Dipole-stabilized carbanions in the series of cyclic aldonitrones
3.* The influence of the configuration of the nitrone group on H—D exchange of the methine hydrogen atom and metallation of aldonitrones

M. A. Voinov★ and I. A. Grigor´ev

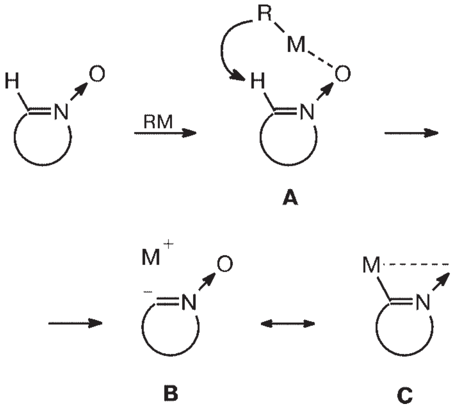
N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences,
9 prosp. Akad. Lavrent´eva, 630090 Novosibirsk, Russian Federation.
Fax: +7 (383 2) 34 4752. E-mail: maxx@nioch.nsc.ru

The spin-spin coupling constants $^3J_{C,H}$ between the hydrogen atom of the aldonitrone group and the carbon atom bound to the nitrogen atom of the N-oxide fragment were determined for a wide range of cyclic and acyclic aldonitrones. Based on comparison of these constants (*trans*-$^3J_{C,H}$ (*E* isomer) > *cis*-$^3J_{C,H}$ (*Z* isomer)), the *Z* configuration was assigned to acyclic nitrones. Coordination of organolithium compounds to the oxygen atom of the N→O group was revealed by ^{13}C NMR spectroscopy. This coordination is the necessary condition for the metallation of aldonitrones. The configuration of the nitrone group is responsible for the ability of the *E* form of acyclic aldonitrones to undergo CD_3ONa-catalyzed isotope exchange of the methine proton in CD_3OD and metallation with Bu^{s}Li.

Key words: cyclic and acyclic aldonitrones, configuration of the nitrone group, spin-spin coupling constants $^3J_{C,H}$, metallation, dipole-stabilized carbanions.

As part of continuing studies of dipole-stabilized carbanions, which are generated upon metallation of cyclic aldonitrones, and their reactions with electrophilic reagents,[1,2] we examined acyclic aldonitrones. However, it has previously been found[2] that acyclic *C*-phenyl-*N*-*tert*-butylnitrone (PBN, **1**) differs dramatically from other cyclic aldonitrones in acidity. The methine H atom in PBN, unlike those in cyclic aldonitrones, is not subjected to CD_3ONa-catalyzed H—D exchange in CD_3OD and is not replaced by the Li atom under the action of LDA and Bu^{n}Li. *C*-Aryl-*N*-alkylnitrones, contrastingly, undergo CD_3ONa-catalyzed exchange of the methine hydrogen atom for deuterium in CD_3OD.[3] In addition, the nitrone group in PBN exists in the *Z* configuration unlike the *E* configuration observed in cyclic aldonitrones.[4] To account for the difference in the reactivity of cyclic aldonitrones and PBN, we suggested that abstraction of the methine H atom is directly preceded by coordination of CD_3ONa or RLi to the oxygen atom of the nitrone group, which is kinetically favorable for H—D exchange and metallation of aldonitrones. Previously,[5—8] an analogous coordination was proposed as an explanation for preferential *syn*-metallation of amides. In the case of cyclic aldonitrones **2—7** (Table 1) existing in the rigidly fixed *E* configuration, the formation of complex **A** (Scheme 1) between the organometallic compound and the oxygen atom of the nitrone group facilitates proton abstraction from the *syn* position with respect to the oxygen atom of the N→O group.

Scheme 1



M is metal

In the case of PBN existing as the *Z* isomer,[4] the configuration of the aldonitrone group does not hinder the formation of the complex but excludes the attack of the electrons of the C—M bond on the H atom located on the opposite side of the C=N bond (Scheme 2).

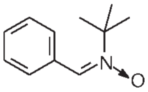
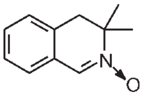
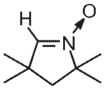
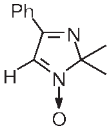
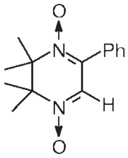
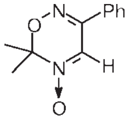
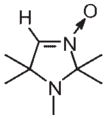
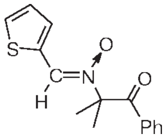
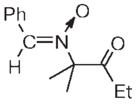
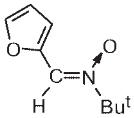
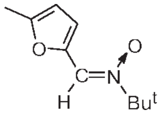
Hence, the configuration of the nitrone group could be a factor responsible for the ability of aldonitrones to undergo H—D exchange and metallation.

---

* For Part 2, see Ref. 1.

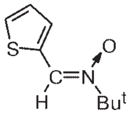
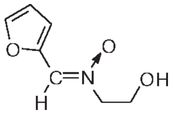
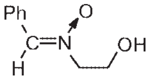
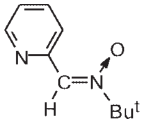
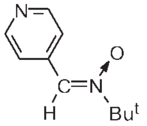
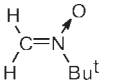
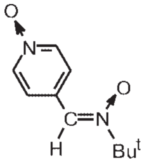
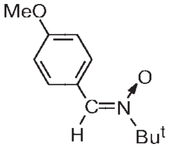
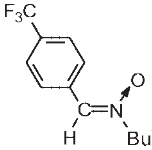
Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 2, pp. 283—290, February, 2002.

