Synthesis of *C*-aryl-*N*-(2-hydroxyphenylmethyl)-nitrones and their reaction with diphenylborinic or carboxylic acid derivatives. Crystal and molecular structures of a free nitrone ligand and its diphenyl–boron chelate[1]

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Abstract: The syntheses of a number of aromatic aldonitrones of *N*-(2-hydroxyphenylmethyl)hydroxylamine and their subsequent reactions with diphenylborinic or carboxylic acid derivatives are reported. Crystals of 8-(4-dimethylaminophenylmethylene)-6,6-diphenyl-5,7-dioxa-8-azonia-6-borata-5*H*-6,7,8,9-tetrahydrobenzocycloheptene, **2*b***, are triclinic, a = 10.6802(8), b = 11.1809(4), c = 10.1520(3) Å, α = 105.847(3)°, β = 92.567(4)°, γ = 84.610(5)°, Z = 2, space group $P\bar{1}$, and those of *C*-(4-dimethylaminophenyl)-*N*-(2-hydroxyphenylmethyl)nitrone, **6*e***, are monoclinic, a = 12.2319(8), b = 7.071(1), c = 17.2005(9) Å, β = 107.520(4)°, Z = 4, space group $P2_1/a$. The structures were solved by direct methods and refined by full-matrix least-squares procedures to R = 0.035 and 0.032 (R_w = 0.036 and 0.032) for 3379 and 1800 reflections with $I \geq 3\sigma(I)$, respectively. Compound **2*b*** is representative of a new type of heterocyclic *B*,*N*-betaine. The solid state structure of **6*e*** (the precursor to **2*b***) shows that only small topological changes, but significant changes in the electron distribution, occur upon the formation of the diphenylboron chelate.

Key words: aromatic aldonitrones, organoboron compounds, crystal structures.

Résumé : On a réalisé la synthèse d'un certain nombre d'aldonitrones aromatiques de la *N*-(2-hydroxyphénylméthyl)-hydroxylamine dont on a examiné les réactions subséquents avec des dérivés des acides diphénylborinique ou carboxylique. Les cristaux du 8-(4-diméthylaminophénylméthylène)-6,6-diphényl-5,7-dioxa-8-azonia-6-borata-5*H*-6,7,8,9-tétrahydrobenzocycloheptène, **2*b***, sont tricliniques, groupe d'espace $P\bar{1}$, avec a = 10,6802(8), b = 11,1809(4) et c = 10,1520(3) Å, α = 105,847(3)°, β = 92,567(4)° et γ = 84,610(5)°, et Z = 2 alors que ceux de la *C*-(4-diméthylaminophényl)-*N*-(2-hydroxyphénylméthyl)nitrone, **6*e***, sont monocliniques, groupe d'espace $P2_1/a$, avec a = 12,2319(8), b = 7,071(1) et c = 17,2005(9) Å, β = 107,520(4)° et Z = 4. On a résolu les structures par des méthodes directes et on les a affinées par la méthode des moindres carrés jusqu'à des valeurs respectives de R = 0,035 et 0,032 (R_w = 0,036 et 0,032) pour 3379 et 1800 réflexions avec $I \geq 3\sigma(I)$. Le composé **2*b*** représente un nouveau type de composé de *B*,*N*-bétaïne hétérocyclique. La structure du composé **6*e*** (précurseur du composé **2*b***) à l'état solide indique que, lors de la formation du chélate diphénylbore, il n'y a que de faibles changements topologiques, toutefois significatifs, qui se produisent dans la distribution électronique.

Mots clés : aldonitrones aromatiques, composés organobore, structures cristallines.

[Traduit par la rédaction]

Introduction

Nitrones of salicylaldehyde react as bidentate ligands with various chelate-forming boron compounds to give heterocyclic *B*,*N*-betaines such as **1** (1) (Scheme 1). An X-ray crystallographic analysis of the diphenylboron derivative of the *N*-methylnitrone (**1**, R = Me) established the seven-membered chelate ring structure with an endocyclic nitrone C═N double bond (2). In the course of this continuing investigation we were interested in the related seven-membered boron chelates **2**, utilizing a similar type of bidentate *N*-oxide–phenolate ligand, differing by having the nitrone C═N bond located outside of the chelate ring ("exocyclic" or "semicyclic" (3)).

An analogous boron chelate ring **3** containing an alcoholate instead of a phenolate ligand moiety had been postulated previously for the crystalline diphenylboron derivatives of *C*-aryl-*N*-(3-hydroxypropyl)nitrones (4). The stability of these type **3** chelates, however, turned out to depend on the *C*-aryl residue, which influences the basicity of the nitrone *N*-oxide function. Thus the derivative of 4-(dimethylamino)benzaldehyde (**3**, Ar = 4-$Me_2NC_6H_4$) proved to be by far the most

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stable of all isolated type **3** chelates, whereas the 4-nitrobenzaldehyde derivative (**3**, Ar = $4\text{-}NO_2C_6H_4$) could not be obtained at all (4). To provide information on the chelate-forming properties of *N*-(2-hydroxyphenylmethyl)nitrones, a series of aromatic aldonitrones was synthesized. The synthesis of these aromatic aldonitrones proceeded from salicylaldoxime **4** via the intermediate hydroxylamine **5** (which could not be isolated) to the nitrones **6**. These aromatic aldonitrones **6** were reacted with diphenylborinic acid anhydride to achieve the synthesis of the diphenylboron chelates **2**. In addition, a possible ring–chain isomerism or a rearrangement of the ligand (**6** $\rightleftharpoons$ **7**) was examined by acylation experiments using an example compound (**6***e*). The same example ligand **6***e* and its diphenylboron chelate **2***b* were subjected to single crystal X-ray crystallographic analysis to provide unambiguous proof of the respective molecular structures and elucidation of possible changes in the molecular geometry concomitant with chelate formation.

Experimental

General procedures

All preparations and reactions were carried out under normal conditions, without protective gas atmosphere. Commercial solvents were used as supplied. Oxybis(diphenylborane) was prepared according to literature methods, from sodium tetraphenylborate (5) or from 2-(diphenylboryloxy)ethylamine (6). Melting points, measured on a Linström SPA-1 apparatus, are uncorrected. Elemental analyses: (C, H, N, O) Carlo Erba Elemental Analyzer 1106; (B) oxidative disintegration (Schöninger) and potentiometric titration. Infrared spectra: Phillips PU 9800 FT-IR spectrometer, V 3.00, and Mattson Genesis Series FTIR Rev. I (ATI Unicam); ^1H nmr: Varian EM 390; ^{11}B nmr: Bruker AC 200. Mass spectra: Finnigan MAT 8430.

8-(4-Methoxyphenylmethylene)-6,6-diphenyl-5,7-dioxa-8-azonia-6-borata-5*H*-6,7,8,9-tetrahydrobenzocycloheptene,[3] 2*a*

6*b* (0.26 g, 1.0 mmol) and oxybis(diphenylborane) (0.17 g, 0.5 mmol) are dissolved in 20 mL of absolute ethanol and refluxed for 10 min. The solvent is distilled off to dryness. Yield: 0.41 g (97%) of slightly discolored white crystals; mp 170–173°C. Infrared (KBr, cm^{-1}): 1650 (C=N), 1599 (C=C); ^1H nmr (90 MHz, $CDCl_3$–TMS), δ (ppm): 3.80 (s, OCH_3), 4.93 (s, NCH_2), 6.85 and 8.09 (d and d, *J* = 9 Hz, AA′BB′ system, OC_6H_4), 6.9–8.0 (m, 14 aromatic H and CH=N); ^{11}B nmr (64 MHz, $CDCl_3$–Et_2OBF_3), δ (ppm): 8.7 ($W_{1/2}$ = 342 Hz), 30.6 ($W_{1/2}$ = 342 Hz), and 46.3 ($W_{1/2}$ = 257 Hz); ratio of peak areas 1:1:1. Anal. calcd. for $C_{27}H_{24}BNO_3$: C 76.97, H 5.74, B 2.57, N 3.32; found: C 76.88, H 5.76, B 2.68, N 3.20. The product gives a blue-colored solution upon the addition of diphenylcarbazone in ethanol, indicating the presence of the chelated diphenylborenium (Ph_2B^+) ion (7).

8-(4-Dimethylaminophenylmethylene)-6,6-diphenyl-5,7-dioxa-8-azonia-6-borata-5*H*-6,7,8,9-tetrahydrobenzocycloheptene,[4] 2*b*

6*e* (0.27 g, 1.0 mmol) and oxybis(diphenylborane) (0.17 g, 0.5 mmol) are dissolved in 20 mL of absolute ethanol and refluxed for 10 min. Upon cooling to room temperature crystallization commences. Yield: 0.42 g (97%) of yellow crystals; mp 205°C (from ethanol). Infrared (KBr, cm^{-1}): 1640 (C=N), 1593 (C=C); ^1H nmr (90 MHz, $CDCl_3$–TMS), δ (ppm): 3.10 (s, $(CH_3)_2N$), 5.06 (s, $N(O)CH_2$), 6.75 and 8.21 (d and d, *J* = 9 Hz, AA′BB′ system, NC_6H_4), 6.9–8.0 (m, 14 aromatic H and CH=N); ^1H nmr (90 MHz, DMSO-d_6–TMS), δ (ppm): 3.05 (s, $(CH_3)_2N$), 5.05 (s, $N(O)CH_2$), 6.79 and 8.13 (d and d, *J* = 9 Hz, AA′BB′ system, NC_6H_4), 6.6–8.0 (m, 14 aromatic H), 8.36 (s, CH=N); ^{11}B nmr (64 MHz, $CDCl_3$–Et_2OBF_3), δ (ppm): 8.5 ($W_{1/2} \approx$ 300 Hz) and 46.5 ($W_{1/2}$ = 260 Hz); ratio of peak areas 1:2. Anal. calcd. for $C_{28}H_{27}BN_2O_2$: C 77.43, H 6.27, B 2.49, N 6.45; found: C 77.43, H 6.24, B 2.45, N 6.48. **2***b* gives a blue-colored solution upon addition of diphenylcarbazone as described for **2***a*. Crystals suitable for X-ray analysis were obtained by slow crystallization from absolute ethanol.

