Dynamic Stereochemistry of Imines and Derivatives. Part 11.[1] Synthesis and Stereochemistry of (*E*)- and (*Z*)-Nitrones

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A range of hindered nitrones [ArCR:N(O)R'; R = H or alkyl] has been synthesized and their stereochemistry has been assigned. The relative proportions of (*E*)- and (*Z*)-nitrone isomers at equilibrium were found to be both substituent- and solvent-dependent. The mechanism of the oxidation of imines to nitrones by peroxy-acid is discussed in relation to the reactant and product stereochemistry. The acidic hydrolysis of *N*-(pentamethylphenylmethylene)alkylamine *N*-oxides has been used as a general synthesis of *N*-alkylhydroxylamines.

NITRONES may be synthesized by several routes,[2] including oxidation of an imine by peroxy-acid, rearrangement of an oxaziridine, and condensation of an aldehyde or a ketone with an *N*-alkylhydroxylamine. All these methods have been used to synthesize the nitrones employed in the present work.

The imines (1)—(9) (Table 1) were obtained from condensation of methyl-substituted benzaldehydes with the corresponding amines. Most were found to exist as a mixture of *E*- and *Z*-isomers in $CDCl_3$, and since imines isomerize rapidly at ambient temperature[3,4] the ratio of isomers given in Table 1 represents the equilibrium distribution. Oxidation of the imines (1)—(9) with *m*-chloroperbenzoic acid (MCPBA) occurred rapidly at room temperature in CH_2Cl_2 to give either an isomeric mixture of nitrones [(14)—(18) and (20)] or a single nitrone isomer [(19), (21), and (22)] (Table 2).

Geometric isomerism in nitrones (imine *N*-oxides) was reported as early as 1918, when *N*-[phenyl-(4-tolyl)-methylene]methylamine *N*-oxide was found to exist in stable, separable *E*- and *Z*-forms.[5] Discrete *E*- and *Z*-isomers were later found in other di-*C*-aryl (R = Ar)[6] and *C*-cyano-*C*-aryl (R = CN)[7,8] nitrones. Although (*E*)- and (*Z*)-nitrone isomers were well authenticated for cases with R ≠ H (*i.e.* 'ketonitrones') prior to the preliminary communication of the present work,[9] previous reports[10] on the detection and isolation of both stable (*E*)- and (*Z*)-nitrone isomers with R = H ('aldonitrones') appear to have been generally discounted.[2,11-13] In view of the detection of both *E*- and

[1] Part 10, W. B. Jennings, S. A. Showiman, M. S. Tolley, and D. R. Boyd, *Org. Magnetic Resonance*, in the press.
[2] J. Hamer and A. Macaluso, *Chem. Rev.*, 1964, **64**, 473.
[3] J. Bjørgo, D. R. Boyd, C. G. Watson, and W. B. Jennings, *J.C.S. Perkin II*, 1974, 757.
[4] J. Bjørgo, D. R. Boyd, C. G. Watson, W. B. Jennings, and D. M. Jerina, *J.C.S. Perkin II*, 1974, 1081.
[5] L. Semper and L. Lichtendstadt, *Ber.*, 1918, **51**, 928.
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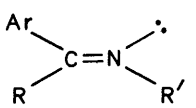
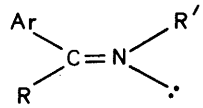
[8] K. Koyana and I. Tanaka, *J. Phys. Chem.*, 1965, **69**, 2545.
[9] J. Bjørgo, D. R. Boyd, and D. C. Neill, *J.C.S. Chem. Comm.*, 1974, 478.
[10] L. I. Smith, *Chem. Rev.*, 1938, **23**, 193 and references therein.
[11] W. D. Emmons, *J. Amer. Chem. Soc.*, 1957, **79**, 5739.
[12] L. W. Boyle, M. J. Peagram, and G. H. Whitham, *J. Chem. Soc.* (*B*), 1971, 1728.
[13] Y. Yoshimura, Y. Mori, and K. Tori, *Chem. Letters*, 1972, 181.