Table 1. H—D exchange rates and the spin-spin coupling constants $^3J_{C,H}$ for cyclic and acyclic aldonitrones

Nitrone		Exchange time/h	[CD_3ONa] /mol L^{-1}	δ_H	$^3J_{C,H}$/Hz
	(**1**)	—[a]	1.2	7.91	1.5
	(**2**)	40	1.2	7.89	4.5
	(**3**)	15	1.2	6.94	7.5
	(**4**)	7	0.5	8.23	7.3
	(**5**)	7	0.85	7.74	5.2
	(**6**)	6	0.5	7.90	3.6
	(**7**)	4	1.2	7.17	—
	(**8**)	—[b]	1.2	8.64	1.4
	(**9**)	—[b]	1.2	8.01	1.8
	(**10**)	90	1.2	8.06	1.5
	(**11**)	88	1.2	7.93	1.5

(*to be continued*)

Table 1 (*continued*)

Nitrone		Exchange time/h	$[CD_3ONa]$ /mol L^{-1}	δ_H	$^3J_{C,H}$/Hz
	**(12)**	75	1.2	8.47	1.4
	**(13)**	22	1.2	8.01	2.2
	**(14)**	>200	1.2	7.84	2.4
	**(15)**	>250	1.2	8.01	1.8
	**(16)**	30	1.2	8.02	1.7
	**(17)**	5	1.2	6.21 6.62	1.5 (*cis*) 6.5 (*trans*)
	**(18)**	16	1.2	8.06	1.5
	**(19)**	—[a]	1.2	7.84	2.0
	**(20)**	—[c]	1.2	7.98	1.8

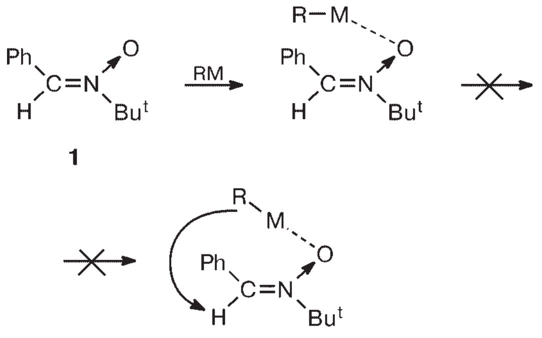
[a] The intensities of the signals for the methine protons remained unchanged over one month.

[b] The compound is unstable under the conditions of H—D exchange.

[c] After one month, 20% of methine protons were exchanged.

The aim of the present study was, first, to reveal the relationship between the configuration of the nitrone group in aldonitrones and their ability to undergo H—D exchange and metallation and, second, to obtain supporting evidence for the formation of a complex between the O atom of the nitrone group and an organometallic compound as a step necessary for the metallation of aldonitrones.

Scheme 2



To reveal the relationship between the configuration of aldonitrones and their ability to undergo metallation, we determined the configurations of acyclic aldonitrones **8—20** (see Table 1), which are structural analogs of PBN, and examined CD_3ONa-catalyzed H—D exchange of the H atom of the aldonitrone group in these compounds as the criterion for their ability to undergo metallation (*cf.* lit. data[2]).

According to data from ^1H and ^{13}C NMR spectroscopy, acyclic nitrones under study exist in solutions as the only isomer. The configuration of the nitrone group was determined using the procedure, which has been employed previously[9,10] in the investigations of the geometry of nitrones. This method is based on the difference in the vicinal spin-spin coupling constants *cis*- and *trans*-$^3J_{C,H}$. In the case of aldonitrones, we determined the spin-spin coupling constant $^3J_{C,H}$ between the H atom of the aldonitrone group and the C atom bound to the N atom of the N→O fragment. Cyclic aldonitrones **2—6** possessing the known fixed *E* configuration and methylenenitrone **17**, which contains the methine H atoms both in the *cis* and *trans* positions with respect to the oxygen atom of N-oxide, were used as the reference compounds. The spin-spin coupling constants for nitrones **2—6** and the constant *trans*-$^3J_{C,H}$ for nitrone **17** (see Table 1) are substantially larger than the corresponding constants for acyclic nitrones and the constant *cis*-$^3J_{C,H}$ for compound **17**, which allowed the unambiguous assignment of the *Z* configuration to nitrones **8—20**. The *Z* configuration of *C*-phenyl-*N*-*tert*-butylnitrone (**1**) has been independently established previously.[4]

The data on the CD_3ONa-catalyzed isotope exchange of the methine proton in aldonitrones in CD_3OD are given in Table 1. As can be seen from these data, there is no direct relationship between the rate of exchange of the methine proton and the electronic effect of the aromatic substituent at the C atom of the nitrone group in the structural analogs of PBN. Thus the influence of the substituents at the α-carbon atom of the nitrone group on the rate of H—D exchange increases in the following series: Ph, p-$CH_3OC_6H_4$ < p-$CF_3C_6H_4$ < 2-pyridyl < 2-furyl < < 2-thienyl < 4-pyridyl < 4-C_5H_4N→O < H.

At the same time, according to the σ_p^- constants,[11—13] which characterize the effect of the substituents on the developing carbanionic center, the above-mentioned substituents are arranged in the following qualitative series: 2-furyl < 2-thienyl < Ph < 2-pyridyl < 4-pyridyl < < 4-C_5H_4N→O.

Hence, the experimental dependence is inconsistent with the published data on the influence of the substituents on the developing carbanionic center. For example, the electron-donating 2-furyl, 2-furyl-5-methyl, and 2-thienyl substituents are similar in their influence on H—D exchange to the electron-withdrawing 4-pyridyl substituent (*cf.* the data on exchange in nitrones **10—12** and **16** given in Table 1). In nitrone **1** containing the phenyl substituent, H—D exchange was not observed at all, while this exchange proceeded most readily in methylenenitrone **17** containing no electron-withdrawing substituents at the α-carbon atom of the nitrone group.

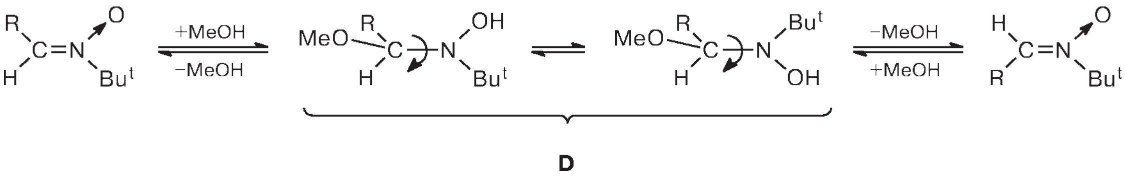
It is known[14—19] that *C*-aryl-*N*-alkylnitrones undergo isomerization with respect to the C=N bond and exist in solutions as an equilibrium mixture of the *E* and *Z* isomers. Apparently, the ease of exchange in acyclic aldonitrones under study could also be associated with their ability to undergo transformation into the *E* isomer.

