1,3-Dipolar cycloaddition of α-phenyl-*N*-*tert*-butylnitrone (PBN) to dichloro- and dibromo-malononitrile, chlorotricyanomethane and tetracyanomethane. Structure of products and kinetics of their formation

Lennart Eberson,*[a] John J. McCullough,[a] Chris M. Hartshorn[b] and Michael P. Hartshorn[b]

[a] *Department of Chemistry, Lund University, PO Box 124, S-221 00 Lund, Sweden*
[b] *Department of Chemistry, University of Canterbury, Christchurch, New Zealand*

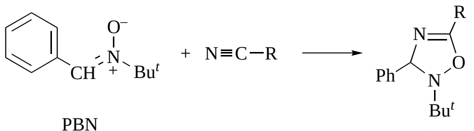
The kinetics of cycloaddition between α-phenyl-*N*-*tert*-butylnitrone (PBN; IUPAC name: *N*-benzylidene-*tert*-butylamine *N*-oxide) and six activated nitriles R–CN, *viz.* dibromo- and dichloro-malononitrile (1a and 1b), chlorotricyanomethane (1c), tetracyanomethane (1d), trichloroacetonitrile (1e) and carbamoylchlorodicyanomethane (5), to give 2-*tert*-butyl-3-phenyl-5-R-2,3-dihydro-1,2,4-oxadiazoles 2a–e have been determined, as well as the similar reaction between 4-NO$_2$PBN and 1c. The second-order rate constants for reaction between PBN and 1 in acetonitrile fall (relative rate constant in parenthesis) in the order of 1d (5.4 × 10^3) > 1c (3.1 × 10^2) > 1b (8) > 1a (1) > 5 (not given) > 1e (9 × 10^{-3}). The rate constants are slightly larger in non-polar solvents. The rate constants of the PBN–1c and PBN–1d cycloadditions (0.15 and 2.6 dm^3 mol^{-1} s^{-1}, respectively) are of the same magnitude as those recently used to classify thioketones as 'superdipolarophiles'.

X-Ray crystal structures are reported for 2-*tert*-butyl-3-phenyl-5-(dichlorocyanomethyl)-2,3-dihydro-1,2,4-oxadiazole (2b) and 2-*tert*-butyl-3-phenyl-5-(chlorodicyanomethyl)-2,3-dihydro-1,2,4-oxadiazole (2c).

Introduction

The effect of cyano-substitution on the electron acceptor properties of unsaturated compounds is well known.[1] The chemistry of compounds such as tetracyanoethylene (TCNE),[1–4] 7,7,8,8-tetracyanoquinodimethane[1,2,4,5] (TCNQ) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[1,4,6,7] depends mainly on the electron-withdrawing effect of the cyano groups. The compounds are all strong electron acceptors, resulting in the formation of charge-transfer complexes and ion pairs with electron donors, and they have a general role as one-electron oxidizing agents.[1–7] Cyano-substitution of ethylenic and aromatic systems also promotes excited state charge transfer leading to exciplex and ion-pair formation and often to photochemical reactions.[8]

In the case of saturated polycyano compounds, an extensive chemistry of malononitrile derivatives exists.[9] However, the electron-acceptor properties of these activated nitriles, in particular dichloro- and dibromo-malononitrile, and the related chlorotricyanomethane and tetracyanomethane have not been much studied.[10] Since spin adduct formation from a spin trap like *N*-*tert*-butyl-α-phenylnitrone (PBN) and a redox active compound can be used as an indicator of the electron-acceptor or -donor properties of the latter,[11] a number of polycyano substituted methanes were prepared and allowed to interact with PBN under oxidizing or reducing conditions.[12] It then became clear that PBN and the substrate were sometimes rapidly depleted in a side reaction, identified as the 1,3-dipolar cycloaddition of PBN to the activated nitrile **1** [reaction (1)]


(1)

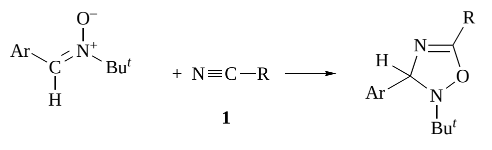
PBN **1** **2**

with formation of a 2,3-dihydro-1,2,4-oxadiazole derivative **2**. This type of reaction has been found recently to occur between PBN and trichloroacetonitrile or other similar nitriles[13] **1**, and the products **2** of reaction (1) were characterized, mainly by mass spectrometry. It was further reasoned that the cycloaddition might deplete the reactants in spin trapping experiments, leading to inefficient spin adduct formation. Thus, in order to plan a study and interpret the results of spin adduct observations from reactions between PBN and activated nitriles (dichloro- and dibromo-malononitrile, chlorotricyanomethane and tetracyanomethane), the role of the cycloaddition as a competing process first had to be assessed. In what follows, we describe the characterization and structures of the cycloadducts, and the kinetics of their formation. In the accompanying paper,[12] we describe the formation of tricyanomethyl–PBN spin adducts which were produced *via* reductive cleavage of chlorotricyanomethane or oxidative processes involving the tricyanomethanide ion.