TABLE 1

N.m.r. data and *E*–*Z* isomer ratios of imines [a]



E



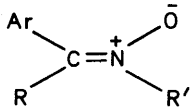
Z

					δ Values for *E*-isomer		δ Values for *Z*-isomer		
	Ar	R′	R	M.p. (°C) [b]	R′	R	R′	R	%Z_e
(1)	2,6-$Me_2C_6H_3$	Me	H		3.51 [c]	8.50	3.04 [c]	8.50	6
(2)	2,4,6-$Me_3C_6H_2$	Me	H		3.50 [c]	8.58	3.03 [c]	8.48	8
(3)	2,3,5,6-Me_4C_6H	Me	H		3.53 [c]	8.50	3.00 [c]	8.50	17
(4)	C_6Me_5	Me	H		3.52 [c]	8.55	3.00 [c]	8.55	21
(5)	C_6Me_5	Et	H	136—138 (sealed tube)	1.33 [d,e]	8.56	1.17 [d,e]	8.56	15
					3.67 [f,g]		3.39 [f,g]		
(6)	C_6Me_5	CH_2Bu^t	H	56—57	1.00 [d]	8.53	0.92 [d]		14
					3.39 [f]		2.85 [f]		
(7)	C_6Me_5	Pr^i	H	157—158	1.29 [d,h]	8.57	1.07 [d,h]	8.57	9
					3.57 [i,j]		[k]		
(8)	C_6Me_5	1-Ad [l]	H	157	1.77	8.58			<1
(9)	C_6Me_5	Bu^t	H	52—54	1.35	8.55			<1
(10)	4-NO_2·C_6H_4	Me	H		3.60	8.40			<1
(11)	4-NO_2·C_6H_4	Me	Me		3.41	2.28	3.06	2.28	3
(12)	4-NO_2·C_6H_4	Pr^i	Me		1.23 [d,h]	2.30	1.08 [d,h]	2.30	5
					3.94 [i,j]		[k]		
(13)	4-NO_2·C_6H_4	Bu^t	Me		1.40	2.40	1.03	2.40	2

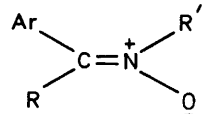
[a] N.m.r. data measured and thermal equilibrations carried out in $CDCl_3$. [b] M.p.s are provided only for new compounds; the corresponding microanalytical data are available as Supplementary Publication No. SUP 21897 (3 pp.). For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1975, Index issue. [c] Previously reported.[4] [d] CH_3. [e] Triplet. [f] CH_2. [g] Quartet. [h] Doublet. [i] CH. [j] Septet. [k] Very low signal intensity. [l] 1-Adamantyl.

TABLE 2

N.m.r. data and *E*–*Z* isomer ratios of nitrones [a]



Z



E

					δ Values for *Z*-isomer		δ Values for *E*-isomer			
	Ar	R′	R	M.p. (°C) [b]	R′	R	R′	R	%E_e	%E^c
(14)	2,6-$Me_2C_6H_3$	Me	H	137—138	3.82	7.52	3.40	7.87	8	86
(15)	2,4,6-$Me_3C_6H_2$	Me	H	166—167 (sealed tube)	3.84	7.48	3.38	7.79	9	85
(16)	2,3,5,6-Me_4C_6H	Me	H	183—185	3.88	7.55	3.40	7.88	15	74
(17)	C_6Me_5	Me	H	198—200	3.89	7.60	3.40	7.92	17	54
(18)	C_6Me_5	Et	H	166—169	1.58 [d,e]	7.64	1.32 [d,e]	7.88	11	39
					3.97 [f,g]		3.55 [f,g]			
(19)	C_6Me_5	CH_2Bu^t	H	182—183	1.18 [d]	7.62			<1	<1
					3.78 [f]					
(20)	C_6Me_5	Pr^i	H	157—158 (sealed tube)	1.49 [d,h]	7.63	1.29 [d,h]	7.83	7	35
					4.23 [i,j]		[k]			
(21)	C_6Me_5	1-Ad [l]	H	205—206 (sealed tube)	1.75	7.63			<1	<1
(22)	C_6Me_5	Bu^t	H	80 (decomp.)	1.62	7.67			<1	<1
(23)	4-NO_2·C_6H_4	Me	H	217—218	3.93	7.51			<1	<1
(24)	4-NO_2·C_6H_4	Me	Me	147—148			3.75	2.49	>99	>99
(25)	4-NO_2·C_6H_4	Pr^i	Me	158—159	1.50 [d,h]	2.67	1.38 [d,h]	2.42	87	>99
							4.40 [i,j]			
(26)	4-NO_2·C_6H_4	Bu^t	Me	129—130	1.70	2.68	1.37 [d]	2.37	79	>99
(27)	2,6-Cl_2-4-NH_2·C_6H_2	Me	H		3.94	7.50	3.58	7.78	8	34

