

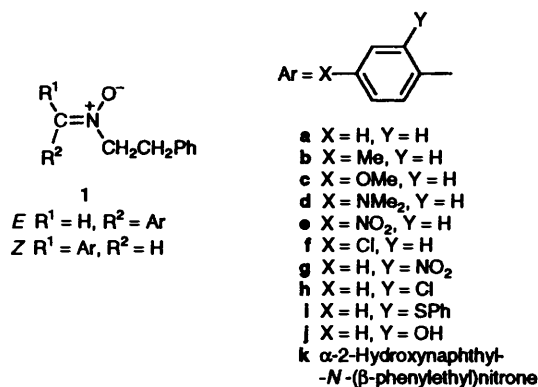
Synthesis and Separation of the *E* and *Z* Isomers of Simple Aldonitrones

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The uncommon *E* isomer of simple aldonitrones has been obtained in significant amounts for the first time in the case of α -phenyl-*N*-(β -phenylethyl)nitrones.

In an attempt to synthesize heterodienes of the type $>C=N-C=C<$, we were interested in the preparation of α -aryl-*N*-(β -phenylethyl)nitrones (*N*-alkylideneamine *N*-oxides), compounds for which there is only one literature report,¹ and this for a α -*p*-nitrophenyl substituted system. On repeating the reported work,¹ we isolated a further compound (m.p. 70–71 °C) in addition to that described earlier (m.p. 155 °C). ¹H NMR and UV evidence established that this additional compound had an *E* configuration, the one reported being the *Z* isomer. In generalizing this study, we have prepared 11 hitherto unknown α -aryl-*N*-(β -phenylethyl)nitrones **1a–k**, in all the cases two isomers being obtained quantitatively (Table 1).



Importance attaches to this finding since the isolation of (*E*)-aldonitrones is rare,² in spite of numerous attempts to obtain them.^{3–9}

In our system the arene aldehydes and *N*- β -phenylethylhydroxylamine obtained from nitrostyrene¹⁰ were heated under reflux in absolute ethanol for *ca.* 30 min and then left overnight. TLC [benzene–CCl₄ (1 : 1) or light petroleum–Et₂O (1 : 1)] established the composition of the product which was then separated either by fractional crystallisation (compounds **1d** and **1e**) or by preferential solubility of the *E* isomer in light petroleum. The stereochemical assignment was made on the basis of ¹H NMR evidence. The appreciable difference in the chemical shifts of the azomethine protons of *Z* and *E* isomers was essentially made use of in determining the geometry. For instance, for all the *Z* aldonitrones (Table 1) the azomethine proton signal appeared at *ca.* δ 7.2–7.4 and for the *E* aldonitrones the corresponding signal was at δ 8.2–8.8. The consistent downfield appearance of the azomethine proton in the *E* isomers is a result of these protons being adjacent to the negatively charged nitron oxygen. In addition, both the methylene protons which appear as triplets in *E* isomers resonate at higher field relative to the corresponding protons in the *Z* isomers. This probably results from the methylene protons being shielded by the proximate phenyl ring which is

Table 1 The overall yield, isomer yield and melting point of *E* and *Z* isomers of α -aryl-*N*-(β -phenylethyl)nitrones prepared as described in a typical example.*

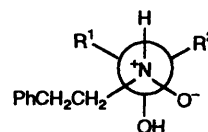
Compound 1	Total yield (%)	% <i>E</i>	% <i>Z</i>	M.p. (°C)	
				<i>E</i>	<i>Z</i>
a	78	35	65	*	66
b	76	36	64	*	*
c	77	31	69	*	65
d	78	32	68	58	87
e	82	30	70	69	155
f	81	30	70	*	89
g	72	45	55	*	*
h	75	41	59	*	108
i	70	98	02	*	*
j	79	23	77	*	98
k	78	22	78	85	*

* Oily or low melting solid. Melting points are uncorrected. All compounds gave satisfactory microanalytical data.

Typical example.—*N*- β -Phenylethylhydroxylamine¹⁰ (1.92 g, 14 mmole) and *p*-nitrobenzaldehyde (1.51 g, 10 mmole) was heated in absolute ethanol (60 cm³) for 30 min. The mixture was then evaporated under reduced pressure and subjected to TLC examination [silica plates, benzene–CCl₄ (1 : 1) or light petroleum–Et₂O (1 : 1)]. Subsequently, the mixture was subjected to fractional crystallisation with absolute alcohol to obtain the *E* and *Z* isomers. In all the remaining cases, the mixture was extracted with light petroleum (4 \times 10 cm³), which, on evaporation, gave the *E* isomer. The remaining *Z* isomer was recrystallised from ethanol.

slightly out of plane with respect to the C=N. The twisting-out of this phenyl ring is also supported by the UV data.

Since the shorter the period under reflux, the greater the amount of *E* isomer obtained, optimization of the yield of *E* isomer was possible by adjusting the reaction conditions. For instance, in a typical example, *N*- β -phenylethylhydroxylamine (1.3 mmol) when condensed with *p*-nitrobenzaldehyde (1.0 mmol) with a reflux period of 120–150 s gave > 75% of *E* isomer; longer periods under reflux gave decreasing yields of *E* isomer until equilibrium was reached. HPLC studies made on two systems, *viz.* compounds **1a** and **1d** suggest that the reaction is initially controlled kinetically and then, later, thermodynamically. The most likely pathway is by formation of the *E* isomer, *via* **2**, with subsequent isomerisation of the former to the *Z* isomer.



2 R¹ = Ph, R² = H
3 R¹ = H, R² = Ph

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Apart from some small steric interaction between the methylene protons and the α -phenyl ring there is no other destabilizing influence in the diastereoisomer **2**: this contrasts with the situation in diastereoisomer **3** which leads to *Z* isomer where there is likely to be a severe repulsive effect between the phenyl ring and the negatively charged oxygen. Such an effect would explain why larger amounts of the *E* isomer are obtained in *ortho* substituted cases (Table 1). The larger amounts of the *Z* isomer for compounds **1j** and **1k** can be well explained in terms of hydrogen bonding between the OH group in the α -phenyl ring and the negatively charged oxygen of the nitron function in the diastereoisomer **3**.

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