Actually, the ease of isomerization of nitrones **10—13** and, consequently, of exchange can result from the electronic character of the aromatic substituents due to Coulomb repulsions between the negatively charged oxygen atom of the nitrone group and the aromatic ring.[15]

Besides, isomerization can proceed by an alternative mechanism through free rotation about the C—N bond in adduct **D** resulted from the reversible addition of MeOH at the C=N bond of the nitrone group (Scheme 3).

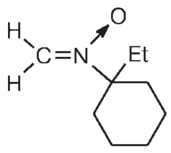
It is quite possible that this pathways is realized in the case of nitrones **15** and **16**. This assumption is evidenced

Scheme 3

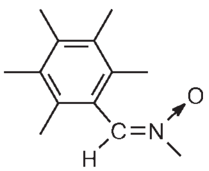


by the following facts. In the UV spectrum of a solution of nitrone **16** in a CD_3ONa—CD_3OD mixture, the extinction coefficient of the band corresponding to the absorption maximum of the nitrone group decreased from 23360 to 2194 upon storage for 10 days. After prolonged storage of nitrones **15** and **16** in a CD_3ONa—CD_3OD solution, their ^{1}H NMR spectra showed signals for the aromatic protons of the starting nitrones (at δ 7.49, 7.95, 8.65, and 9.02 for **15** and at δ 8.25 and 8.64 for **16**) along with sets of signals, which are analogous in multiplicities to the above-mentioned signals but are shifted upfield (at δ 7.28, 7.49, 7.80, and 8.48 for **15** and at δ 7.49 and 8.45 for **16**). The ratio of the signals were 1 : 2.5 (>3 days for nitrone **15**) and 1 : 3.5 (after 30 h for nitrone **16**) with the starting compounds predominating. The minor signals can be assigned to an addition product of MeOH to the nitrone group, which was accumulated in the reaction mixture. The signals for the aromatic protons in the *Z* isomers of the starting nitrones are shifted downfield due to the deshielding effect of the oxygen atom of the N-oxide group.[20—23] In the ^{13}C NMR spectrum of the reaction mixture (for nitrone **16**), the intensity of the signal for the C atom of the nitrone group at δ 130.77 is decreased and the minor signals appeared at δ 25.48, 123.05, 149.74, and 139.83. The latter signals are assigned respectively to the *tert*-butyl group and the C(3), C(2), and C(4) atoms of the pyridine ring in the adduct with MeOH.

In methylenenitrone **17**, the H atoms located both in the *cis* and *trans* positions with respect to the O atom of the nitrone group are exchanged for the deuterium atoms with equal facility, the H—D exchange in nitrone **17** proceeding most rapidly compared to all the other acyclic aldonitrones under study. Consequently, if our assumption is correct, nitrone **17** should be characterized by the lowest barrier to isomerization with respect to the C=N bond. The rate constant of the configuration exchange (k) in nitrone **17** was determined (in 1,2-dichlorobenzene, k = 88.6 s^{-1} at 133 °C) and the activation energy for isomerization was estimated ($\Delta G^{\neq}$ = 20.3 kcal mol^{-1}) by ^{1}H NMR spectroscopy at the temperature of coalescence of the signals for the methylene protons.[24] The $\Delta G^{\neq}$ value determined by us is somewhat lower than that reported for *N*-(1-ethylcyclohexyl)methylideneamine N-oxide (**21**) (k = 53.5 s^{-1} at 180 °C, $\Delta G^{\neq}$ = 23.2 kcal mol^{-1})[25] and is substantially lower than that for *C*-substituted nitrone *N*-(2,3,4,5,6-pentamethylbenzylidene)methylamine N-oxide (**22**) ($k = 0.9 \cdot 10^{-5}$ s^{-1} at 147 °C, $\Delta G^{\neq}$ = 34.6 kcal mol^{-1}).[15] Hence, the rate of isotope exchange in acyclic aldonitrones can actually be associated with the ease of isomerization with respect to the C=N bond.



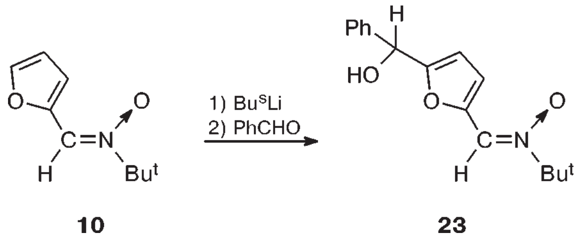
21



22

According to the data from ^{1}H NMR spectroscopy, treatment of aldonitrones **1** and **19** with Bu^sLi at −70 °C for 2 h followed by quenching of the reaction mixture with D_2O did not lead to exchange of the methine H atom for the D atom. Treatment of nitrones **15—17** with Bu^sLi followed by the addition of PhCHO was accompanied by destruction of the starting compounds. Under the above-mentioned conditions, nitrone **10** was metallated at position 5 of the furyl ring to form *N*-*tert*-butyl[5-(α-hydroxybenzyl)-2-furfurylideneamine] N-oxide (**23**) in 65% yield (Scheme 4).

Scheme 4



10 **23**

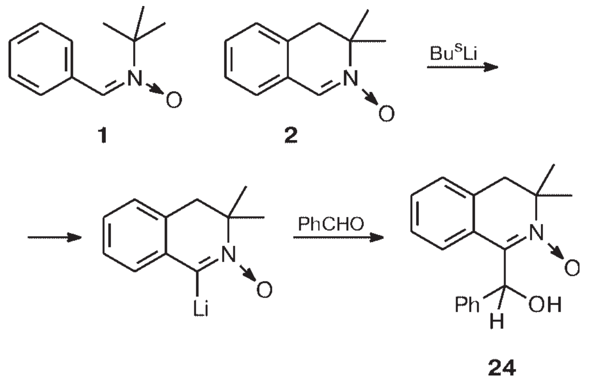
In the case of nitrone **11**, metallation cannot proceed at position 5 of the furyl ring and the starting compound was completely recovered.

