Preparation and reactivity of some stable nitrile oxides and nitrones

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To Otto on the occasion of his 65th birthday

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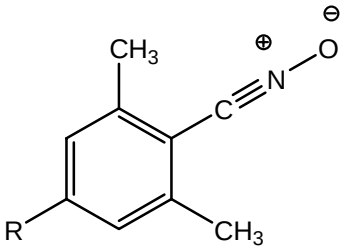
Abstract

a,b;g,d-Unsaturated nitrile oxides 6, 13 have been prepared from the corresponding aldehydes *via* sequential oxime formation, chlorination, and dehydrochlorination. These nitrile oxides show unexpected stability, presumably due to delocalisation, and can be isolated. 2,6-Diphenylbenzonitrile oxide 13b was particularly stable and a single crystal X-ray structure was obtained. 3,3-Diphenylpropenitrile oxide 6 was also isolated but could be dimerized, to give a 1,4,2,5-dioxadiazine 7 or furoxan 8, *via* slight modifications to the conditions employed. The corresponding nitrones 14, 17 have also been prepared, *via* the reaction of the a,b;g,d-unsaturated aldehydes 10a,b with substituted hydroxylamines, isolated and trapped.

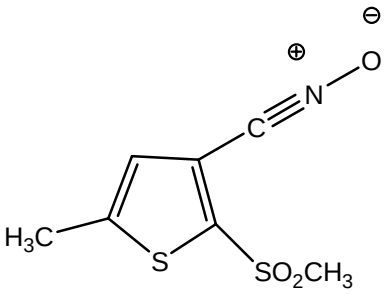
Keywords: Nitrile oxides, nitrones, dimerization, X-ray crystal structure

Introduction

The majority of nitrile oxides, like the other classes of nitrilium betaine 1,3-dipoles, are chemically unstable and undergo dimerization to either 1,4,2,5-dioxadiazines or furoxans.[1] Relatively stable nitrile oxides can be obtained as a result of steric shielding of the nitrile oxide moiety,[2] *e.g.* 4-substituted-2,6-dimethylbenzonitrile oxides 1, or by electrostatic (donor-acceptor) interactions,[3] *e.g.* methylsulphonylthiophenecarbonitrile oxide 2. Stabilization by steric shielding produces nitrile oxides which are unreactive in both the solid and solution states, whilst stabilization due to electrostatic interactions generally gives nitrile oxides which are stable in the solid state, but which are reactive in solution. This latter class of nitrile oxides dimerize, or react with dipolarophiles, in solution.



1a R = Br
b R = OCH_3



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Nitrones are reactive 1,3-dipoles of the allyl class which are also usually generated *in situ*. Nitrones have proved to be very useful tools in the construction of structurally complex molecules, usually allowing a high degree of diastereocontrol. In this context, both the nitrone [3+2] cycloaddition to alkenes[4] and the alkylation of nitrones by organometallic reagents[5] have been extensively developed and have become reliable synthetic procedures. In addition, nitrones are useful spin trap reagents, and are thus widely employed in biological systems.[6]

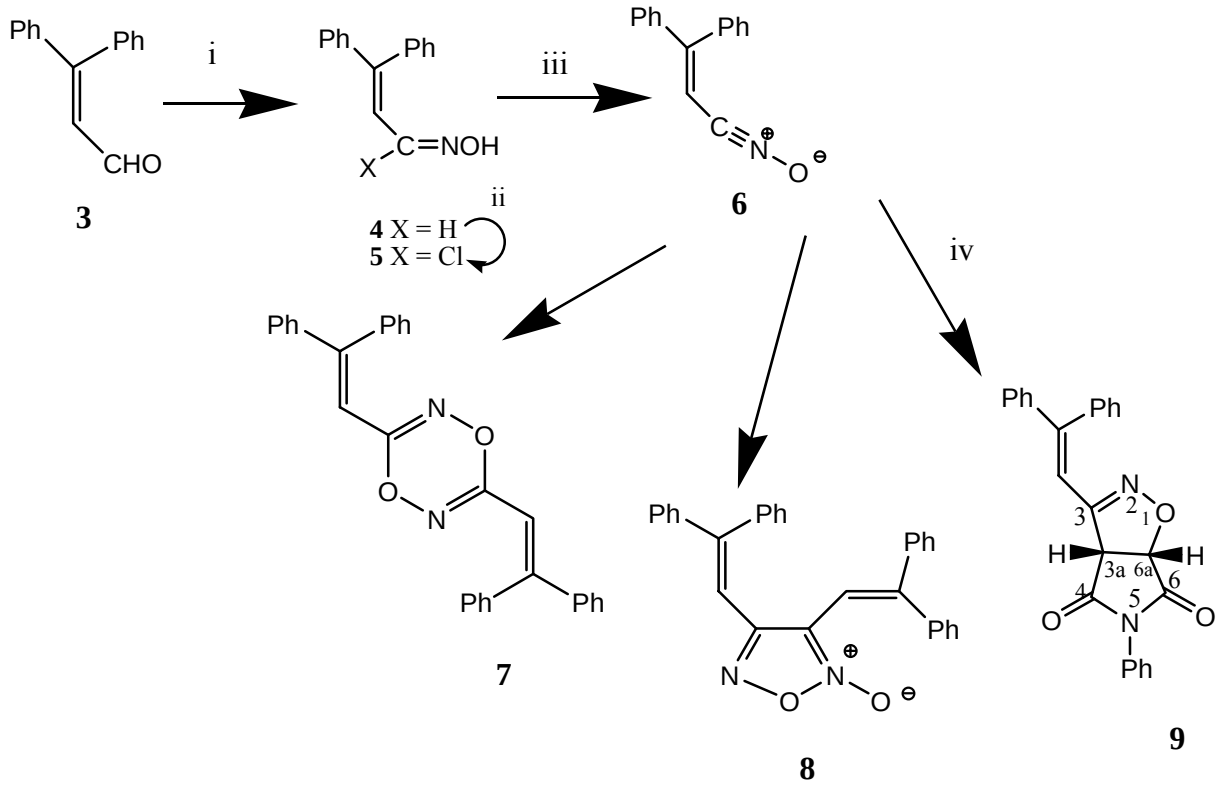
We wish to report here the preparation of some nitrile oxides and nitrones with a,b;g,d-unsaturation, which show unexpected stability in the solid state, presumably due to resonance stabilization, but which undergo dimerization, or can be trapped by dipolarophiles, in solution. The intramolecular reactivity of C-(1-buten-3-ynyl)-nitrones has been studied in detail by Eberbach,[7] but no data are available on the reactivity of the analogous C-(1,3-butadienyl)-derivatives.