8-(4-Diethylaminophenylmethylene)-6,6-diphenyl-5,7-dioxa-8-azonia-6-borata-5H-6,7,8,9-tetrahydrobenzocycloheptene, 2*c*

6*f* (0.30 g, 1.0 mmol) and oxybis(diphenylborane) (0.17 g, 0.5 mmol) are dissolved in 20 mL of absolute ethanol and refluxed for 10 min. Crystallization starts upon cooling. Yield: 0.26 g (56%) of yellowish crystals; mp 183°C (from ethanol). Infrared (KBr, cm^{-1}): 1642 (C=N), 1593 (C=C); ^1H nmr (90 MHz, $CDCl_3$ – TMS), δ (ppm): 1.16 (t, *J* = 8 Hz, 2 CH_3), 3.35 (q, *J* = 8 Hz, 2 NCH_2), 4.83 (s, $N(O)CH_2$), 6.55 and 7.95 (d and d, *J* = 9 Hz, AA′BB′ system, NC_6H_4), 6.7–7.8 (m, 14 aromatic H and CH=N); ^{11}B nmr (64 MHz, $CDCl_3$–Et_2OBF_3), δ (ppm): 8.8 ($W_{1/2}$ = 550 Hz) and 46.6 ($W_{1/2}$ = 430 Hz); ratio of peak areas 5:1. Mass spectrum (EI, 150°C), *m/z* (%): 385 (74) [$M^+ - C_6H_5$], 369 (43) [$M^+ - C_6H_5 - O$], 298 (44) [$6f^+$], 282 (21) [$6f^+ - O$], 192 (59), 177 (100), 161 (42), 133 (32), 105 (26), 78 (38), 77 (32). Anal. calcd. for $C_{30}H_{31}BN_2O_2$: C 77.93, H 6.76, B 2.34, N 6.06; found: C 77.93, H 6.90, B 2.35, N 6.09. **2***c* gives a blue-colored solution upon addition of diphenylcarbazone as described for **2***a*.

Synthesis of *C*-aryl-*N*-(2-hydroxyphenylmethyl)nitrones, 6 (general procedure)

Salicylaldoxime, **4** (13.7 g, 100 mmol) is dissolved in 50 mL of methanol. After the addition of sodium cyanotrihydroborate[5] (4.2 g, 67 mmol), 50 mL of 2 N HCl solution is added dropwise under stirring, the mixture being kept at a constant pH of 3 using a pH-stat automatic titrator. The consumption is finished after about 40 min and the solution is brought to pH 6.5 with 2 N NaOH solution. A third of this solution (~40 mL), containing the hydroxylamine **5**, is mixed with 30 mmol

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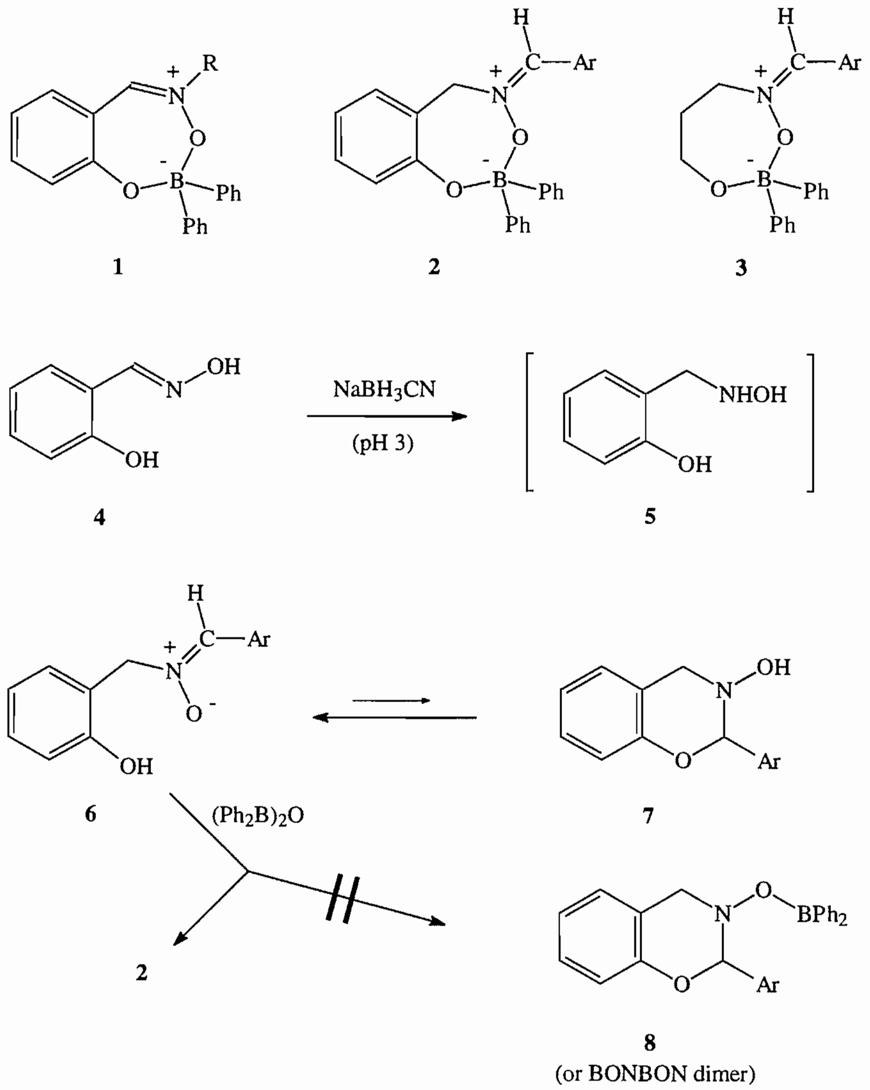
[3] Alternative nomenclature: *N*-(4-methoxyphenylmethylene)-*N*-[(2-diphenylboryloxyphenyl)methyl]amine *N*-oxide (O→B complex).

[4] Alternative nomenclature: *N*-(4-dimethylaminophenylmethylene)-*N*-[(2-diphenylboryloxyphenyl)methyl]amine *N*-oxide (O→B complex).

[5] Sodium cyanoborohydride ($NaBH_3CN$).

Scheme 1.



	Ar
2*a*	4-$MeOC_6H_4$
2*b*	4-$Me_2NC_6H_4$
2*c*	4-$Et_2NC_6H_4$

	Ar
6*a*	C_6H_5
6*b*	4-$MeOC_6H_4$
6*c*	4-$O_2NC_6H_4$
6*d*	4-ClC_6H_4
6*e*	4-$Me_2NC_6H_4$
6*f*	4-$Et_2NC_6H_4$
6*g*	2,4,6-$Me_3C_6H_2$
6*h*	1-naphthyl

of an aromatic aldehyde and is refluxed for 30 min.[6] Upon cooling, the nitrone **6** precipitates and is recrystallized from ethanol.

*C-Phenyl-*N*-(2-hydroxyphenylmethyl)nitrone, **6**a*

From benzaldehyde (3.18 g, 30 mmol). Yield: 5.46 g (80%) of colorless crystals; mp 174°C. Infrared (KBr, cm^{-1}): 3000–1700 ("curtain", O-H), 1609 (C=N), 1595 (C=C); ^1H nmr (90 MHz, $CDCl_3$–TMS), δ (ppm): 5.07 (s, NCH_2), 6.8–7.5 (m, 7 aromatic H), 7.50 (s, CH=N), 8.1–8.3 (m, 2 aromatic H), 11.35 (s, broad, exchangeable, OH). Anal. calcd. for

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[6] The remaining two thirds of the solution are reacted similarly with aromatic aldehydes to give the nitrones **6**.

Table 1. Crystallographic data.[a]

Compound	**2***b*	**6***e*
Formula	$C_{28}H_{27}BN_2O_2$	$C_{16}H_{18}N_2O_2$
FW	434.34	270.33
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$ (No. 2)	$P2_1/a$ (No. 14)
a, Å	10.6802(8)	12.2319(8)
b, Å	11.1809(4)	7.071(1)
c, Å	10.1520(3)	17.2005(9)
α, °	105.847(3)	90
β, °	92.567(4)	107.520(4)
γ, °	84.610(5)	90
V, Å^3	1160.8(1)	1418.8(2)
Z	2	4
ρ_{calc}, g/cm^3	1.242	1.265
F(000)	460	576
μ(Cu K_α), cm^{-1}	5.74	6.42
Crystal size, mm	0.12 × 0.30 × 0.35	0.08 × 0.25 × 0.40
Transmission factors	0.90–1.00	0.88–1.00
Scan type	ω–2θ	ω–2θ
Scan range, deg in ω	1.31 + 0.20 tan θ	1.31 + 0.20 tan θ
Scan speed, deg/min	32 (up to 9 scans)	32 (up to 9 scans)
Data collected	$+h, \pm k, \pm l$	$+h, +k, \pm l$
$2\theta_{max}$, deg	155	155
Crystal decay, %	Negligible	Negligible
Total reflections	5015	3266
Total unique reflections	4754	3116
R_{merge}	0.023	0.011
Reflections with $I \geq 3\sigma(I)$	3379	1800
No. of variables	383	254
R	0.035	0.032
R_w	0.036	0.032
gof	2.37	2.08
Max Δ/σ (final cycle)	0.0007	0.0003
Residual density e/Å^3	–0.10 to 0.12	–0.08 to 0.13

[a] Temperature 294 K, Rigaku AFC6S diffractometer, Cu K_α radiation (λ = 1.54178 Å), graphite monochromator, takeoff angle 6.0°, aperture 6.0 × 6.0 mm at a distance of 285 mm from the crystal, stationary background counts at each end of the scan (scan/background time ratio 2:1), $\sigma^2(F^2) = [S^2(C + 4B)]/\mathrm{Lp}^2$ (S = scan rate, C = scan count, B = normalized background count), function minimized $\Sigma w(|F_o| - |F_c|)^2$ where $w = 4F_o^2/\sigma^2(F_o^2)$, $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $R_w = (\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2)^{1/2}$, and gof $= [\Sigma w(|F_o| - |F_c|)^2/(m - n)]^{1/2}$. Values given for R, R_w, and gof are based on those reflections with $I \geq 3\sigma(I)$.

