stereo-selectivity. With dipolarophile **1a** arylazides and benzonitrile oxides attack, preferentially, the electron-poor tetrasubstituted double bond, while in the case of **1b** and **1c** is the substituted double bond which enters the cycloaddition. By contrast, 2-diazopropane and C-phenyl-N-methylnitrone react with the sole tetrasubstituted double bond of **1a–c** in stereo- and site-specific cycloadditions. The quantitative evaluation of the two possible reaction paths was performed by glc analysis. The compounds detected were those arising from Diels–Alder cycloreversions of the thermally labile intermediate adducts **2** and **3** (Scheme 1). The results were rationalized on the basis of a qualitative perturbation treatment which considers frontier orbital interactions only.

Being easily accessible and suitable for studies of reactivity,[1,2] stereochemistry[1,3–8] and synthesis,[9–12] norbornadiene and derivatives have gained the interest of a large number of researchers.

We planned this work with the aim to compare the relative reactivity of electron-rich vs electron-poor double bonds in cycloadditions with different 1,3-dipole and therefore we choose norbornadienes **1** as suitable models for such an investigation.

The usefulness of compounds **1**, as masked acetylene derivatives in the synthesis of pentaatomic heterocycles, has already been proved by reacting various 1,3-dipoles with **1a** and **1b**.[9,12,13]

In the present work we have studied the relative reactivity of the two double bonds of compounds **1a–c** towards 1,3-dipoles having different FO discussing the results in a PMO treatment context.[14]

RESULTS

The reactions of 1,3-dipoles with a large excess of norbornadiene **1** (molar ratio 1:5) in order to prevent the formation of bis-adducts were carried out in anhydrous benzene. Azides, mesitonitrile oxide, 2 - diazopropane (DP) and C - phenyl - N - methylnitrone were reacted as such; benzonitrile oxides and diphenylnitrile imine (DPNI) were generated *in situ* from the corresponding benzhydroximic acid chlorides and N(α - chlorobenzylidene) - N′ - phenylhydrazine, respectively, by adding a stoichiometric amount of triethylamine.

The reactions of nitrile oxides, DPNI, DP with dipolarophiles **1a–c** and those of azides and C - phenyl - N - methylnitrone with **1a** went to completion at room temperature while the reactions of azides and C - phenyl - N - methylnitrone with **1b** and **1c** required more drastic conditions (Experimental). The results are collected in Schemes 1 and 2 and Table 1.

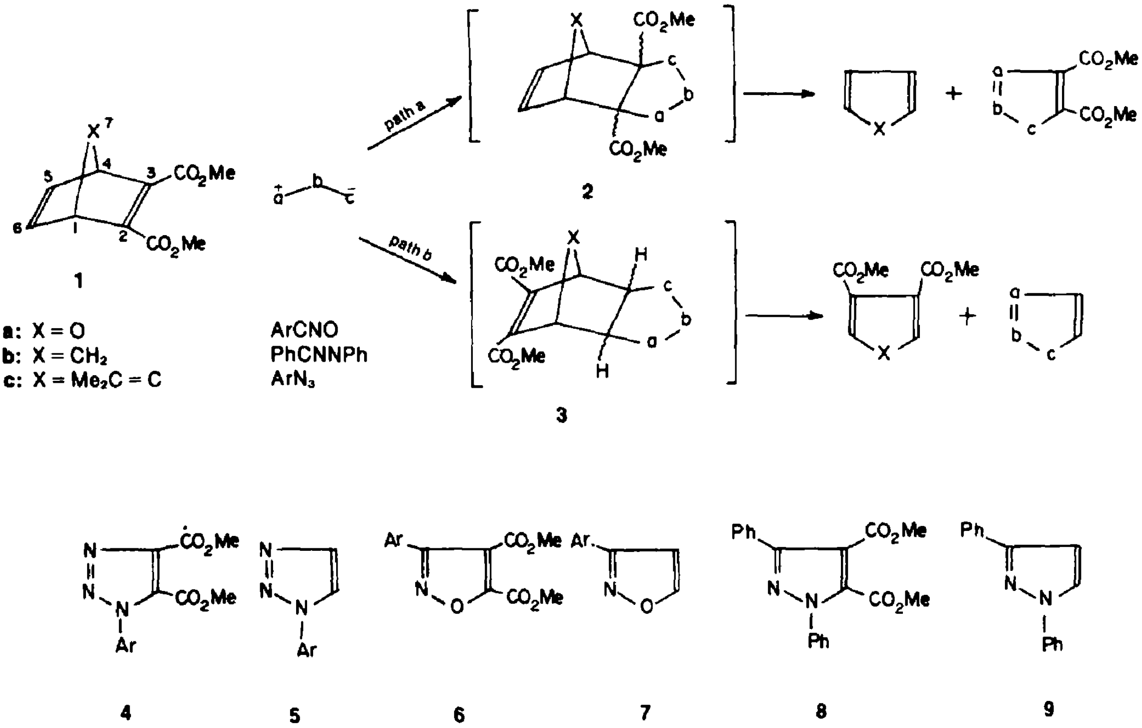
Intermediate cycloadducts **2** and **3** generally were neither isolated nor detected because they decompose under reaction conditions, as shown in Scheme 1, to give heterocycles **4–9**.

Since we were mainly interested to determine ratios path a/path b, in the case of stable intermediate adducts (e.g. the reaction of benzonitrile oxides with **1b**) the Diels–Alder cycloreversion was promoted by heating the reaction mixtures at 120° until the tlc disappearance of compounds **2** and **3**; the resulting **4/5**, **6/7** and **8/9** ratios were evaluated as usual by glc analysis (Table 1).

