α-Hydroxyalkyl(benzyl)furazans and α-hydroxyalkyl(benzyl)furoxans Synthesis and reactivity

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A general and simple preparative method for the synthesis of α-hydroxyalkyl(benzyl)furazan and -furoxan derivatives is proposed. The method involves reduction of acyl or ethoxycarbonyl substituents in these heterocyclic compounds with $NaBH_4$ in ethanol. Based on the alcohols thus prepared, a number of previously unknown functional derivatives (α-nitroxyalkyl-, α-haloalkyl-, and α-azidoalkylfurazans and -furoxans) have been synthesized.

Key words: furazans, furoxans, reduction, nucleophilic substitution.

Until recently, the set of known functionally substituted furazans and furoxans, which permit target-directed syntheses of various derivatives of these heterocyclic compounds as possible biologically active materials, has been quite limited. Compounds with substituents containing a carbonyl group in the α-position could serve as suitable objects for extending the range of accessible furazan and furoxan derivatives. The development of convenient methods for the preparation of these compounds[1–3] allowed us to begin a systematic study of their reactivities. Previously, bromination[4] and nitrosation[5] of acetylfurazans and acetylfuroxans have been studied. The present paper is devoted to the investigation of the reduction of the acyl and ethoxycarbonyl substituents in these heterocyclic compounds to α-hydroxyalkyl and α-hydroxybenzyl groups and to the synthesis of various functional derivatives of furazan and furoxan based on the compounds obtained.

Only a few examples of the reduction of carbonyl-containing groups in the derivatives of furazan and furoxan have been reported; in all cases, $NaBH_4$ was used as the reducing agent. For example, treatment of 3,4-dibenzoylfuroxan (**1a**) with $NaBH_4$ in ethanol led to the reduction of both carbonyl groups in this compound to hydroxyl groups and gave 3,4-bis(α-hydroxybenzyl)furoxan (**2a**) in 75% yield.[6] When the mixed anhydride obtained *in situ* from 4-phenylfurazan-3-carboxylic acid and ethyl chlorocarbonate was reduced with the same reagent, 3-hydroxymethyl-4-phenylfurazan was isolated in 91 % yield.[7] The carbonyl group was reduced to an alcoholic group in 60 % yield when 5-bromo-4,4-dimethyl-6-oxocyclohexanofuroxan was treated with $NaBH_4$ in dioxane.[8] However, no examples of reduction of alkoxycarbonyl groups in furazan and furoxan derivatives have been reported. Data on the reactivities of hydroxyl-containing derivatives of these heterocyclic compounds are also lacking.

Based on this information, we decided to study in more detail the reduction of acetyl and benzyl groups in furazan and furoxan derivatives to the corresponding α-hydroxy-derivatives through the action of $NaBH_4$ and also to study the possibility of using this reagent for the reduction of the ethoxycarbonyl groups in these heterocyclic derivatives to hydroxymethyl groups. $NaBH_4$ is known to be usually relatively ineffective for the reduction of ester groups; therefore, this reduction is normally carried out using $LiAlH_4$.[9] However, the furoxan ring is unstable in the presence of $LiAlH_4$.[10] At the same time, 4-nitro- and 2,4-dinitrophenyl esters of aliphatic carboxylic acids are known[11] to be successfully reduced with $NaBH_4$ to their hydroxymethyl derivatives, which has been explained by the strong electron-withdrawing effect of nitroaromatic compounds. Since both furazan and furoxan rings exhibit clear-cut electron-withdrawing effects,[12] it might have been expected that alkoxycarbonylfurazans and -furoxans would be reduced with $NaBH_4$ to the corresponding α-hydroxymethyl derivatives.