$C_{14}H_{13}NO_2$: C 74.00, H 5.77, N 6.16; found: C 73.94, H 5.78, N 6.09.

C-*(4-Methoxyphenyl)*-N-*(2-hydroxyphenylmethyl)nitrone,* *6*b
From 4-methoxybenzaldehyde (4.08 g, 30 mmol). Yield: 6.20 g (80%) of colorless crystals; mp 166°C. Infrared (KBr, cm^{-1}): 3100–1700 (“curtain”, O-H), 1603 (C=N, C=C); ^{1}H nmr (90 MHz, $CDCl_3$−TMS), δ (ppm): 3.80 (s, OCH_3), 5.02 (s, NCH_2), 6.86 and 8.13 (d and d, *J* = 9 Hz, AA′BB′ system, OC_6H_4), 6.66–7.36 (m, 4 aromatic H), 7.43 (s, CH=N), 11.75 (s, exchangeable, OH). Anal. calcd. for $C_{15}H_{15}NO_3$: C 70.02, H 5.88, N 5.44; found: C 69.90, H 5.87, N 5.37.

C-*(4-Nitrophenyl)*-N-*(2-hydroxyphenylmethyl)nitrone,* *6*c
From 4-nitrobenzaldehyde (4.53 g, 30 mmol). Yield: 6.42 g (79%) of yellow crystals; mp 174°C. Infrared (KBr, cm^{-1}): 3200–1700 (“curtain”, O-H), 1598 and 1579 (C=N, C=C); ^{1}H nmr (90 MHz, $CDCl_3$ – TMS), δ (ppm): 5.15 (s, NCH_2), 6.76–7.43 (m, 4 aromatic H), 7.66 (s, CH=N), 8.20 and 8.35 (d and d, *J* = 9 Hz, AA′BB′ system, $O_2NC_6H_4$), 10.43 (s, exchangeable, OH). Anal. calcd. for $C_{14}H_{12}N_2O_4$: C 61.76, H 4.44, N 10.29; found: C 61.21, H 4.47, N 9.99.

C-*(4-Chlorophenyl)*-N-*(2-hydroxyphenylmethyl)nitrone,* *6*d
From 4-chlorobenzaldehyde (4.22 g, 30 mmol). Yield: 5.78 g (74%) of colorless needles; mp 174°C. Infrared (KBr, cm^{-1}): 3000–1700 (“curtain”, O-H), 1588 (C=N, C=C); ^{1}H nmr (90 MHz, $CDCl_3$−TMS), δ (ppm): 5.10 (s, NCH_2), 6.73–7.56 (m, 4 aromatic H), 7.38 and 8.20 (d and d, *J* = 9 Hz, AA′BB′ sys-

tem, ClC_6H_4), 7.52 (s, CH=N), 11.13 (s, exchangeable, OH). Anal. calcd. for $C_{14}H_{12}ClNO_2$: C 64.25, H 4.62, Cl 13.55, N 5.35; found: C 64.25, H 4.60, Cl 13.19, N 5.23.

C-*(4-Dimethylaminophenyl)*-N-*(2-hydroxyphenylmethyl)-nitrone,* ***6*e**

From 4-dimethylaminobenzaldehyde (4.48 g, 30 mmol). Yield: 7.20 g (89%) of pale yellow crystals; mp 200°C. Infrared (KBr, cm^{-1}): 3000–1700 ("curtain", O-H), 1618 (C=N), 1589 (C=C); ^1H nmr (90 MHz, $CDCl_3-TMS$), δ (ppm): 3.07 (s, $(CH_3)_2N$), 5.04 (s, $N(O)CH_2$), 6.96 and 8.13 (d and d, J = 9 Hz, AA′BB′ system, NC_6H_4), 6.80–7.33 (m, 4 aromatic H), 7.36 (s, CH=N), 12.25 (s, exchangeable, OH). Anal. calcd. for $C_{16}H_{18}N_2O_2$: C 71.09, H 6.71, N 10.36; found: C 71.07, H 6.77, N 10.37. Crystals suitable for X-ray analysis were obtained by very slow cooling of a saturated solution of **6*e*** in ethyl acetate, mp 201°C.

C-*(4-Diethylaminophenyl)*-N-*(2-hydroxyphenylmethyl)-nitrone,* ***6*f**

From 4-diethylaminobenzaldehyde (5.32 g, 30 mmol). Yield: 5.43 g (61%) of pale yellow crystals; mp 176°C. Infrared (KBr, cm^{-1}): 3100–1700 ("curtain", O-H), 1597 and shoulder at 1610 (C=N, C=C); ^1H nmr (90 MHz, $CDCl_3-TMS$), δ (ppm): 1.18 (t, J = 8 Hz, 2 CH_3), 3.38 (q, J = 8 Hz, 2 NCH_2), 5.02 (s, $N(O)CH_2$), 6.63 and 8.08 (d and d, J = 9 Hz, AA′BB′ system, NC_6H_4), 6.50–7.30 (m, 4 aromatic H), 7.33 (s, CH=N), 12.36 (s, exchangeable, OH). Anal. calcd. for $C_{18}H_{22}N_2O_2$: C 72.45, H 7.43, N 9.39; found: C 72.52, H 7.39, N 9.39.

C-*(2,4,6-Trimethylphenyl)*-N-*(2-hydroxyphenylmethyl)-nitrone,* ***6*g**

From 2,4,6-trimethylbenzaldehyde (4.45 g, 30 mmol). Yield: 4.96 g (61%) of a colorless powder; mp 166°C. Infrared (KBr, cm^{-1}): 3200–1900 ("curtain", O-H), 1592 and shoulder at 1600 (C=N, C=C); ^1H nmr (90 MHz, $CDCl_3-TMS$), δ (ppm): 2.16 (s, 2 *o*-CH_3), 2.26 (s, *p*-CH_3), 5.08 (s, NCH_2), 6.70–7.40 (m, 6 aromatic H), 7.75 (s, CH=N), 11.30 (s, exchangeable, OH). Anal. calcd. for $C_{17}H_{19}NO_2$: C 75.81, H 7.11, N 5.20; found: C 75.96, H 7.12, N 5.20.

C-*(1-Naphthyl)*-N-*(2-hydroxyphenylmethyl)nitrone,* ***6*h**

From 1-naphthylbenzaldehyde (4.69 g, 30 mmol). Yield: 6.34 g (76%) of colorless crystals; mp 164°C. Infrared (KBr, cm^{-1}): 3100–1800 ("curtain", O-H), 1604 (C=N), 1590 (C=C); ^1H nmr (90 MHz, $CDCl_3-TMS$), δ (ppm): 5.23 (s, NCH_2), 6.73–8.10 (m, 10 aromatic H), 8.30 (s, CH=N), 9.35 (d, J = 7.5 Hz, 1 aromatic H), 11.30 (s, exchangeable, OH). Anal. calcd. for $C_{18}H_{15}NO_2$: C 77.96, H 5.45, N 5.05; found: C 77.89, H 5.26, N 4.74.

3-Acetyloxy-2-(4-dimethylaminophenyl)-3,4-dihydro-2*H*-1,3-benzoxazine, 9*a* (Scheme 2)

A solution of acetylchloride (0.08 g, 1.0 mmol) in 5 mL of benzene is slowly added to a solution of **6*e*** (0.27 g, 1.0 mmol) and triethylamine (0.10 g, 1.0 mmol) in 20 mL of dry benzene. After 2 h of stirring at 50°C the precipitated triethylammonium chloride is filtered off, and the solution is evaporated in vacuo. The remaining oil is brought to crystallization with petroleum ether and (or) diethyl ether. Yield: 0.20 g (64%) of a slightly discolored white powder; mp 129°C (from benzene). Infrared (KBr, cm^{-1}): 1749 (C=O), 1612 (C=C); ^1H nmr (90 MHz, $CDCl_3-TMS$), δ (ppm): 1.93 (s, CH_3CO), 2.96 (s, $(CH_3)_2N$), 4.33 (s, broad, $N(O)CH_2$), 6.02 (s, O-CH-N), 6.72 and 7.46 (d and d, J = 7 Hz, AA′BB′ system, NC_6H_4), 6.9–7.4 (m, 4 aromatic H). Anal. calcd. for $C_{18}H_{20}N_2O_3$: C 69.21, H 6.45, N 8.97; found: C 68.90, H 6.56, N 8.84.