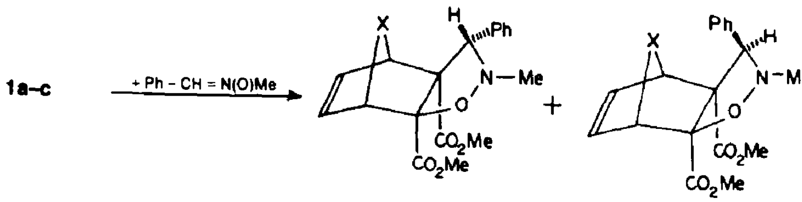
The effect of solvent polarity on the path a/path b ratio was investigated by reacting mesitonitrile oxide with **1a** in a number of solvents. The results obtained are gathered in Table 2. The increase in path b/path a ratio parallels the increase in solvent polarity with the exception of methanol and ethanol whereby ratio value falls to a minimum.

In contrast to the behaviour of **2** and **3**, adducts **10a–c** and **11a** were easily isolated from the reactions of C - phenyl - N - methylnitrone and **1a–c** (Scheme 2). In agreement with the attributed structures **10a–c** and **11a**, the ^1H NMR spectra of these compounds exhibited the characteristic resonance of vinyl protons. Site-specific addition of nitrone to the tetrasubstituted double bond of compounds **1** is thus proved. Furthermore, catalytic hydrogenation of **10a–c** and **11a** gave compounds **13a–c** and **14a**, respectively, which were also obtained from reaction of C - phenyl - N - methylnitrone with **12a–c** (Scheme 3).

Structures **10**, **11**, **13** and **14** are assigned on the basis of the present findings and also taking into account the strict *syn*-methylene specificity found in previously reported reactions of norbornene derivatives with numerous 1,3-dipoles.[15] Finally, the *cis*-relationship between phenyl and methoxycarbonyl groups in compounds **10** and **13** follows from the strong shielding experienced by a methoxycarbonyl group [$\delta(CDCl_3)$ 3.04–2.97] in comparison to the other one [$\delta(CDCl_3)$ 3.71 – 3.84]. The methoxycarbonyl groups of **11a** and **14a** resonate at similar field (e.g. **11a**: $\delta(CDCl_3)$ 3.78 and 3.63)



Scheme 1.



	Total Yield (%)	10(%)	11(%)
1a	85	70	30
1b	73	100	0
1c	76	100	0

Scheme 2.

values. Structure **14a** was further substantiated by its synthesis from **19a** as shown in Scheme 3.

The attack of the borohydride ion was shown to occur with high selectivity from the least hindered side of the molecule.[16] Also the attack of 2-diazopropane to compounds **1** to give adducts **15** was stereo- and site-specific, yielding the sole *syn*-methylene adducts at the tetrasubstituted double bond. Compound **15a** was too labile to be isolated and the cycloreversion product **17** was obtained in quantitative yield.

In order to evaluate the influence of the X bridge on the reaction rates of 1,3-dipoles with compounds **1** a kinetic investigation of the reaction between mesitonitrile oxide and dipolarophiles **12** was carried out (Scheme 5).

A second order rate constant ($k_2 = 2.21 \times 10^{-3}\,l\,mol^{-1}\,sec^{-1}$) was determined by reacting mesitonitrile oxide with an excess of **12a** (1:3) in ethanol at 25°, following the disappearance of the 1,3-dipole UV absorption at 260 nm. The ratio values $k_{12a}/k_{12b} = 48.1$ and $k_{12b}/k_{12c} = 1.1$ obtained according to the competitive method allowed the other two constants reported in Scheme 5 be evaluated.

DISCUSSION

Norbornadiene is a classic example of molecule in which a through space interaction between two double bonds is operative.[17] Significant overlap between the two degenerate orbitals beneath the carbon skeleton results in two new molecular orbitals (HOMO and NHOMO). The splitting (0.85 eV) between the bonding and antibonding combinations has been determined by photoelectron (PE) measurements.[18] Similarly, the unoccupied orbitals π^* mix to give LUMO and NLUMO. In both cases, as a consequence of the molecular symmetry, the MO coefficients at the four involved carbon atoms are

Table 1. Path a : path b ratios for the reactions of aryl-nitrile oxides, aryl-azides, DPNI[a], DP[b] and C-phenyl-N-methylnitrone with dipolarophiles **1**[c]

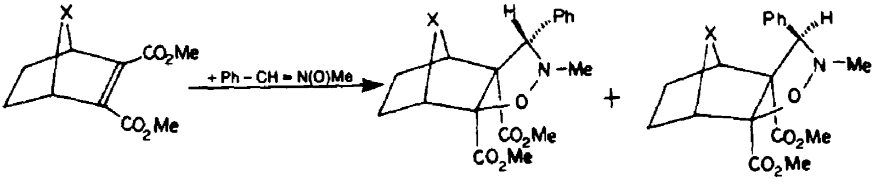
1,3-dipole	Dipolarophile	path a (%)	path b (%)
$a=\overset{\oplus}{b}-\overset{\ominus}{c}$	**1**		
4-MeO-C_6H_4CNO	**1a**	87.3	12.7
C_6H_5CNO	**1a**	75.0	25.0
4-NO_2-C_6H_4CNO	**1a**	56.4	43.6
4-MeO-C_6H_4CNO	**1b**	10.6	89.4
C_6H_5CNO	**1b**	13.5	86.5
4-NO_2-C_6H_4CNO	**1b**	3.8	96.2
4-MeO-C_6H_4CNO	**1c**	16.7	83.3
C_6H_5CNO	**1c**	10.4	89.6
4-NO_2-C_6H_4CNO	**1c**	5.3	94.7
4-MeO-$C_6H_4N_3$	**1a**	90.8	9.2
$C_6H_5N_3$	**1a**	82.4	17.6
4-NO_2-$C_6H_4N_3$	**1a**	51.6	48.4
4-MeO-$C_6H_4N_3$	**1b**	22.5	77.5
$C_6H_5N_3$	**1b**	23.0	77.0
4-NO_2-$C_6H_4N_3$	**1b**	8.5	91.5
4-MeO-$C_6H_4N_3$	**1c**	22.4	77.6
$C_6H_5N_3$	**1c**	17.0	83.0
4-NO_2-$C_6H_4N_3$	**1c**	6.2	93.8
DPNI	**1a**	99.4	0.6
DPNI	**1b**	80.5	19.5
DPNI	**1c**	82.4	17.4
DP	**1a**	d	
DP	**1b**	d	
DP	**1c**	d	
Ph-CH=N(O)Me	**1a**	d	
Ph-CH=N(O)Me	**1b**	d	
Ph-CH=N(O)Me	**1c**	d	