Results

Formation of oxazolidines

The reactions studied are shown in Scheme 1. From a synthetic viewpoint, these cycloadditions are remarkably simple to carry out. The nitrone and nitrile components are mixed at *ca.* 20 °C


1 **2**

1a R = CBr$_2$CN
1b R = CCl$_2$CN
1c R = CCl(CN)$_2$
1d R = C(CN)$_3$
1e R = CCl$_3$

2a Ar = Ph, R = CBr$_2$CN
2b Ar = Ph, R = CCl$_2$CN
2c Ar = Ph, R = CCl(CN)$_2$
2d Ar = Ph, R = C(CN)$_3$
2e Ar = Ph, R = CCl$_3$
2f Ar = 4-NO$_2$C$_6$H$_4$, R = CCl(CN)$_2$

Scheme 1

in acetonitrile, dichloromethane or [^{2}H]chloroform and left for an appropriate time. The course of the reaction can be easily monitored by ^{1}H NMR spectroscopy.

Usually an excess of the nitrile was used since this is easily separated from the adduct by evaporation or washing the crystalline products with pentane. In the case of the PBN–tetracyanomethane reaction, a 1 : 1 stoichiometry was used to avoid difficulties with the removal of unreacted tetracyanomethane which is less volatile and soluble than the other nitriles. The PBN–tetracyanomethane adduct **2d** also differed from the other cycloadducts in being less stable. Dilute solutions of **2d** in acetonitrile, dichloromethane or [^{2}H]chloroform could be kept for days at 4 °C, but concentrated solutions and solvent-free material deteriorated rapidly and hence attempts to recrystallize **2d** were unsuccessful. This decay reaction may involve loss of the tricyanomethyl side chain as the tricyanomethanide ion, a good leaving group in view of the high acidity of the conjugate acid ($pK = -5$).[14]

Previous work on nitrone–nitrile cycloadditions reported that the reactions were regiospecific and the 2,3-dihydro-1,2,4-oxadiazole ring system, shown in Scheme 1, was assigned to the adducts formed. The structural assignments were based on spectral[13] or chemical evidence,[15] and in one case X-ray crystallography was used.[16,17] In the present study, the structures of two cycloadducts (**2b** and **2c**) were determined by X-ray crystallography, and the remaining structures (**2a**, **2d**–**f**) were shown to be structurally analogous by comparison of spectral data (see following sections).

Mass spectrometry

The mass spectra of cycloadducts **2a**–**d**, **2f** were similar to those described for **2e** and related compounds.[13] Molecular ions of 1 : 1 adducts were observed in all cases. The intensity ratios of halogen isotope peaks at M, M + 2 and M + 4 were consistent with the number of chlorine or bromine atoms expected from the nitrile used.[18] The fragmentation patterns are given in the Experimental section, the most prominent ions being reported. The base peak in all cases had *m*/*z* 57 accompanied by a less intense (usually *ca.* 35% of *m*/*z* 57) at *m*/*z* 56. These ions are derived from loss of the *tert*-butyl side chain. In the spectra of **2a**–**c**, peaks were also observed at *m*/*z* 343, 255 and 246, respectively (M − 56), corresponding to loss of 2-methylpropene from the molecular ions. All the adducts except **2f** showed a peak at *m*/*z* 77 due to the phenyl ion, while the PBN adducts **2a**–**c** also showed ions at *m*/*z* 177, 146 and 121 derived from PBN.[13]

From **2d**, a fragmentation ion at *m*/*z* 116 (6%) was observed. This corresponds to the molecular ion of tetracyanomethane but is unlikely to arise from unreacted tetracyanomethane, the molecular ion of which is of very low intensity (<1%) in the EI spectrum of the pure compound. Observation of *m*/*z* 116 in the mass spectrum of **2d** and 177 in the mass spectra of **2a**–**c** indicates that retrocycloaddition occurs to some extent on electron impact.

NMR spectroscopy

The ^{1}H NMR spectra of dihydrooxadiazoles **2a**–**f** were useful not only for structural assignments, but also for establishing purity, reaction progress and cycloaddition kinetics of the less reactive nitriles. The spectra of **2a**–**e** were similar showing a nine-proton singlet at 1.23 ppm (Bu^t), a one-proton singlet at 6.13 ppm (benzylic CH), and a five-proton multiplet at 7.42 ppm (H in Ph). The adducts were easily distinguished from PBN which has singlets at 1.60 and 7.53 ppm (Bu^t and benzylic CH), while the phenyl group gives two multiplets at 7.39 and 8.29 ppm.

In the spectrum of the 4-nitrophenyl adduct **2f**, the aromatic region shows two multiplets at 7.70 and 8.29 ppm (described as doublets in the Experimental section). These are due to the AA′XX′ system of the 1,4-disubstituted benzene ring. The coupling constant from the most intense lines in the multiplets[19] gives $J_{\mathrm{AX}} = J_{ortho} = 8.9$ Hz.

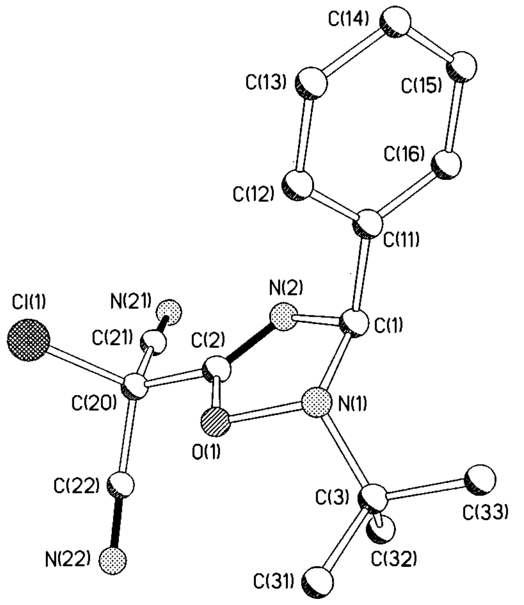


Fig. 1 Perspective drawing of compound **2c**. Double and triple bonds are shown in black.