[a] N.m.r. data measured and thermal equilibrations carried out in $CDCl_3$. [b] M.p.s are provided only for new compounds; the corresponding microanalytical data are available in the Supplementary Publication (see footnote *b*, Table 1). [c] %*E*-isomer found directly after synthesis. [d] CH_3. [e] Triplet. [f] CH_2. [g] Quartet. [h] Doublet. [i] CH. [j] Septet. [k] Very low signal intensity. [l] 1-Adamantyl.

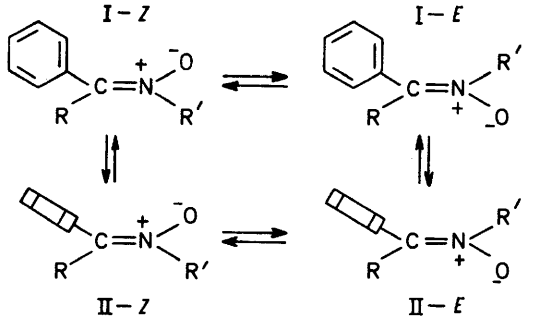
Z-isomers of imines [4] and the relatively high barrier to isomerization of (*E*)- and (*Z*)-ketonitrones,[8,14] it appeared possible that earlier attempts to obtain both aldonitrone isomers may have been thwarted by an unsuitable choice of substituents around the nitrone group. A similar rationalization appeared possible for *C*-alkyl-*C*-aryl ketonitrones where only one isomer was formed.[13]

The aldonitrones (19), (21), and (22) obtained by oxidation of the corresponding imines (6), (8), and (9) with MCPBA showed n.m.r. data consistent with a *Z*-configuration (Table 2). However, the aldonitrones (14)—(18) and (20) obtained by the same method from the aldimines (1)—(5) and (7) respectively, were each found to be a mixture of the anticipated *Z*-isomer and a second product identified as the *E*-isomer on the basis of chemical shift positions, peak multiplicity, and the thermal isomerization of *E*- and *Z*-isomers in $CDCl_3$ solution which was facilitated by a trace of benzoic acid.

The assignment of stereochemistry to the aldonitrones (14)—(22) (Table 2) was based upon a comparison of δ values with those obtained for other *C*-aryl aldonitrones [*e.g.* (23)] for which a *Z*-configuration had been established by a range of independent unequivocal methods.[2,12,15] Thus, (*E*)-aldonitrones [by analogy with the (*Z*)-aldimines; Table 1] showed upfield n.m.r. signals for the substituents R′ [as compared with the (*Z*)-aldonitrones] owing to the shielding influence of the proximate aryl ring. The upfield shift of the methine proton (R) signal of the aldonitrones (14)—(23), relative to the corresponding aldimines (1)—(10), is in concurrence with previous studies on heterocyclic *N*-oxides.[16,17] Similarly, the consistent downfield shift of the signal due to the methine proton in the (*E*)-aldonitrones (relative to the *Z*-isomer) is in agreement with an earlier proposal that protons adjacent to a negatively charged oxygen atom of an *N*-oxide will resonate at lower field.[18,19] The methine proton shift will also be affected by the conformation of the aryl ring which, however, should be almost orthogonal for both *E*- and *Z*-isomers of (14)—(22).

Oxidation of the imines (1)—(5) and (7) yielded both (*E*)- and (*Z*)-aldonitrones. The syntheses of (14)—(17) by condensation of the corresponding aldehydes with *N*-methylhydroxylamine gave <1, <1, 27, and 86% *E*-isomer, respectively. From these results it appeared that the formation of the less stable *E*-isomer was facilitated by substitution at the 2- and 6-positions of the aryl ring. Accordingly, the original synthesis [20] of the nitrone (27) from 3-amino-2,6-dichlorobenzaldehyde and *N*-methylhydroxylamine was reinvestigated. Analysis by n.m.r. showed both *E*- and *Z*-isomers to be present. On heating, the proportion of (27*E*) decreased from 34 to 8%. These results now confirm the validity of this early report [20] on the synthesis of (*E*)- and (*Z*)-aldonitrones. It appears, however, that Meisenheimer *et al.*[20] were unable to detect both isomers after heating, owing to the relatively small proportion of *E*-isomer at equilibrium (8%).