[a] Diphenylnitrilimine. [b] 2-Diazopropane. [c] All the reactions were carried out in benzene. [d] 100% path a.

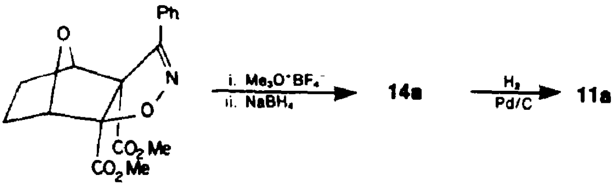
Table 2. Solvent effect for the reaction of mesitonitrile oxide with dipolarophile 1a[a]

Solvent	$E_T^{13,14}$	$\pi(=\pi^*)^{15}$	path a (%)	path b (%)
$MeNO_2$	46.3	.848	36.2	63.8
DMF	43.8	.875	39.9	60.1
CH_2Cl_2	41.1		40.6	59.4
MeCOMe	42.2	.683	43.1	56.9
MeCN	46	.86	44.2	55.8
$CHCl_3$	39.1		46.6	53.4
$MeCO_2Et$	38.1	.545	46.5	53.5
THF	37.4	.576	49.4	50.6
CS_2	32.6		53.3	46.7
Et_2O	34.6	.273	55.5	44.5
C_6H_6	34.5		57.1	42.9
CCl_4	32.5		61.8	38.2
C_6H_{12}	31.2	.000	64.7	35.3
$n\text{-}C_6H_{14}$	30.9	-.081	61.0	39.0
EtOH	51.9		67.8	32.2
MeOH	55.5		65.2	34.8

[a] The values reported in this table were evaluated by a GLC analysis of the reaction mixtures taking into account the relative amounts of compounds 6(Ar=Mes) and 7(Ar=Mes).

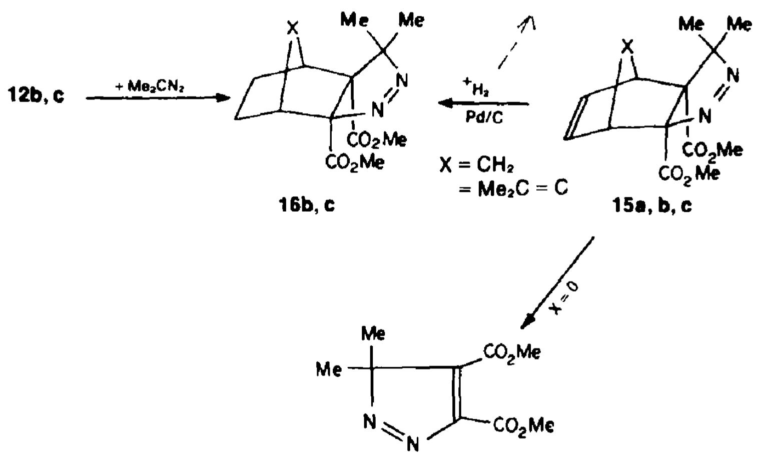


12	Total Yield (%)	13 (%)	14 (%)
a: X = O	80	90	10
b: X = CH_2	70	100	0
c: X = $Me_2C = C$	77	100	0

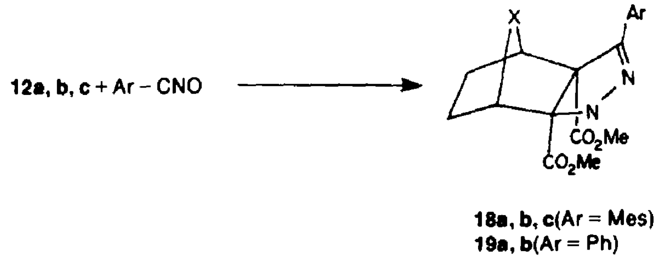


19a

Scheme 3.



Scheme 4.



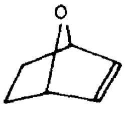
Dipolarophile	1,3-dipole	k_2 l mol^{-1} s^{-1})10^5
12a	Mes − CNO	221
12b	Mes − CNO	4.59
12c	Mes − CNO	4.18

Scheme 5. Second-order rate constants (l mol^{-1} s^{-1}) for cycloadditions of mesitonitrile oxide to **12a–c** in ethanol at 25°.