Results and Discussion

The nitrile oxide 6 was prepared *via* the corresponding aldoxime 4,[8] generated from b-phenylcinnamaldehyde 3 and hydroxylamine hydrochloride, in the presence of a base. The oxime 4 was obtained as a mixture of *syn* and *anti* forms and was used in the next step without further purification. Conversion to the corresponding nitrile oxide 6 was achieved by chlorination with *N*-chlorosuccinimide in DMF to give the hydroximoyl chloride 5 followed by base-catalysed dehydrochlorination, Scheme 1.[9]

When the hydroximoyl chloride was prepared at 35°C, in the absence of base, the dioxadiazine 7 was obtained, whereas at 40°C, in the presence of triethylamine, dimerisation afforded the furoxan 8. The two products were characterised by high resolution mass spectrometry and NMR spectroscopy. The proton NMR spectrum of dioxadiazine 7 shows a singlet for the equivalent alkene protons, at d6.49, whilst that of the furoxan 8 shows 1H singlets at d6.59 and d6.74.

When the reaction was repeated, and the aldoxime chlorinated at 40°C, followed by additional stirring at 25°C overnight, with subsequent dehydrochlorination by treatment with triethylamine and standard work-up, 3,3-diphenylpropenitrile oxide 6 was isolated as a stable product. The IR spectrum shows an intense peak at 2287 cm^{-}



Scheme 1. *Reagents and conditions*; I, NH_2OH, NaOH, EtOH, H_2O, reflux, 30 min, 78%; ii, NCS, DMF; iii, Et_3N, Et_2O; iv, *N*-phenylmaleimide, Et_2O.

for Cthree=N^+-O^- and the proton NMR spectrum shows a singlet at d5.76. The structure was confirmed by high resolution mass spectrometry. This nitrile oxide is stable when stored at 0C, presumably due to the extended conjugation in this system, Figure 1, giving rise to resonance stabilization. The reactivity of this stable nitrile oxide was then investigated by generation in the presence of *N*-phenylmaleimide to give the cycloadduct 9 in excellent yield, Scheme 1.

In the same way, nitrile oxides 13 were generated from the corresponding aldehydes 10 *via* oxime 11 formation, chlorination to the hydroximoyl chlorides 12, and dehydrochlorination with base, Scheme 2. 2,6-Diphenylbenzonitrile oxide 13b was obtained as a crystalline solid and is also stable upon storage. In this case, the stability presumably arises from both resonance stabilization and steric shielding of the nitrile oxide group. No products from the dimerisation of these nitrile oxides were obtained.

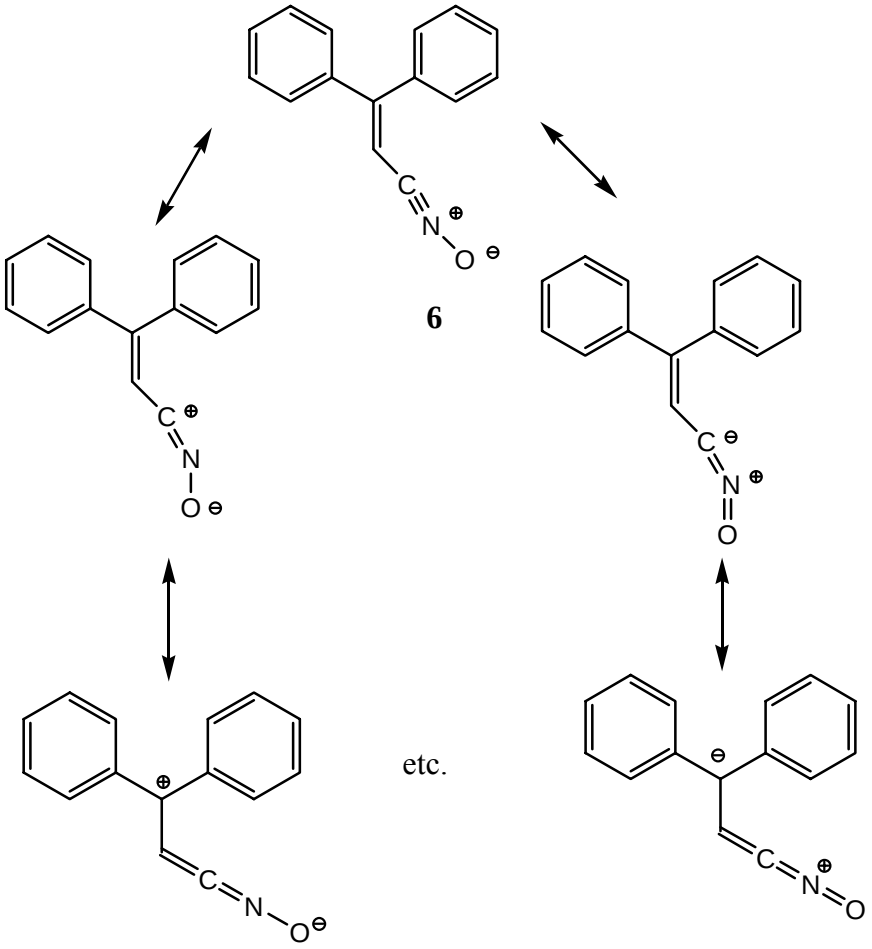
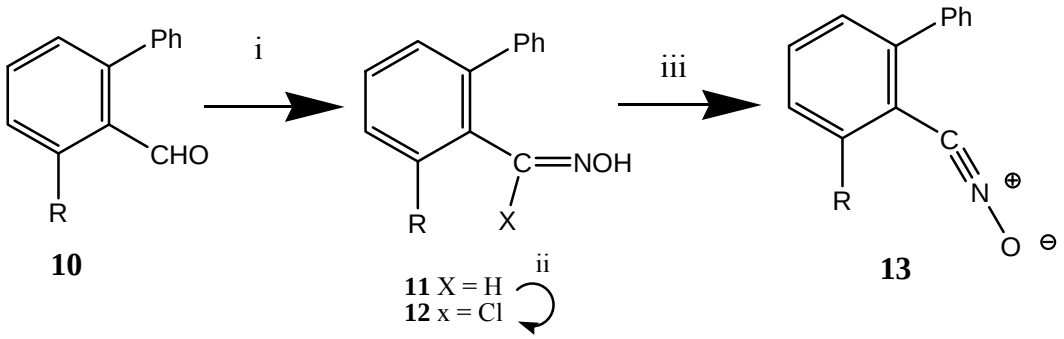