The equilibration of the (*E*)- and (*Z*)-nitrones in refluxing $CDCl_3$ (containing a trace of benzoic acid) was monitored by n.m.r. and the results are shown in Table 2 (% E_e). In parallel with the corresponding imines,[4] the aldonitrones (14)—(23) showed a marked preference for a configuration with the methine proton and R′ adjacent (*Z*). The *E*–*Z* configurations and extreme conformations of aldonitrones are shown in Scheme 1. Several factors



SCHEME 1 Dynamic stereochemistry of nitrones

will affect the preferred stereochemistry of the (*E*)- and (*Z*)-aldonitrones at equilibrium, as follows. (i) In aldonitrones (14)—(22) the largest substituents are clearly the *C*-aryl and *N*-alkyl substituents, and the preference for the *Z*-configuration reflects these non-bonded interactions. (ii) Resonance stabilization would favour the coplanar conformations I-*Z* and I-*E*. (iii) Substitution of the 2- and 6-positions of the aryl ring will increase the steric interactions in conformations I-*Z* and I-*E* and will lead to a preference for conformations II-*Z* and II-*E* where these steric effects are minimal. The increase in the proportion of *E*-isomer (8 ⟶ 17% *E*) along the series (14)—(17) is analogous to the trend previously reported for the imines (1)—(4) (6% ⟶ 21% *Z*).[4] This might also be attributed to the buttressing effect of the *m*-methyl substituents, which increases the net steric effect of the *ortho*-substituents in conformations I-*Z* and I-*E*, thus favouring the orthogonal conformations (II-*Z* and II-*E*). (iv) The adjacent negatively charged oxygen atom and aryl group in conformation II-*Z* may experience a repulsive effect which would favour the alternative configuration and conformations. Thus the increase in % *E*-isomer at equilibrium associated with the increase in the number of electron-donating methyl substituents on the aryl ring could originate from an augmentation of the repulsive interaction.

[14] T. S. Dobashi, M. H. Goodrow, and E. J. Grubbs, *J. Org. Chem.*, 1973, **38**, 4440.
[15] D. R. Boyd, W. B. Jennings, R. Spratt, and D. M. Jerina, *Chem. Comm.*, 1970, 745.
[16] G. Englert, *Z. analyt. Chem.*, 1961, **181**, 447.
[17] R. K. Harris, A. R. Katritzky, S. Øksne, A. S. Bailey, and W. G. Paterson, *J. Chem. Soc.*, 1963, 197.
[18] K. Koyano and H. Suzuki, *Bull. Chem. Soc. Japan*, 1969, **42**, 3306.
[19] E. J. Grubbs, R. J. Milligan, and M. H. Goodrow, *J. Org. Chem.*, 1971, **36**, 1780.
[20] J. Meisenheimer, W. Theilacker, and O. Beisswenger, *Annalen*, 1932, **495**, 253.

Although the factors (i)—(iv) may each influence the equilibrium position in the aldonitrones (14)—(22), normal steric effects appear to dominate in all cases. With the exception of the aldonitrone (19) the steric effects in these nitrones are generally analogous to those shown by the corresponding imines (4)—(9). Space-filling models of the anomalous neopentyl-substituted nitrone (19) indicate considerable non-bonded interactions between the t-butyl group and the aryl ring or oxygen atom in the *E*-isomer (even in the least hindered conformation). These interactions may be less severe in the corresponding imine (6*Z*) owing to the absence of the oxygen atom. The non-bonded interactions were also considerable between the *N*-t-butyl or *N*-adamantyl group and the aryl ring or oxygen atom in the nitrones (22*E*) or (21*E*), respectively. Thus although a neopentyl group (*A* value 2.0 [21]) is normally considered to be smaller than an isopropyl group (*A* value 2.15 [21]), the reverse appears to be the case for these nitrones.