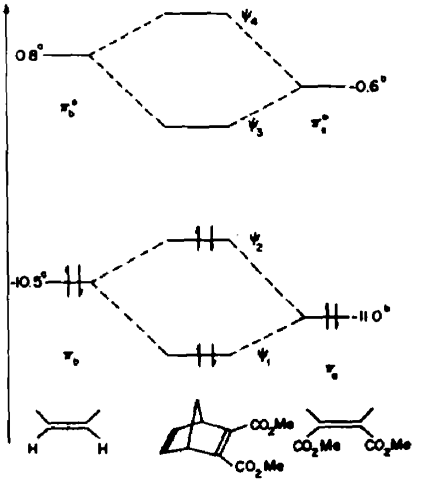
identical. In norbornadiene derivative **1b** the localized orbitals π_a, π_b (and π_a^*, π_b^*) are separated by an energy gap which can be estimated from the known ionization energies (IE) (and electron affinities EA) of ethylene 10.5 (and −0.84) eV[19] and dimethylmaleate 11.0 (and 0.6) eV.[19]

Therefore the HOMO and LUMO (resulting from a $\pi_a - \pi_b$ and a $\pi_a^* + \pi_b^*$ conbinations, respectively) extend again over the two double bonds but they are now mainly localized on the disubstituted and on the tetrasubstituted double bond respectively. In other words, the coefficients of ψ_2 (ψ_3) are larger at the disubstituted (tetrasubstituted) double bond because this is closer in energy to π_b (π_a^*). By replacing the methylene bridge with an oxygen atom, that is on going from **1b** to **1a**, the most relevant change is a stabilization of all the orbitals as suggested by PE measurements on the model compound **20**.[20]

Compound **20** shows an IE of 9.44 eV which is 0.47 eV higher than that of norbornene (8.97 eV);[17] the above statement is also supported by the *ab initio* MO calculations performed on norbornadiene (HOMO, −6.94 eV; LUMO, 7.92 eV) and 7-oxanorbornadiene (HOMO, −7.07 eV; LUMO, 7.62 eV).[21] It will follow that 1,3-dipolar cycloadditions controlled by the HOMO (1,3-dipole)-LUMO (dipolarophile) interaction will proceed



20



ᵃValues relative to ethylene
ᵇValues relative to dimethylmaleate

Fig. 1. A qualitative representation of the F.O. energies in **1b**.

along path a whereas path b will be favoured by the LUMO (1,3-dipole)-HOMO (dipolarophile) interaction. Moreover the path a/path b ratio should increase both on passing from **1b** to **1a** and by changing electron-poor with electron-rich 1,3-dipoles as expected for a stronger HOMO (1,3-dipole)-LUMO (dipolarophile) interaction.

The results were in full agreement with this hypothesis. In fact the electron-rich 1,3-dipoles 2-diazopropane (IE = 7.9 eV)[22] and C - phenyl - N - methylnitrone (IE = 8.01 eV),[23] whose dominant interaction with dipolarophile is HOMO (1,3-dipole)-LUMO (dipolarophile) (Fig. 2), react with all cycloaddends according the sole path a.

Moreover, the contribute of path a progressively decreases along the series DPNI, phenylazide (IE = 8.72 eV)[23] and benzonitrile oxide (IE = 8.92 and 10.5 eV)[23,24] (Table 1) as expected from the HOMO energies of these 1,3-dipoles. A similar trend was also found for substituted azides and nitrile oxides where the introduction of an electron-withdrawing group (e.g. nitro) group) enhances the relative rate of attack to the disubstituted double bond of dipolarophiles **1a–c** (path b) while smaller and somewhat irregular effect was found for the OMe-group.

The increased path a/path b ratio on going from benzonitrile oxide or phenylazide to DPNI supports previous data which indicated an higher donor character for DPNI in comparison to the former two dipoles.[25] The results of Table 1 show that both FO interactions are at work in the reactions of DPNI, benzonitrile oxides and arylazides: the HOMO (1,3-dipole)-LUMO (dipolarophile) interaction is dominant in the reactions of DPNI with **1a–c** and in the reactions of nitrile oxides and arylazides with **1a** whereas the reactions of benzonitrile oxides or arylazides with **1b** or **1c** are characterized by a LUMO (1,3-dipole)-HOMO (dipolarophile) control.

The same conclusions may be drawn from the kinetic data reported in Scheme 5; the reaction rate for the cycloaddition of mesitonitrile oxide to dipolarophile **12** is strongly accelerated by the introduction of an electron-withdrawing substituent in the dipolarophile (e.g. **12a**). It should be pointed out also that path a/path b ratios are at best a minimum estimate of the electronic factors because the attack to π_a is obviously sterically disfavoured as can be seen comparing the results of the sterically encumbered mesitonitrile oxide (IE = 8.35 eV) with those of benzonitrile oxide (Table 2).

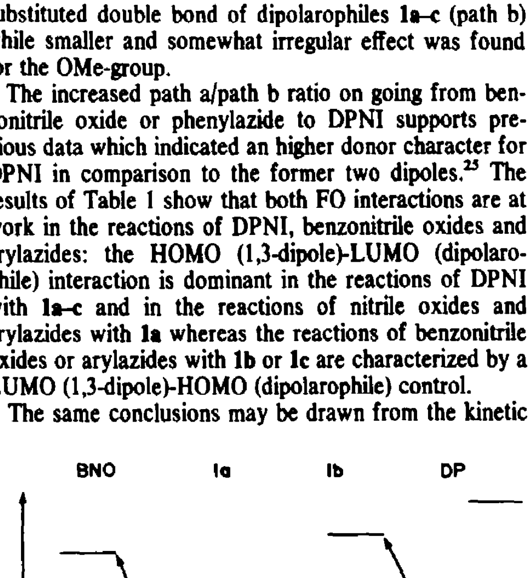


Fig. 2. Qualitative diagram of the frontier orbital energies for Ia, Ib, 2-diazopropane(DP) and benzonitrile oxide. The dominant interactions are indicated (solid arrows).