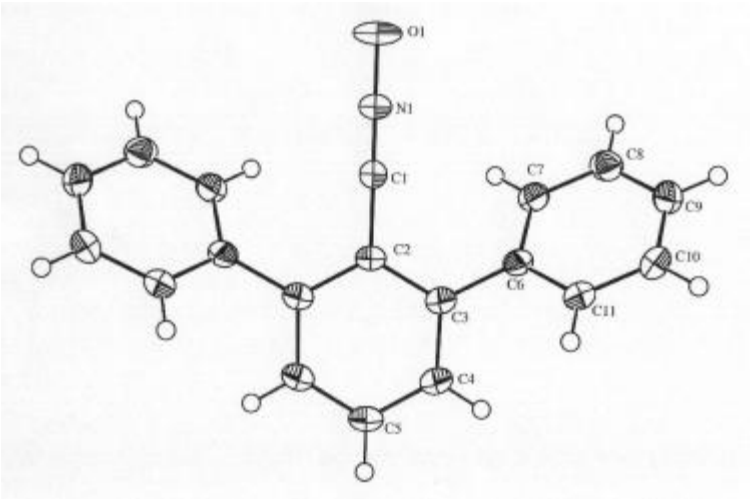
Figure 1



a R = H; **b** R = Ph

Scheme 2. *Reagents and conditions*; I, NH_2OH, NaOH, EtOH, H_2O, reflux, 30 min, 78%; ii, NCS, DMF; iii, Et_3N, Et_2O.

A single crystal X-ray structure of this nitrile oxide was obtained, the key feature of which is the linear nitrile oxide group with a bond angle ÐCºN-O of 179.4°, Figure 2.



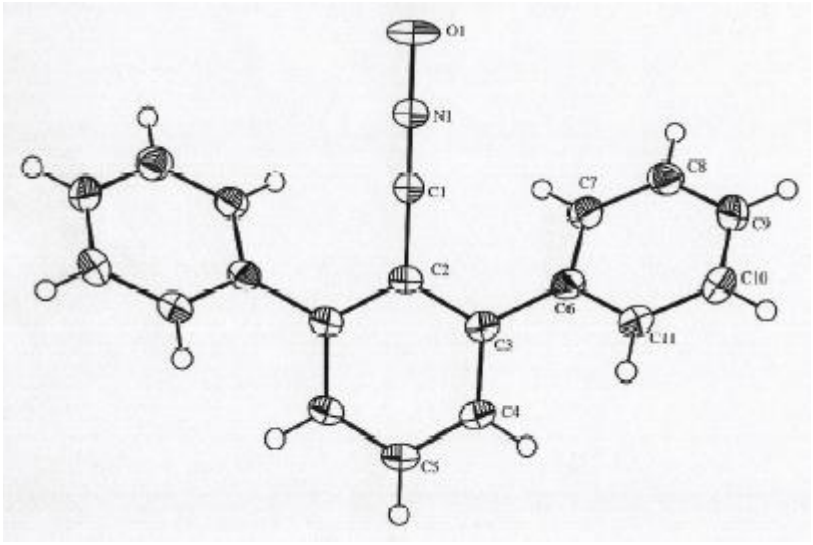
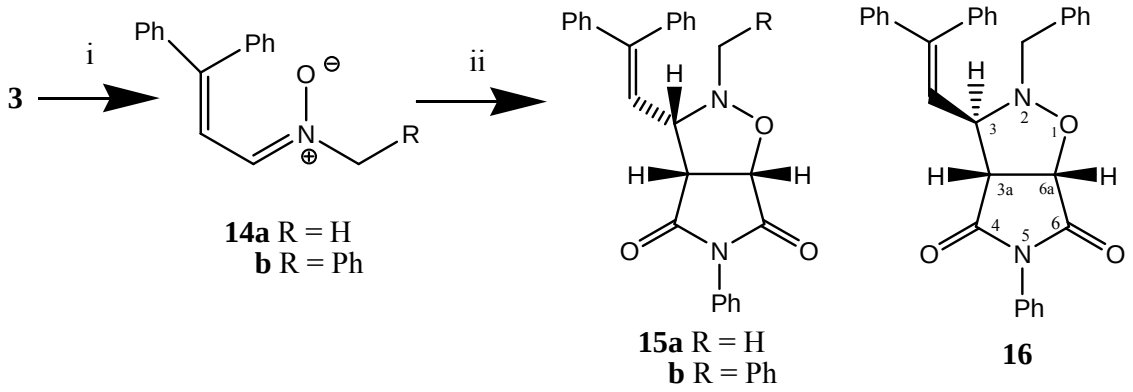