Inertness of nitrone **11** with respect to Bu^sLi, even though it rather readily undergoes CD_3ONa-catalyzed isotope exchange, is probably associated with "freezing" of the *E—Z* isomerization of the nitrone relative to the C=N bond at the temperature of metallation (−70 °C). In this case, the thermodynamically more stable *Z* isomer remains in solution and metallation does not take place. Apparently, this conclusion can be extended not only to the nitrones under study but also to all acyclic aldonitrones.

To some approximation, cyclic aldonitrone **2** can be considered as the fixed *E* form of nitrone **1**. In compound **2**, the H atom of the aldonitrone group was rather readily exchanged for the D atom (see Table 1), and nitrone **2** was metallated with Bu^sLi at —70 °C to form a bright-violet solution whose reaction with PhCHO gave rise to 1-(α-hydroxybenzyl)-3,3-dimethyl-3,4-dihydroisoquinoline 2-oxide (**24**) (Scheme 5).

Probably, it is this difference in the configuration of the nitrone groups that is responsible for such different behavior of nitrones **1** and **2** in metallation. A change in CH-acidity of the aldonitrone group upon its incorporation into the dihydroisoquinoline ring owing to changes in the bond angles seems to be unlikely because it is highly improbable that the incorporation of the C atom into the weakly strained six-membered ring can lead to a substan-

Scheme 5



tial change in the s character of the orbital of the C atom involved in the C—H bond. This statement is supported by the similarity of the chemical shifts of the C atoms of the nitrone group in these compounds (δ 127.17 and 129.64 for **1** and **2**, respectively; the spectra were measured in CCl_4). We believe that this comparison for structurally similar nitrones **1** and **2** is acceptable. In addition, we determined the spin-spin coupling constants $J_{C,H}$ for the aldonitrone group in compounds **1** and **2** (170 and 182 Hz, respectively) from their ^{13}C NMR spectra. Taking into account the well-known correlation[26] between the spin-spin coupling constants and the s character of the orbitals of the C atom, we estimated the s character of the exocyclic orbital of the α-carbon atom of the nitrone group (0.34 and 0.36 in compounds **1** and **2**, respectively). These values indicate that the structural differences have a negligible effect on thermodynamical CH-acidity of nitrones **1** and **2**. Consequently, the formation of the complex between the organolithium compound and the oxygen atom of the nitrone group could be kinetically favorable for metallation of the *E* isomer of nitrone.

The complex of type **A** (see Scheme 1, M = Li) of the RLi compound with the O atom of the N→O group was detected by ^{13}C NMR spectroscopy. We used $LiClO_4$, which is readily soluble in ether-type solvents, as a compound simulating RLi because we could not use LDA and Bu^sLi in the case of cyclic aldonitrones. We found that the addition of $LiClO_4$ to solutions of aldonitrones **1**, **2**, **4**, **7**, and **11** in THF led to a noticeable downfield shift of the signal for the C atom of the nitrone group in the ^{13}C NMR spectra (Table 2).

These changes in the chemical shifts are analogous to those observed[27] upon protonation of the O atom of the nitrone group and are indicative of the interaction between the N→O group and the Li ion.

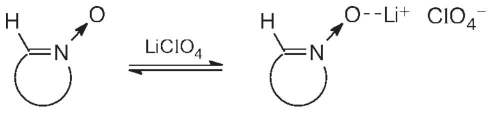


Table 2. Chemical shifts (δ) of the methine C atom in the ^{13}C NMR spectra of compounds **1**, **2**, **4**, **7**, and **11** in the presence of variable amounts of $LiClO_4$

Nitrone	δ (THF)	$δ_1$ (2 equiv. of $LiClO_4$)	$δ_2$ (5 equiv. of $LiClO_4$)	Δδ ($δ_2$ – δ)
1	127.25	129.02 128.06*	130.77	3.52
2	129.31	134.45 131.76*	135.42	6.11
4	123.79	125.90	127.95	4.16
7	132.45	140.54	140.70	8.25
11	119.18	120.17	123.11	3.93

* The chemical shifts in the presence of 2 equiv. of dicyclohexano-18-crown-6.

Upon the addition of dicyclohexano-18-crown-6 to the sample under study, the signal for the C atom of the nitrone group was shifted back to high field. This fact indicates that the downfield shift of the signal for the C atom of the nitrone group is not a consequence of the increase in polarity of the solution upon addition of $LiClO_4$.

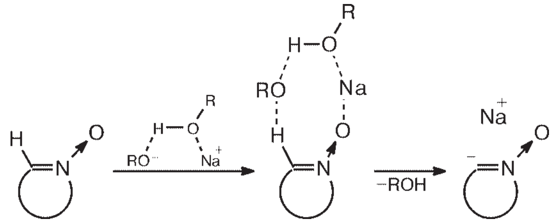
The difference between the chemical shifts of the starting nitrone and the coordinated form increases with increasing concentration of $LiClO_4$ due to the shift of the equilibrium to the coordinated form. As can be seen from Table 2, the difference (Δδ) between the chemical shifts of free (δ) and coordinated ($δ_2$) forms are noticeably different for cyclic and acyclic nitrones. For example, the values Δδ for structurally similar nitrones **1** and **2** differ by a factor of ~2. Apparently, this is associated with the difference in efficiency of the conjugation between the nitrone group and the aromatic substituent in the compounds under study. As a result, in the case of formation of the complex of type **A** (see Scheme 1), nitrone **7** containing the isolated aldonitrone group cannot compensate for deficiency of the electron density on the C atom of the nitrone group at the expense of other fragments of the molecule through the conjugation system. Because of this, Δδ for compound **7** has the maximum value (see Table 2).