In fact, we found that this reagent in ethanol is effective for the transformation of both acyl and ethoxycarbonyl groups in furazan and furoxan derivatives to the corresponding α-hydroxyalkyl or α-hydroxybenzyl substituents (Scheme 1). The reduction of ethoxycarbonyl groups in furoxans was found to require merely a somewhat greater amount of the reductive agent than the reduction of acyl derivatives. It should be noted that to isolate the final reaction products, alcohols of the furazan and furoxan series, the reaction mixture needs in all cases to be treated with excess HCl, which is necessary for the hydrolysis of the borates of the obtained alcohols. The position of the *N*-oxide oxygen atom in the furoxan ring has no effect on the ability of the acyl and ethoxycarbonyl groups to be reduced. For example, in the case of 3,4-diacetylfuroxan (**1b**), both carbonyl-containing fragments are reduced. The reduc-

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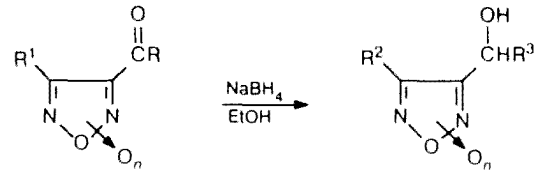
tion of both the 3- and 4-ethoxycarbonyl substituents in 4-amino-3-ethoxycarbonylfuroxan (**1h**) and 4-ethoxycarbonyl-3-methylfuroxan (**1i**) (Scheme 1) also occurs successfully.

Scheme 1

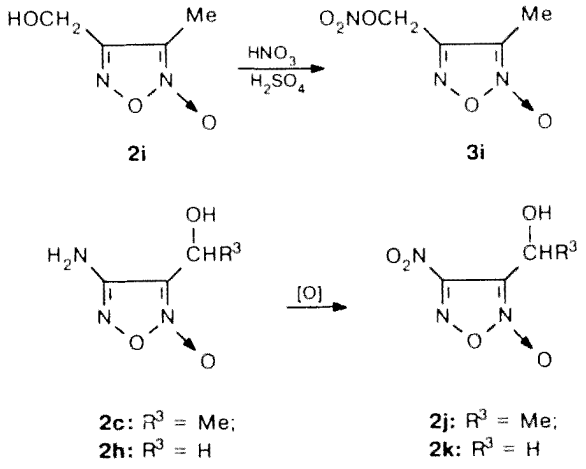


1b—i **2b—i**

Compound	R	R^1	n	Compound	R^2	R^3	n
1b	Me	MeCO	1	**2b**	Me(OH)CH	Me	1
1c	Me	4-NH_2	1	**2c**	4-NH_2	Me	1
1d	Ph	4-NH_2	1	**2d**	4-NH_2	Ph	1
1e	Me	MeCO	0	**2e**	Me(OH)CH	Me	0
1f	Me	4-NH_2	0	**2f**	4-NH_2	Me	0
1g	Ph	4-NH_2	0	**2g**	4-NH_2	Ph	0
1h	OEt	4-NH_2	1	**2h**	4-NH_2	H	1
1i	OEt	3-Me	1	**2i**	3-Me	H	1

The large number of hydroxy-derivatives **2a—i** obtained made it possible to study their reactivities. For example, using the hydroxymethyl derivative **2i** as an example we showed that the hydroxy group is readily nitrated by a mixture of HNO_3 and H_2SO_4 to give the corresponding nitroxymethyl derivative (**3i**). We also found that the amino group in amino-derivatives **2c** and **2h** can be oxidized by peroxide oxidants to a nitro group (the hydroxyl fragment remaining unaffected), thus yielding nitro derivatives **2j** and **2k** (Scheme 2).

Scheme 2

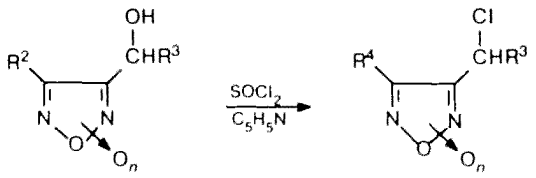


2i **3i**

2c: R^3 = Me; **2h**: R^3 = H **2j**: R^3 = Me; **2k**: R^3 = H

In addition, the hydroxyl group in the alcohols synthesized is successfully replaced by a chlorine atom through the action of the $SOCl_2$—pyridine complex in CH_2Cl_2 or in dioxane to give previously unknown α-chloroalkyl or α-chlorobenzyl furazan and furoxan derivatives (**4a—c,f—k**) in preparative yields (Scheme 3).