3-Benzoyloxy-2-(4-dimethylaminophenyl)-3,4-dihydro-2*H*-1,3-benzoxazine, 9*b*

6*e* (0.27 g, 1.0 mmol), triethylamine (0.10 g, 1.0 mmol), and benzoylchloride (0.14 g, 1.0 mmol) are reacted as described for **9*a***. Yield: 0.25 g (67%) of a colorless white powder; mp 129°C (from benzene – petroleum ether). Infrared (KBr, cm^{-1}): 1748 (C=O), 1615 (C=C); ^1H nmr (90 MHz, $CDCl_3-TMS$), δ (ppm): 2.90 (s, $(CH_3)_2N$), 4.50 (m, $N(O)CH_2$), 6.16 (s, O-CH-N), 6.68 and 7.88 (d and d, J = 8 Hz, AA′BB′ system, NC_6H_4), 6.8–7.6 (m, 9 aromatic H). Anal. calcd. for $C_{23}H_{22}N_2O_3$: C 73.78, H 5.92, N 7.48; found: C 74.06, H 6.10, N 7.27.

C-(4-Dimethylaminophenyl)-*N*-[2-(phenylcarbamoyloxy)-phenylmethyl]nitrone, 10

6*e* (0.27 g, 1.0 mmol) in 30 mL of dry benzene is mixed with phenylisocyanate (0.12 g, 1.0 mmol) and refluxed for 6 h. The solvent is distilled off and the residue recrystallized from benzene – petroleum ether. Yield: 0.17 g (44%) of pale yellow crystals; mp 131°C. Infrared (KBr, cm^{-1}): 3409 (N-H), 1755 and 1741 (C=O), 1618 and 1590 (C=N, C=C); ^1H nmr (90 MHz, $CDCl_3-TMS$), δ (ppm): 3.04 (s, $(CH_3)_2N$), 5.03 (s, $N(O)CH_2$), 6.68 and 8.12 (d and d, J = 9 Hz, AA′BB′ system, NC_6H_4), 6.7–7.4 (m, 9 aromatic H), 7.35 (s, CH=N), ~11 (very broad, exchangeable, NH). Anal. calcd. for $C_{23}H_{23}N_3O_3$: C 70.93, H 5.95, N 10.79; found: C 70.72, H 5.99, N 10.75.

X-ray crystallographic analyses of 2*b* and 6*e*

Crystallographic data appear in Table 1. The final unit-cell parameters were obtained by least squares on the setting angles for 25 reflections with 2θ = 86.6°–93.5° for **2*b*** and 88.2°–95.9° for **6*e***. The intensities of three standard reflections, measured every 200 reflections throughout the data collections, showed only small random fluctuations for both compounds. The data were processed,[7] and corrected for Lorentz and polarization effects and for absorption (based on azimuthal scans).

The structures were solved by direct methods, the coordinates of the non-hydrogen atoms being determined from *E*-maps or from subsequent difference Fourier syntheses. All non-hydrogen atoms were refined with anisotropic thermal parameters. For **2*b*** a difference map indicated that the NMe_2 hydrogen atoms (associated with C(27) and C(28)) were 3:2 twofold disordered with respect to rotation about

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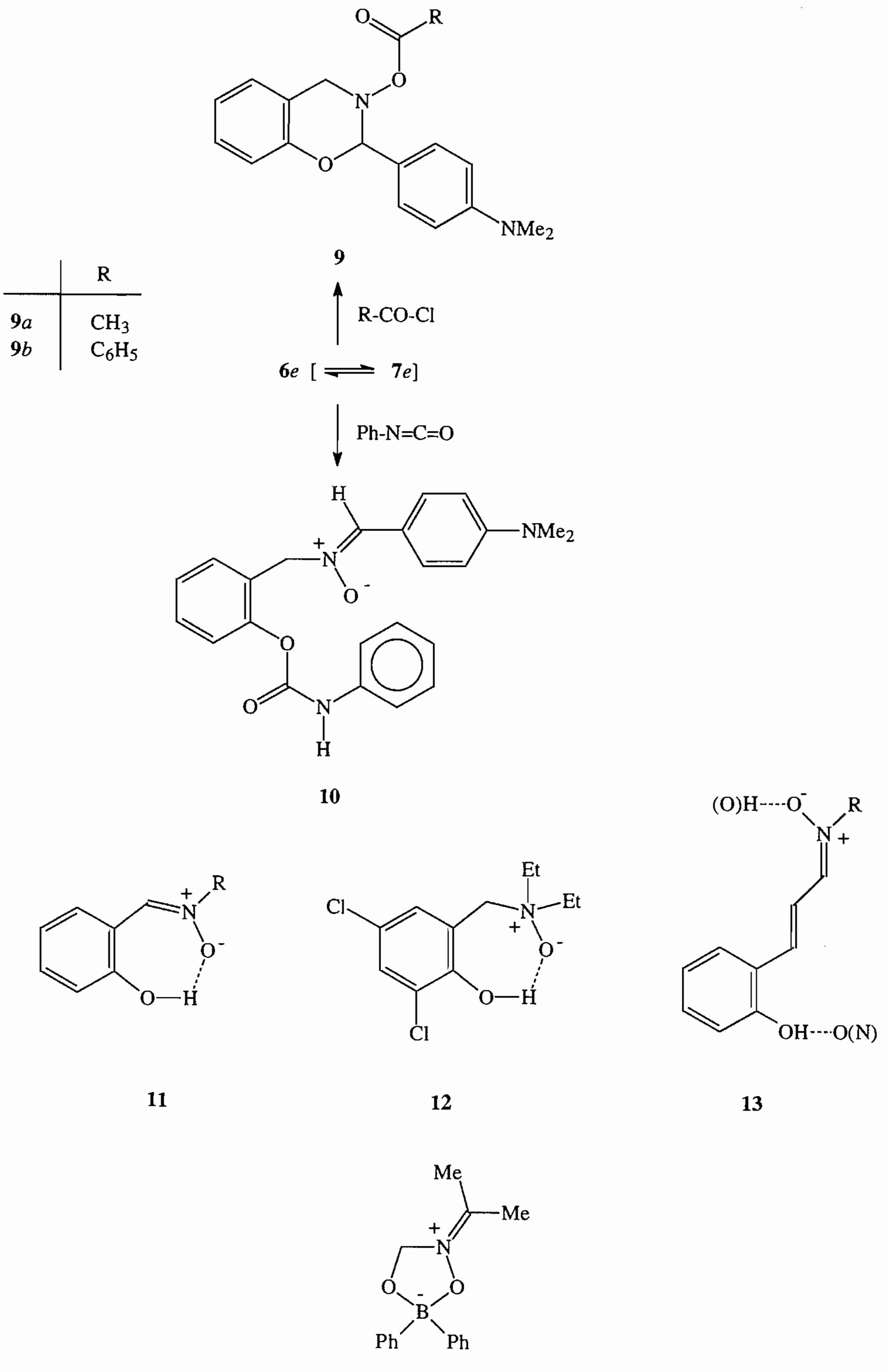
[7] *teXsan*: Crystal structure analysis package. Unix version 1.7. Molecular Structure Corporation. The Woodlands, Tex., U.S.A. 1995.

Scheme 2.



the N—C bonds. These disordered hydrogen atoms were fixed in calculated positions with C—H = 0.98 Å and B_H = 1.2 $B_{\text{bonded atom}}$ and all remaining hydrogen atoms of **2***b* and all those of **6***e* were refined with isotropic thermal parameters. Corrections for secondary extinction were applied (Zachariasen type, isotropic, Gaussian), the final values of the extinction coefficients being 7.8(2) × 10^{-6} for **2***b* and 7.73(11) × 10^{-6} for **6***e*. Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from the *International tables for X-ray crystallography* (8). Final atomic coordinates and equivalent isotropic thermal parameters, bond lengths, bond

Table 2. Final atomic coordinates (fractional) and B_{eq} (Å^2).[a]

