Tetrahedron Vol 39, No 22, pp. 3833 to 3841, 1983
Printed in Great Britain

0040-4020/83 $3.00 + .00
Pergamon Press Ltd.

C-SUBSTITUTION REACTIONS OF *C,N*-DIARYL NITRONES.

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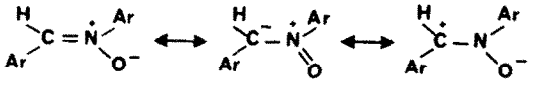
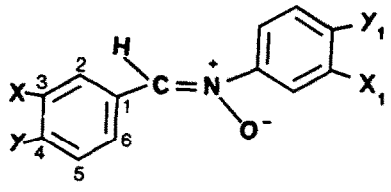
(*Received in UK* 26 *July* 1983)

Abstract- *C,N*-Diaryl nitrones react rapidly with *N*-bromosuccinimide in an aprotic solvent to yield among other products, the **E** and **Z** isomers of the *C*-succinimidyl substituted nitrones and a small amount of the corresponding hydroxamic acid. The stereochemistry of the *C*-succinimidyl nitrones was confirmed by an X-ray structure determination of the *C,N*-(dimethoxyphenyl) derivative **8e**. In the presence of the base DABCO the formation of hydroxamic acids is suppressed and the **Z** *C*-succinimidyl nitrone forms more rapidly than the more stable **E** isomer. Several mechanistic rationalisations of this observed stereochemistry are discussed.

The functionalisation of *C,N*-diaryl nitrones at the α position has considerable synthetic utility, since these compounds are potential precursors for a wide variety of compounds.[1] Such functionalisation can in principle be accomplished by either nucleophilic or electrophilic substitution at the α carbon atom of the nitrone, *via* either of the two canonical forms shown below.



Several reagents [*e.g.* $Pb(OAc)_4$[2], $KMnO_4$[3] or $FeCl_3$[4]] have in the past been used in this way to generate hydroxamic acids from nitrones, but these reactions have limitations in the range of substrates that can be functionalised. Attempted electrophilic substitution at the α carbon of the nitrone **1a** with *N*-bromosuccinimide or bromine has been previously reported[5] to lead to the formation of *N*-(*p*-bromophenyl), *C*-phenyl nitrone (**2**) and its decomposition products.



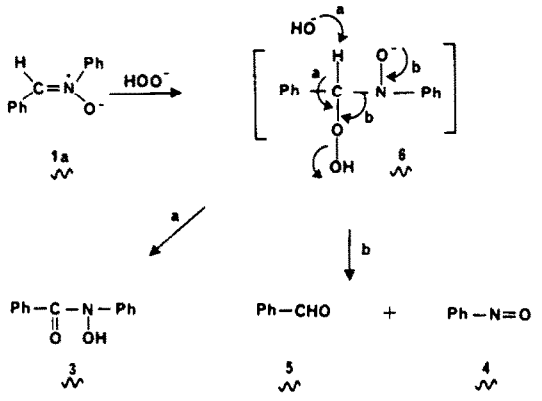
	X	Y	X_1	Y_1
1a	H	H	H	H
1b	H	Br	H	H
1c	H	NO_2	H	H
1d	OMe	OMe	H	H
1e	OMe	OMe	OMe	OMe

We report in this paper our investigations into the reactions of diaryl nitrones with hydrogen peroxide and *N*-bromosuccinimide (NBS).

RESULTS AND DISCUSSION

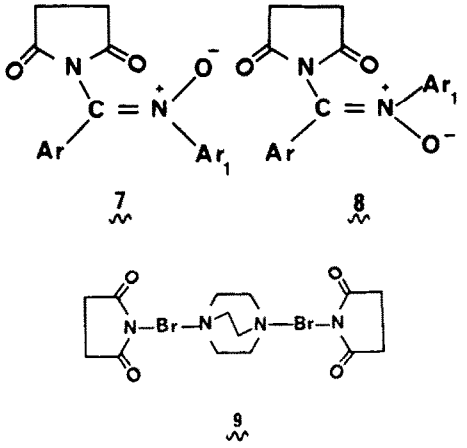
Reaction of Nitrones with H_2O_2— On treatment with aqueous alkaline hydrogen peroxide at -30° to -50°C, *C,N*-diphenyl nitrone [**Z** *N*-phenylmethylene benzeneamine *N*-oxide] (**1a**) yielded rapidly but in minor amounts, the hydroxamic acid **3** (5-10%), the major products being nitrosobenzene **4** and benzaldehyde **5**. The formation of the products could be

rationalised on the basis of two concurrent reactions (path **a** and **b**) involving the common intermediate **6** (Scheme 1).