IR spectra

The IR spectra of dihydrooxadiazoles **2a**–**d** are very similar and in agreement with the assigned structure. First comparing **2a**–**c** (run in KBr discs), the spectra showed a series of bands between 3100 and 2850 cm^{-1} due to CH vibrations, a nitrile band at *ca.* 2240 cm^{-1} and a band at *ca.* 1660 cm^{-1} assigned to the C=N bond. In cycloadducts **2a**–**d**, the latter was not resolved from the weak aromatic C=C band at *ca.* 1600 cm^{-1}. In **2f** the aromatic band at 1605 cm^{-1} was of medium intensity and well resolved from the C=N band at 1670 cm^{-1}. The nitrile band was weak in all cases and particularly so in the dibromomalononitrile adduct **2a**. This is common for saturated nitriles, substituted at the α-position with electron-withdrawing substituents.[20]

Because of the difficulties with the isolation of the PBN–tetracyanomethane adduct **2d**, the IR spectrum was obtained from a solution in CCl_4. The spectrum showed similar features to **2a**–**c** described above, including a weak nitrile band at 2245 cm^{-1} and a C=N band at 1675 cm^{-1}.

X-Ray crystallography and stereochemistry

The structure of the PBN–chlorotricyanomethane adduct (**2c**) and the PBN–dichloromalononitrile adduct (**2b**) were determined by single crystal X-ray analyses. Perspective drawings of the structures of **2c** and **2b** are presented in Figs. 1 and 2, respectively.

The nitrone–nitrile cycloadditions result in the formation of the 2,3-dihydro-1,2,4-oxadiazole ring system. Such a structure was proposed previously for cycloadducts from α,*N*-diarylnitrones and TCNE,[15] and from PBN and halogenated acetonitriles,[13] and was verified by the X-ray crystal structure analysis of the cycloadduct **4** of nitrone **3** and 7,7-dicyanonorcarane.[16,17] The 2,3-dihydro-1,2,4-oxadiazole ring is formed with complete regioselectivity, the anionic oxygen of the nitrone adding to the electron-deficient nitrile carbon.

The crystal structures show that the geometric configuration of the starting nitrone is retained in the oxadiazole products. Only one isomer (*Z*) is observed for aldonitrones, *e.g.* PBN, which have bulky substitutents such as *tert*-butyl.[21] In this configuration the phenyl and *tert*-butyl groups are *trans*, as they are in the oxadiazoles **2c** and **2b** (Figs. 1 and 2). As expected, the *trans* structures of Figs. 1 and 2 are the forms present in the

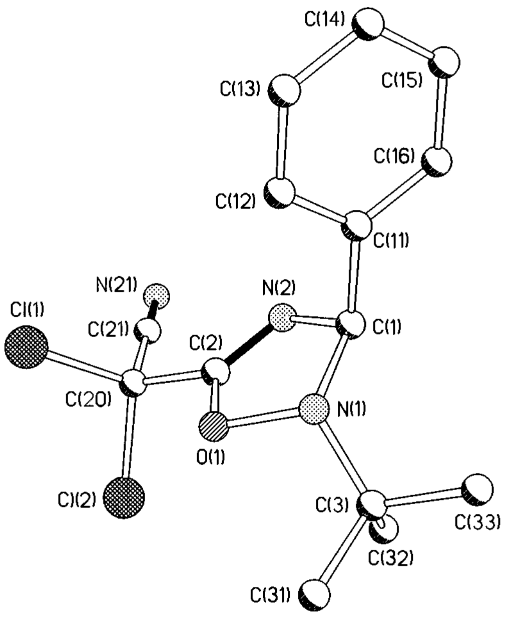
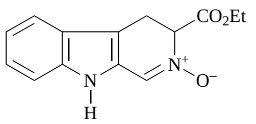


Fig. 2 Perspective drawing of compound **2b**. Double and triple bonds are shown in black.



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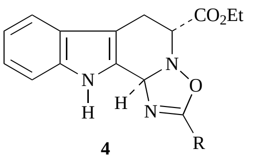

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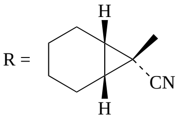


crystalline state, but they are most likely retained in solution. The *cis* configuration would have the phenyl and *tert*-butyl groups eclipsed and should possess higher energy. AM1 calculations (Hyperchem®) indeed showed the *cis* compound to be 6 kcal mol^{-1} higher in energy than the *trans* compound for both **2b** and **2c**.

A further point of interest is the geometry of the five-membered dihydrooxadiazole ring. As noted above, the same ring system is present in **4**. The conformation was described, but the dihydrooxadiazole ring was constrained by being part of a bicyclic system.[16,17] In the monocyclic dihydrooxadiazoles, the heterocyclic ring is very close to the envelope conformation. Considering the PBN–chlorotricyanomethane adduct **2c** (Fig. 1), a plane containing O(1), C(2) and N(2) can be defined. Then C(1) lies 0.018 Å on one side of the plane, while N(1) is located 0.1245 Å above the opposite side. Thus O(1), C(2), N(2) and C(1) are almost coplanar, with N(1) displaced significantly out of the plane defined.