Atom	x	y	z	B_{eq}
		2*b*		
O(1)	0.25618(9)	0.18444(8)	0.47205(10)	3.44(2)
O(2)	0.2527(1)	0.05590(10)	0.2275(1)	4.41(3)
N(1)	0.3157(1)	0.0955(1)	0.5285(1)	3.34(3)
N(2)	0.3279(1)	0.5637(1)	1.0859(1)	4.43(3)
C(1)	0.3158(2)	−0.0357(1)	0.4446(2)	3.95(4)
C(2)	0.1918(1)	−0.0593(1)	0.3732(2)	3.65(3)
C(3)	0.1647(2)	−0.0087(1)	0.2637(2)	3.94(3)
C(4)	0.0523(2)	−0-0303(2)	0.1904(2)	5.26(5)
C(5)	−0.0309(2)	−0.1022(2)	0.2285(2)	5.90(5)
C(6)	−0.0049(2)	−0.1517(2)	0.3369(2)	5.43(5)
C(7)	0.1063(2)	−0.1299(1)	0.4103(2)	4.48(4)
C(8)	0.3524(1)	0.1250(1)	0.6557(2)	3.44(3)
C(9)	0.3475(1)	0.2419(1)	0.7561(2)	3.37(3)
C(10)	0.2905(2)	0.3561(1)	0.7420(2)	3.80(3)
C(11)	0.2858(2)	0.4610(1)	0.8487(2)	4.04(4)
C(12)	0.3365(1)	0.4604(1)	0.9794(2)	3.61(3)
C(13)	0.3957(2)	0.3460(2)	0.9936(2)	4.11(4)
C(14)	0.3996(2)	0.2418(2)	0.8860(2)	4.00(4)
C(15)	0.1924(1)	0.2904(1)	0.2910(2)	3.77(4)
C(16)	0.1589(2)	0.4028(2)	0.3861(2)	4.91(4)
C(17)	0.0859(2)	0.5001(2)	0.3521(2)	5.77(5)
C(18)	0.0445(2)	0.4864(2)	0.2197(3)	6.11(6)
C(19)	0.0749(2)	0.3769(2)	0.1229(3)	6.30(6)
C(20)	0.1472(2)	0.2806(2)	0.1580(2)	5.18(5)
C(21)	0.4309(1)	0.1925(1)	0.3049(2)	3.77(3)
C(22)	0.4999(2)	0.1192(2)	0.1935(2)	4.47(4)
C(23)	0.6246(2)	0.1355(2)	0.1756(2)	5.68(5)
C(24)	0.6844(2)	0.2267(2)	0.2701(3)	6.22(6)
C(25)	0.6198(2)	0.3014(2)	0.3804(3)	5.99(6)
C(26)	0.4949(2)	0.2841(2)	0.3974(2)	4.85(4)
C(27)	0.2654(2)	0.6803(2)	1.0723(2)	5.98(5)
C(28)	0.3744(2)	0.5619(2)	1.2219(2)	5.44(5)
B(1)	0.2839(2)	0.1774(2)	0.3215(2)	3.59(4)
		6*e*		
O(1)	0.37986(9)	0.1588(2)	0.28554(8)	5.29(3)
O(2)	0.4404(1)	0.3113(2)	0.17254(9)	6.46(4)
N(1)	0.2665(1)	0.1598(2)	0.25789(8)	4.08(3)
N(2)	0.2872(1)	0.1491(2)	0.64420(8)	4.55(4)
C(1)	0.2183(2)	0.1708(3)	0.1674(1)	4.60(5)
C(2)	0.2375(1)	0.3613(3)	0.13453(9)	3.94(4)
C(3)	0.3467(1)	0.4187(3)	0.13657(10)	4.64(4)
C(4)	0.3610(2)	0.5893(4)	0.1002(1)	5.91(6)
C(5)	0.2675(2)	0.6995(4)	0.0631(1)	6.30(7)
C(6)	0.1598(2)	0.6461(4)	0.0617(1)	6.13(6)
C(7)	0.1448(2)	0.4763(3)	0.0975(1)	4.95(5)
C(8)	0.2001(1)	0.1543(2)	0.3037(1)	4.02(4)
C(9)	0.2309(1)	0.1491(2)	0.39115(10)	3.73(4)
C(10)	0.3423(1)	0.1462(3)	0.4454(1)	4.02(4)
C(11)	0.3602(1)	0.1443(3)	0.5280(1)	4.07(4)
C(12)	0.2689(1)	0.1468(2)	0.5616(1)	3.80(4)
C(13)	0.1575(1)	0.1469(3)	0.5071(1)	4.27(4)
C(14)	0.1401(1)	0.1484(3)	0.4246(1)	4.17(4)
C(15)	0.4016(2)	0.1581(4)	0.7000(1)	5.86(6)
C(16)	0.1921(2)	0.1616(4)	0.6775(1)	5.24(5)

[a] $B_{eq} = (8/3)\pi^2\Sigma\Sigma(U_{ij}a_i{*}a_j{*}(\mathbf{a}_i.\mathbf{a}_j))$.

Table 3. Bond lengths (Å) with estimated standard deviations in parentheses.

Bond	Length	Bond	Length
2b			
O(1)—N(1)	1.371(1)	O(1)—B(1)	1.549(2)
O(2)—C(3)	1.357(2)	O(2)—B(1)	1.488(2)
N(1)—C(1)	1.482(2)	N(1)—C(8)	1.294(2)
N(2)—C(12)	1.349(2)	N(2)—C(27)	1.445(2)
N(2)—C(28)	1.451(2)	C(1)—C(2)	1.492(2)
C(2)—C(3)	1.387(2)	C(2)—C(7)	1.388(2)
C(3)—C(4)	1.389(2)	C(4)—C(5)	1.385(3)
C(5)—C(6)	1.368(3)	C(6)—C(7)	1.379(3)
C(8)—C(9)	1.419(2)	C(9)—C(10)	1.402(2)
C(9)—C(14)	1.408(2)	C(10)—C(11)	1.361(2)
C(11)—C(12)	1.412(2)	C(12)—C(13)	1.413(2)
C(13)—C(14)	1.361(2)	C(15)—C(16)	1.387(2)
C(15)—C(20)	1.392(2)	C(15)—B(1)	1.613(2)
C(16)—C(17)	1.390(2)	C(17)—C(18)	1.369(3)
C(18)—C(19)	1.366(3)	C(19)—C(20)	1.383(3)
C(21)—C(22)	1.396(2)	C(21)—C(26)	1.394(2)
C(21)—B(1)	1.616(2)	C(22)—C(23)	1.387(3)
C(23)—C(24)	1.378(3)	C(24)—C(25)	1.371(3)
C(25)—C(26)	1.391(3)		
		6e	
O(1)—N(1)	1.324(2)	O(2)—C(3)	1.359(2)
N(1)—C(1)	1.491(2)	N(1)—C(8)	1.291(2)
N(2)—C(12)	1.370(2)	N(2)—C(15)	1.440(2)
N(2)—C(16)	1.446(2)	C(1)—C(2)	1.507(3)
C(2)—C(3)	1.385(2)	C(2)—C(7)	1.385(2)
C(3)—C(4)	1.394(3)	C(4)—C(5)	1.372(3)
C(5)—C(6)	1.363(3)	C(6)—C(7)	1.387(3)
C(8)—C(9)	1.437(2)	C(9)—C(10)	1.400(2)
C(9)—C(14)	1.396(2)	C(10)—C(11)	1.371(2)
C(11)—C(12)	1.404(2)	C(12)—C(13)	1.403(2)
C(13)—C(14)	1.370(2)		

angles, and intra-annular torsion angles appear in Tables 2–5, respectively. Hydrogen atom parameters, anisotropic thermal parameters, and torsion angles, intermolecular contacts, and least-squares planes are included as supplementary material.[8]

Results and discussion

Synthesis and structure of the nitrones 6

N-(2-Hydroxyphenylmethyl)hydroxylamines **5** were generated by the reduction of salicylaldoximes **4** with $NaBH_3CN$ at pH 3 (9) for the synthesis of the nitrones **6**. The hitherto unknown hydroxylamine **5** appears to be a very unstable compound and could not be isolated, neither as a free base nor as a hydrochloride salt. It was possible, however, to trap compound **5** in situ as its nitrone derivatives **6** by the addition of an aromatic aldehyde to the reaction mixture of the salicylaldoxime reduction. The condensation products **6** crystallized in good yields.

Since it has been reported that *N*-(2-hydroxyalkyl)nitrones (10), *N*-(3-hydroxyalkyl)nitrones (11), and also *N*-(2-hydroxynaphthylmethyl)nitrones (12) can isomerize to cyclotautomeric *N*-hydroxy-oxazolidine or *N*-hydroxy-perhydro-1,3-oxazine derivatives, an isomerism between the open-chain nitrone form **6** and the cyclic form **7** had to be considered. It is known from the literature (4, 10–13) that nitrones derived from aromatic aldehydes are very stable in their open-chain nitrone form, and that no trace of the ring form is detectable by spectroscopic means in inert solvents. Only aliphatic aldo- or ketonitrones display evidence of both forms in their nmr spectra.

The nitrone structure cannot be deduced unequivocally from the infrared spectra of **6** (KBr pellets) because the

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[8] Copies of material on deposit may be purchased from: The Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, Canada K1A 0S2. Tables of hydrogen atom coordinates and bond lengths and angles involving hydrogen atoms have also been deposited with the Cambridge Crystallographic Data Centre and can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.

Table 4. Bond angles (deg) with estimated standard deviations in parentheses.

