Configurationally Stable *E–Z*-Aldonitrones

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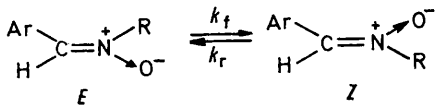
Summary The elusive *E*-isomer of aldonitrones was formed in two independent kinetically controlled reactions; the observation of both the *E*- and the *Z*-aldonitrones at equilibrium, and their subsequent separation, permitted an estimation of rotational barriers by direct thermal stereomutation.

WHILE several reports have appeared on the detection, separation, and equilibration of *E–Z*-ketonitrones,[1,2] to date the corresponding aldonitrones have been observed exclusively in the thermodynamically preferred *Z* form at equilibrium. That configurational instability has been reported for *E*-aldonitrones formed after BF_3-catalysed rearrangement of an oxaziridine[3] or after photochemical rearrangement of the *Z*-isomer,[4] is in accord with the only previous report of a rotation barrier for an aldonitrone (*ca.* 23 kcal mol^{-1}).[5]



E *Z*

	Ar	R	% *E* [a]	*E*[b]	*Z*[b]
(**1**)	2,6-$Me_2C_6H_3$ ..	Me	9(9)	6·60	6·18
(**2**)	2,4,6-$Me_3C_6H_2$ ..	"	10(11)	6·62	6·16
(**3**)	2,3,5,6-Me_4C_6H ..	"	15(21)	6·60	6·12
(**4**)	C_6Me_5	"	17(23)	6·60	6·11
(**5**)	9-Anthryl	"	30[c]	6·54	5·88
(**6**)	C_6Me_5	Et	12(20)	8·68[d]	8·42[d]
(**7**)	"	Pr^i	8(13)	8·71[d]	8·51[d]
(**8**)	"	Bu^t	<1(<1)	—	8·38[d]

[a] Equilibrium distribution obtained by n.m.r. integration in $CDCl_3$ (results in parentheses in Bu^tOH). [b] NMe signals. [c] Insoluble. [d] NCMe signals.

After equilibration, the aldonitrones (**1**)—(**5**) (Table; formed from the corresponding aldehyde and *N*-alkylhydroxylamine) showed n.m.r. peaks due to both the expected *Z*-isomer and a second component which is now identified as the *E*-isomer on the basis of the following evidence [exemplified by compound (**4**)]. (i) The aldonitrone *Z*-(**4**) showed, in addition to the pentamethyl signals, peaks at τ 6·11 (NMe) and 2·41 (vinyl-CH). The aldonitrone *E*-(**4**) showed peaks at τ 6·60 (NMe) and 2·10 (vinyl-CH). The upfield shift of the NMe signal in *E*-(**4**) resulted from the shielding influence of the proximate aryl ring by analogy with the corresponding imines.[6] (ii) The importance of kinetic control during the condensation route to aldonitrones was evident from the formation of *E*-(**4**) with a stereopreference of $> 85\%$. When the latter isomeric mixture was heated in $CDCl_3$, the proportion of *E*-(**4**) decreased concomitantly with an increase in the *Z*-isomer concentration until equilibrium was established.

The *E–Z* aldonitrones (**1**)—(**4**) and (**6**)—(**8**) were also obtained by oxidation with *m*-chloroperoxybenzoic acid (5 min at 42 °C in CH_2Cl_2) of the corresponding *E–Z*-aldimines. The proportion of *E–Z*-nitrone and/or *E–Z*-oxaziridine varied according to the number of electron-donating methyl substituents on the aryl ring. The aldonitrones (**4**), (**6**), (**7**), and (**8**) were thus free from oxaziridine in the product mixture. The proportion of *E*-aldonitrone formed by oxidation under the stated conditions was consistently higher than the aldonitrone equilibrium ratio (kinetic control). The observation that the oxaziridines [formed simultaneously with the nitrones (**1**)—(**3**)] do not rearrange to the corresponding nitrones under identical experimental conditions is in concurrence with the recent suggestion that the oxaziridine and the nitrone resulting from peroxyacid oxidation of a common cyclic imine are each formed by a different mechanism.[7] The equilibrium distribution of the separated *E*- and *Z*-aldonitrones† in Bu^tOH and $CDCl_3$ (Table) provides evidence for a differential solvation effect. The interconversion barriers of the *E*- and *Z*-isomers of compound (**4**) were obtained using the direct thermal stereomutation technique (n.m.r.) in purified diphenyl ether: temp., 147 °C, $k_f = 5{\cdot}3 \pm 0{\cdot}2 \times 10^{-5}\ s^{-1}$, $\Delta G_f^{\ddagger} = 33{\cdot}1$ kcal mol^{-1}; $k_r = 0{\cdot}9 \pm 0{\cdot}2 \times 10^{-5}\ s^{-1}$, $\Delta G_r^{\ddagger} =$

† The *E*- and *Z*-aldonitrones were found to be separable by chromatography on base-treated silica gel or by recrystallization from solvent containing traces of base.

34·6 kcal mol^{-1}. Traces of benzoic acid had a marked catalytic effect on the rate of interconversion: temp. 64 °C (after addition of benzoic acid), $k_f = 2{\cdot}1 \times 10^{-3}$ s^{-1}, $\Delta G_f^{\ddagger} = 23{\cdot}9$ kcal mol^{-1}; $k_r = 2{\cdot}6 \times 10^{-4}$ s^{-1}, $\Delta G_r^{\ddagger} = 25{\cdot}4$ kcal mol^{-1}.

Thus, in the absence of carboxylic acid, *E*–*Z*-aldonitrones can show considerable configurational stability, comparable to that reported for ketonitrones.[2] The significant proportion of *E*-isomer at equilibrium in aldonitrones (**1**)—(**7**) may be rationalized in terms of classical nonbonded interactions [*cf.* (**4**), (**6**), (**7**), and (**8**)], plus conformation and electronic effects similar to those proposed for *E*–*Z* aldimines.[6]

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