An analogous change in the chemical shift was observed in the ^{13}C NMR spectrum of nitrone **1** recorded in an ethereal solution of LDA at –70 °C. In this case, the signal for the C atom of the nitrone group is shifted downfield (from 127 to 140 ppm). In addition, the ^{13}C NMR spectrum recorded under the conditions of monoresonance shows spin-spin coupling between the C atom of the nitrone group and the methine hydrogen atom ($J_{C,H}$ = 170 Hz), which confirms the absence of exchange of the H atom for the Li atom.

When equimolar amounts of dicyclohexano-18-crown-6 and Bu^sLi were mixed before the addition of aldonitrone **4**, the reaction mixture did not develop a bright-crimson color characteristic of metallated aldonitrone. Treatment of the reaction mixture with PhCHO followed by its quenching with water led only to recovery of the starting compound. Apparently, efficient binding of Li of the organolithium compound to crown ether prevents coordination of the R—Li molecule to the oxygen atom of the nitrone group (*cf.* lit. data[28]) and, hence, inhibits metallation. Thus, coordination of the organometallic compound to the O atom of the nitrone group (the formation of complex **A**, see Scheme 1) is a prerequisite step preceding deprotonation.

The above-described experiments on the influence of coordination of the RLi molecule with the N→O group on metallation suggest that the mechanism of metallation with organolithium compounds in aprotic solvents, which was postulated in the introduction to the present study, is similar to the mechanism of CD_3ONa-catalyzed deprotonation in CD_3OD. Actually, deprotonation in MeOH proceeded, most likely, under the action of the solvent-separated ion pair $Na^+...O(R)—H...^-OR$ (it is known[29—32] that CH_3ONa exists in this form in solution). Due to coordination with the N→O group, the cation, which is involved in the Coulomb interaction with the anion, brings the latter to the hydrogen atom to be abstracted (Scheme 6).

Scheme 6



To summarize, the above-considered experimental data provide evidence in favor of the assumption that the ability of aldonitrones to undergo metallation and H—D exchange is determined by the configuration of the nitrone group. This steric requirement is apparently associated with the fact that deprotonation occurs in the complex formed by an organometallic compound or alkoxide and the oxygen atom of the nitrone group in the step directly preceding proton abstraction. The formation of this complex is kinetically favorable for proton abstraction from the *Z* position with respect to the N-oxide group. Taking into account that this complex is involved in deprotonation, metallation of aldonitrones can be assigned to CIPE-controlled processes[33] (CIPE is Complex Induced Proximity Effect).

Experimental

The IR spectra were recorded on Specord-IR and Bruker Vector-22 spectrometers in KBr pellets. The UV spectra were measured on a Specord UV-VIS spectrometer in EtOH. The ^1H and ^{13}C NMR spectra were recorded on Bruker AC-200 (200.132 and 50.323 MHz for ^1H and ^{13}C, respectively) and Bruker AM-400 instruments (400.136 and 100.614 MHz for ^1H and ^{13}C, respectively) with the use of the signal of the solvent as the internal standard. The melting points were determined on a Kofler plate. Elemental analyses were carried out at the Laboratory of Microanalysis of the N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry of the Siberian Branch of the Russian Academy of Sciences. Nitrones **2**,[34] **4**,[35] **7**,[36] **8**,[37] **9**,[38] **13**,[19] and **14** [19] were synthesized according to procedures reported previously. Nitrone **3** was kindly supplied by Prof. V. A. Reznikov. Nitrones **5** and **6** were prepared by D. G. Mazhukin and I. A. Kirilyuk and will be described elsewhere.

Synthesis of acyclic aldonitrones 10—12, 15, 16, and 18—20 (general procedure). A solution of *N-tert*-butylhydroxylamine hydrochloride ($1.35 \cdot 10^{-2}$ mol) in MeOH (5 mL) was added to a solution of the corresponding aldehyde ($1.4 \cdot 10^{-2}$ mol) in MeOH (5 mL). The reaction mixture was cooled to 5—10 °C, made alkaline with 1 *M* solution of MeONa in MeOH (pH ≈ 10), and kept for two days. Then the reaction mixture was poured into water (50 mL) and extracted with CH_2Cl_2 (5×10 mL). The extract was dried with K_2CO_3, the solvent was distilled off under reduced pressure, and the solution of the residue in $CHCl_3$ was passed through a column with SiO_2. The spectroscopic characteristics of nitrones **16**,[39] **19**,[40] and **20** [41] are identical with those reported in the literature.

***N-tert*-Butyl(2-furfurylideneamine) N-oxide (10).** The yield was 65%, m.p. 64—66 °C (from light petroleum). Found (%): C, 64.51; H, 7.77; N, 8.43. $C_9H_{13}NO_2$. Calculated (%): C, 64.67; H, 7.78; N, 8.38. IR, ν/cm^{-1}: 1550 (C=N). UV, λ_{max}/nm (ε): 305 (23780). ^1H NMR (acetone-d$_6$), δ: 1.53 (s, 9 H, 3 Me); 6.56, 7.62, and 7.69 (all m, 1 H each, furyl); 7.83 (s, 1 H, H—C=N). ^{13}C NMR (acetone-d$_6$), δ: 28.20 ($C(\underline{C}H_3)_3$); 70.33 ($\underline{C}(CH_3)_3$); 112.50 (C(3), furyl); 113.84 (C(4), furyl); 143.95 (C(5), furyl); 120.42 (C=N); 149.45 (C(2), furyl).

***N-tert*-Butyl(5-methyl-2-furfurylideneamine) N-oxide (11).** The yield was 68%, m.p. 82—84 °C (from hexane). Found (%): C, 66.38; H, 8.31; N, 7.68. $C_{10}H_{15}NO_2$. Calculated (%): C, 66.30; H, 8.29; N, 7.73. UV, λ_{max}/nm (ε): 314 (28280). ^1H NMR (acetone-d$_6$), δ: 1.52 (s, 9 H, 3 Me); 2.29 (s, 3 H, Me); 6.16 and 7.58 (both d, 1 H each, furyl, $^3J_{H,H}$ = 3.5 Hz); 7.73 (s, 1 H, H—C=N). ^{13}C NMR (acetone-d$_6$), δ: 13.59 (Me); 28.21 ($C(\underline{C}H_3)_3$); 69.89 ($\underline{C}(CH_3)_3$); 108.90 (C(4), furyl); 115.29 (C(3), furyl); 120.25 (C=N); 148.11 (C(2), furyl); 153.75 (C(5), furyl).