Bonds	Angle(deg)	Bonds	Angle(deg)
	2*b*		
N(1)-O(1)-B(1)	118.3(1)	C(3)-O(2)-B(1)	119.7(1)
O(1)-N(1)-C(1)	116.5(1)	O(1)-N(1)-C(8)	120.3(1)
C(1)-N(1)-C(8)	122.4(1)	C(12)-N(2)-C(27)	121.7(1)
C(12)-N(2)-C(28)	121.8(1)	C(27)-N(2)-C(28)	116.4(1)
N(1)-C(1)-C(2)	110.8(1)	C(1)-C(2)-C(3)	116.8(1)
C(1)-C(2)-C(7)	123.0(2)	C(3)-C(2)-C(7)	120.2(2)
O(2)-C(3)-C(2)	118.4(1)	O(2)-C(3)-C(4)	122.0(2)
C(2)-C(3)-C(4)	119.6(2)	C(3)-C(4)-C(5)	119.2(2)
C(4)-C(5)-C(6)	121.4(2)	C(5)-C(6)-C(7)	119.6(2)
C(2)-C(7)-C(6)	120.1(2)	N(1)-C(8)-C(9)	131.0(1)
C(8)-C(9)-C(10)	126.9(1)	C(8)-C(9)-C(14)	116.5(1)
C(10)-C(9)-C(14)	116.5(1)	C(9)-C(10)-C(11)	121.5(2)
C(10)-C(11)-C(12)	121.8(1)	N(2)-C(12)-C(11)	121.6(1)
N(2)-C(12)-C(13)	121.5(1)	C(11)-C(12)-C(13)	116.8(1)
C(12)-C(13)-C(14)	120.6(2)	C(9)-C(14)-C(13)	122.7(1)
C(16)-C(15)-C(20)	115.4(2)	C(16)-C(15)-B(1)	125.3(1)
C(20)-C(15)-B(1)	119.2(2)	C(15)-C(16)-C(17)	122.8(2)
C(16)-C(17)-C(18)	119.6(2)	C(17)-C(18)-C(19)	119.5(2)
C(18)-C(19)-C(20)	120.4(2)	C(15)-C(20)-C(19)	122.3(2)
C(22)-C(21)-C(26)	115.9(2)	C(22)-C(21)-B(1)	122.1(2)
C(26)-C(21)-B(1)	121.9(2)	C(21)-C(22)-C(23)	122.3(2)
C(22)-C(23)-C(24)	119.8(2)	C(23)-C(24)-C(25)	119.7(2)
C(24)-C(25)-C(26)	120.0(2)	C(21)-C(26)-C(25)	122.3(2)
O(1)-B(1)-O(2)	111.2(1)	O(1)-B(1)-C(15)	103.5(1)
O(1)-B(1)-C(21)	110.6(1)	O(2)-B(1)-C(15)	110.5(1)
O(2)-B(1)-C(21)	108.2(1)	C(15)-B(1)-C(21)	112.8(1)
	6*e*		
O(1)-N(1)-C(1)	114.7(1)	O(1)-N(1)-C(8)	124.3(1)
C(1)-N(1)-C(8)	121.0(1)	C(12)-N(2)-C(15)	120.9(2)
C(12)-N(2)-C(16)	120.8(2)	C(15)-N(2)-C(16)	118.0(2)
N(1)-C(1)-C(2)	112.4(1)	C(1)-C(2)-C(3)	120.7(2)
C(1)-C(2)-C(7)	119.9(2)	C(3)-C(2)-C(7)	119.3(2)
O(2)-C(3)-C(2)	121.5(2)	O(2)-C(3)-C(4)	119.0(2)
C(2)-C(3)-C(4)	119.5(2)	C(3)-C(4)-C(5)	120.0(2)
C(4)-C(5)-C(6)	121.1(2)	C(5)-C(6)-C(7)	119.2(2)
C(2)-C(7)-C(6)	120.8(2)	N(1)-C(8)-C(9)	128.7(2)
C(8)-C(9)-C(10)	126.4(1)	C(8)-C(9)-C(14)	116.2(1)
C(10)-C(9)-C(14)	117.4(2)	C(9)-C(10)-C(11)	120.7(2)
C(10)-C(11)-C(12)	121.9(2)	N(2)-C(12)-C(11)	121.7(2)
N(2)-C(12)-C(13)	121.1(1)	C(11)-C(12)-C(13)	117.2(2)
C(12)-C(13)-C(14)	120.6(2)	C(9)-C(14)-C(13)	122.2(2)

Table 5. Intra-annular torsion angles (deg) for **2*b*** with standard deviations in parentheses.

Atoms	Value (deg)	Atoms	Value (deg)
O(1)-N(1)-C(1)-C(2)	−40.0(2)	C(3)-O(2)-B(1)-O(1)	25.7(2)
N(1)-C(1)-C(2)-C(3)	73.2(2)	O(2)-B(1)-O(1)-N(1)	58.3(2)
C(1)-C(2)-C(3)-O(2)	1.3(2)	B(1)-O(1)-N(1)-C(1)	−46.6(2)
C(2)-C(3)-O(2)-B(1)	−67.7(2)		

Fig. 1. Stereoview of **6***e*; 33% probability thermal ellipsoids are shown for the non-hydrogen atoms. Unfilled bonds and fine lines represent hydrogen bonds and C—H···O interactions, respectively.

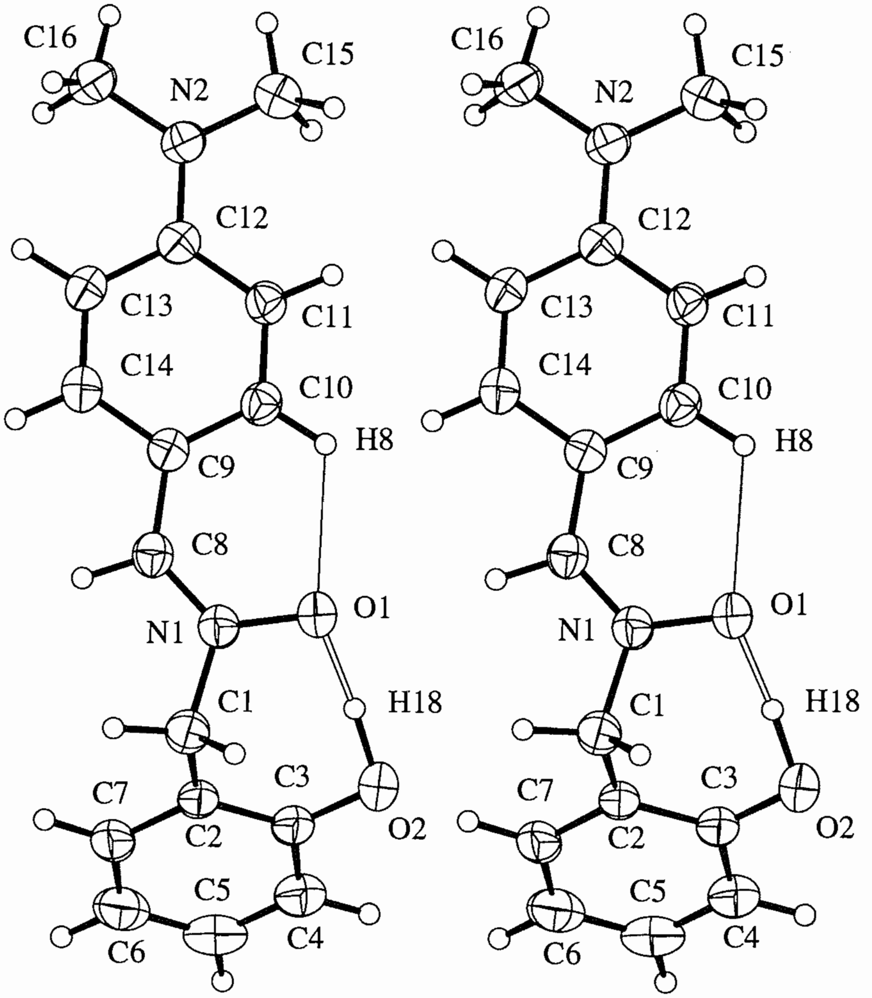
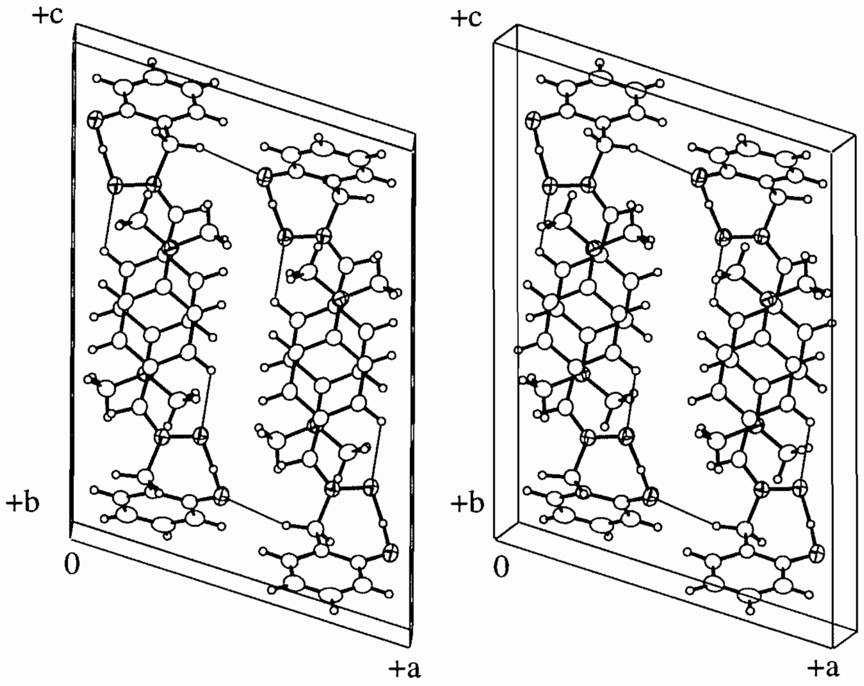


Table 6. Comparison of selected ^{1}H nmr data of 4-substituted benzaldehyde nitrones **6** and pK_a values of the corresponding *N*-methylnitrones (15).

Ar	$\delta_{CH=N}$ (ppm)	δ_{OH} (ppm)	p*K*a values for Ar-CH=N(O)Me (15)
4-$NO_2C_6H_4$ (**6***c*)	7.66	10.43	6.10
4-ClC_6H_4 (**6***d*)	7.52	11.13	7.67
C_6H_5 (**6***a*)	7.50	11.35	8.26
4-$MeOC_6H_4$ (**6***b*)	7.43	11.75	9.43
4-$Me_2NC_6H_4$ (**6***e*)	7.36	12.25	11.94
4-$Et_2NC_6H_4$ (**6***f*)	7.33	12.36	—

expected C=N stretching vibrations near 1600 cm^{-1} coincide with the ν_{16} C=C ring stretching of the aromatic ring systems in these molecules, and the distinction is further complicated by resonance interactions between the nitrone and the conjugated aryl group. Very broad "curtain" type O-H association bands between 3100 and 1700 cm^{-1}, however, are consistent with the nitrone form **6** having an intramolecular hydrogen bond involving the "chelated" phenolic proton like those known for salicylaldonitrones **11** (1, 14) (Scheme 2). The nitrone form is clearly demonstrated in the ^{1}H nmr spectra of **6** by signals for the CH=N methine proton at ~7.5 ppm, similar to those observed for other *C*-arylnitrones (1, 4, 10*a*, 12, 14*b*, 15). Signals for the O-CH-N methine protons of the cyclic form **7**, typically around 5–6 ppm, were not detected. In accor-

Fig. 2. Stereoview of the packing arrangement of **6***e*; 33% probability thermal ellipsoids are shown for the non-hydrogen atoms. Unfilled bonds and fine lines represent hydrogen bonds and C—H···O interactions, respectively.