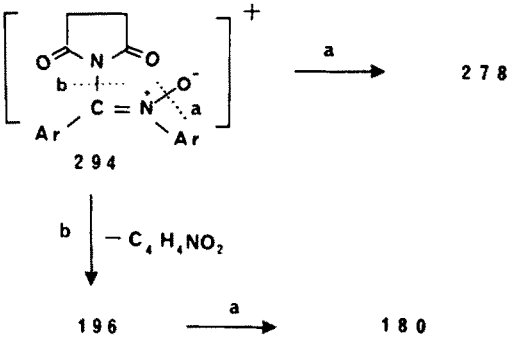
Scheme 1

Reaction of Nitrones with N-Bromosuccinimide— Contrary to an earlier report[5] we have found that *N*-bromosuccinimide reacted rapidly (30 min.) at room temperature with **1a** in dry benzene to give a variety of products (t.l.c.) from which the compounds **7a**, **8a** and **3** were isolated in yields of 20%, 24% and 4% respectively. The results obtained with various nitrones are collected in Table 1.



The same reaction, when conducted in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO), led to a slower (2-3 days) but a much cleaner reaction and the products isolated were initially the isomer **7a** and after thermal equilibration, **8a**. NBS and DABCO are known[6] to form a crystalline 2:1 (NBS:DABCO) complex when mixed in solution. This complex is known[6a] to be a powerful source of "Br^+" and has been recently shown[6b] to contain a linear N-Br-N bridge (*e.g.* **9**) in which the N-Br bonds are longer and the bromine more electrophilic than in NBS itself.

The structures **7a** and **8a** attributed to the products are based on the following evidence. The infra-red spectra of compounds **7a** and **8a** both contained bands at 1785 and 1725 cm^{-1} strongly suggesting the incorporation of the succinimidyl group into the nitrone molecule. Prominent peaks in the mass spectra of both compounds at m/z 294 (M^+), 278 (M^+ - 16), 196 (M^+ - 98) and 180 (M^+ - 16 - 98) also led to the same conclusion (Scheme 2). A similar fragmentation pattern was observed for all the other compounds synthesised, *e.g.* **7b** - **7e** and **8b** - **8e** from the nitrones **1b** - **1e**.



Scheme 2

The proton spectra of the succinimidyl region of the nitrones **7** and **8** all show a characteristic AA'BB' coupling pattern, with a much larger difference in the chemical shifts between the A and B protons in the case of **8** than **7**. Iterative analysis of the 250 MHz ^1H spectra gave almost exact fits in terms of ABCD spin systems, although the deviation from exact AA'BB' symmetry was small (Figure 1). The spectra were sufficiently second order that in each case the *relative* signs of the coupling constants could be determined (Table 2). These proton spectra are noteworthy in several respects. The presence of complex coupling patterns suggests that there is a significant barrier to rotation of the succinimidyl ring about the C-N bond. For **7c** this complex coupling pattern was observed to persist up to least 100°C, which corresponds to $\Delta G^{\neq}$ of at least 18 kcal.mol^{-1} for the rotation process. The coupling constants of absolute value 18 to 19 Hz (Table 2) can be assigned to the geminal coupling between the two protons in a methylene group. These pairs of protons (*i.e.* A and D or B and C) have different chemical shifts, suggesting that the two faces of the succinimidyl ring have different chemical environments. Thus the suc-