The effect of solvent upon the equilibrium ratio of nitrones (17*E* and *Z*) is summarized in Table 3. Preliminary experiments showed that the proportion of (17*E*) decreased slightly at higher nitrone concentrations. Unfortunately the nitrone (17) was relatively insoluble in most of the common solvents examined, and the equilibrium distribution of isomers was frequently obtained for saturated solutions. These variable concentrations and low solubilities preclude any meaningful discussion of relative solvation effects.

Alternative mechanisms for the oxidation of imines to oxaziridines by peroxy-acids have recently been proposed to account for the kinetic results observed.[22,23] The possible relevance of a stereochemical investigation of reactant (imine) and product (oxaziridine) to the mechanism of this oxygen atom transfer process has also been considered.[24] Ogata and Sawaki [23] have provided kinetic evidence for the existence of different mechanisms for the production of either nitrone or oxaziridine in the oxidation of cyclic imines. Thus it was proposed that oxaziridines are formed by attack of peroxy-acid from above or below the imine molecular plane (orthogonal attack) whereas nitrones would result from direct electrophilic attack along the molecular plane at the nitrogen lone pair (coplanar attack). Unfortunately the imines selected for study [23] precluded a reactant–product analysis of stereochemistry since this was fixed by the cyclic structure. The acyclic imines (1)—(9) which were present in both *E*- and *Z*-forms, on oxidation with MCPBA were found to produce both (*E*)- and (*Z*)-nitrones [from (1)—(9)] and *cis*- and *trans*-oxaziridines [from (1) and (2)].[24] When the oxaziridines formed by oxidation of the imines (1) and (2) [or by photochemical rearrangement of the nitrone (17)] were subjected to the conditions of peroxy-acid oxidation and work-up no trace of the isomeric nitrones was found. Thus, it is probable that the nitrones and oxaziridines resulting from oxidation of the acyclic imines (1)—(9) were each formed by a different mechanism.

Coplanar oxidation of the (*E*)- and (*Z*)-imine isomers should be faster at the less hindered nitrogen lone pair of the (*Z*)-aldimine *i.e.* $k_2 > k_1$ in Scheme 2. The predominance of the less stable (*E*)-nitrone (kinetic control) produced on oxidation of the imines (1)—(4) agrees with the latter proposal.

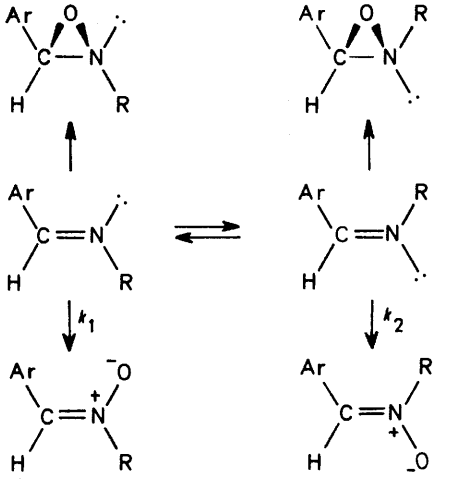
TABLE 3

Solvent effects on the equilibrium distribution of (*E*)- and (*Z*)-aldonitrones (17) [a]

Solvent:	$(CD_3)_2SO$	$(CD_3)_2CO$ [b]	1,2-$Cl_2C_6H_4$	CD_3OD [c]	$CDCl_3$ [b,c]	C_6D_6	ButOH	CCl_4
$\%E$ [e]	4	5	11	<12	17	21	24	28

[a] Saturated solution containing benzoic acid (5 mg) equilibrated at 35 °C. [b] Equilibrated at 60 °C. [c] 0.005M; 0.75 ml containing benzoic acid (5 mg).

During the synthesis of nitrones from aldehydes and *N*-alkylhydroxylamines [15] the requirement for a convenient and general route to *N*-alkylhydroxylamines became evident. The acid-catalysed hydrolysis of aldonitrones appeared to provide a possible solution (Scheme 3). Among the features of this cycle which appeared to add to the synthetic potential were: (i) the availability of pure pentamethylbenzaldehyde in a single-step high-yield synthesis from pentamethylbenzene; (ii) the rapid syntheses of imine, nitrone, and alkylhydroxylamine salt in good yield; and (iii) the ease of recovery (low water solubility) and purification (sublimation or crystallization) of the aldehyde after hydrolysis.