UV spectroscopy

The UV absorption spectra of PBN, 4-NO_2-PBN, nitriles **1a–d** and cycloadducts **2a–d,f** were needed to determine reaction conditions for the kinetics and for experiments in which radicals were produced by direct irradiation of the nitriles (*e.g.* **1c**).[12] The spectrum of PBN in ethanol showed maxima at 294 and 226 nm, and a shoulder at *ca.* 205 nm ($\varepsilon_{max} = 1.81 \times 10^4$ and 7.64×10^3 dm^3 mol^{-1} cm^{-1}, respectively). This agrees with the published spectrum[22] of *N*-methyl-α-phenylnitrone in methanol with maxima at 288, 221.5 and 206.5 nm ($\varepsilon_{max} = 1.65 \times 10^4$, 9.93×10^3 and 7.46×10^3 dm^3 mol^{-1} cm^{-1}, respectively). In acetonitrile, PBN displayed maxima at 298 and 230 nm, and a shoulder at *ca.* 210 nm ($\varepsilon_{max} = 1.87 \times 10^4$ and 6.95×10^3 dm^3 mol^{-1} cm^{-1}, respectively). The position of the long-wavelength band of PBN was solvent dependent, ranging from 300 nm in cyclohexane or dichloromethane to 282 nm in HFP. The spectrum of 4-NO_2-PBN in acetonitrile displayed maxima at 360 and 254 nm ($\varepsilon_{max} = 1.66 \times 10^4$ and 1.06×10^4 dm^3 mol^{-1} cm^{-1}, respectively). For kinetics measurements, the concentration of 4-NO_2-PBN was monitored at 360 nm.

The UV spectra of **1a–c** and the related carbamoylchlorodicyanomethane **5** were rather featureless. Dibromomalononitrile

$(NC)_2C(Cl)CONH_2$

5

1a was the only compound showing a maximum, with ε_{max} at 240 nm = 607 dm^3 mol^{-1} cm^{-1}, and also the only one with significant absorption at the PBN maximum, ε_{298} being 86 dm^3 mol^{-1} cm^{-1}. At wavelengths < 240 nm, **1b**, **1c** and **5** showed end absorptions, shoulders being observed for **1b** and **5**.

The spectrum of **1c** in 95% ethanol was reported as having maxima at *ca.* 212 and 229 nm.[23] Our sample of **1c** showed similar spectra in ethanol, but the spectra changed with time. Also, on addition of 4% water, the spectrum of **1c** in acetonitrile changed to one resembling the spectrum in ethanol. Thus the spectra of **1c** in ethanol and hydroxylic media in general appear to be derived from compounds resulting from reaction between **1c** and the solvent.

The spectrum of tetracyanomethane **1d** in acetonitrile showed absorptions of very low intensity with $\lambda_{max} = 214$ nm. This absorption increased rapidly on addition of small amounts of water, and the band shape was identical with that of tetrabutylammonium and potassium tricyanomethanide. Authentic[12] $Bu_4NC(CN)_3$ in acetonitrile had λ_{max} at 214, 238 and 278 nm ($\varepsilon_{max} = 2.73 \times 10^4$, 1.17×10^3 and 1.64×10^2 dm^3 mol^{-1} cm^{-1}, respectively). The spectrum was similar to those reported[23,24] for aqueous solutions of $KC(CN)_3$. Hydrolysis of tetracyanomethane to form ammonium tricyanomethanide is a known reaction[25] which would readily explain our observations. In the absence of hydrolysis products, tetracyanomethane is transparent in acetonitrile at wavelengths >200 nm.

The UV spectra of cycloadducts **2a–d** were very similar. The spectrum of **2b** in acetonitrile, showing a maximum at 256 nm ($\varepsilon = 1.0 \times 10^3$ dm^3 mol^{-1} cm^{-1}) and a shoulder at 210 nm ($\varepsilon = 1.0 \times 10^4$ dm^3 mol^{-1} cm^{-1}), was typical. At the λ_{max} of PBN, 298 nm, **2a–d** all had extinction coefficients <3% of the ε_{max} of PBN. Finally, adduct **2f** from 4-NO_2-PBN and chlorotricyanomethane **1c** had the expected absorption band due to the nitrophenyl group at $\lambda_{max} = 264$ nm ($\varepsilon_{max} = 1.1 \times 10^4$ dm^3 mol^{-1} cm^{-1}).

Kinetics

Table 1 lists second-order rate constants for reactions of nitriles **1a–e** with PBN and **1c** with 4-NO_2-PBN at 22 °C. Calculated half-lives are given for the case of a pseudo-first-order reaction with one component in excess and at a concentration of 0.1 mol dm^{-3} in order to give an impression of the timescales of the various reactions. Rates were measured under pseudo-first order conditions, with the nitrile in excess, and were carried out at least in duplicate. There was good agreement between runs, and the figures given in Table 1 are averages.