***N-tert*-Butyl(2-thienylmethylideneamine) N-oxide (12).** The yield was 85%, m.p. 162—164 °C (from AcOEt). Found (%): C, 59.22; H, 7.18; N, 7.40. $C_9H_{13}NOS$. Calculated (%): C, 59.02; H, 7.10; N, 7.65. IR, ν/cm^{-1}: 1577 (C=N). UV, λ_{max}/nm (ε): 312 (18692). ^1H NMR ($CDCl_3$), δ: 1.56 (s, 9 H, 3 Me); 7.10 (dd, 1 H, H(4) thienyl, $^3J_{H,H}$ = 4 Hz, $^3J_{H,H}$ = 5 Hz); 7.38 (dd, 1 H, H(5) thienyl, $^3J_{H,H}$ = 5 Hz, $^4J_{H,H}$ = 1 Hz); 7.41 (dd, 1 H, H(3) thienyl, $^3J_{H,H}$ = 4 Hz, $^4J_{H,H}$ = 1 Hz); 8.00 (s, 1 H, H—C=N). ^{13}C NMR ($CDCl_3$), δ: 27.97 ($C(\underline{C}H_3)_3$); 68.76 ($\underline{C}(CH_3)_3$); 125.30 (C=N); 126.16, 128.04, 128.96 (thienyl); 133.23 (C(2), thienyl).

***N-tert*-Butyl(2-pyridylmethylideneamine) N-oxide (15).** The yield was 70%, m.p. 63—65 °C (from light petroleum). Found (%): C, 67.41; H, 7.89; N, 15.71. $C_{10}H_{14}N_2O$. Calculated (%): C, 67.42; H, 7.86; N, 15.73. IR, ν/cm^{-1}: 1555 (C=N). UV, λ_{max}/nm (ε): 302 (16800). ^{1}H NMR (acetone-d$_6$), δ: 1.59 (s, 9 H, 3 Me); 7.31, 7.82, 8.62, and 9.18 (all m, 1 H each, py); 7.85 (s, 1 H, H—C=N). ^{13}C NMR (acetone-d$_6$), δ: 28.33 (C($\underline{C}H_3)_3$); 72.11 ($\underline{C}(CH_3)_3$); 123.37 (C(5), py); 124.44 (C(3), py); 137.17 (C(4), py); 150.30 (C(6), py); 151.92 (C(2), py); 131.20 (C=N).

***N-tert*-Butyl(4-pyridylmethylideneamine) N-oxide (16).** ^{13}C NMR (acetone-d$_6$), δ: 28.35 (C($\underline{C}H_3)_3$); 72.78 ($\underline{C}(CH_3)_3$); 122.11 (C(3), py); 139.02 (C(4), py); 150.94 (C(2), py); 127.95 (C=N).

***N-tert*-Butyl(methylideneamine) N-oxide (17).** A solution of *N-tert*-butylhydroxylamine hydrochloride (2 g, $1.6 \cdot 10^{-2}$ mol) in MeOH (5 mL) was made alkaline with 1 *M* solution of MeONa in MeOH (pH $\approx$ 10), and cooled to 5 °C. Then 30% formaline (3.5 mL) was added, whereupon the reaction mixture slightly warmed up. After 15 min, the reaction mixture was concentrated and water (3 mL) was added. The reaction mixture was extracted with CH_2Cl_2 (5×10 mL), the extract was dried with $MgSO_4$, the solvent was distilled off under reduced pressure, and the residue was sublimed. The yield was 1.13 g (70%). The spectroscopic characteristics are identical with those reported in the literature.[42] ^{13}C NMR ($CDCl_3$), δ: 27.92 (C($\underline{C}H_3)_3$); 69.87 ($\underline{C}(CH_3)_3$); 119.44 (C=N).

Study of H—D exchange in acyclic aldonitrones. Nitrone ($3.8 \cdot 10^{-5}$ mol) was placed in an NMR tube, a freshly prepared solution (0.5 mL) of CD_3ONa in CD_3OD was added, and the reaction mixture was stirred until the sample was completely dissolved. The concentrations of the solutions of CD_3ONa in CD_3OD are given in Table 1. The course of the isotope exchange was monitored by ^{1}H NMR spectroscopy by following the changes in the integral intensity ratio of the signals for the methine proton and the signals for the protons of the geminal Me groups (for cyclic aldonitrones), the protons of the *tert*-butyl group (for *C*-R-*N-tert*-butylnitrones), or the aromatic H atoms (for nitrones **13** and **14**). The course of the reaction was monitored until the conversion reached ~85% (the ratio of the signals for the methine proton and the protons of the *tert*-butyl group was 1 : 60 and the ratio of the signals for the methine proton and the protons of the geminal Me groups was 1 : 40).

Study of the reactions of aldonitrones with Bu^{s}Li. A solution of Bu^{s}Li in hexane (2.3 mL, $2.3 \cdot 10^{-3}$ mol) was placed in a flask (which was preliminarily filled with argon) equipped with a magnetic stirred, a dropping funnel, and a thermometer and cooled to −70 °C. Then a solution of aldonitrone **1**, **2**, **10**, **11**, **15—17**, or **19** ($1.9 \cdot 10^{-3}$ mol) in THF (2 mL) was added dropwise to a solution of Bu^{s}Li over 15 min. The reaction mixture was stirred at −70 °C for 10—15 min and a solution of PhCHO ($2.5 \cdot 10^{-3}$ mol) in THF (3 mL) was added. The reaction mixture was stirred at −70 °C for 10 min, warmed to −20 °C, and quenched with water (2 mL). The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (2×5 mL). The combined organic extracts were dried with $MgSO_4$ and concentrated. The recovery of nitrones **1**, **11**, and **19** was 95—98%. The identity of the compounds isolated and the starting nitrones were determined by comparing their IR and ^{1}H NMR spectra. Nitrones **23** and **24** were isolated by preparative TLC.