TABLE 1. Physical Properties of the C-Succinimidyl Nitrones 7 and 8

COMPOUND X	Y	X_1	Y_1		Yield(7+8)[c] (%)	m.p. (°C)	I.R.(KBr) (cm^{-1})	^1H NMR ($CDCl_3$) δ (ppm)	m/e[d] (M^+)	(M^+-O)	($M^+-C_4H_4NO_2$)	($M^+-C_4H_4NO_2$-O)
H	H	H	H	7a	56	≈ 130[a]	1785, 1725	7.36-7.17 (10H, m, ArH) 3.17-2.81 (4H, m, $-CH_2-CH_2-$)	294	278	196	180
				8a		170-172	1785, 1725	8.46-7.88 (2H, m, ArH) 7.50-7.41 (8H, m, ArH) 2.98-2.18 (4H, m, $-CH_2-CH_2-$)	"	"	"	"
H	Br	H	H	7b	60	92-102[a]	1785, 1720	7.36-6.95 (9H, m, ArH) 3.11-2.78 (4H, m, $-CH_2-CH_2-$)	373	357	275	259
				8b		102-104	1792, 1723	7.43-7.29 (8H, m, ArH) 7.00 (1H, d, J 3Hz, ArH) 3.09-2.86 (4H, m, $-CH_2-CH_2-$)	"	"	"	"
H	NO_2	H	H	7c	83	(a)	1788, 1723	8.07 (2H, d, J 8Hz, ArH) 7.42-7.36 (7H, m, ArH) 3.19-2.86 (4H, m, $-CH_2-CH_2-$)	339	323	241	225
				8c		187(dec.)	1790, 1726	8.34 (4H, d, J 2.4Hz, ArH) 7.44 (5H, s, ArH) 2.91-2.29 (4H, m, $-CH_2-CH_2-$)	"	"	"	"
OMe	OMe	H	H	7d	40	(b)	—	—			—	
				8d		186(dec.)	1785, 1730	8.78 (1H, d, J_m 2.1 Hz, 2-H) 7.43 (5H, s, ArH) 7.12 (1H, dd, J_o 8.7 Hz, J_m 2.1 Hz, 6-H) 6.89 (1H, d, J_o 8.7 Hz, 5-H) 3.98 (3H, s, CH_3O) 3.94 (3H, s, CH_3O) 2.94-2.19 (4H, m, $-CH_2-CH_2-$)	354	338	256	240
OMe	OMe	OMe	OMe	7e	64	(b)	—	—			—	
				8e		185-190 (dec.)	1785, 1730	8.77 (1H, d, J_m 2.2 Hz, 2-H) 7.14-6.75 (5H, m, ArH) 3.96, 3.93, 3.90, 3.86 (4 x 3H, 4S, 4 x CH_3O) 2.95-2.29 (4H, m, $-CH_2-CH_2-$)	414	398	316	300

(a) On heating compounds (7) isomerise slowly to (8)

(b) Detected only on t.l.c. of the reaction mixture, but on attempted crystallisation isomerised to (8)

(c) Crude yield

(d) Accurate mass measurement for (M^+) confirmed the molecular formulae.

cinimidyl ring must be approximately orthogonal to the plane of the nitrone C=N−O atoms, and the slight distortions from AA'BB' symmetry suggests that the molecules may not have an exact plane of symmetry. Since this behaviour is shown by both the **Z** and **E** nitrones (**7** and **8**) any steric effects that might cause this cannot be due to the *N*-aryl group and are more probably due to the *C*-aryl group. This aryl group is known to be approximately co-planar with the nitrone C=N−O plane in *C,N,N*-triphenyl nitrone[7] and if this is so in **7** or **8** hindered rotation of the succinimidyl ring would not be unexpected. As usual in a planar 5-membered ring,[8] J^{trans} is less than J^{cis}. The chemical shifts of the two protons on one face of the succinimidyl ring in **8** are shifted upfield by *ca* 0.4 ppm compared with **7**, and we interpret this as resulting from these two protons being close to the shielding face of the *N*-aryl group. This allows the assignment of the **E** configuration to **8**, and implies that the *N*-aryl group is also twisted significantly out of the nitrone plane.

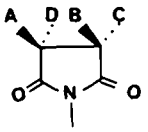


Table 2. ^{1}H NMR Constants for the Succinimidyl Region of the Nitrones **7** and **8**.

	8c	8e	7c
δ_A, ppm	2.402	2.448	2.954
δ_B	2.403	2.448	2.954
δ_C	2.838	2.818	3.073
δ_D	2.838	2.818	3.073
J_{AB}, Hz	10.26	10.07	10.18
J_{AC}	4.69	5.41	4.30
J_{AD}	-18.40	-18.16	-18.63
J_{BC}	-19.00	-18.08	-18.85
J_{BD}	4.96	5.40	5.11
J_{CD}	10.31	9.98	10.16

To test these conclusions, and also to assign unambiguously the **E** configuration to **8** and the **Z** configuration to **7**, X-ray analysis of the tetramethoxy-nitrone derivative **8e** was undertaken. The results (Figure 2a) confirmed the conclusions based on the n.m.r. evidence, showing that the *C*-aryl group is approximately co-planar with the plane of the C=N−O atoms, and that the *N*-aryl and *C*-succinimidyl groups are approximately orthogonal to this plane. The positional co-ordinates of the non-hydrogen atoms are given in Table 3, while Table 4 shows the bond lengths and bond angles about the nitrone moiety.

Table 3. Fractional coordinates of the non-hydrogen atoms of **8e**, with estimated standard deviations in parentheses.