In most kinetic runs, only the absorption at the PBN maximum was monitored, but in the reaction of PBN with **1c** and **1d** the time dependence of the absorption spectrum from 200 to 500 nm was also determined. No evidence of charge transfer absorption was seen at any stage of the reaction. Such absorption was observed from solutions of nitrones and TCNE.[15]

In order to check for products other than dihydrooxadiazoles, spectra of all kinetic samples were scanned from 200 to

Table 1 Rate constants of the reaction between PBN or 4-NO_2-PBN and nitriles at 22 °C

Nitrile	Nitrone	Solvent	k/dm^3 mol^{-1} s^{-1}	$\tau_{\frac{1}{2}}$/h[a]	Method
Cl_3CCN (**1e**)	PBN	$CDCl_3$	4.2×10^{-6}	460	NMR
$Cl_2C(CN)_2$ (**1b**)	PBN	CH_2Cl_2	1.9×10^{-3}	1.0	UV
$Cl_2C(CN)_2$ (**1b**)	PBN	CH_3CN	4.0×10^{-3}	0.5	UV
$Br_2C(CN)_2$ (**1a**)	PBN	CH_3CN	4.8×10^{-4}	4.0	NMR, UV
$ClC(CN)_3$ (**1c**)	PBN	CH_2Cl_2	0.30	0.006	UV
$ClC(CN)_3$ (**1c**)	PBN	CH_3CN	0.15	0.012	UV
$ClC(CN)_3$ (**1c**)	PBN	CH_3CN–HFP (4:1)	8.0×10^{-2}	0.024	UV
$ClC(CN)_3$ (**1c**)	4-NO_2-PBN	CH_3CN	2.5×10^{-2}	0.08	UV
$C(CN)_4$ (**1d**)	PBN	CH_3CN	2.6	0.0007	UV
$ClC(CN)_2CONH_2$ (**5**)	PBN	CH_3CN	*b*	33	
$KC(CN)_3$	PBN	CH_3CN	No reaction[c]		UV
—	PBN	CH_3CN	No reaction[d]		

[a] As calculated for a pseudo-first-order reaction at $[PBN]_o$ or $[\mathbf{1}]_o = 0.1$ mol dm^{-3}. [b] This reaction was not first-order and thus only an approximate $\tau_{\frac{1}{2}}$ could be estimated. [c] In 4 h. [d] In >300 h.

500 nm on reaction completion. Only in the case of PBN–**1c** in dichloromethane was an additional product observed. This had $\lambda_{max} = 262$ nm, with an intensity *ca.* 50% of the initial PBN absorbance, but did not absorb strongly at the monitoring wavelength (300 nm). Formation of this minor product seems to be due to the large excess of chlorotricyanomethane used for kinetics; it was not observed in the preparation described[26] for dihydrooxadiazole **2c**, as established by UV monitoring of the crude product. Dihydrooxadiazole **2c** could be isolated in yields of 90% or greater from solutions in which this minor product was observed.

Since mixtures of PBN and tricyanomethanide salts were used in spin trapping experiments,[12] we included potassium tricyanomethanide as a nitrile in Table 1. No measurable reaction occurred in *ca.* 4 h, the maximal period for the spin trapping experiments. Similarly, and consistent with an earlier report for nitrone **3**,[27] PBN was found not to react with acetonitrile. The UV absorption of PBN in acetonitrile did not change on keeping the solution for several weeks.

It can be seen from Table 1 that the reactivities of the nitriles used in this study are in most cases such that the reaction with PBN is rapid at room temperature, with tetracyanomethane **1d** as the most reactive compound.

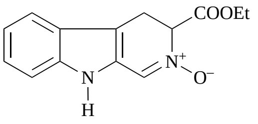
Discussion

Kinetics of the nitrile–PBN cycloaddition

The general reactivity of simple nitriles towards 1,3-dipoles, including nitrones, has been previously studied kinetically. Acetonitriles with electronegative α-substituents reacted readily with organic azides forming tetrazoles[28a] and with nitrones forming dihydrooxadiazoles.[13,26] In these additions, trichloroacetonitrile was often the most reactive nitrile used. TCNE also reacted with nitrile oxides,[28b] nitrile sulfides[28b] and nitrones,[15] cycloaddition occurring at the nitrile groups of TCNE. Nitrones add to TCNE forming products assigned as tricyanovinyldihydrooxadiazoles.[15] The kinetics of the latter cycloaddition were studied using α,*N*-diarylnitrones. It was found that the reaction rate was increased by electron-donating groups in the α-phenyl ring, while electron-withdrawing groups had the reverse effect. We find a similar substituent effect in the addition of PBN or 4-NO_2-PBN and **1c**, the latter reaction being six times slower (Table 1).

Table 2 Rate constants of the reaction with nitrone **6** in 2-methoxyethanol at 85 °C

Dipolarophile	k_2/dm^{-3} mol^{-1} s^{-1}
Ethyl crotonate	5.6×10^{-3}
Dimethylmalononitrile	2.0×10^{-3}
4-Nitrobenzonitrile	2.1×10^{-4}
4-Formylbenzonitrile	9.2×10^{-5}
4-Chlorobenzonitrile	5.4×10^{-5}
Benzonitrile	3.0×10^{-5}
4-Methoxybenzonitrile	2.0×10^{-5}



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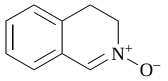

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In another study, the kinetics of the cycloaddition between simple nitriles and nitrone **6** were determined.[27] Some examples of the rate constants, obtained in 2-methoxyethanol at 85 °C, are given in Table 2. These rate data show that even a reactive alkylated nitrile, such as dimethylmalononitrile, reacts somewhat slower than the moderately reactive olefinic dipolarophile, ethyl crotonate. The reaction of benzonitriles was favoured by electron-withdrawing substituents in the benzene ring. The effect of solvent polarity was also studied for the reaction between nitrone **7** and dimethylmalononitrile, and showed that the effect of solvent polarity was small,[27] as found for other types of nitrone cycloadditions.[29] The ratio of $k_{toluene}/k_{2\text{-methoxyethanol}}$ was about 11.