***N-tert*-Butyl[5-(α-hydroxybenzyl)-2-furfurylideneamine] N-oxide (23)** was isolated by chromatography on SiO_2 (1 : 20 CH_2Cl_2—MeOH mixture as the eluent), m.p. 199—201 °C (hexane—EtOAc, 1 : 20). Found (%): C, 70.33; H, 7.22; N, 5.26. $C_{16}H_{19}NO_3$. Calculated (%): C, 70.33; H, 6.96; N, 5.13. IR ($CHCl_3$), ν/cm^{-1}: 1525 (C=N), 3605 (OH). IR (KBr), ν/cm^{-1}: 1518 (C=N), 3220 (OH). UV, λ_{max}/nm (ε): 314 (17078). ^{1}H NMR ($CDCl_3$), δ: 1.52 (s, 9 H, Me); 2.91 (d, 1 H, OH, $^3J_{H,H}$ = 4.5 Hz); 5.79 (d, 1 H, CH, $^3J_{H,H}$ = 4.5 Hz); 6.28 and 7.63 (both d, 1 H each, furyl, $^3J_{H,H}$ = 3.9 Hz); 7.32—7.42 (m, 5 H, Ph); 7.65 (s, 1 H, H—C=N). ^{13}C NMR ($CDCl_3$), δ: 27.95 (Me); 69.60 ($\underline{C}(CH_3)_3$); 70.10 (CH); 109.96, 115.50 (CH, furyl); 121.37 (C=N); 126.53 (*o*-C(Ph)); 129.12 (*p*-C(Ph)); 129.44 (*m*-C(Ph)); 140.35 (*ipso*-C(Ph)); 147.36, 158.93 (2 *ipso*-C(furyl)).

1-(α-Hydroxybenzyl)-3,3-dimethyl-3,4-dihydroisoquinoline 2-oxide (24) was isolated by chromatography on Al_2O_3 (a 3 : 2 light petroleum—AcOEt mixture as the eluent). The yield was 75%, m.p. 166—168 °C (hexane—AcOEt, 1 : 1). Found: C, 76.92; H, 6.79; N, 4.91. $C_{18}H_{19}NO_2$. Calculated: C, 76.87; H, 6.76; N, 4.98. IR, ν/cm^{-1}: 1529 (C=N), 3213 (OH). UV, λ_{max}/nm (ε): 303 (14428). ^{1}H NMR ($CDCl_3$), δ: 1.35 and 1.47 (both s, 3 H each, 2 Me); 3.01 and 3.14 (AB system, 2 H, CH_2, $J_{H,H}$ = 16 Hz); 5.98 (d, 1 H, CH, $^3J_{H,H}$ = 11 Hz); 7.18—7.43 (m, 9 H, arom.); 7.49 (d, 1 H, OH, $^3J_{H,H}$ = 11 Hz). ^{13}C NMR ($CDCl_3$), δ: 23.76, 24.46 (Me); 41.54 (CH_2); 66.70 (C(3)); 71.09 (HCOH); 125.80 (*o*-C(Ph)); 128.03 (*p*-C(Ph)); 128.52 (*m*-C(Ph)), 123.33 (Ar); 127.61 (Ar); 129.52 (Ar); 128.33, 130.66 (*ipso*-C(Ar)); 140.63 (*ipso*-C(Ph)); 144.14 (C=N).

In an independent experiment with nitrone **1**, the reaction mixture was kept at −70 °C for 2 h and warmed to −20 °C. Then D_2O (2 mL) was added. The organic layer was separated and dried with $MgSO_4$ and the solvent was distilled off under reduced pressure. Analysis of the residue by ^{1}H NMR spectroscopy (in CD_3OD) revealed the presence of the signal for the methine proton (δ 7.91) with the intensity ratio of 1 : 5 relative to the signals for the aromatic protons.

Study of coordination of the N$\rightarrow$O group of aldonitrones with $LiClO_4$ and LDA. ***A.*** Nitrone **1**, **2**, **4**, **7**, or **11** ($1.3 \cdot 10^{-4}$ mol) was placed in an NMR tube and a solution (0.5 mL) of $LiClO_4$ in dry THF was added ($LiClO_4$ was preliminarily calcined at 120 °C for 24 h). The resulting mixture was stirred until the compound under study was completely dissolved and then kept for 0.5 h.

B. A solution of nitrone **1** (0.3 g, $1.9 \cdot 10^{-3}$ mol) in ether (5 mL) was added to an ethereal solution of LDA (25 mL, $9.5 \cdot 10^{-3}$ mol), which was preliminarily cooled to −70 °C, under argon. The resulting mixture was stirred at −70 °C for 10 min and then transferred into an NMR tube filled with argon and placed in solid carbon dioxide. The ^{13}C NMR spectrum was recorded at −70 °C.

We thank O. P. Shkurko for helpful discussion.

This study was financially supported by the Russian Foundation for Basic Research (Project No. 97-03-32864a).