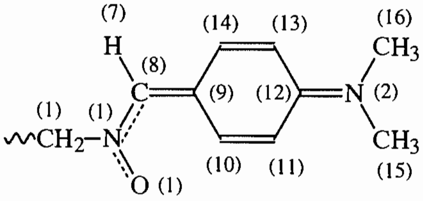
dance with the predominant or exclusive open-chain nitrone form **6** in solution, the "chelated" phenolic proton gives rise in each case to a downfield signal at ~11.4 ppm, characteristic for intramolecular hydrogen bonds of this type (1, 12*a*, 12*c*, 14*a*, 16). Comparison of the ^{1}H nmr spectra of the 4-substituted benzaldonitrones **6** (see Table 6) shows that the increasing downfield shift of the OH signal reflects the strengthening of the hydrogen bond due to the increasing basicity of the azomethine *N*-oxide group, going from the 4-nitro- to the 4-diethylaminophenyl derivative. For comparison, Table 6 also lists the pK_a values reported for the *N*-methylnitrones having the corresponding 4-substituents at the *C*-aryl residue (17). There is also an increasing, though less distinct, balancing upfield shift of the signals assigned to the CH═N methine protons in the same sequence of nitrones **6** (Table 6), indicating the gain in shielding by the electron-donating substituents in the 4-position.

The X-ray analysis of **6***e* establishes the nitrone structure of the type **6** compounds, at least in the crystalline state, and shows the intramolecular hydrogen bond between the phenolate and *N*-oxide oxygen atoms, already suggested by the ^{1}H nmr and infrared spectra (Fig. 1). In the crystal of **6***e* this O(2)—H(18)···O(1) hydrogen bond (O—H = 1.13(3) Å, O···H = 1.40(3) Å, O···O = 2.521(3) Å, O—H···O = 174(2)°) represents a strong hydrogen bond (18) within a seven-membered "proton chelate" having metrical parameters similar to those of two other phenolic *N*-oxides with intramolecular H-bridges: the *N*-*tert*-butylsalicylaldonitrone **11** (R = CMe_3) (19) and the 2-(diethylaminomethyl)-4,6-dichlorophenol *N*-oxide **12** (20) with H···O (O···O) distances of 1.53 Å (2.47 Å) and 1.22/1.31 Å (2.407/2.425 Å), respectively. The nearly linear O—H...O angle in **6***e* may contribute to the bonding energy and lies in between the corresponding values of 170.6° in **11** (19) and 175/177° in **12** (20). The nearly linear intramolecular O—H...O angles in **6***e*, **11**, and **12** are comparable to those reported for *inter*molecular O—H···O(N) hydrogen bonds in various vinyl salicylaldonitrones like **13** (21) that cannot form intramolecular H-bridges and crystallize in "head-to-tail" chains via O–H...O hydrogen bonds (O···H = 1.44–1.96 Å, O···O = 2.567–2.662 Å, O—H···O = 135°–180°). Furthermore, the (*Z*) arrangement at the nitrone double bond allows the formation of an intramolecular C—H···O hydrogen bond (C(10)—H(8)...O(1): C—H = 1.00(1) Å, O···H = 2.30(1) Å, C···O = 2.922(2) Å, C—H...O = 119(1)°). The geometry of this intramolecular C—H···O interaction is clearly consistent with the presence of a hydrogen bond (22) which may play a role in determining the solid state molecular conformation.

The crystal packing of **6***e* (Fig. 2) is dominated by three intermolecular C—H···O contacts that meet the requirements of hydrogen bonding (22): C(1)—H(2) and C(8)—H(7) both interact with the same phenolic oxygen atom O(2) to link *a*-glide related "helical enantiomers" into linear chains, and one of the *N*-methyl groups forms the C(15)—H(14)...O hydrogen bond to a neighboring nitrone oxygen atom cross-linking the chains along *b*. The geometry of these interactions is as follows: C(1)—H(2)...O(2)($-1/2 + x$, $1/2 - y$, z), C(8)—H(7)···O(2)($-1/2 + x$, $1/2 - y$, z), C(15)—H(14)···O(1)($1 - x$, $-y$, $1 - z$); C—H = 1.03(2), 1.00(2), 1.01(2) Å; H···O = 2.47(2), 2.48(2), 2.47(2) Å; C···O = 3.429(2), 3.306(2), 3.439(2) Å; and C—H···O = 153(1)°, 165(1)°, 160(2)°; respectively.

The C═N bond length (1.291(2) Å) does not differ significantly from the values found for other nitrones (19, 21, 23, 24) whereas the N—O bond (1.324(2) Å) is slightly longer, prob-

Fig. 3. Mesomeric electron distribution in the 4-dimethylaminophenylmethylidene resonance system.



ably because of the involvement of the nitrone oxygen atom in the very strong intramolecular hydrogen bond. As a consequence of the interaction of the nitrone group and the 4-dimethylaminophenyl π-system, an approximate coplanarity is seen in this part of the molecule. The relatively short bond lengths for N(2)—C(12) (1.370(2) Å), C(10)—C(11) (1.371(2) Å), C(13)—C(14) (1.370(2) Å), and C(8)—C(9) (1.437(2) Å) are indicative of a significant contribution from the 4-dimethylaminomethylidene resonance form having double bonds at these locations (Fig. 3). The phenolic ring system of C(2)—C(7) plus O(2) is twisted out of the mean plane of the remainder of the molecule by about 60°.

Synthesis and structure of the boron chelates 2

To examine the chelate-forming properties of the nitrones **6** by replacement of the "chelated" phenolic proton with a diphenylborenium ion (Ph_2B^+), the compounds **6** were reacted with diphenylborinic acid anhydride, $(Ph_2B)_2O$, in ethanol. Only the 4-dialkylaminophenyl derivatives **6***e* and **6***f* gave crystalline diphenylboron chelates (**2***b* and **2***c*) stable enough for recrystallization. The 4-methoxyphenyl derivative **2***a* could be obtained only as a crude crystalline product that decomposes easily by solvolysis. In all the other cases the respective bidentate ligand **6** was recovered unchanged, even from water-free aprotic media like benzene with continuous removal of reaction water by azeotropic distillation (Dean–Stark trap).

Thus details of the formation of the seven-membered boron chelates **2** resembles the results reported for the synthesis of type **3** chelates (4). Both ring systems show that the ring enlargement of stable six-membered boron chelates derived from aromatic aldonitrones (10*a*) to seven-membered chelates is disadvantageous with respect to the stability of these compounds if the nitrone N=C bond appears as a substitutive (exocyclic) double bond. In the case of the salicylaldonitrone boron chelates **1**, however, with the N=C nitrone double bond being part of the chelate ring (endocyclic), the chelate stability is adequate for various derivatives that could be recrystallized without difficulties despite the enlarged ring system (1, 2). As for the boron chelates **3**, the electron-donating 4-dialkylamino substituent of the *C*-aryl residue of the chelates **2***b* and **2***c* increases the basicity at the nitrone oxygen enough to enable the formation of a chelate sufficiently stable for recrystallization or for analyses of solutions. A similar, though weaker, effect is achieved by the 4-methoxy substituent in the chelate **2***a*.

The solvolytic sensitivity of **2** becomes obvious in the ^{11}B nmr spectra where, in addition to signals for tetracoordinate (sp^3) boron at δ (Et_2OBF_3) = 8.5–8.8 ppm, second signals appear at 46.3–46.6 ppm indicating the presence of a trivalent (sp^2) boron atom of a Ph_2B-O-R moiety (25) that might result from ring opening at the weaker O—B bond to the nitrone oxygen ligand in solution. The solvolysis observed in the $CDCl_3$ solutions of the ^{11}B nmr experiments is a partial solvolysis, the mechanism of which is not yet clear. Other solvents like DMSO-d_6 are even less suitable because of water content. While we are not sure just what Ph_2B-O-R moiety (possibly the ring-opened compound **2** or free diphenylborinic acid) gives rise to the signal at 46.6 ppm, this species should be a trivalent Ph_2B-O-R moiety. The additional peak at 30.6 ppm in the spectrum of **2***a* points to more extensive decomposition of the diphenylborinic acid component that may result from dephenylation by moisture (H_2O traces, or even HCl traces in the $CDCl_3$) or from oxidation by atmospheric oxygen in the solvent, resulting in a $Ph_2B(OR)_2$ phenylboronic acid derivative (25). Experiments with special precautions to exclude water or oxygen in the nmr experiments have not been performed.

The ^1H nmr spectra of **2** do not display any signals at 5–6 ppm indicative of an N-CH-O methine signal that could be assigned to the diphenylborinate **8** (or its BONBON dimer[9]) deriving from a possible cyclotautomer **7**. The CH=N methine signal indicating the nitrone form **2** appears hidden behind the multiplets arising from the aromatic proton signals in each case.

The infrared spectra of **2** show a distinct shift, about 30 cm^{-1}, of the nitrone C=N stretching band to higher frequencies compared to the respective free ligands **6**, indicating the increased iminium salt character of the nitrone moiety in the boron chelates **2**. Similar tendencies have also been observed in the formation of boron chelates from other nitrone ligands (1, 4, 10).