Inspection of Table 1 and Scheme 5 reveals a similar behaviour for **1b**, **c** and **12b**, **c** in all the examinated reactions; the symmetry allowed interaction between the exocyclic double bond and ψ_2 in **1c** (π_a in **12c**) gives rise to apparent effect neither on the site-selectivity (Table 1) nor on the cycloaddition rate of mesitonitrile oxide with dipolarophile **12b**, **c** (Scheme 5).[26]

In previous papers we have reported the influence of the solvent polarity on the regio-[27] and *syn–anti* selectivity;[28] the data of Table 2 show a great influence of the solvent polarity on site-selectivity. These findings once more suggest that caution should be used in the attempts to rationalize, in terms of MO perturbational approach, the selectivity data for reactions carried out in different media.† A point of Table 2 which deserves a comment is the lowest path a/path b ratios found for methanol and ethanol in disagreement with the trend of the solvent effect. An hydrogen bond between these two solvent and nitrile oxide should give both to a stabilization of the frontier orbitals, with a consequent major LUMO(1,3-dipole)-HOMO(dipolarophile) control and an increase of the steric requirements for the 1,3-dipole; both effects act together in lowering the reaction rate at the tetrasubstituted double bond.

EXPERIMENTAL

^1H NMR spectra were recorded at 36° for $CDCl_3$ solns with a Varian A-60 (60 MHz) spectrometer ($SiMe_4$ as internal standard); Microanalysis were performed on a Carlo Erba Analyzer, Mod. 1106; all new compounds gave satisfactory elemental analysis (±0.3%). Glc analysis were performed on a Carlo Erba Gaschromatograph 2300 with internal normalization. Hplc analysis were carried out on a Perkin–Elmer S.3 with an ODS Silix 1 column, eluent: methanol–acetonitrile; detector LC65T (240 nm).

Dipolarophiles **1a**[29] **1b**[30] and **1c**[31] were prepared by standard methods whereas dipolarophiles **12a**,[32] **12b** [b.p. = 92–93°/0.4 mmHg] and **12c** [m.p. = 54–56° from light petroleum] were obtained by hydrogenation of the corresponding diene as previously reported for **12a**.

Synthesis of standards **4–9**. Compounds **4**,[33] **6**[34] and **8**[35] were obtained, in high yield, from the 1,3-dipolar cycloaddition of dimethyl acetypendicarboxylate to arylazides, benzonitrile oxides and diphenylnitrile imine respectively.

Compounds **5** synthesized as previously reported for 1 - phenyl - 1,2,3 - triazole[36][1 - *p* - methoxyphenyl - 1,2,3 - triazole m.p. = 80–82°; 1 - *p* - nitrophenyl - 1,2,3 - triazole m.p. = 207°].

Compounds **7** and **9**[35] were prepared by heating under reflux an HCl soln of the adducts of vinyl acetate to benzonitrile oxides[37] and diphenylnitrilimine respectively. The physical data of these compounds are in agreement with those reported in the cited literature; analytical samples of these heterocycles were used in glc calibration.

Cycloaddition of benzonitrile oxides with dipolarophiles **1a–c**. To a soln of **1a**, **b** or **c** (10.0 mmol) and the appropriate benzohydroximic acid chloride (3.0 mmol) in benzene (50 ml) a stoichiometric amount of Et_3N in benzene (20 ml) was added over a period of 2 hr under stirring. The organic layer was separated, dried and evaporated to give a residue which was glc analyzed; the mixtures derived from **1b** were previously heated at 120° (2 hr) in order to promote the decomposition of the inter-

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†The relative rate enhancement of path a promoted by an increased solvent polarity (Table 2) suggests a smaller dipole moment of the transition state which leads to adducts **2** than that leading to adduct **3**. As matter of fact, cycloadduct **3**, isolated from the reaction of benzonitrile oxide with **1b**, is characterized by an higher R_F value than that of the related compound **2** (see Experimental) in agreement with a lower dipole moment for the former in comparison with the latter.

mediate adducts which proved stable at room temp. Three out of the four possible intermediate adducts, derived from the reaction benzonitrile oxide (Ar=Ph)-**1b**, were isolated by column chromatography using cyclohexane–EtOAc 4:1 as eluent.

We obtained, in order of elution: excess dipolarophile, 0.122 g of the *syn*-methylene adduct **2**[m.p. 117–118° as colourless prism from MeOH; ^{1}H NMR δ(CDCl$_3$): 6.7 and 6.1 (m, 2H, olefinic); 3.8 and 3.5 (s, 6H, OMe)], 0.9023 g of the *syn*-derivative **3**[m.p. 104–6° as colourless prism from EtOH; ^{1}H NMR δ(CDCl$_3$): 5.2 (d, 1H, H-2) $J_{2,6} = 8.0$Hz; 4.05 (d, 1H, H-6); 3.85 and 3.80 (s, 6H, OMe)] and 0.1633 g of the *anti*-adduct **3**,[m.p. 122–124° as colourless prism from EtOH; ^{1}H NMR δ(CDCl$_3$): 5.6 (dd, 1H, H-2) $J_{1,2} = 4.3$Hz, $J_{2,6} = 9.3$Hz; 4.3 (dd, 1H, H-6); 3.8 and 3.2 (s, 6H, OMe)]. The *syn*-structure **3** was attributed taking into account the low coupling constant between H-2 and H-6 ($J_{1,2} \simeq$ 0Hz) while the *syn*-structure **2** gained evidence from its catalytic hydrogenation to the dihydro-derivative **19b** (Ar=Ph) which, in turn, was obtained from the cycloaddition of benzonitrile oxide (Ar=Ph) to **12b**. The glc analysis were performed with a glass column of OV 17 (3%) on GCPS 100–120 mesh.