Our rate data follow similar trends. The effect of solvent polarity is small, the ratio between rate constants in the nonpolar dichloromethane and the strongly polar CH_3CN–HFP (4:1) mixture being about 4. The effect of successively replacing chlorine atoms with cyano groups upon the rate constant for cycloaddition to PBN in the series CCl_3CN, $CCl_2(CN)_2$, $CCl(CN)_3$ and $C(CN)_4$ is 950, 38 and 17, respectively. The reactivity of a nitrile group in each of these compounds can also be expressed relative to that of trichloroacetonitrile (**1e**). The statistically corrected relative rates for $CCl_2(CN)_2$, $CCl(CN)_3$ and $C(CN)_4$ are 4.8×10^2, 1.2×10^4 and 1.6×10^5, respectively, which places the two latter compounds in the class of 'superdipolarophiles'. This classification[30] was based upon the large rate constants observed for reactions between *N*-methyl-*C*-phenylnitrone **8** (IUPAC name: *N*-benzylidenemethylamine *N*-oxide) and thioketones at 25 °C in relation to the previously most reactive olefin, dimethyl acetylenedicarboxylate (Table 3).

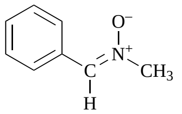

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Table 3 Rate constants for the reaction with nitrone **8** at 25 °C

Dipolarophile	k_2/dm^{-3} mol^{-1} s^{-1}
Methyl propiolate	5.5×10^{-6}
Dimethyl acetylenedicarboxylate	4.1×10^{-4}
Heptane-4-thione	0.15
Adamantanethione	0.62

The practical implication of this study for spin trapping involving nitriles **1a**–**e** is that only nitriles **1c** and **1d** react fast enough with PBN to warrant special precautions to avoid depletion of the reactants in attempted spin trappings. This problem is treated in the accompanying paper.[12]

Experimental

General methods

Melting points were measured on a Kofler hot-stage microscope and are reported uncorrected. IR spectra were run on a Perkin-Elmer 298 spectrometer, as KBr discs unless stated otherwise. Mass spectra were run on a JEOL JMS-SX102 instrument while for NMR spectra a Varian XL-300 spectrometer was used (*J* values are given in Hz). For UV-VIS spectra and kinetic spectroscopy an HP-8452 diode array spectrometer was used. Elemental analyses were by Mikrokemi AB, Uppsala.

Materials

PBN and 4-NO$_2$-PBN were purchased from Aldrich and used as received. Dichloromalononitrile (**1b**) was from Aldrich or Lancaster Synthesis and was distilled, bp 100 °C at 760 mmHg. Dibromomalononitrile[31] (**1a**) was prepared by the bromination of malononitrile and had bp 30 °C at 1 mmHg (lit.,[31] 49.2 °C at 10 mmHg). Chlorotricyanomethane (**1c**) was prepared by an improved method[26] and had mp 45–47 °C (lit.,[32] 46–47 °C). Tetracyanomethane (**1d**) was prepared from cyanogen chloride (Merck Schuchardt, 98%) and silver tricyanomethanide[32] by the method of Mayer[25] as modified by Makhon'kov and Zefirov.[33] The product partially sublimed and sintered without melting at 170–180 °C in a sealed capillary. *m*/*z* (EI) 117 (*M* + H; 0.5%), 116 (*M*, 0.5), 90 (3), 76 (1), 64 (100), 52 (1), 50 (2), 38 (15); *cf.* ref. 33.

Acetonitrile (Merck, LiChrosolv) and dichloromethane (Merck, Suprasolv) were used as received or dried over 4 Å molecular sieves. Deuteriated solvents were from Glaser AG, Basel.

Cycloaddition kinetics

The reactions of Scheme 1 were carried out under pseudo-first-order conditions at 22 ± 1 °C, with the nitrile component in *ca.* 10-fold excess over the nitrone. For the faster reactions, the disappearance of PBN or 4-NO$_2$-PBN was monitored by UV spectroscopy, mostly in quartz cuvettes of 1 mm pathlength. For **1d**, the faster rate required use of the Rapid Kinetics Accessory RX.1000 from Applied Photophysics, London, which has a cell of 2 mm length. The initial nitrone concentrations were *ca.* 1 mmol dm^{-3}. Monitoring was performed at the absorption maximum of the nitrone which for PBN is solvent dependent in the range of 282–300 nm. In acetonitrile PBN had $\lambda_{max} = 298$ nm, $\varepsilon = 1.87 \times 10^4$ dm^3 mol^{-1} cm^{-1} while 4-NO$_2$-PBN had $\lambda_{max} = 360$ nm, $\varepsilon = 1.66 \times 10^4$ dm^3 mol^{-1} cm^{-1}. The Hewlett-Packard 89532K UV–Visible Kinetics Software package was used to record absorbance *vs.* time and to calculate the first-order rate constant by eqn. (2), where A_o, A_t and A_∞ are the absorbances at

$$\ln(A_t - A_\infty) = -kt + \ln(A_o - A_\infty) \qquad (2)$$

time 0, *t* and infinity, respectively, and *k* is the pseudo-first-order rate constant. Since the cycloaddition products and starting nitriles (except for dibromomalononitrile) have low absorbances at 290–300 nm (see text), A_∞ values were usually small, *ca.* 0.05 AU while A_o was in the range of 1.3–1.7 AU (AU = absorbance units).