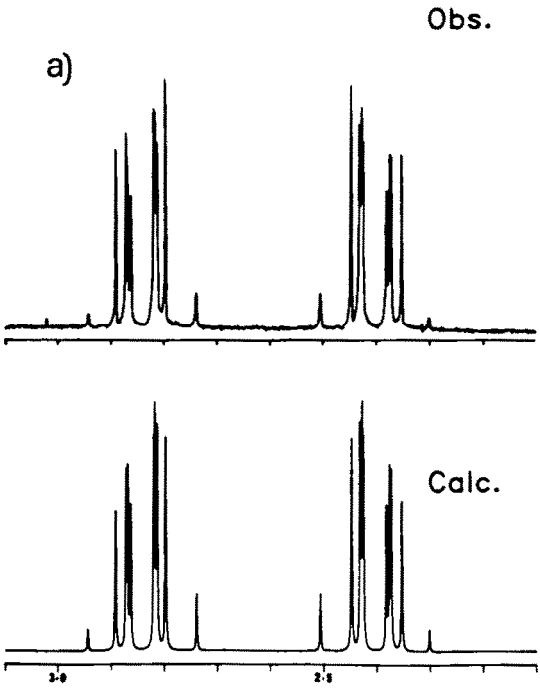
Atom	*x*	*y*	*z*
O(1)	-0.0836(2)	0.5967(2)	0.13500(9)
N(1)	-0.0285(2)	0.4926(2)	0.16790(10)
C(1)	0.0301(2)	0.4854(2)	0.24209(11)
C(11)	0.0407(2)	0.5916(2)	0.29774(11)
C(12)	-0.0335(2)	0.7031(2)	0.28123(11)
C(13)	-0.0214(2)	0.7999(2)	0.33600(12)
O(13)	-0.0910(2)	0.9098(2)	0.32614(9)
C(131)	-0.1739(3)	0.9340(3)	0.25236(15)
C(14)	0.0646(2)	0.7886(2)	0.40891(12)
O(14)	0.0655(1)	0.8890(2)	0.45878(9)
C(141)	0.1474(3)	0.8810(3)	0.53531(15)
C(15)	0.1370(2)	0.6798(2)	0.42503(12)
C(16)	0.1254(2)	0.5818(2)	0.37028(11)
C(21)	-0.0367(2)	0.3835(2)	0.11392(12)
C(22)	-0.1377(2)	0.3058(2)	0.09509(12)
C(23)	-0.1543(2)	0.2131(2)	0.03700(12)
O(23)	-0.2487(2)	0.1300(2)	0.01279(11)
C(231)	-0.3429(3)	0.1453(4)	0.04593(22)
C(24)	-0.0696(2)	0.1996(2)	-0.00211(12)
O(24)	-0.0952(1)	0.1067(2)	-0.05897(8)
C(241)	-0.0090(2)	0.0872(3)	-0.09878(14)
C(25)	0.0293(2)	0.2780(2)	0.01816(13)
C(26)	0.0459(2)	0.3715(2)	0.07653(14)
N(31)	0.0864(2)	0.3627(2)	0.26794(9)
C(32)	0.0365(2)	0.2668(2)	0.30345(15)
O(32)	-0.0607(2)	0.2764(2)	0.31054(13)
C(33)	0.1253(2)	0.1575(3)	0.32831(17)
C(34)	0.2285(2)	0.1950(2)	0.30110(16)
C(35)	0.2007(2)	0.3286(2)	0.26651(13)
O(35)	0.2615(1)	0.3988(2)	0.24082(10)

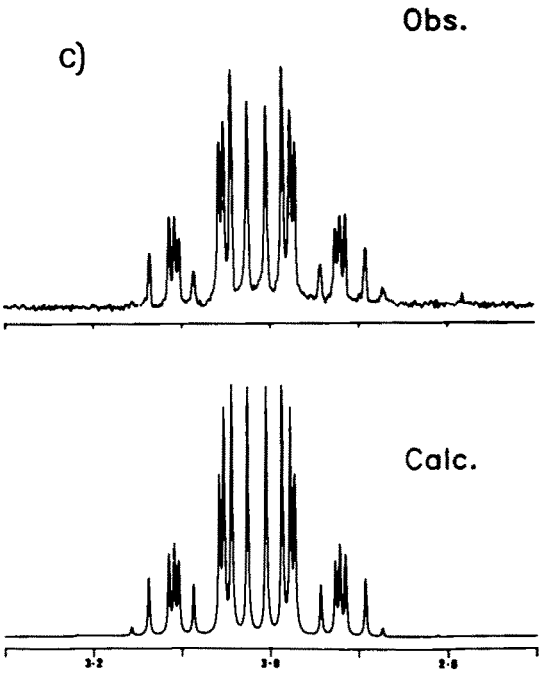
Table 4. The more important bond lengths (Å) and bond angles (°) of **8e**, with estimated standard deviations in parentheses.