Solvent effect. The reactions were carried out, at room temp, by mixing 3 mmol of **1a** and 2 mmol of mesitonitrile oxide in 30 ml of the solvents listed in Table 2. The solvents were carefully dried with standards methods;[38] the end of the reactions were detected by tlc disappearance of the 1,3-dipole. The ratios reported in Table 2 were obtained by glc with a QF1 (3%) glass column in isothermal (146°) conditions.

Cycloadditions of arylazides to **1a–c**. To a soln of **1a**, **b** or **c** (10.0 mmol) in benzene (50 ml), 3.0 mmol arylazides were added. The reactions of **1a** took place at room temp whereas those of **1b** and **1c** were carried out under reflux (24 hr). In all cases, we were not able to detect the intermediate adducts **2** or **3**. Gas chromatographic analyses were done using a 3% OV-225 (on GGS 80–100 mesh) glass column.

Cycloadditions of diphenylnitrile imine with **1a–c**. To a soln of **1a** (**1b** or **1c**) (10.0 mmol) and N(α-chlorobenzylidene) N'-phenylhydrazine (3.0 mmol) in benzene (50 ml), a slight excess of Et$_3$N in benzene (20 ml) was added. The organic layer was separated, dried and evaporated to give a residue which was glc analyzed. Tlc analysis of the mixture **1b**-diphenylnitrile imine showed the presence of intermediate adducts which slowly decomposed at room temp. To secure a quantitative decomposition, the mixture was heated at 100° for a short time and then glc analyzed.

Cycloadditions of 2-diazopropane with **1a–c** *and* **12b**, **c**. An ethereal soln of 2-diazopropane was added, in small amounts, to a two fold excess of **1a–c**. The soln was left aside at 0° for 24 hr then the solvent evaporated; column chromatography of the residue afforded adducts **17b**, **17c** and the pyrazole **18** in nearly quantitative yield.

Compounds **12b**, **c**, reacted with excess of 2-diazopropane under similar conditions, furnished, in quantitative yield, adducts **16b** and **16c**.

Cycloadditions of C - phenyl - N - methylnitrone to **1a** *and* **12a**. A soln of C - phenyl - N - methylnitrone (3 mmol) and **1a** or **12a** (10 mmol), in benzene (50 ml) was left aside, at room temp, for 20 days, until the tlc disapparence of the 1,3-dipole. After evaporation of the solvent, a column chromatography (silica gel, cyclohexane–EtOAc 4:1 as eluent) of the residue, afforded, in order of elution adducts **11a** (or **14a**) and **10a** (or **13a**). Reaction yields and isomer ratios are reported in Schemes 2 and 3; spectroscopic and analytical data are collected in Tables 3 and 4.

Cycloadditions of C - phenyl - N - methylnitrone to **1b–c** *and* **12b**, **c**. A soln of C - phenyl - N - methylnitrone (3.0 mmol) and **1b**, **c**, **12b**, **c**, in benzene (50 ml), were heated under reflux for 10 days. After evaporation of the solvent, a column chromatography of the residue [silica gel, cyclohexane–EtOAc 4:1 as eluent] allowed to separate adducts **10b**, **c** and **13b**, **c** from the excess dipolarophile; yields are given in Schemes 2 and 3. Spectroscopic and analytical data are gathered in Tables 3 and 4.

Cycloadditions of mesitonitrile oxide to **12a**, **b**, **c**. An ethereal soln of mesitonitrile oxide and a slight excess of **12a**, **b**, **c** was left

Table 3. ^{1}H NMR [δ(CDCl$_3$)] data for compounds **10–19**

Compound	H-1	H-5	H-7	H-8	H-9	OMe	OMe
10a	5.0	3.80	4.75	6.55	6.37	3.77	3.04
10b	3.22	3.66	3.02	6.28		3.78	2.97
10c	3.65	3.40	3.48	6.33		3.70	3.05
11a	5.03	4.28	4.67	6.57	6.42	3.75	3.63
13a	4.74	3.93	4.47	1.7–2.20		3.84	3.15
13b	2.70	3.60	2.45	1.65–1.40		3.79	3.01
13c	3.15	3.54	2.92	1.9–1.55		3.79	3.17
14a	4.84	4.50	4.40	2.0–1.6		3.83	3.76
15b	3.46		3.07	6.57	5.96	3.70	3.60
15c	4.06		3.55	6.75	6.20	3.75	3.64
16b	3.0		2.48	1.70–1.5		3.77	3.70
16c	3.45		2.82	1.7–1.4		3.74	3.70
18a	4.92		4.92	2.10–1.60		3.84	3.54
18b	2.98		2.85	1.60–1.4		3.80	3.50
18c	3.40		3.28	1.65–1.40		3.78	3.47
19a	4.95		4.95	1.90–1.65		3.83	3.61
19b	2.92		2.73	2.0–1.1		3.80	3.55