Figure 2



14a R = H
b R = Ph

15a R = H
b R = Ph

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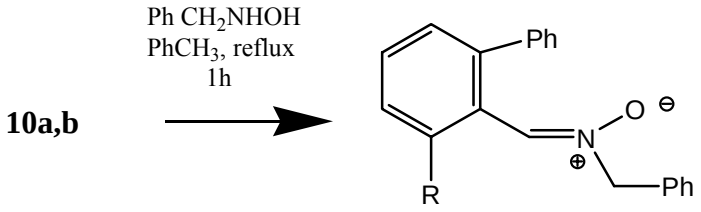
Scheme 3. *Reagents and conditions*; I, RCH_2NHOH, Et_3N, $PhCH_3$, reflux, 1h; ii, *N*-phenylmaleimide, $PHCH_3$, reflux.

Nitrones are easily available from aldehydes or ketones and *N*-monosubstituted hydroxylamines. In this manner -phenylcinnamaldehyde 3 was reacted with *N*-methyl- and *N*-benzylhydroxylamine, Scheme 3. From both these reactions a stable, isolable nitrone 14a,b was formed and characterized (by elemental analysis or high resolution mass spectrometry). The stability of these nitrones is presumably also attributable to resonance stabilization. Although stable, these dipoles were easily trapped, in solution, by alkenic dipolarophiles in refluxing toluene, giving the corresponding cycloadducts 15 and 16. In the case of the *N*-methylnitrone this cycloaddition with *N*-phenylmaleimide was completely *endo*-selective giving 15a, whilst the *N*-benzyl

derivative gave a 1:1 mixture of *endo*- 15b and *exo*-products 16 which were separated by crystallization.

The stereochemistry of the cycloadducts was deduced by n.O.e. experiments (Tables 1 and 2). The most important, decisive information obtained from these experiments is the presence / absence of the n.O.e. interaction between the H-3 and H-3a protons in the *endo*- and *exo*-cycloadducts, respectively. The stereochemistry of the *N*-methyl adduct 15a was assigned by comparison with the *N*-benzyl analogues.



17a R = H
b R = Ph

Scheme 4

The nitrones themselves proved to be remarkably stable upon refluxing in toluene or xylene. No 1,7-electrocyclisation reaction was observed, in contrast to other allylic dipoles, such as azomethine[10] or carbonyl ylides,[11] and only slow decomposition was observed after a few days reaction time.

Experimental Section

General Procedures. M.p.s were determined on a Gallenkamp apparatus and are uncorrected. Elemental analyses were performed on a Perkin-Elmer 240C or Carlo Erba 1106 Elemental Analyser. IR spectra were recorded on a Perkin-Elmer 1600 series FTIR or Unicam research series FTIR spectrophotometer using sodium chloride plates. ^{1}H NMR spectra were acquired on a Jeol GSX 270 FT NMR at 270 MHz, a Bruker AC 250 at 250 MHz, or a Bruker AVANCE 300 at 300MHz. Coupling constants are given in Hz and all chemical shifts are relative to an internal standard of tetramethylsilane. ^{13}C NMR spectra were obtained on a Jeol GFX 270 FT NMR (68 MHz) spectrometer or a Bruker AC 250 (63 MHz). Low resolution electron impact mass spectra were obtained on a Trio 2000 VG. High resolution spectra were obtained on a VG ZAB-E spectrometer (E.P.S.R.C. Mass Spectrometry Service Centre, Swansea) or Bruker

APEX II ICR-MS. Thin layer chromatography was performed on Merck silica gel $60F_{254}$. All solvents were purified according to standard procedures. Diethyl ether was freshly distilled over sodium wire with a trace of benzophenone. Toluene was distilled from, and stored over, sodium wire. Fisons silica gel 60 (35-70 micron) was used for wet flash chromatography. The samples were applied in liquid form or were pre-adsorbed onto silica 60 (35-70 micron) from dichloromethane solutions. 2-Phenylbenzaldehyde and 2,6-diphenylbenzaldehyde were prepared by the method of Sharp and Cullen.[12] 3,3-Diphenyl-2-propenaldoxime was prepared by the method of Lachman.[8]

Crystal data for 2,6-diphenylbenzonitrile oxide (13b)

$C_{19}H_{13}NO$, M = 271.30. Monoclinic, a = 9.839 (2), b = 14.195 (3), c = 10.0298 (10) Å, β = 96.989° (10) (by least squares refinement of the setting angles for 2942 reflections within = 2.50 - 26.30°), V = 1390.3 (4) $Å^3$, space group P2(1)/m, Z = 4, D_m = 1.296 g cm^{-3}. F(000) = 568. White crystals. Crystal dimensions 0.40x0.35x0.35 mm, (Mo-K) = 0.080 mm^{-1}.

Data collection and processing

From the ranges scanned, 2942 data were collected (2.50 26.30°), 2942 unique (R_{int} = 0.024).