Scheme 3

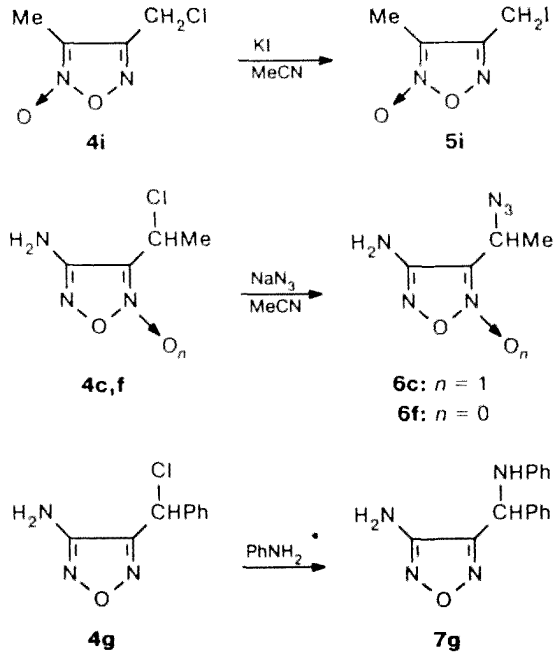


2a—c,f—k **4a—c,f—k**

Compound	R^3	n	2, R^2	4, R^4
a	Ph	1	Ph(OH)CH	PhCH(Cl)
b	Me	1	Me(OH)CH	MeCH(Cl)
c	Me	1	4-NH_2	4-NH_2
f	Me	0	4-NH_2	4-NH_2
g	Ph	0	4-NH_2	4-NH_2
h	H	1	4-NH_2	4-NH_2
i	H	1	3-Me	3-Me
j	Me	1	4-NO_2	4-NO_2
k	H	1	4-NO_2	4-NO_2

The development of a fairly convenient method for the synthesis of α-chloroalkyl and α-chlorobenzyl derivatives of furazan and furoxan makes it possible to substantially extend the set of accessible functional derivatives of these heterocyclic compounds. Scheme 4 shows several examples of replacement of the chlorine atom by various nucleophiles (I, N_3, NHPh). It is obvious that these transformations by no means exhaust the possibili-

Scheme 4



4i **5i**

4c,f **6c**: n = 1 **6f**: n = 0

4g **7g**

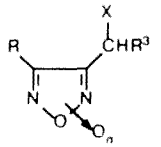
Table 1. Characteristics of furoxan and furazan derivatives