N(1)-C(1) 1.309(2)	C(1)-C(11) 1.455(3)
N(1)-O(1) 1.286(2)	C(1)-N(31) 1.421(2)
N(1)-C(21) 1.461(3)	
O(1)-N(1)-C(1) 123.5(2)	
N(1)-C(1)-C(11) 125.1(2)	
O(1)-N(1)-C(21) 113.2(2)	
N(1)-C(1)-N(31) 115.5(2)	
C(1)-N(1)-C(21) 123.3(2)	
C(11)-C(1)-N(31) 119.4(2)	

A space filling diagram (Figure 2b) shows that interaction between the carbonyl groups of the succinimidyl ring and the *o*-hydrogens from the *C*-aryl

Figure 1. Observed ^{1}H n.m.r. spectra for the succinimidyl region of (*a*) **8c**, (*b*) **8e**, and (*c*) **7c**, and the corresponding ABCD spectra calculated using the parameters reported in Table 2.





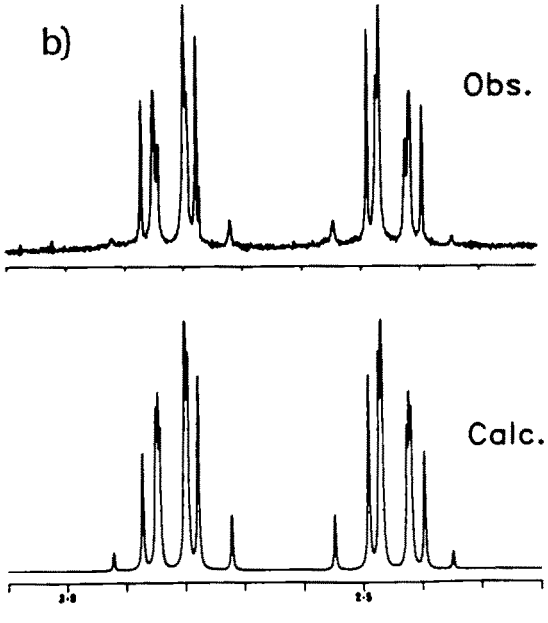
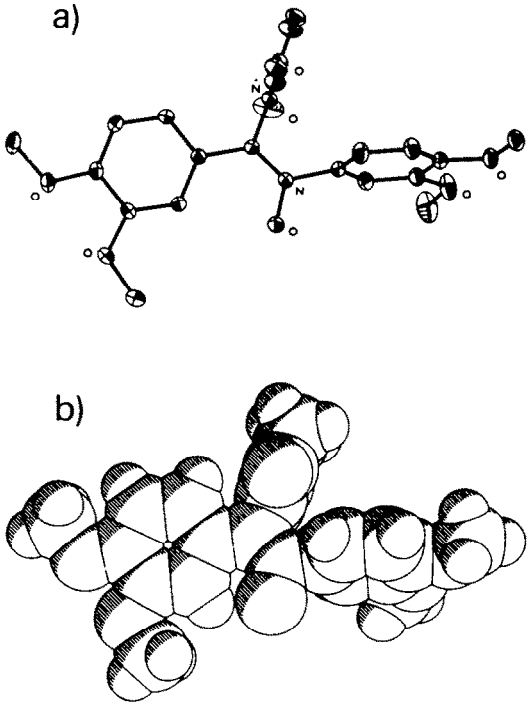


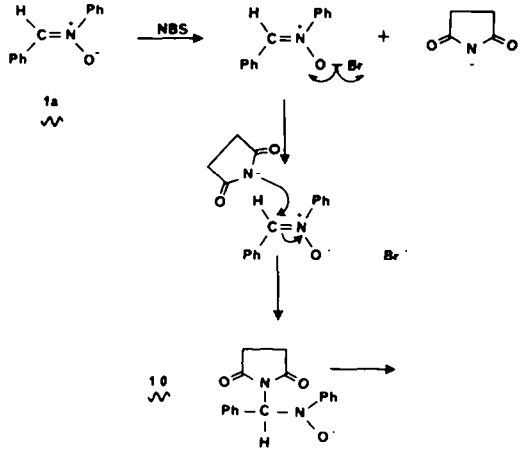
Figure 2. X-Ray structure of **8e** showing (*a*) the thermal ellipsoids and (*b*) shown as a space filling representation.



ring would indeed prevent free rotation.