Structural analysis and refinement

The structure was solved *via* direct methods (SHELX-S)[13] and refined on F_o^2 by full-matrix least-squares (SHELXL-93)[14] using all unique data corrected for Lorentz and polarisation factors to final *wR* (on F_o^2) and *R* (on *F*) values of 0.1375 and 0.0651 for 205 parameters (non-hydrogen atoms anisotropic; hydrogens in idealised positions with U_{iso}s tied to the U_{eq}s of the parents). The corresponding *R*-values for data with I > 2s(I) are 0.1276 and 0.0451, respectively. The weighting scheme used was $w = 1/[s^2(F_o^2) + (0.0467P)^2]$, where $P = [\max(F_o)^2 + 2(F_c)^2]/3$; this gave satisfactory agreement analyses. Sources of scattering factors as in ref. 14. Full details of data collection and structure refinements, atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

Isolation of nitrile oxides.General procedure

To a solution of the oxime(0.86 mmol) in dry DMF (10 cm^3) was added *N*-chlorosuccinimide (0.86 mmol) in dry DMF (5 cm^3), dropwise, over 10-15min., at 40°C. After stirring for 3h., the water bath was removed and the reaction mixture stirred at 25°C, overnight. The reaction was quenched by pouring the mixture onto ice-water (30 cm^3) and extracted with ether (3 20 cm^3). The combined organic extracts were washed with ice-water (10 cm^3) and brine solution (10 cm^3), dried ($MgSO_4$) and solvent

evaporated under reduced pressure to give a pale brown oil. The product was dissolved in ether (6 cm^3) and a solution of triethylamine (1 equiv.) in ether (3 cm^3) was added dropwise over 20min., at 0°C. The mixture was stirred at 0°C for 1h. and allowed to reach room temperature overnight. The salt was filtered and the solvent removed under reduced pressure to give the nitrile oxide.

3,3-Diphenylpropenitrile oxide (6). From b-phenylcinnamaldehyde 3 asa pale brown oil (0.181 g, 94%) (Found: M^+, 221.084. Calc. for $C_{15}H_{11}NO$: *M*, 221.084); ν_{max} (liquid film)/cm^{-1} 2287 (CN), 1598 (C=C); δH (270 MHz, $CDCl_3$) 5.76 (1H, s, C=CH), 7.17-7.35 (10H, m, Ar-H); *m/z* 221 (M^+, 90%), 205 (100), 191 (38), 179 (28), 166 (61).

2-Phenylbenzonitrile oxide (13a). From 2-phenylbenzaldehyde 10a as a yellow oil (0.29g, 74%) (Found: MH^+, 196.076. Calc. for $C_{13}H_{10}NO$: *MH*, 196.076); ν_{max} (liquid film)/cm^{-1} 2296 (CN); δH (270 MHz, $CDCl_3$) 7.15-7.50 (17H, m); *m/z* 196 (MH^+, 69%), 180 (63), and 178 (100).

2,6-Diphenylbenzonitrile oxide 13b. From 2,6-diphenylbenzaldehyde 10b as white crystals (0.46 g, 79%), mp 167-169C (Found: MH^+, 272.107. Calc. for $C_{19}H_{14}NO$: *MH*, 272.1075); ν_{max} (liquid film)/cm^{-1} 2297 (CN); δH (270 MHz, $CDCl_3$) 7.39-7.59 (13H, m); *m/z* 272 (MH+, 52%), 256 (35) and 254 (100).

Trapping of 3,3-diphenylpropenitrile oxide 6

Method 1

N-Chlorosuccinimide (0.042 g, 0.31 mmol) was added to a solution of 3,3-diphenyl-2-propenaldoxime 4 (0.35 g, 1.57 mmol) in DMF (24 cm^3), with stirring, under N_2. The reaction was initiated by bubbling the gas from the head space of a concentrated HCl bottle through the solution. A further aliquot of *N*-chlorosuccinimide (0.168 g, 1.25 mmol) was then added, ensuring that the temperature remained below 35°C. The reaction was again purged with HCl (g), then poured into 4 volumes of ice-water. The reaction mixture was extracted with ether (3 10 cm^3). The combined ether extracts were washed with water (30 cm^3), dried ($CaSO_4$) and evaporated under reduced pressure to give a dark brown oil (0.29 g, 42%). This dark brown oil was purified by column chromatography on silica, eluting with ether / petroleum ether 40-60°C (0:100 to 10:90), to give 3,6-bis(2',2'-diphenylethenyl)-1,4,2,5-dioxadiazine 7 as a pale brown oil (0.17 g, 49%) (Found: M, 442.166. Calc. for $C_{30}H_{22}N_2O_2$: *M*, 442.168); ν_{max} (liquid film)/cm^{-1} 1650 (C=N), 1599 (C=C); δH (360 MHz, $CDCl_3$) 6.49 (2H, s, C=CH), 7.02-7.36 (20H, m, Ar-H); *m/z* 442 (M^+, 7%), 221 (100), 205 (60), 191 (79), and 179 (60).

Method 2

To a solution of 3,3-diphenyl-2-propenaldoxime 4 (0.18 g, 0.807 mmol) in DMF (3 cm^3) was added *N*-chlorosuccinimide (0.107 g, 0.807 mmol) in DMF (2 cm^3), with stirring over *ca.* 10min., at 40°C under N_2. The mixture was stirred for a further 1h., and allowed to reach room temperature overnight. The reaction mixture was poured onto ice