Table 4. Physical and analytical data for compounds **10–19**

Compound	Cryst. Solvent	M.p. (T/°C)	Found % C	Found % H	Found % N	Formula	Required % C	Required % H	Required % N
10a	EtOH[a]	126-127	62.48	5.60	4.18	$C_{18}H_{19}NO_6$	62.60	5.55	4.06
11a		Yellow oil	62.55	5.65	4.12				
10b	EtOH[a]	113-115	66.30	6.14	4.17	$C_{19}H_{21}NO_5$	66.46	6.16	4.08
10c	EtOH[a]	102-104	68.98	6.48	3.58	$C_{22}H_{25}NO_5$	68.91	6.57	3.65
13a	EtOH[b]	114	62.29	6.01	4.10	$C_{18}H_{21}NO_6$	62.24	6.09	4.03
14a		Yellow oil	62.18	6.04	4.12				
13b	Cyclohexane[a]	133-135	66.02	6.70	4.01	$C_{19}H_{23}NO_5$	66.07	6.71	4.06
13c	Cyclohexane[a]	110-112	68.43	7.02	3.71	$C_{22}H_{27}NO_5$	68.55	7.06	3.63
15b	Cyclohexane[a]	117-118	60.30	6.41	10.03	$C_{14}H_{18}N_2O_4$	60.42	6.52	10.07
15c	Cyclohexane[a]	121-122	64.18	6.85	8.85	$C_{17}H_{22}N_2O_4$	64.13	6.97	8.80
16b	Cyclohexane[a]	101-103	59.84	7.21	9.78	$C_{14}H_{20}N_2O_4$	59.98	7.19	9.99
16c	Cyclohexane[a]	134-135	63.58	7.52	8.81	$C_{17}H_{24}N_2O_4$	63.73	7.55	8.74
18a	EtOH[a]	158-160	64.21	6.32	3.84	$C_{20}H_{23}NO_6$	64.33	6.21	3.75
18b	EtOH[b]	156-157	67.70	6.86	3.86	$C_{21}H_{25}NO_5$	67.91	6.78	3.77
18c	EtOH[a]	186-188	69.87	7.21	3.52	$C_{24}H_{29}NO_5$	70.05	7.10	3.40
19a	EtOH[a]	156-157	61.55	5.28	4.32	$C_{17}H_{17}NO_6$	61.63	5.17	4.23
19b	EtOH[a]	137-139	65.48	5.88	4.37	$C_{18}H_{19}NO_5$	65.64	5.81	4.25

[a] As colourless prism [b] As colourless needles

aside, at room temp, until the tlc disapparence of the 1,3-dipole. Adducts **18a**, **b**, **c** were isolated in nearly quatitative yield.

Cycloadditions of benzonitrile oxide to **12a**, **b**. To a soln of **12a**, **b** (2.2 mmol) and benzhydroximic acid chloride (2.0 mmol) in ether (50 ml) a stoichiometric amount of Et_3N was added over 2 hr under stirring. The ethereal soln was filtered and evaporated to give adducts **19a**, **b** in high yield (≥75%).

Synthesis of **14a**. To a nitromethane solnn of **19a** (0.5 g), a large excess of trimethyloxonium fluoborate was added; the reaction proceeded at room temp (24 hr). The solvent was evaporated *in vacuo* and the residue dissolved in 30 ml of abs EtOH. An excess of $NaBH_4$ was added, in small portions, during 30 min and stirring was continued for about 30 min. The solvent was removed, the residue treated with water and extracted with ether. After usual work up, compound **14a** was obtained in 73% yield.

Catalytic hydrogenation of compounds **10a–c**, **11a**, **15b**, **c**. Compounds **10a–c**, **11a**, **15b**, **c** (100 mg) were dissolved in EtOH (95%; 10 ml) and catalytically (Pd/C 5%; 15 mg) reduced with H_2 at 760 Torr and room temp. After uptake of 1.0 equiv, the reaction was interrupted and the soln filtered and evaporated. The resulting dihydro derivatives resulted identical in every respect with compounds **13a–c**, **14a** and **16b**, **c** obtained by cycloadditions of **12** with C - phenyl - N - methylnitrone and 2 - diazopropane respectively.

Kinetics. Kinetic data for MNO addition to **12a** were obtained for solns containing an excess of dipolarophiles by following spectrophotometrically the disappearance of the nitrile oxide. The samples were accurately weighed into standard flasks and made up to 50 ml with spectroscopic grade EtOH, then placed in a thermostatted bath at 25°.

After the two solns were mixed together in a 100 ml volumetric flask; portions (1 ml) were pipetted at suitable intervals into EtOH (50 ml) and cooled to prevent further reaction. The second-order rate constants were determined in the usual way from expression (1) where $\underline{a}$ is the initial concentration of MNO, $\underline{b}$ that of dipolarophile **12a**, $\underline{x}$ the concentration of MNO at time t and κ_2 the second-order

$$\kappa_2 t = \frac{2.303}{b-a}\log\frac{a(b-x)}{b(a-x)} \qquad (1)$$

rate coefficient in $1\,mol^{-1}\,s^{-1}$. The amount of MNO at any time was determined from the UV absorption, λ_{max} 260 nm (ϵ = 16,500), and the concentration in the original soln was calculated. The kinetic data for MNO addition to **12b** and **12c** were obtained from competition experiments with **12a**.

To a soln of **12b** (20 mmol) and **12a** (0.5 mmol) or **12b** (20 mmol) and **12c** (20 mmol), in EtOH (100 ml), a deficiency of MNO (0.4 mmol) was added; the mixture was left aside at 25° until the 1,3-dipole disappearence (tlc analysis). The mixture was hplc analyzed and the relative amounts of adducts **18** were evaluated in comparison with standard binary mixtures of the same compounds. The results were evaluated according to Huisgen *et al.*[39]

Acknowledgements—We thank Prof. G. Bianchi and P. Grünanger for helpful discussions, Dr. C. Bugatti for glc analysis and the C.N.R. (Rome) for financial support.

REFERENCES

[1] M. A. Battiste, J. F. Timberlake and H. Malkus, *Tetrahedron Letters* 2529 (1976).

[2] H. R. Pfaendler, H. Tanida and E. Haselbach, *Helv. Chim. Acta* **57**, 383 (1974).

[3]G. W. Klumpp, A. H. Veefkind, W. L. de Graaf and F. Bickelhaupt, *Ann. Chem.* **706**, 47 (1967).

[4]K. B. Astin and K. Mackenzie, *J. Chem. Soc.* Perkin II 1004 (1975).