On heating compound **7a** in toluene for 3 days conversion to **8a** was observed. This is consistent with evidence which suggests that the most stable configuration of *C,N*-diaryl nitrones is with the two aryl groups *trans* with respect to each other[9] The thermal isomerisation **7** to **8** could also be detected in attempted recrystallisations of compounds **7d** and **7e**, which afforded the isomers **8d** and **8e** respectively, and is probably the reason for the ill-defined melting points of the pure compounds **7**. This facile thermal isomerisation may well account for the high final proportion of **8d** and **8e** in the reaction of **1** with NBS in the presence of DABCO. The presence of electron-donating substituents in the aromatic rings of the nitrone must significantly lower the energy barrier of **Z** to **E** interconversion, since the activation energy for the thermal isomerisation of nitrones with no such aryl substituents is quite high (*e.g.* **Z** *C*-cyano-*C,N*-diphenyl nitrone[10], 24.6 kcal.mol^{-1}, *N*-benzyl, *C,C*-diaryl nitrones[9], 33.6 kcal.mol^{-1}).

The reaction of **1a** with NBS in benzene, when monitored by e.s.r. spectroscopy, gave rise to a complex spectrum indicating the intermediacy of a nitroxide radical of type **10**[11] (a_N = 10.8G, a_H = 2.5G). Decomposition and/or disproportionation could lead to the array of products obtained (*cf* Scheme 3).



Scheme 3

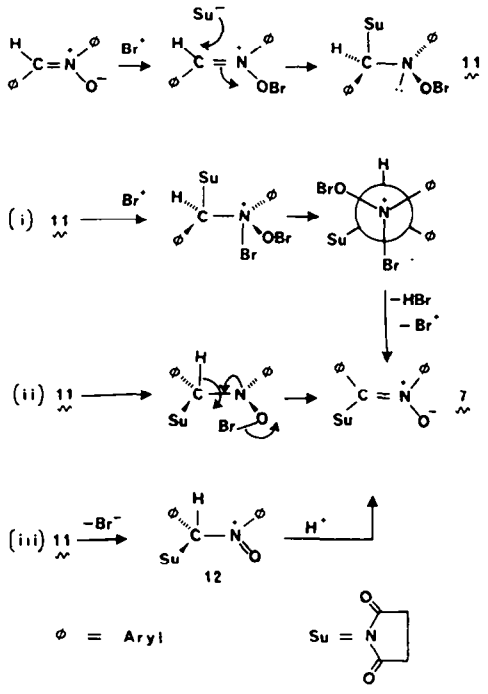
However, when the same reaction was conducted in the presence of DABCO no detectable e.s.r. spectrum was observed and the product formed initially in each case was the *less stable* **Z** isomer **7**. The reaction was also carried out in tetrachloroethylene, a solvent which is too weakly nucleophilic to react with a Br^+ species but which does react with bromine atoms. The reaction took twice as long, possibly due to the reduced solubility of the complex **9** in this solvent, but the formation of the same array of products was still observed. This tends to suggest that in the presence of DABCO, radical pathways are suppressed and an ionic pathway operates.

Any mechanistic rationalisation of this reaction must explain the initial predominant formation of the *less* stable **Z** nitrone **7** rather than **8**. We envisage at least three mechanisms as being possible (Scheme 4).

The initial substrate is assumed to be the more stable **Z** nitrone **1**, and not the less stable **E** isomer.[9] We postulate that initial bromination on the oxygen is followed by nucleophilic addition involving the succinimidyl moity to give an intermediate **11** in which the lone pair that develops on the nitrogen atom of the nitrone and the incoming nucleophile are now antiperiplanar. Such stereoelectronic effects have ample precedence.[12] Several mechanistic pathways are now possible (Scheme 4). (*i*) Quaternisation at the hydroxylamine nitrogen with a second "Br^+" is assumed to occur with no racemisation at the nitrogen centre. This seems a reasonable assumption, since hydroxylamines are known[13] to have a relatively high barrier to inversion at nitrogen ($\Delta G^{\ddagger}$ *ca* 14 kcal.mol^{-1}). Stereospecific *antiperiplanar* elimination of HBr would eventually result in exclusive formation of the *less* stable nitrone **7**. (*ii*) The intermediate **11** could undergo a concerted *syn* elimination of HBr *via* a 5-centre transition state. Such eliminations *via* 4 and 6-centre transition states with all carbon skeletons are known to have relatively high activation energies[14], but it is possible that the presence of two heteroatoms would render such a 5-centre elimination facile. (*iii*) The preceding mechanism could occur in a stepwise fashion, involving unimolecular elimination of Br· from **11** to give the species **12**, followed by a base catalysed deprotonation. The observed stereochemistry of the product **7** requires that a stabilising interaction between one of the carbonyl groups and the N=O group be present in the transition state for deprotonation of **12**. This stabilisation cannot be present in **7** itself (since it is *less*

stable than **8**); such selectivity could be a result of the bond angle at the electrophilic carbon in an early transition state for deprotonation (*ca* 109°) which allows such an interaction, and an angle in the product nitrone (*ca* 120°) which prohibits it.