(11 g) and extracted with ether (3 15 cm^3). The combined organic extracts were washed with ice-cold water (5 cm^3), brine solution (3 cm^3), dried (Na_2SO_4) and solvent evaporated under reduced pressure to give a brown oil (0.16 g). The crude oil was dissolved in dry ether (5 cm^3) to which a solution of triethylamine (0.11 g, 0.15 cm^3, 0.11 mmol) in ether (5 cm^3) was added over *ca*. 20 min., under N_2. The mixture was stirred at room temperature and the precipitated salt filtered. The reaction was monitored by t.l.c., which showed a mixture of products. The filtrate was evaporated under reduced pressure to give a brown oil (0.08g, 22%). The oil was purified by column chromatography on silica, eluting with ether / petroleum ether 40-60^oC (0:100 to 30:70), from which 3,4-bis(2',2'-diphenylethenyl)furoxan 8 was isolated as a pale brown oil (0.05 g, 28%) (Found: MH^+, 443.175. Calc. for $C_{30}H_{23}N_2O_2$: *MH*$^+$, 443.175); ν_{max} (liquid film)/cm^{-1} 1662 (C=N), 1598 (C=C); δ_H (360 MHz, $CDCl_3$) 6.59 (1H, s, C=CH), 6.74 (1H, s, C=CH), 7.07-7.48 (20H, m, Ar-H); *m/z* 443 (MH^+, 6%), 425 (42), 222 (100), 206 (94), and 180 (39); δ_C (68 MHz, $CDCl_3$), 110.1 (CH), 113.0 (CH), 128.4 (2 × CH), 128.5 (2 × CH), 128.55 (2 × CH), 128.6 (2 × CH), 128.7 (3 × CH), 128.75 (3 × CH), 128.9 (2 × CH), 129.15 (quat.), 129.2 (quat.), 129.95 (3 × CH), 130.0 (quat.), 130.3 (quat.), 138.5 (quat.), 141.2 (quat.), 142.1 (quat.), 152 (quat.), 155.5 (quat.).

Trapping of 3,3-diphenylpropenitrile oxide 6 with *N*-phenylmaleimide

To a solution of 3,3-diphenyl-2-propenaldoxime 4 (0.0966 g, 0.433 mmol) in dry DMF (10 cm^3) was added *N*-chlorosuccinimide in dry DMF (5 cm^3), dropwise over 10-15min., at 40^oC. After stirring for 3h., the water bath was removed and the reaction mixture allowed to stir at 25^oC, overnight. The reaction was quenched by pouring the mixture into ice (10 g) and extracted with ether (3 20 cm^3). The combined organic extracts were washed with ice-water (10 cm^3), brine solution (10 cm^3), dried (Na_2SO_4) and the solvent evaporated under reduced pressure to give a pale brown oil (0.084 g). The product was dissolved in ether (6 cm^3) and *N*-phenylmaleimide (0.056 g, 0.326 mmol) added, with stirring, under N_2. A solution of triethylamine (0.065 g, 0.089 cm^3, 0.326 mmol) in ether (3 cm^3) was added dropwise over 1h., at 0^oC then the mixture was allowed to reach room temperature overnight. The precipitated solid was filtered and solvent evaporated under reduced pressure to give 4,6-dioxo-5-phenyl-3-(2,2-diphenylethenyl)-2,5-diaza-1-oxabicyclo[3.3.0]octane 9 as a dark brown oil (0.152 g, 89%). The dark brown oil was purified by wet flash column chromatography on silica, eluting with ethyl acetate / petroleum ether 60-80^oC (0:100 to 20:80) (0.149g, 87%) (Found: M, 394.132. Calc. for $C_{25}H_{18}N_2O_3$: *M*, 394.132); δ_H (270 MHz, $CDCl_3$) 3.93 (1H, d, *J* 9.8, H-3*a*), 5.27 (1H, d, *J* 9.9, H-6*a*), 6.82 (1H, s, H-3'), 7.18-7.38 (15H, m, Ar-H); δ_C (18MHz, $CDCl_3$) 53.8 (CH), 79.4 (CH), 112.6 (CH), 128.1 (6xCH), 128.5 (6xCH), 129.2 (4xCH), 130.6 (quat.), 138.9 (quat.), 140.8 (quat.), 152.3 (quat.), 152.7

(quat.), 169.3 (quat., C=O), 170.7 (quat., C=O); *m/z* 394 (M^+, 100%), 366 (5), 247 (58), 205 (60).

General procedure for Isolation of nitrones.

The aldehyde (0.10 g, 0.48 mmol) and the *N*-substituted hydroxylamine (0.48 mmol) were dissolved in dry toluene (5 cm^3) and triethylamine (0.07 cm^3, 0.05 g, 0.5 mmol) was added. The reaction mixture was refluxed for one hour under Dean and Stark conditions and an argon atmosphere. After cooling, the precipitated triethylamine hydrochloride was filtered off, and the solution was evaporated. The residue was triturated with ether to give the product.

***N*-Methyl-*N*-(3,3-diphenylpropenyl)nitrone (14a).** From β-phenylcinnamaldehyde 3 and *N*-methylhydroxylamineas awhite powder, mp 148-150 ^oC (90 mg, 79 %)) (Found: C, 80.9; H, 6.3; N, 5.9. $C_{16}H_{15}NO$ requires C, 81.0; H, 6.4; N, 5.9%) (Found: MH^+, 238.122. Calc. for $C_{16}H_{16}NO$: *MH*, 238.123. Found: MNa^+, 260.1045. Calc. for $C_{16}H_{15}NONa$: *MNa*, 260.105); δH (250 MHz, $CDCl_3$) 3.66 (3H, s, Me), 7.04 (1H, d, *J* 9.5), 7.19-7.27 (2H, m), 7.27-7.38 (5H, m), 7.39-7.48 (4H, m); δC (63 MHz, $CDCl_3$) 52.7 (CH_3), 117.4 (CH), 128.2 (2 CH), 128.5 (2 CH), 128.6 (CH), 128.7 (2 CH), 129.0 (quat.), 130.2 (2 CH), 136.7 (CH), 138.7 (quat.), 140.7 (quat.), 149.6 (quat.); ν_{max} (KBr)/cm^{-1} 1540 (C=C); *m/z* 238 (M^+, 100), 222 (29), 209 (13), 181 (4), 144 (3), 107 (4), 85 (10), 71 (9), and 57 (26).