Compound	Yield (%)	M.p./°C	R_f	Found / Calculated (%) C	H	N	Molecular formula	IR, ν/cm^{-1}	MS, m/z (I_{rel} (%))	^{14}N (^{15}N) NMR (CD_3COD_3), δ, J/Hz
Furoxans										
3,4-Bis(1-hydroxyethyl)-furoxan (**2b**)	92	Oil[a]	0.49[b]					1385, 1460, 1635, 2955, 2995		
4-Amino-3-(1-hydroxy-ethyl)furoxan (**2c**)	84	102—103 (from $CHCl_3$)	0.35[b]	32.65 / 33.09	4.59 / 4.86	29.27 / 28.96	$C_4H_7N_3O_3$	1630, 2945, 2990, 3005, 3235, 3320, 3390, 3415	145 [M$^+$](24), 115(22), 97(31), 85(14), 70(100)	
4-Amino-3-(α-hydroxy-benzyl)furoxan (**2d**)	41	116—118	0.46[b]	51.81 / 52.17	4.77 / 4.38	20.03 / 20.28	$C_9H_9N_3O_3$	1320, 1380, 1450, 1485, 1625, 2940, 2985, 3310, 3395		
4-Amino-3-hydroxy-methylfuroxan (**2h**)	53	106—108	0.26[b]	27.42 / 27.48	4.10 / 3.84	30.73 / 31.11	$C_3H_5N_3O_3$	1620, 1640, 2960, 3240, 3340, 3435	131 [M$^+$](25), 101(19), 83(25), 74(33), 71(41), 70(100)	
4-Hydroxymethyl-3-methylfuroxan (**2i**)	85	Oil[a]	0.41[b]					1610, 2930, 2980, 3430	130 [M$^+$](100), 100(86), 70(37), 69(90)	
3-(1-Hydroxyethyl)-4-nitrofuroxan (**2j**)	41	Oil[a]	0.28[c]					1360, 1460, 1635, 2940, 3005, 3430		
3-Hydroxymethyl-4-nitrofuroxan (**2k**)	81	Oil[a]	0.55[c]					1360, 1580, 1640, 2860, 2940, 3400	162 [M$^+$+1](2), 115(25), 86(4), 85(100), 84(72)	
3-Methyl-4-nitroxy-methylfuroxan (**3i**)	81	13—16	0.26[d]	27.35 / 27.44	3.13 / 2.88	23.72 / 24.00	$C_4H_5N_3O_5$	1280, 1620, 1650, 2930 2970, 3030	175 [M$^+$](24), 145(16), 130(16), 115(24), 113(40), 100(20), 99(88), 97(20)	^{14}N: −50.0 br. (ONO_2), −19.0 br. (N_{ring})
3,4-Bis(α-chlorobenzyl)-furoxan (**4a**)	81	Oil[a]	0.64[b]					1380, 1455, 1600, 1650, 2795, 3055		
3,4-Bis(1-chloroethyl)-furoxan (**4b**)	68	Oil[a]	0.57[b]					1390, 1470, 1520, 1620, 2900, 2955, 3010		^{14}N: −13.3 br. (N_{ring})
4-Amino-3-(1-chloroethyl)-furoxan (**4c**)	72	69—71	0.42[b]	29.55 / 29.37	3.79 / 3.70	25.26 / 25.69	$C_4H_6ClN_3O_2$	1385, 1450, 1490, 1610, 1645, 2980, 3250, 3330, 3430		
4-Amino-3-chloromethyl-furoxan (**4h**)	38	101—102	0.47[b]	24.30 / 24.09	2.77 / 2.68	28.28 / 28.10	$C_4H_3ClN_3O_2$	1615, 3245, 3340, 3430		^{15}N: −337.50 (NH_2)
4-Chloromethyl-3-methylfuroxan (**4i**)	70	Oil[a]	0.24[e]							1620, 1630, 2860, 2930, 2980, 3040 2980, 3040
3-(1-Chloroethyl)-4-nitrofuroxan (**4j**)	86	Oil[a]	0.50[d]					1360, 1580, 1635, 1650, 2940, 3030		