For kinetics by ^{1}H NMR spectroscopy, pseudo-first-order conditions were again used. [PBN] was *ca.* 0.06 mol dm^{-3}, with the nitrile in 10-fold excess. Solvents used were [^{2}H$_3$]-acetonitrile or CDCl$_3$, and dichloromethane was added as an internal standard. The disappearance of PBN was monitored by using the integral of the Bu^t singlet at δ 1.68 relative to that of dichloromethane at δ 5.35. Plots of ln[Int(PBN-Bu^t)/Int(CH$_2$Cl$_2$)] *versus t* were linear with slope of $-k$. This method was used for dibromomalononitrile and trichloroacetonitrile.

Reaction of PBN and dibromomalononitrile. Dihydrooxadiazole 2a

A solution of PBN (73 mg, 0.41 mmol) and dibromomalononitrile (124 mg, 0.55 mmol) in CDCl$_3$ (1.5 ml) was left for 24 h at 20 °C in a stoppered flask. No residual PBN (singlets at δ 1.60 and 7.53) was seen. Evaporation under vacuum afforded a clear oil (221 mg) which crystallized on standing. The crystals were washed with diethyl ether–pentane and filtered to give 2-*tert*-butyl-3-phenyl-5-(dibromocyanomethyl)-2,3-dihydro-1,2,4-oxadiazole (**2a**, 132 mg, 80%), mp 115–117 °C. An analytical sample had mp 116–117.5 °C (from cyclohexane) (Found: C, 42.1; H, 3.9; N, 10.3; Br, 39.7. $C_{14}H_{15}Br_2N_3O$ requires C, 41.9; H, 3.8; N, 10.5; Br, 39.8%); *m*/*z* (EI) 399 (M, 5%), 343 (10), 233 (10), 185 (12), 146 (22), 121 (35), 104 (15), 77 (17), 57 (100), 56 (37); δ_H(CDCl$_3$) 1.23 (9 H, s, Bu^t), 6.12 (1 H, s, 3-H), 7.40 (5 H, m, H in Ph); ν_{max}/cm^{-1} 3020, 2960 and 2920 (C–H), 2240 (C≡N, w), 1650 (C=N), 1365, 1220, 1200, 1040, 905, 690, 650.

Reaction of PBN and dichloromalononitrile. Dihydrooxadiazole 2b

To a solution of PBN (89 mg, 0.5 mmol) in dichloromethane (4 ml) was added dichloromalononitrile (136 mg, 1.0 mmol). The solution was left in a stoppered flask for 18 h at 20 °C. Evaporation under vacuum gave crude 2-*tert*-butyl-3-phenyl-5-(dichlorocyanomethyl)-2,3-dihydro-1,2,4-oxadiazole (**2b**, 160 mg), mp 61–65 °C. No residual PBN was seen (^{1}H NMR spectroscopy). Recrystallization from heptane gave pure **2b** (127 mg, 81%), mp 65–67 °C (Found: M$^+$, 311.0593. $C_{14}H_{15}Cl_2N_3O$ requires *M*, 311.0594); *m*/*z* (EI) 311 (M, 10%), 255 (20), 189 (10), 146 (20), 121 (18), 104 (13), 77 (15), 57 (100), 56 (36); δ_H(CDCl$_3$) 1.22 (9 H, s, Bu^t), 6.13 (1 H, s, 3-H), 7.41 (5 H, m, H in Ph); ν_{max}/cm^{-1} 3020, 2980 and 2920 (C–H), 2242 (C≡N, w), 1655 (C≡N), 1365, 1230, 1200, 1060, 1040, 910, 800, 760, 695, 660.

Crystals suitable for X-ray crystallography were grown from a solution in heptane by slow evaporation at 20 °C.

Reaction of PBN and chlorotricyanomethane. Dihydrooxadiazole 2c

This compound was prepared as reported.[26] The analytical sample had the following additional characteristics: *m*/*z* (EI) 302 (M, 22%), 268 (4), 246 (6), 212 (11), 180 (10), 146 (18), 132 (9), 104 (24), 77 (18), 57 (100), 56 (36), 41 (13); ν_{max}/cm^{-1} 3025, 2965 and 2920 (C–H), 2250 (C≡N, w), 1670 (C=N), 1450, 1365, 1230, 1200, 1060, 1025, 910, 780, 745, 690, 660.

Crystals suitable for X-ray crystallography were grown from a solution in heptane containing CH$_2$Cl$_2$ (*ca.* 2%). The solution was left in a covered vessel in the refrigerator at 4 °C for 3 days, and crystals were selected before the solution had evaporated to dryness.

Reaction of 4-NO$_2$-PBN and chlorotricyanomethane. Dihydrooxadiazole 2f

4-NO$_2$-PBN (44 mg, 0.20 mmol) and chlorotricyanomethane (38 mg, 0.30 mmol) were dissolved in acetonitrile (45 ml) and left at 20 °C for 15 h. Evaporation under vacuum gave an oil which was dissolved in pentane and evaporated to give crystals, mp 140–144 °C. Recrystallization from heptane gave 2-*tert*-butyl-3-(4-nitrophenyl)-5-(chlorodicyanomethyl)-2,3-dihydro-1,2,4-oxadiazole (**2f**, 66 mg, 96%), mp 140–142.5 °C (Found: C, 51.6; H, 3.9; N, 19.9; Cl, 10.6. $C_{15}H_{14}ClN_5O_3$ requires C, 51.8; H, 4.1; N, 20.1; Cl, 10.2%). *m*/*z* (EI) 347 (M, 2%), 313 (4.5), 298 (2), 257 (4), 232 (25), 191 (25), 57 (100), 56 (11); δ_H($CDCl_3$) 1.24 (9 H, s, Bu^t), 6.25 (1 H, s, 3-H), 7.70 (2 H, d, *J* 8.8 H in Ph), 8.29 (2 H, d, *J* 9.0, H in Ph); ν_{max}/cm^{-1} 2980 and 2930 (C–H), 2245 (C≡N, w), 1670, 1605, 1520 (NO_2), 1340 (NO_2), 1200, 1030, 855, 840, 750.