***N*-Benzyl-*N*-(3,3-diphenylpropenyl)nitrone (14b).** From β-phenylcinnamaldehyde 3 and *N*-benzylhydroxylamineas awhite powder, mp 120-2 ^oC (110 mg, 71 %) (Found: MH^+, 314.154. Calc. for $C_{22}H_{20}NO$: *MH*, 314.154. Found: MNa^+, 336.136. Calc. for $C_{22}H_{20}NONa$: *MNa*, 336.136); δH(250 MHz, $CDCl_3$) 4.86 (2H, s, CH_2), 7.08 (1H, d, *J*10), 7.19-7.13 (2H, m), 7.27-7.43 (14H, m); δC (63 MHz, $CDCl_3$) 69.6 (CH_2), 117.5 (CH), 128.3 (2 CH), 128.5 (2 CH), 128.6 (3 CH), 128.9 (quat.), 129.0 (3 CH), 129.2 (2 CH), 130.3 (2 CH), 133.4 (CH), 135.8 (quat.), 138.8 (quat.), 140.8 (quat.), 149.9 (CH); ν_{max} (KBr)/cm^{-1} 1684 (C=C), 1540 (C=C); *m/z* 314 (7%, M^+), 250 (7), 237 (18), 222 (28), 209 (100), 146 (5), 134 (14), 106 (67), 85 (27), 71 (23), and 57 (78).

***N*-Benzyl-*N*-(2-phenylbenzylidene)nitrone (17a).** From 2-phenylbenzaldehyde 10a and *N*-benzylhydroxylamineas ayellow oil (0.28 g, 65%)(Found: MH^+, 314.154. Calc. for $C_{20}H_{18}NO$: *MH*, 314.154. Found: MNa^+, 310.120. Calc. for $C_{20}H_{17}NONa$: *MNa*, 310.120); δH(270 MHz, $CDCl_3$) 4.72 (2H, s, CH_2), 7.05-7.29 (14H, m), 9.32 (1H, m); δC (68 MHz, $CDCl_3$) 70.7 (CH_2), 126.8 (CH), 126.9 (CH), 127.1 (CH), 127.2 (CH), 127.7 (2xCH), 128.0 (CH), 128.1 (2xCH), 128.5 (2xCH), 128.9 (quat.), 129.1 (2x CH), 129.15 (CH), 131.7 (CH), 132.6 (quat.), 139.0 (quat.), 141.2 (quat.); ν_{max} (KBr)/cm^{-1} 1576, 1555 (C=C).

***N*-Benzyl-*N*-(2,6-diphenylbenzylidene)nitrone (17b).** From 2,6-diphenylbenzaldehyde 10b and *N*-benzylhydroxylamineas awhite solid after trituration

with ether, mp 176-178°C (0.44 g, 81%)(Found: MH^+, 364.169. Calc. for $C_{26}H_{22}NO$: *MH*, 364.170. Found: MNa^+, 386.1515. Calc. for $C_{26}H_{21}NONa$: *MNa*, 386.152); δ_H(270 MHz, $CDCl_3$) 4.55 (2H,s, CH_2), 7.04-7.47 (19H, m); δ_C (68 MHz, $CDCl_3$) 69.4, 127.0, 127.3 (2x CH), 128.0 (4xCH), 128.05 (4xCH), 128.6 (2xCH), 128.9 (2xCH), 129.2, 129.5 (2xCH), 132.15, 134.2 (2xCH), 140.85 (2xCH), 142.6 (2x CH); ν_{max} (KBr)/cm^{-1} 1649 (C=C); m/z 364 (MH^+, 100%), 348 (39), 259 (8), and 241 (18).

General procedure for the trapping of nitrones with *N*-phenylmaleimide

The nitrone (0.38 mmol) and *N*-phenylmaleimide (70 mg, 0.40 mmol) were dissolved in toluene (5 cm^3) and the solution was refluxed for 3 hours. The solvent was removed and the residue was purified by column chromatography and / or recrystallization [from hexane - ethyl acetate (3:1)].

2-Methyl-4,6-dioxo-5-phenyl-3-(2',2'-diphenylethenyl)-2,5-diaza-1-oxabicyclo-[3.3.0]octane 15a. From*N*-methyl-*N*-(3,3-diphenylpropenyl)nitrone 14a and *N*-phenylmaleimide as a pale yellow oil after column chromatography (70 mg, 45 %) (Found: C, 74.8; H, 5.4; N, 6.9. $C_{26}H_{22}N_2O_3.1/2H_2O$ requires C, 74.5; H, 5.5; N, 6.7%) (Found: MH^+, 411.170. Calc. for $C_{26}H_{23}N_2O_3$: *MH*, 411.170. Found: MNa^+, 433.152. Calc. for $C_{26}H_{22}N_2O_3Na$: *MNa*, 433.152); δ_H(250 MHz, $CDCl_3$) 2.66 (3H, s, N-C*H*$_3$), 3.43 (1H, dd, *J* 7.6 and 7.2, H-3*a*), 3.51 (1H, dd, *J* 9.5 and 7.6, H-3), 4.84 (1H, d, *J* 7.2, H-6*a*), 5.82 (1H, d, *J* 9.5, H-3'), 7.22 - 7.53 (15H, m, Ar-H); δ_C (63 MHz, $CDCl_3$) 42.3 (CH_3), 53.0 (CH), 70.5 (CH), 75.9 (CH), 126.2 (CH), 126.3 (2xCH), 127.5 (2xCH), 127.8 (CH), 128.3 (2xCH), 128.6 (2xCH), 128.8 (CH), 129.1 (2 ´ CH), 129.2 (2x CH), 129.7 (CH), 131.5 (quat.), 139.2 (quat.), 140.9 (quat.), 148.6 (quat.), 172.5 (C=O), 174.6 (C=O).