No molecular ion peak was observed in the mass spectrum of **2***c* (investigated as an example). As noted earlier for the seven-membered boron chelates **3** (4), only a dephenylated fragment (M^+ − 77) could be detected. This is typical for diphenylboron chelates and points to a preferred transition of the zwitterionic compound **2***c* to the stable (**2***c* − $C_6H_5)^+$ ion.

An X-ray analysis of **2***b*, derived from the free ligand **6***e* (see above), establishes the seven-membered boron chelate structure **2** (Fig. 4), which represents a new type of heterocyclic *B*,*N*-betaine (27). The proton of the intramolecular O—H···O moiety in **6***e* is replaced by the diphenylborenium cation, leading to some changes in the geometry of **2***b*. Besides the C(10)—H(8)...O(1) intramolecular contact, which is maintained in the chelate **2***b* without any significant changes, three additional intramolecular C—H···O interactions (all involving the phenolate oxygen atom O(2)) are noted: (C(10)—H(8)···O(1), C(1)—H(1)···O(2), C(20)—H(16)···O(2), C(22)—H(17)···O(2); C—H = 0.96(2), 0.99(2), 1.02(2), 0.96(2) Å; H···O = 2.32(2), 2.43(2), 2.50(2), 2.46(2) Å; C···O = 2.915(2), 2.708(2), 2.906(2), 2.857(2); Å; C—H···O = 119(1)°, 95(1)°, 103(1)°, 103(1)°, respectively). The relatively acute C—H···O angles for the three interactions involving O(2) suggest that these weak interactions probably have little influence on the molecular conformation (22). As noted above for **6***b*, the *C*-arylnitrone moiety is

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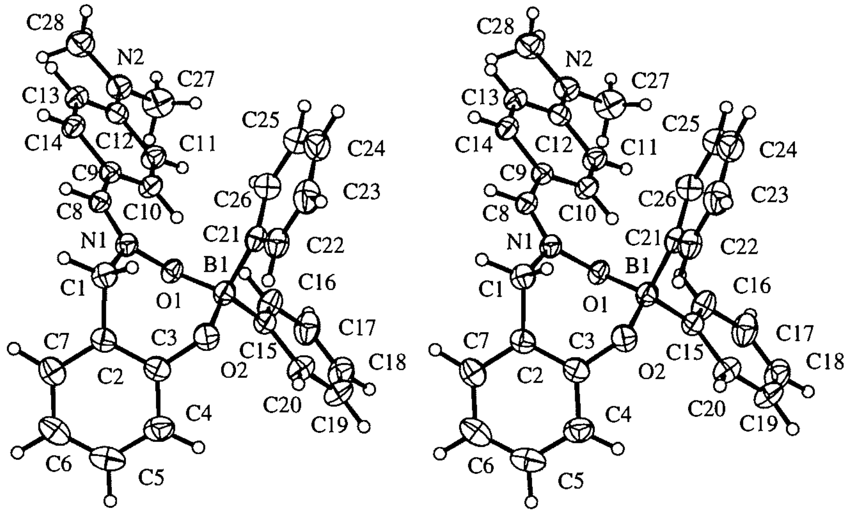
[9] For more information about BONBON dimers of borinates from hydroxylamine derivatives see ref. 26 and papers cited therein.

Fig. 4. Stereoview of **2***b*; 33% probability thermal ellipsoids are shown for the non-hydrogen atoms.



roughly coplanar. The *C*-arylnitrone mean plane makes a dihedral angle of about 67° with that of phenolate system C(2)—C(7) plus O(2), indicating a somewhat larger rotation in **2***b* than in the free ligand **6***e*. The centrosymmetric structure of **2***b*, like that of **6***e*, contains pairs of "helical enantiomers." Molecules of **2***b* are separated by normal van der Waals distances, the shortest intermolecular distance between non-hydrogen atoms being N(2)···C(13) = 3.407(2) Å.

The insertion of the Lewis acid diphenylboron group in place of the phenolic hydrogen of **6***e* enhances the iminium salt character of the nitrone moiety in **2***b*. Within the 4-dimethylaminophenylmethylidene moiety (Fig. 3) of **2***b*, the double bond character of the N(2)—C(12), C(10)—C(11), C(13)—C(14), and C(8)—C(9) bonds is even more pronounced than in **6***e* (for **2***b*: 1.349(2), 1.361(2), 1.361(2), and 1.419(2) Å, respectively; for **6***e*: 1.370(2), 1.371(2), 1.370(2), and 1.437(2) Å). The N—O bond of the nitrone group in **6***e* (1.324(2) Å), already longer than those for nitrone groups not involved in hydrogen bonding, is further lengthened by about 0.05 Å in the boron chelate **2***b* (1.371(1) Å). This represents a decrease in the π-bond order of the nitrone N—O bond from 0.35 in the free ligand **6***e* to 0.22 in the chelate **2***b*, estimated from plots of bond distance vs. HMO–π-bond order (28*b*). The $C{=}N^+$ nitrone double bond, however, remains practically unchanged (1.291(2) Å in **6***e* and 1.294(2) Å in **2***b*) with an estimated (28*a*) HMO–π-bond order of 0.82 in both the ligand and the chelate, and is comparable to the $C{=}N^+$ bond in **1** (R = Me) (1.291(4) Å) (2). It is somewhat surprising that the chelate formation, i.e., the incorporation of the Lewis acid boron nucleus, has a more profound effect on the more distant 4-dimethylaminophenyl resonance system than on the conjugated nitrone $C{=}N^+$ group.

As in **1** (R = Me) (2) and other boron chelates obtained from bidentate ligands having *N*-oxide and alcoholate or phenolate oxygen donor atoms (23, 29), the (N)O—B bond in **2***b* is longer (1.549(2) Å) than the (C)O—B bond (1.488(2) Å). The sum of the bond lengths about the boron atom in **2***b* (6.266 Å) is about the same as in the other type of seven-membered diphenylboron chelate **1** (R = Me) (6.276 Å) (2), consistent with the observation that for a given chelate ring size this sum is essentially constant (30). The mean (phenyl)C—B bond length in **2***b* (1.615(2) Å) is similar to corresponding values observed for **1** (R = Me) (2) and other Ph_2BO_2 chelates (29*a*–*d*, 29*g*, 30–32). The mean C—B/mean O—B bond length ratio for **2***b* (1.063) indicates a slightly increased binding strength of the bidentate ligand with respect to the diphenylboron moiety compared to the other type of seven-membered chelate **1** (R = Me) (2), which has an average C—B/O—B ratio of 1.054. Similar values calculated from the bond lengths observed for various six-membered "Ph_2BO_2" chelates provide a good estimate of overall chelate binding strength (31).

The chelate ring geometry of **2***b* (with an exocyclic N═C double bond) generally allows somewhat smaller intracyclic angles at the ring member atoms than does the geometry of **1** (2) with an endocyclic N═C double bond. In **1** nearly all of the chelate ring angles are widened: the sum of the intracyclic bond angles is 858.4° compared to 811.7° in **2***b*. If the differing alkylidene substituents are not considered, the new boron chelates **2** may be formally regarded as ring-enlarged "phenylogues" (by *o*-phenyl insertion) of the five-membered diphenylboron chelate **14**, which has been fully characterized by X-ray crystallographic analysis (29*g*). Comparing the dimensions of the chelate rings in **2***b* and **14**: similar bond distances are found at the "Ph_2BO_2" moiety and wider ring angles are found at all ring member atoms of **2***b*, in particular the N-O-B angle that changes from 104.7(2)° in **14** to 118.3(1)° in **2***b*.

Acylation of the nitrones 6

Since the attack of the Lewis acid diphenylborinic acid at the nitrone groups leads preferentially to the boron chelates **2** rather than to an *O*-borylated cyclotautomerization product **8**, acylation was attempted with an acyl halide and an isocyanate. Thus the reaction of **6***e* with acetyl chloride (R = Me) and benzoyl chloride (R = Ph) resulted in the crystalline benzoxazine derivatives **9**, whereas the reaction with phenyl isocyanate gave the phenylcarbamoylated phenol **10** with an intact nitrone function. The *N*-acyloxy derivatives **9***a*,*b* display ester carbonyl C═O stretching bands in the infrared spectra at about 1750 cm^{-1} and have the typical O-CH-N acetalic methine proton signal near $\delta = 6.1$ ppm in the ^1H nmr spectra. Comparable acylations of the ring tautomers of *N*-(2-hydroxyalkyl)nitrones (10), *N*-(3-hydroxyalkyl)nitrones (4), and *N*-(2-hydroxynaphthylmethyl)nitrones (12*b*, 12*c*, 33) have been reported. Compound **10** is not only characterized by urethane C=O and nitrone C=N stretching bands in the infrared spectrum, but also by the typical $CH{=}N^+$ methine proton signal at 7.35 ppm in the ^1H nmr spectrum. The latter excludes not only a 1,3-benzoxazine derivative like **9**, but also an isoxazolidine derivative as a result of the possible 1,3-dipolar cycloaddition of phenylisocyanate to the nitrone group. It should be noted that the ester or urethane C=O stretch is not a good means for discrimination and it serves only for the characterization of both compounds. It is also *not* the 7.35 ppm signal in the ^1H nmr (buried under the multiplet of aromatic protons) that discriminates, but rather the *absence* of the acetalic O-CH-N methine signal around 6 ppm that suggests the open-chain nitrone form of **10**. X-ray analysis would certainly establish these structures, but it has not yet been possible to obtain suitable crystals of **9** and **10**.

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