References

1. M. A. Voinov, I. A. Grigor´ev, and L. B. Volodarsky, *Tetrahedron,* 2000, **56**, 4071.

2. M. A. Voinov, I. A. Grigor´ev, and L. B. Volodarsky, *Heterocycl. Commun.*, 1998, **4**, 261.
3. N. N. Zatsepina, I. F. Tupitsyn, A. I. Belyashova, E. A. Medyantseva, I. M. Andreeva, and V. I. Minkin, *Reakts. Sposobn. Organ. Soedinenii* [*Reactivities of Organic Compounds*], 1975, **12**, 223.
4. D. E. Gallis, J. A. Warshaw, B. J. Acken, and D. R. Crist, *J. Org. Chem.*, 1991, **56**, 6352.
5. R. Schlecker, D. Seebach, and W. Lubosch, *Helv. Chim. Acta*, 1978, **61**, 512.
6. N. G. Rondan, K. N. Houk, P. Beak, W. J. Zajdel, J. Chandrasekhar, and P. v. R. Schleyer, *J. Org. Chem.*, 1981, **46**, 4108.
7. P. Beak and W. J. Zajdel, *J. Am. Chem. Soc.*, 1984, **106**, 1010.
8. D. R. Hay, Z. Song, S. G. Smith, and P. Beak, *J. Am. Chem. Soc.*, 1988, **110**, 8145.
9. Y. Inouye, K. Takaya, and H. Kakisawa, *Magn. Reson. Chem.*, 1985, **23**, 101.
10. E. Kleinpeter, C.-P. Maschmeier, J. Krahnstover, H. Matschiner, and H. Kohler, *J. Prakt. Chem.*, 1990, **332**, 261.
11. V. P. Mamaev, O. P. Shkurko, and S. G. Baram, *Adv. Heterocycl. Chem.*, 1987, **42**, 1.
12. H. H. Szmant and C. M. Harmuth, *J. Am. Chem. Soc.*, 1964, **86**, 2909.
13. B. B. Jarvis and B. A. Marien, *J. Org. Chem.*, 1977, **42**, 2676.
14. T. S. Dobashi, M. H. Goodrow, and E. J. Grubbs, *J. Org. Chem.*, 1973, **38**, 4440.
15. J. Bjorgo, D. R. Boyd, and D. C. Neill, *J. Chem. Soc., Chem. Commun.*, 1974, 478.
16. W. B. Jennings, D. R. Boyd, and L. C. Waring, *J. Chem. Soc., Perkin Trans. 2*, 1976, 610.
17. J. Bjorgo, D. R. Boyd, D. C. Neill, and W. B. Jennings, *J. Chem. Soc., Perkin Trans. 1*, 1977, 254.
18. W. Kliegel and H. Becker, *Chem. Ber.*, 1977, **110**, 2067.
19. S. M. Bakunova, I. A. Grigor´ev, and L. B. Volodarskii, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 1403 [*Russ. Chem. Bull.*, 1999, **48**, 1389 (Engl. Transl.)].
20. K. Koyano and H. Suzuki, *Tetrahedron Lett.*, 1968, 1859.
21. K. Koyano and H. Suzuki, *Bull. Chem. Soc. Jpn.*, 1969, **42**, 3306.
22. I. A. Grigor´ev, M. M. Mitasov, G. I. Shchukin, I. K. Korobeinicheva, and L. B. Volodarskii, *Zh. Org. Khim.*, 1977, **13**, 1532 [*J. Org. Chem. USSR*, 1977, **13** (Engl. Transl.)].
23. S. Sivasubramanian, P. Mohan, M. Thirumalaikumar, and S. Mathusubramanian, *J. Chem. Soc., Perkin Trans. 1*, 1994, 3353.
24. H. Kessler, *Angew. Chem., Int. Ed. Engl.*, 1970, **9**, 219.
25. L. W. Boyle, M. J. Peagram, and G. H. Whitham, *J. Chem. Soc. B*, 1971, 1728.
26. C. Juan and H. S. Gutowsky, *J. Chem. Phys.*, 1962, **37**, 2198.
27. I. A. Grigor´ev, V. I. Mamatyuk, G. I. Shchukin, V. V. Martin, and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.*, 1986, 1065 [*Chem. Heterocycl. Compd.*, 1986, **22** (Engl. Transl.)].
28. P. Beak, G. R. Brubaker, and R. Farney, *J. Am. Chem. Soc.*, 1976, **98**, 3621.
29. K. Boeden and R. C. Cook, *J. Chem. Soc. B*, 1968, 1529.
30. P. B. Beronius, G. Wikander, and A. M. Nilsson, *J. Phys. Chem.*, 1970, **70**, 52.
31. R. L. Kay, *J. Am. Chem. Soc.*, 1960, **82**, 2099.
32. V. I. Slovetskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1970, 1768 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1970, **19**, 1667 (Engl. Transl.)].
33. P. Beak and A. I. Meyers, *Acc. Chem. Res.*, 1986, **19**, 356.
34. T. J. N. Watson, *J. Org. Chem.*, 1998, **63**, 406.
35. I. A. Kirilyuk, I. A. Grigor´ev, and L. B. Volodarskii, *Izv. Akad. Nauk, Ser. Khim.*, 1992, 1064 [*Bull. Russ. Acad. Sci., Div. Chem. Sci.*, 1992, **41**, 834 (Engl. Transl.)].
36. I. A. Grigor´ev, G. I. Shchukin, V. V. Martin, and V. I. Mamatyuk, *Khim. Geterotsikl. Soedin.*, 1985, 247 [*Chem. Heterocycl. Compd.*, 1985, **21** (Engl. Transl.)].
37. I. A. Kirilyuk, I. A. Grigor´ev, and L. B. Volodarskii, *Izv. SO Akad. Nauk SSSR, Ser. Khim.*, 1989, 99 [*Bull. Sib. Branch Russ. Acad. Sci., Div. Chem. Sci.*, 1989 (Engl. Transl.)].
38. L. B. Volodarskii and T. K. Sevast´yanova, *Zh. Org. Khim.*, 1971, 1687 [*J. Org. Chem. USSR*, 1971, **7** (Engl. Transl.)].
39. E. G. Janzen, R. L. Dudley, and R. V. Shetty, *J. Am. Chem. Soc.*, 1979, **101**, 243.
40. D. St. C. Black and K. G. Watson, *Austr. J. Chem.*, 1973, **26**, 2159.
41. B. S. Selinsky, L. A. Levy, A. G. Motten, and R. E. London, *J. Magn. Res.*, 1989, **81**, 57.
42. M. L. Druelinger, R. W. Shelton, and S. R. Lammert, *J. Heterocycl. Chem.*, 1976, **13**, 1001.

Received August 21, 2000;
in revised form July 24, 2001