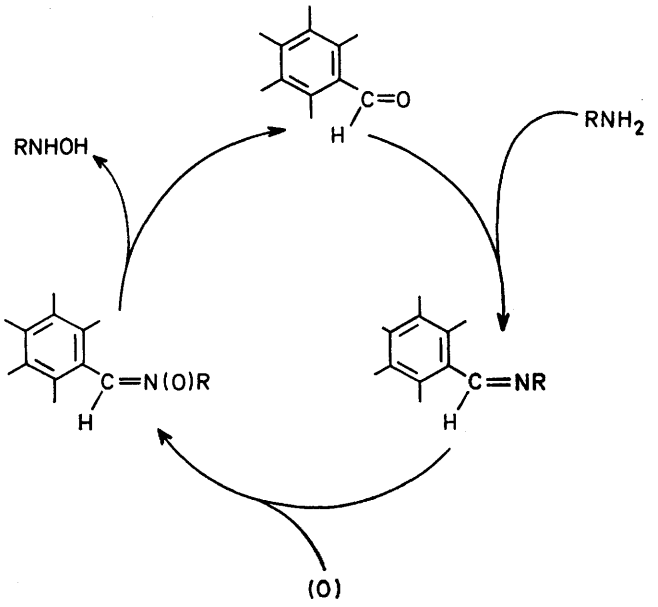


SCHEME 2

The yields at each step in the cycle for the synthesis of

[21] J. A. Hirsch, *Topics Stereochem.*, 1967, **1**, 199.
[22] V. Madan and L. B. Clapp, *J. Amer. Chem. Soc.*, 1969, **91**, 6078; 1970, **92**, 4902.
[23] Y. Ogata and Y. Sawaki, *J. Amer. Chem. Soc.*, 1973, **95**, 4687, 4692.
[24] D. R. Boyd, D. C. Neill, C. G. Watson, and W. B. Jennings, *J.C.S. Perkin II*, 1975, 1813.

a range of *N*-alkylhydroxylamines are shown in Table 4. Although no attempts were made to optimize the reaction conditions the method does appear to be of synthetic value. The lower yield of *N*-(1-adamantyl)-hydroxylamine (49%) and the recovery of the nitrone



SCHEME 3

(22) after attempted acidic hydrolysis are probably a reflection of the stabilizing influence of bulky substituents like t-butyl and pentamethylphenyl.

TABLE 4

Yields of imines, nitrones, and *N*-alkylhydroxylamine hydrochlorides

				(RNHOH,HCl)	
Imine	(%)	Nitrone	(%)	R	(%)
(4)	91	(17)	93	Me	88
(5)	90	(18)	89	Et	83
(7)	87	(20)	96	Pr^i	80
(8)	83	(21)	79	1-Ad [a]	49
(9)	89	(22)	80	Bu^t	*b*

[a] 1-Adamantyl. [b] Nitrone recovered quantitatively.

Ketonitrones are generally more difficult to synthesize than aldonitrones. Thus, the ketonitrone (24) was obtained only in low yield by methylation of the *p*-nitroacetophenone oxime anion. The ketonitrones (25) and (26) were available by photochemical rearrangement of the corresponding oxaziridine isomers.[25]

The ketonitrones *N*-(α-methylbenzylidene)- and *N*-(*p*,α-dimethylbenzylidene)-methylamine *N*-oxide had been reported to exist exclusively in the *E*-form on the basis of chemical reactivity, the intensity of u.v. absorption peaks, the low field shift of an *N*-methyl signal in the n.m.r. spectrum, and the results of application of the paramagnetic shift reagent tris(dipivaloylmethanato)europium.[13]

The n.m.r. shift data for the ketonitrones (24)—(26) obtained directly after synthesis were consistent with the presence of a single isomeric form. Comparison with the published data just mentioned suggested that the same configuration was common to all these nitrones. Thermal equilibration of (25) and (26) in $CDCl_3$ showed the formation of a second component which was identified as the other isomer from n.m.r. data (δ values and peak multiplicity). Furthermore, n.m.r. analysis of the heated nitrone samples showed that the increase in signal intensity of the new component was in concert with the diminution of signal for the starting material.