[5]H. Taniguchi, T. Ikeda, Y. Yoshida and E. Imoto, *Bull. Chem. Soc. Japan* **50**, 2694 (1977).

[6]J. W. Wilt and W. N. Roberts, *J. Org. Chem.* **43**, 170 (1978).

[7]M. Franck-Neumann and M. Sedrati, *Angew. Chem.* Int. Ed. Engl. **13**, 606 (1974).

[8]D. Cristina, C. De Micheli and R. Gandolfi, *J. Chem. Soc.* Perkin I, 2891 (1979); C. De Micheli, R. Gandolfi and R. Oberti, *J. Org. Chem.* **45**, 1209 (1980).

[9]D. N. Reinhoudt and C. G. Kouwenhoven, *Recl. Trav. Chim. Pays-Bas*, **95**, 67 (1976).

[10]R. K. Lustgarten and H. G. Richey, Jr., *J. Am. Chem. Soc.* **96**, 6393 (1974).

[11]R. N. Warrener, C. H. Anderson, I. W. McCay and M. N. Paddon-Row, *Aust. J. Chem.* **30**, 1481 (1977).

[12]H. Matsukubo and H. Kato, *J. Chem. Soc.* Perkin I 2565 (1976).

[13]C. Dietrich-Buchecker, D. Martina and M. Franck-Neumann, *J. Chem. Res.* 78 (1978).

[14a]M. J. S. Dewar, *The Molecular Orbital Theory of Organic Chemistry*, pp. 191–247. McGraw-Hill, New York (1969); [b]For application to 1,3-dipolar cycloaddition see: G. Bianchi, C. De Micheli and R. Gandolfi, *The Chemistry of Functional Groups*, Supplement A (Edited by S. Patai). Interscience, New York (1977).

[15]Ref. 14*b*, pp. 438–9, 451–3 and 458–9; Ref. 5 and the lit cited therein; T. Saito and S. Motoki, *J. Org. Chem.* **44**, 2493 (1979).

[16]A. Cerri, C. De Micheli and R. Gandolfi, *Synthesis* 710 (1974).

[17]R. Hoffmann, *Acc. Chem. Res.* **4**, 1 (1971).

[18]P. Bishof, T. A. Hashmall, E. Heilbronner and V. Hornung, *Helv. Chim. Acta* **52**, 1745 (1969); E. Heilbronner and H. D. Martin, *Ibid.* **55**, 1490 (1972); L. M. Domelsmith, P. D. Mollere, K. N. Houk, R. C. Hahn and R. P. Johnson, *J. Am. Chem. Soc.* **100**, 2959 (1978).

[19]K. N. Houk, J. Sims, R. E. Duke, Jr., R. W. Strozier and J. K. George, *Ibid.* **95**, 7287 (1973).

[20]R. S. Brown and R. W. Marcinko, *Ibid.* **100**, 5721 (1978).

[21]C. W. Jefferson, W. de los Heros, J. C. E. Gehret and G. Wipff, *Tetrahedron Letters* 1629 (1980).

[22]E. Heilbronner and H. D. Martin, *Chem. Ber.* **106**, 3376 (1973).

[23]J. Bastide, J. P. Maier and T. Kubota, *J. Electron Spectrosc. Relat. Phenom.* **9**, 307 (1976).

[24]K. N. Houk, P. Caramella, L. L. Murchausen, Y. M. Chang, A. Battaglia, J. Sims and D. C. Kaufman, *Ibid.* **10**, 441 (1977).

[25]An estimated value of 7.5 kcal/mol was calculated for the I.E. of D.P.N.I.: K. N. Houk, J. Sims, C. R. Watts and L. J. Luskus, *J. Am. Chem. Soc.* **95**, 7301 (1973).

[26]A reduced effect of the exocyclic double bond on the reaction rate was also observed in the Diels–Alder cycloadditions of norbornadienes to 9,10-dimethylanthracene.[2]

[27]G. Bianchi, C. De Micheli, R. Gandolfi, P. Grünanger, P. Vita Finzi and O. Vajna de Pava, *J. Chem. Soc.* Perkin I 1148 (1973).

[28]G. Bianchi, C. De Micheli, A. Gamba and R. Gandolfi, *Ibid.* Perkin I 137 (1974).

[29]H. Prinzbach, M. Argüelles and E. Druckrey, *Ang. Chem.* Int. Ed. Engl. 7, 1039 (1966).

[30]Diels–Alder, *Ann. Chem.* **490**, 236 (1931).

[31]Diels–Alder, *Ibid.* **566**, 24 (1950).

[32]G. Stork, E. E. van Tamelen, L. J. Friedmann and A. W. Brgsthaler, *J. Am. Chem. Soc.* **75**, 384 (1953).

[33]R. Huisgen, R. Knorr, L. Moebius and G. Szeimes, *Chem. Ber.* **98**, 4014 (1965).

[34]J. E. Franz and H. K. Pearl, *J. Org. Chem.* 41, 1296 (1976).

[35]R. Fusco, *The Chemistry of Heterocyclic Compounds* (Edited by A. Weissberger). Interscience, New York (1967).

[36]R. Huisgen, L. Moebius, G. Müller, H. Stangl, G. Szeimies and J. M. Vernon, *Chem. Ber.* **98**, 3992 (1965).

[37]C. Grundmann and P. Grünanger, *The Nitrile Oxides*, Springer-Verlag, New York (1971).

[38]J. Bergon, Z. Hamlet and W. Mueller, *J. Am. Chem. Soc.* **84**, 297 (1962); S. Smith, A. Fainberg and S. Winstein, *Ibid.* **83**, 618 (1961).

[39]K. Bast, M. Christl, R. Huisgen and W. Mack, *Chem. Ber.* **106**, 3312 (1973).