Further mechanistic investigations of the unusual stereochemistry of these reactions are in progress.



Scheme 4

EXPERIMENTAL

^{1}H n.m.r. spectra were recorded in $CDCl_3$, unless otherwise stated, with tetramethylsilane as an internal standard on a JEOL JNM-PS-100 or a Bruker WM 250 spectrometer. I.r. spectra were recorded on a Perkin Elmer 457 instrument. Melting points were determined with a Kofler hot stage apparatus and are uncorrected. T.l.c. was carried out on silica gel (GF_{254}) (0.5 mm layer for preparative work, p.t.l.c.). Mass spectra were obtained on an A.E.I. MS-9 (70 eV) and accurate mass measurements were carried out on a VG Micromass 7070B spectrometer. E.s.r. spectra were obtained on a Bruker ER 200tt spectrometer.

The nitrones required for the present study were prepared by condensation of the appropriate hydroxylamine and the aromatic aldehyde in ethanol under reflux.[15] When the aromatic hydroxylamine proved to be too unstable (*e.g.* polyalkoxy hydroxylamines) the nitrone was prepared by condensing the aromatic aldehyde with the hydroxylamine generated *in situ* by reduction of the corresponding aromatic nitro compound, in a heavily buffered solution, involving a modification of Wiemann and Glacet's method.[16]

General Procedure for the Synthesis of Nitrones— To the aromatic nitro compound (1 mmole) and the appropriate aldehyde (1 mmole) in a mixture of methanol:water:tetrahydrofuran (2:1:6) (10 mmoles of acetic acid, 5 mmoles of sodium hydroxide), and kept at -2 to -8°C was added slowly with stirring zinc dust (2 mmoles). The reaction was monitored by t.l.c. for the complete disappearance of the starting materials. The mixture was diluted with brine and extracted with dichloromethane. The organic phase was dried (Na_2SO_4), and after filtration and removal of the solvent under reduced pressure, the residue obtained was recrystallised from benzene:*n*-hexane.

The following nitrones were thus prepared:

N-phenyl-*C*-phenyl nitrone (**1a**), m.p. 109.5-110.5° (Lit.[15] m.p. 112);

N-phenyl-*C*-(*p*-bromophenyl) nitrone (**1b**), m.p. 162-164° (Lit.[17] m.p. 161.5);

N-phenyl-*C*-(*p*-nitrophenyl) nitrone (**1c**), m.p. 187-189° (Lit.[15] m.p. 189);

N-phenyl-*C*-(3,4-dimethoxyphenyl) nitrone (**1d**), m.p. 95-97°, ν_{max} (cm^{-1}) (KBr) 1502, 1270, δ ($CDCl_3$, TMS) 8.57 (1H, d, J 1.5Hz, 2-H), 7.87 (1H, s, C-H), 7.78 (2H, dd, J_o 8.1Hz, J_m 1.5Hz, 2'-H, 6'-H), 7.64 (1H, dd, J_o 8.1Hz, J_m 1.5Hz, 6-H), 7.49-7.46 (3H, m, 3'-H, 4'-H, 5'-H), 6.96 (1H, d, J_o 8.1Hz, 5-H), 4.00 (6H, 2s, 2x OMe).

(Found: C, 70.12; H, 5.88; N, 5.47%. $C_{15}H_{15}NO_3$ requires C, 70.02; H, 5.87; N, 5.45%).

N-(3',4'-dimethoxyphenyl)-*C*-(3,4-dimethoxyphenyl) nitrone (**1e**), m.p. 131.5-132.5, ν_{max} (cm^{-1}) (KBr) 1512, 1280, δ ($CDCl_3$, TMS) 8.58 (1H,d, J_m 2 Hz, 2-H), 7.85 (1H,s, *C*-H), 7.48 (1H, dd, J_o 8.1 Hz, J_m 2Hz, 6-H), 7.37 (1H, d, J_m 2.2 Hz, 2'-H),

7.22 (1H, dd, J_o 8.5 Hz, J_m 2.2 Hz, 6'-H), 6.84 (1H, d, J_o 8.1 Hz, 5-H), 6.76 (1H, d, J_o 8.5 Hz, 5'-H), 4.00, 3.96, 3.94 (12H, 3s, 4xOMe).

(Found: C, 64.04; H, 6.1; N, 4.2%. $C_{17}H_{19}NO_5$ requires C, 64.35; H, 5.9; N, 4.4%).