Compound	Yield (%)	M.p./°C	R_f	Found / Calculated (%) C	H	N	Molecular formula	IR, ν/cm^{-1}	MS, m/z (I_{rel} (%))	^{14}N (^{15}N) NMR (CD_3COD_3), δ, J/Hz
3-Chloromethyl-4-nitrofuroxan (**4k**)	51	Oil[a]	0.67[b]					1340, 1570, 1620, 2820, 2980, 3040		^{14}N: −34.7 br. (NO_2)
4-Iodomethyl-3-methylfuroxan (**5i**)	94	Oil[a]	0.48[d]							^{15}N: −22.75 (N_{ring}-2), $^5J_{^{15}N-^1H}(CH_2)$ = 3.5; −12.63 (N_{ring}-5), $^3J_{^{15}N-^1H}(CH_3)$ = 3.3
4-Amino-3-(1-azidoethyl)-furoxan (**6c**)	54	Dec. without melting[a]	0.52[b]					1320, 1370, 1390, 1450, 1490, 1550, 1610, 2125, 2940, 2990, 3360, 3450		^{14}N: −159.57 (−NNN), −137.31 (−NNN), −17.4 br. (N_{ring})
Furazans										
3,4-Bis(1-hydroxyethyl)-furazan (**2e**)	90	Oil[a]	0.53[b]					1380, 1420, 1455, 2950, 2995		
4-Amino-3-(1-hydroxyethyl)-furazan (**2f**)	93	73 (from $CHCl_3$)	0.31[b]	37.02 / 37.21	5.33 / 5.46	32.74 / 32.56	$C_4H_7N_3O_2$	1325, 1380, 1420, 1450, 1530, 1635, 2945, 2995		
4-Amino-3-(α-hydroxy-benzyl)furazan (**2g**)	87	90–92[a] (from $CHCl_3$)	0.71[g]					1330, 1405, 1450, 1495, 1520, 1625, 3050, 3300, 3400		
4-Amino-3-(1-chloroethyl)-furazan (**4f**)	56	47–48 (from $CHCl_3$+ C_6H_{14})	0.48[b]	32.38 / 32.56	4.22 / 4.10	28.13 / 28.48	$C_4H_6ClN_3O$	1380, 1440, 1530, 1630, 2940, 2960, 3330, 3460		
4-Amino-3-(α-chlorobenzyl)-furazan (**4g**)	54	63–65 (from C_6H_{14})	0.72[b]	51.12 / 51.57	3.75 / 3.85	19.88 / 20.04	$C_9H_8ClN_3O$	1360, 1440, 1460, 1495, 1525, 1635, 3070, 3340, 3480		
4-Amino-3-(1-azido-ethyl)furazan (**6f**)	38	Dec. without melting[a]	0.48[b]					1390, 1445, 1530, 1640, 2125, 2940, 3000, 3360, 3440		^{14}N: −347 br. (NH_2), −164.0 (−NNN), −136.2 (−NNN), 22.9 br. (N_{ring})
4-Amino-3-[(α-phenylamino)-benzyl]furazan (**7g**)	67	98–99 (from C_6H_{14})	0.55[d]	66.80 / 66.65	5.56 / 5.30	21.70 / 21.04	$C_{15}H_{14}N_4O$	1320, 1435, 1500, 1605, 1625, 3040, 3060, 3365, 3460		

[a] The compound could not be isolated in an analytically pure state. [b] $CHCl_3$: Pr^iOH = 9 : 1. [c] PhH : EtOAc = 3 : 1. [d] $CHCl_3$, [e] CCl_4 : $CHCl_3$ = 1 : 1. [g] $CHCl_3$: MeCOMe = 3 : 1.