Reaction of PBN and tetracyanomethane. Dihydrooxadiazole 2d Tetracyanomethane (24 mg, 0.21 mmol) in dry acetonitrile (5 ml) was mixed with PBN (37 mg, 0.21 mmol) in acetonitrile (5 ml) at 20 °C, and the solution was left protected from the atmosphere for 4 h. A 5 ml aliquot was evaporated under vacuum without heating, to give 2-*tert*-butyl-3-phenyl-5-(tricyanomethyl)-2,3-dihydro-1,2,4-oxadiazole (**2d**, 60 mg, 100%), mp 50–55 °C (decomp.). No residual PBN was seen (^{1}H NMR spectroscopy). The product deteriorated upon attempted recrystallization, and was characterized in solution as follows. (*i*) A 1 ml aliquot of the above acetonitrile solution was diluted with 4 ml of dichloromethane, and this solution was used to obtain mass spectra (Found: M$^+$, 293.1279. Calc. for $C_{16}H_{15}N_5O$: *M*, 293.1281); *m*/*z* (EI) 293 (M, 15%), 254 (3), 180 (3), 146 (10), 116 (6), 104 (4), 77 (12), 57 (100), 56 (35). (*ii*) A 2 ml aliquot was evaporated and used for a ^{1}H NMR spectrum. δ_H($CDCl_3$) 1.24 (9 H, s, Bu^t), 6.18 (1 H, s, 3-H), 7.45 (5 H, m, H in Ph). (*iii*) A 2 ml aliquot was evaporated and redissolved in CCl_4 for an IR spectrum. ν_{max}/cm^{-1} 3060, 3020, 2960, 2920 (C–H), 2245 (C≡N, w), 1675, 1450, 1360, 1200, 1025, 690.

Crystallography

Crystal data, established from precession photographs and measured accurately, by means of a Siemens R3m/V four-circle diffractometer [molybdenum X-radiation, λ(Mo-Kα) 0.71069 Å from a crystal monochromator] are given below.† The space group was determined unambiguously as a result of the structure analyses reported below, but initially indicated by conditions limiting possible reflections. ω-Scans were used to collect reflection intensities out to a maximum Bragg angle θ, given below. The cell parameters were determined by least-squares refinements for which the setting angles of accurately centred high-angle reflections were used.

Crystal data

Dihydrooxadiazole 2c. $C_{15}H_{15}ClN_4O$, *M* 302.76, orthorhombic, space group *Pbca*, *a* 19.199(3), *b* 7.653(2), *c* 21.265(5) Å, *V* 3124(1) Å^3, D_c 1.287 g cm^{-3}, *Z* 8, μ(Mo-Kα) 2.49 cm^{-1}. The crystal was colourless and of approximate dimensions 0.58 × 0.53 × 0.50 mm. Data were collected at 163(2) K out to a maximum Bragg angle θ 27.5°. Number of independent reflections measured 3554, 2061 with $I > 2\sigma(I)$. Absorption corrections were not applied; g_1 0.0961, g_2 0.0000; $R_{(obs)}$-factor 0.062, $\omega R_{(all\ data)}$ 0.206.

Dihydrooxadiazole 2b. $C_{14}H_{15}Cl_2N_3O$, *M* 312.19, monoclinic, space group $P2_1/c$, *a* 10.417(1), *b* 18.721(2), *c* 7.887(1) Å, β 94.47(1)°, *V* 1533.4(3) Å^3, D_c 1.352 g cm^{-3}, *Z* 4, μ(Mo-Kα) 4.22 cm^{-1}. The crystal was colourless and of approximate dimensions 0.69 × 0.63 × 0.36 mm. Data were collected at 163(2) K out to a maximum Bragg angle θ 27.5°. Number of independent reflections measured 3529, 1752 with $I > 2\sigma(I)$. Absorption corrections were not applied; g_1 0.0593, g_2 0.0000; $R_{(obs)}$-factor 0.047, $\omega R_{(all\ data)}$ 0.126.

Structure determination

The structures were solved by direct methods and difference-Fourier syntheses. Full-matrix least-squares refinements (SHELXL-93)[34] were employed. This program is based on intensities and uses all data. The observed threshold $I > 2\sigma(I)$ was used only for calculating $R_{(obs)}$, shown here as a comparison for the refinements based on *F*. Reflection weights $1/[\sigma^2(F_o^2) + (g_1P)^2 + g_2P]$, where $P = (F_o + 2F_c^2)/3$, were used. All non-hydrogen atoms were assigned anisotropic thermal parameters. Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. Final Fourier syntheses show no abnormal discrepancies between observed and calculated structure factors.

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† Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 2*, available *via* the RSC Web pages (http://chemistry.rsc.org/rsc/p1pifa.htm). Any request to the CCDC for this material should quote the full literature citation and the reference number 188/115.

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