2-benzyl-4,6-dioxo-5-phenyl-3-(2',2'-diphenylethenyl)-2,5-diaza-1-oxabicyclo-[3.3.0]octane 15b, 16. From *N*-benzyl-*N*-(3,3-diphenylpropenyl)nitrone (14b) and *N*-phenylmaleimide. *exo* adduct 16;white powder, recrystallised after column chromatography, mp 129-132 °C (30 mg, 19 %) (Found: MH^+, 487.202. Calc. for $C_{32}H_{27}N_2O_3$: *MH*, 487.202); δ_H(250 MHz, $CDCl_3$) 3.74 (1H, dd, *J* 7.3 and 2.1, H-3*a*), 3.87 (1H, d, *J* 13.9, PhC*H*$_2$), 4.22 (2H, m, PhC*H*$_2$ and H-3*a*), 4.99 (1H, d, *J* 7.3, H-6*a*), 6.34 (1H, d, *J* 9.9, H-3'), 7.10 - 7.55 (20H, m, Ar-H); δ_C (63 MHz, $CDCl_3$) 55.1 (CH), 56.2 (CH_2), 66.1 (CH), 75.7 (CH), 122.3 (CH), 126.3 (CH), 126.6 (CH), 127.4 (CH), 127.6 (CH), 127.9 (CH), 128.4 (CH), 128.9 (CH), 129.2 (CH), 129.8 (CH), 131.4 (quat.), 136.2 (quat.), 137.9 (quat.), 141.3 (quat.), 147.6 (quat.), 165.8 (C=O), 173.8 (C=O).

endo adduct **15b**. white powder recrystallised after column chromatography, mp 138-140 °C (80 mg, 52 %) (Found: C, 78.5; H, 5.4; N, 5.7. $C_{32}H_{26}N_2O_3$ requires C, 79.0; H, 5.4; N, 5.75%) (Found: MH^+, 487.202. Calc. for $C_{32}H_{27}N_2O_3$: *MH*, 487.202. Found:

MNa^+, 509.184. Calc. for $C_{32}H_{26}N_2O_3Na$: *MNa*, 509.184); $_{\delta H}$(250 MHz, $CDCl_3$) 3.54 (1H, t, *J* 7.5, H-3*a*), 3.66 (1H, dd, *J* 9.4 and 7.7, H-3), 3.79 (1H, d, *J* 14.9, PhCH_2), 4.20 (1H, d, *J* 14.9, PhCH_2), 4.85 (1H, d, *J* 7.5, H-6*a*), 5.79 (1H, d, *J* 9.4, H-3'), 7.15 - 7.48 (20H, m, Ar-H); $_{\delta C}$ (63 MHz, $CDCl_3$) 52.9 (CH), 58.5 (CH_2), 68.4 (CH), 76.0 (CH), 120.4 (CH), 126.0 (CH), 126.3 (2xCH), 127.6 (2xCH), 127.9 (q), 128.0 (CH), 128.1 (CH), 128.2 (2xCH), 128.3 (2xCH), 128.4 (2xCH), 128.6 (2xCH), 129.1 (CH), 129.2 (2xCH), 131.5 (CH), 134.2 (CH), 136.0 (quat.), 139.3 (quat.), 140.9 (quat.), 148.0 (quat.), 172.3 (C=O), 174.1 (C=O).

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References

1. (a) DeSarlo, F. *J. Chem. Soc., Perkin Trans. I*, **1974**, 1951. (b) Grundmann, Ch.; Grunanger P. *The Nitrile Oxides*; Springer-Verlag: Berlin, 1971; p 242.
2. (a) Shiro, M.; Yamakawa, M.; Kubota, T. *Acta Crystallogr*. **1979**, B35, 712. (b) Shiro, M.; Yamakawa, M.; Kubota, T.; Koyama, H. *J. Chem. Soc., Chem. Commun*. **1968**, 1409.
3. Krayushkin, M. M.; Vorontsova, L. G.; Kurella, M. G.; Kalik, M. A. *Russ. Chem. Bull.* **1993**, 42, 689.
4. Confalone, P. N.; Huie, E. M. *Org. React.* **1988**, 36, 1; Torsell, K. B. G. *Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis*; H. Feuer Ed.; VCH Publishers: New York, 1988.
5. Bloch, R. *Chem. Rev.* **1998**, 98, 1407.
6. Fevig, T. L.; Bowen, S. M.; Janowick, D. A.; Jones, B. K.; Munson, H. R.; Ohlweiler, D. F.; Thomas, C. E. *J. Med. Chem.* **1996**, 39, 4988.
7. Eberbach, W.; Roser, J. *Tetrahedron Lett.* **1987**, 28, 2689.
8. Lachman, *Org. Synth*; Coll: 1943; Vol. 2, p 70.
9. Liu, K.-C.; Shelton, B. R.; Howe, R. K. *J. Org. Chem*. **1980**, 45, 3916.
10. (a) Groundwater, P. W.; Nyerges, M. *Adv. Het. Chem.* **1999**, 73, 97. (b) Arany, A.; Bendell, D.; Groundwater, P. W.; Garnett, I.; Nyerges, M. *J. Chem. Soc. Perkin Trans. 1,* **1999**, 2605.

11. Eberbach, W.; Buchardt, B.; Trostmann, *U. Tetrahedron Lett.* **1979**, 19, 4049. (b) O'Shea, D. F.; Sharp, J. T. *J. Chem. Soc. Perkin Trans. 1,* **1997**, 3025.
12. Cullen, K. E.; Sharp, J. T. *J. Chem.Soc., Perkin Trans. I*, **1993**, 2961.
13. Sheldrick, G. M. *Acta Crystallogr. Sect. A*, **1990**, 46, 467.
14. Sheldrick, G. M. SHELXL-93: *Program for Crystal Structure Refinement*; University of Göttingen: Germany.