Table 2. ^{1}H NMR spectra of the furoxan and furazan derivatives

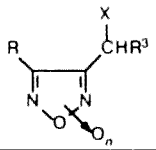


Compound	Solvent	δ, *J*/Hz					
		R	X	R^3	Me [Ph]	CH [CH_2]	OH [NH_2]
		Furoxans (*n* = 1)					
2b	$CDCl_3$	4-MeCH[OH]	OH	Me	1.42 d (^3J = 1.0), 1.43 d (^3J = 1.0), 1.53 d (^3J = 6.5), 1.55 d (^3J = 6.5)	4.88 q (^3J = 1.0), 4.89 q (^3J = 1.0), 4.92 q (^3J = 6.5), 4.97 q (^3J = 6.5)	4.48 br.s
2c	CD_3COCD_3	4-NH_2	OH	Me	1.47 d	4.97 q	5.16 s [5.53 br.s]
2d	CD_3CN	4-NH_2	OH	Ph	7.38–7.51 m	5.90 s [5.10 br.s]	4.85 br. s
2h	$CDCl_3$ + CF_3COOD	4-NH_2	OH	H		[4.57 s]	5.34 br.s [OH+NH_2]
2i	CD_3COCD_3	3-Me	OH	H	2.01 s	[4.63 s]	4.68 br.s
2j	CD_3COCD_3	4-NO_2	OH	Me	1.56 d (^3J = 3.5)	5.2 q (^3J = 3.5)	4.80 br.s
2k	CD_3COCD_3	4-NO_2	OH	H		[4.77 s]	4.41 br.s
3i	CD_3COCD_3	3-Me	ONO_2	H	2.17 s	[5.52 s]	
4a	CD_3CN	4-PhCHCl	Cl	Ph	[7.33–7.48 m]	6.20 s, 6.26 s, 6.30 s, 6.33 s	
4b	CD_3COCD_3	4-MeCHCl	Cl	Me	1.73–1.83 m	5.65 q (2 H, ^3J = 6.3), 6.04 q (^3J = 6.9), 6.10 q (^3J = 6.9)	
4c	$CDCl_3$	4-NH_2	Cl	Me	1.82 d (^3J = 4.5)	5.08 q (^3J = 4.5)	[4.82 br.s]
4h	CD_3COCD_3	4-NH_2	Cl	H		[4.68 s]	[5.95 br.s]
4i	CD_3COCD_3	3-Me	Cl	H	2.24 s	[4.77 s]	
4j	$CDCl_3$	4-NO_2	Cl	Me	1.89 d (^3J = 3.4)	5.54 q (^3J = 3.4)	
4k	CD_3COCD_3	4-NO_2	Cl	H		[5.09 s]	
5i	$CDCl_3$	3-Me	I	H	2.20 s	[4.26 s]	
6c	$CDCl_3$	4-NH_2	N_3	Me	1.50 d (^3J = 2.6)	4.79 q,	[4.88 s]
		Furazans (*n* = 0)					
2e	CD_3COCD_3	MeCH[OH]	OH	Me	1.61 d (^3J = 3.3)	5.22 q (^3J = 3.3)	4.20 br.s
2f	CD_3COCD_3	NH_2	OH	Me	1.5 d (^3J = 2.2)	5.12 q (^3J = 2.2)	5.05 br.s
2g	CD_3COCD_3	NH_2	OH	Ph	[7.34–7.54 m]	6.20 d (^3J = 2.3)	5.57 d (^3J = 2.3) [5.37 br.s]
4f	$CDCl_3$	$CDCl_3$	NH_2	Cl	Me	1.94 d (^3J = 2.3)	5.39 q (^3J = 2.3) [4.64 s]
4g	$CDCl_3$	NH_2	Cl	Ph	[7.42–7.48 m]	6.33 s	[4.16 br.s]
6f	$CDCl_3$	NH_2	N_3	Me	1.95 d (^3J = 2.5)	5.39 q (^3J = 2.5)	[5.61 br.s]
7g	$CDCl_3$	NH_2	NHPh	Ph	[6.73–7.48 m]	5.87 s	4.52 br.s [NH_2+NH]

ties for the synthesis of new functionally substituted furazans and furoxans opened by this study.

It should be noted that, according to NMR spectroscopy, compounds **2b** and **2e**, obtained by the reduction