Reaction between 1a and hydrogen peroxide— A vigorously stirred mixture of *N*-phenyl-*C*-phenyl nitrone (94 mg) and aqueous hydrogen peroxide (0.8 ml; 30%) and methanol (2ml) was treated with aq. NaOH (5N, 0.1ml) at -30°C. After completion of the reaction (*ca.* 5 min., t.l.c. control) examination of the crude reaction mixture (t.l.c.) revealed the presence of benzaldehyde (positive DNP test, identical Rf with authentic material), nitrosobenzene (identical with an authentic sample) and the hydroxamic acid **3** (in 5-10%).

Reaction between 1a and N-bromosuccinimide— To *N*-phenyl-*C*-phenyl nitrone (200 mg) in dry benzene (5 ml), protected from light, was added with stirring *N*-bromosuccinimide (174 mg) at room temperature in one lot. After the exothermic reaction had subsided (5 min.) the mixture was stirred for a further 30 min. and filtered. The filtrate was evaporated to dryness under reduced pressure to give a gum which was purified (p.t.l.c.; SiO_2, CH_2Cl_2) to give *N*-phenyl-benzohydroxamic acid (**3**) (8 mg; identical with an authentic sample (m.p., m.m.p., Rf, ^1H n.m.r.)), **7a** (41 mg, colourless needles, m.p. 130°C) and **8a** (48 mg, colourless needles, m.p. 170-172°C).

Reaction between Nitrones and N-bromosuccinimide in the presence of DABCO— To the nitrone (1 equiv.) dissolved in 12 ml of dry tetrahydrofuran (other solvents that can be used without significant reduction in yields are benzene, dichloromethane or chloroform) was added DABCO (2 equiv.) and NBS (2 equiv.) and the reaction mixture, protected from light, was left stirring at room temperature until the disappearance of the starting material was observed (t.l.c. control; 2-3 days). The product was exclusively **7** (t.l.c.) in the initial stages of the reaction, but the percentage of isomer **8** (particularly **8d** and **8e**) increased with time. The reaction mixture was filtered and the filtrate evaporated to yield a semicrystalline solid from which the isomers **7** and **8** were separated (p.t.l.c.; SiO_2, CH_2Cl_2:MeOH, 100:2). The isomers **7** had a markedly lower Rf value than isomers **8**. The pure isomers were further purified by crystallisation from a mixture of benzene, dichloromethane and *n*-hexane. The physical data of the compounds **7** and **8** thus prepared are collected in Table 1.

Computational Procedures— The iterative NMR analysis of the ^1H n.m.r. spectra was carried out using an interactive graphical program written by J. C. Burgess and H. S. Rzepa. The r.m.s. errors between the calculated and the observed line frequencies were similar to the digital resolution used in recording the spectra (0.15Hz/point).

Crystallographic Studies on 8e— X-ray intensity data were collected using a Nicolet R3m/Eclipse S140 diffractometer system. Graphite monochromated Cu-Kα radiation was used with the Omega-scan measuring routine. Intensities were measured for 2766 independent reflections ($2<2\vartheta<104°$), of which 2317 were judged to be observed ($I > 3\sigma(I)$). Unit-cell dimensions and the orientation matrix were based on 21 automatically centred reflections.

Crystal Data.

$C_{21}H_{22}N_2O_7$, mol. wt. 414.4, monoclinic, a = 11.778(1), b = 10.158(1), c = 18.119(2) **A**, β = 108.06(1)°, U = 2061.0**A**^{3} (at 19°C), space group $P2_1/n$ (no. 14), Z = 4, D_c = 1.333 g cm^{-3}, F(000) = 871.9, μ(Cu-Kα) = 8.1 cm^{-1}.

Structure Solution and Refinement.

The structure was solved by direct methods. All non-hydrogen atoms were refined anisotropically, the methyl hydrogen atoms were refined as rigid groups with an isotropic factor for each group of three hydrogens, and the ring hydrogen atoms were placed at calculated positions and allowed to ride on their parent carbon atoms. The SHELXTL program system[18] was used throughout the calculations, and atomic scattering factors were taken from reference 19. Least squares refinement was by the block cascade method, typical of the SHELXTL system. The final R factor was 0.039, and in the final difference Fourier synthesis the largest remaining peak was 0.14e**A**^{2}.

Tables of anisotropic temperature factors, hydrogen co-ordinates, and bond lengths and bond angles for the whole molecule, have been deposited with the

Cambridge Crystallographic Data Centre.

ACKNOWLEDGEMENTS. We thank the Foundation Calouste Gulbenkian, the Instituto Nacional de Investigação Científica for partial financial support, NATO for grant No. 1971, Junta Nacional de Investigação Científica e Tecnológica for grant No. 117-79-78, and the S.E.R.C for the diffractometer system. The interactive NMR analysis was carried out on the CDC Cyber 174 computer at Imperial College Computer centre and the text was set using the program MTROFF and the Imperial College Autologic micro-5 phototypesetter.

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