The values in Table 2 indicate that the nitrones (24)—(26) which were obtained directly after synthesis had an *E*-configuration, in agreement with that proposed for the reported ketonitrones.[13] This may be deduced from the shielding effect of the aryl ring on the adjacent *N*-alkyl group which moves the R′ signal upfield. The high field shift of the *C*-methyl substituent in the (*E*)-ketonitrone isomers (24)—(26) (relative to the *Z*-forms) contrasts with a low field shift of the C–H signal found in (*E*)-aldonitrones (14)—(20).

The clear trend towards a higher proportion of the *E*-isomer ($\%E_e$) with decreasing size of R′ shown by the ketonitrones (24)—(26) may be rationalized in terms of the aryl ring in an orthogonal conformation being slightly ' larger ' than the *C*-methyl substituent and an electronic repulsion between the negatively charged oxygen atom and the aryl ring in the *Z*-configuration. Thus it may be concluded that (as with the corresponding imines) both *E*- and *Z*-isomers of aldonitrones and of *C*-alkyl-*C*-arylketonitrones do often exist in significant proportions at equilibrium.

EXPERIMENTAL

N.m.r. spectra were obtained with Varian XL-100 and A-60 instruments. The *E*–*Z* isomer ratios were estimated after duplicate experiments from the n.m.r. integration (±2%).

Pentamethylbenzaldehyde.— Pentamethylbenzaldehyde was synthesized by the method previously reported for mesitaldehyde.[26] An improvement in the reported procedure, which avoided the tedious steam distillation, involved purification by passage down a column of active alumina followed by sublimation (140—150° and 0.01 mmHg). Pentamethylbenzaldehyde, m.p. 148—150° [from light petroleum (b.p. 60—80 °C)], was obtained in >65% yield (lit.,[27] 148—150°).

Imines.—The amines (1)—(9) were synthesized from the corresponding aldehydes and amines.[4] Characteristics of imines which have not been synthesized previously [3,4] are given in Table 1.

Nitrones.—The nitrones (14)—(22) and the oxaziridines isomeric with (14) and (15) were all synthesized in >80% yield by oxidation of the corresponding imines with MCPBA as reported previously for oxaziridines.[24]

The nitrone (23) was obtained by condensation of *p*-nitrobenzaldehyde with *N*-methylhydroxylamine. The nitrone (24) was synthesized by methylation (Me_2SO_4–

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NaOH) of *p*-nitroacetophenone oxime (9% yield). The synthetic methods used for (23), (24), and (27) have been used extensively for other nitrones.[2]

The nitrones (25) and (26) were obtained by u.v. irradiation of the corresponding oxaziridines in $CHCl_3$ and were separated (silica gel chromatography) from starting material as reported.[25]

The thermal equilibrations reported in Table 2 were carried out with the nitrone (0.000 5 M) in $CDCl_3$ (0.75 ml) at 60 °C containing benzoic acid (0.005 g) and were monitored (>24 h) by n.m.r. (±2%). M.p. data for new nitrones are given in Table 2. The nitrone (27) had the same m.p. as reported.[20]

N-*Alkylhydroxylamines*.—The nitrone was refluxed for 1 h with an equimolar quantity of 5N-HCl and then poured into an equal volume of water. The regenerated aldehyde was obtained by extraction with ether. The aqueous portion was concentrated under vacuum to give the crude *N*-alkylhydroxylamine (Table 4). *N*-Methylhydroxylamine hydrochloride had m.p. 85—87° (lit.,[28] 85—86°). N-*Ethylhydroxylamine hydrochloride* had m.p. 35—36° (Found: C, 24.6; H, 8.3; N, 14.6. C_2H_8ClNO requires C, 24.6; H, 8.3; N, 14.4%). *N*-Isopropylhydroxylamine hydrochloride had m.p. 50—54° (lit.,[29] 55°). *N*-1-Adamantylhydroxylamine hydrochloride had m.p. 227° (decomp.) (lit.,[30] 192—195°) (Found: C, 58.9; H, 9.0; N, 7.0. Calc. for $C_{10}H_{18}ClNO$: C, 59.0; H, 8.9; N, 6.9%).

We thank W. J. Swindall and H. B. McKnight for microanalyses, the Northern Ireland Ministry of Education for a Studentship (to D. C. N.), and the Queen's University of Belfast for a Demonstratorship (to J. B.).

[6/1171 *Received*, 18*th June*, 1976]

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