Table 3. ^{13}C NMR spectra of the furoxan and furazan derivatives



Compound	R	R^1	R^2	δ, J/Hz			
				CH_3 [Ph]	CH[CH_2]	C_{ring}-3	C_{ring}-4
				Furoxans (n = 1)			
2b[a]	4-MeCH(OH)	OH	Me	19.38, 19.50, 19.81, 20.13	61.49, 61.71, 62.39, 62.41	117.79, 117.96	159.56, 159.67
2d[a]	4-NH_2	OH	Ph	[117.60, 126.14, 128.84, 128.90, 138.93]	67.37	111.99	156.72
3i[b]	3-Me	ONO_2	H	7.46	[63.61]	111.56	151.02
4a[a]	4-PhCHCl	Cl	Ph	[128.23—136.19]	51.68, 51.72, 53.70, 53.82	115.35, 118.20	156.68, 156.92
4b[b]	4-MeCHCl	Cl	Me	20.00, 20.23, 21.66, 21.72	46.27, 46.29, 47.62, 48.01	115.33, 115.51	157.47, 157.54
4c[c]	4-NH_2	Cl	Me	21.11	46.01	111.21	155.49
4h[b]	4-NH_2	Cl	H		[32.74]	109.23	157.19
4i[a]	3-Me	Cl	H	7.78	[35.07]	96.60	155.61
4k[b]	4-NO_2	Cl	H		[33.16 ($^1J_{^{13}C-^1H}$ = = 160)]	110.23 $^2J_{^{13}C-^1H}(CH_2)$ = = 5.2	158.80 ($^1J_{^{13}C-^1H}(NO_2)$ = = 18.1)
5i[c]	3-Me	J	H	7.93 ($^1J_{^{13}C-^1H}$ = 133)	[−13.25 $^2J_{^{13}C-^1H}(CH_3)$ = = 155)]	111.85 ($^2J_{^{13}C-^1H}(CH_3)$ = = 7.4)	155.53 ($^2J_{^{13}C-^1H}(CH_2)$ = = 4.8)
6c[c]	4-NH_2	N_3	Me	15.86	51.22	110.63	155.32
				Furazans (n = 0)			
2e[c]	MeCH(OH)	OH	Me	21.49, 21.51	61.46, 61.60	156.18, 156.35	
2f[b]	NH_2	OH	Me	22.17	62.37	151.03, 156.40 (C_{ring}—NH_2)	
2g[b]	NH_2	OH	Ph	[127.16, 128.67, 128.95, 129.44, 129.73]	69.17	150.19, 156.37 (C_{ring}—NH_2)	
4f[c]	NH_2	Cl	Me	22.17	46.61	147.57, 154.27 (C_{ring}—NH_2)	
4g[c]	NH_2	Cl	Ph	[127.28, 127.73, 129.06, 129.47]	52.51	146.44, 154.13 (C_{ring}—NH_2)	
6f[b]	NH_2	N_3	Me	22.60	47.17	149.34, 155.79 (C_{ring}—NH_2)	
7g[c]	NH_2	NHPh	Ph	[114.20, 119.68, 127.00, 128.76, 129.27, 129.36, 137.95, 145.93]	54.48	147.99, 154.65 (C_{ring}—NH_2)	

Note. Solvents: [a]CD_3CN, [b]CD_3COCD_3, [c]$CDCl_3$.

of diacetylfuroxan and diacetylfurazan, as well as the products of the replacement of the hydroxyl groups in **2b** and in 3,4-bis(α-hydroxybenzyl)furoxan **2a** by chlorine (compounds **4b** and **4a)** are mixtures of diastereomers consisting of racemates and meso-forms.

Experimental

IR spectra were recorded on a UR-20 spectrometer for pellets or for thin films between pieces of KBr glass. ^1H, ^{13}C, ^{14}N, and ^{15}N NMR spectra were obtained on a Bruker AM-300 instrument operating at 300, 75.5, 21.5, and 21.5 MHz, re-

spectively. Chemical shifts were measured relative to internal tetramethylsilane (for ^1H and ^{13}C NMR) or to external $MeNO_2$ (for ^{14}N and ^{15}N NMR). Mass spectra were obtained on a Varian MAT CH-6 instrument at an ionization energy of 70 eV. TLC was carried out on Silufol UV-254 plates; the eluents used are listed below Table 1. The main characteristics of the compounds synthesized, including data of their IR spectra, mass spectra, and ^{14}N and ^{15}N NMR spectra, are given in Table 1, and the ^1H and ^{13}C NMR spectral data are presented in Tables 2 and 3, respectively.

General procedure for the preparation of hydroxy-derivatives by the reduction of furazan and furoxan carbonyl derivatives (2b—2i). A carbonyl derivative (10 mmol; or 8 mmol for compounds **1b**, **1e**, **1h**, and **1i**, or 20 mmol for **1d**) was added at 10—15 °C to $NaBH_4$ (0.23 g, 6 mmol) in 30 mL of anhydrous ethanol (in the cases of compounds **1d**, **1h**, and **1i**, the reactants were mixed in the reverse order). The reaction mixture was stirred at this temperature for 10 min (or for 1 h in the case of compound **1h**), concentrated HCl (0.7 mL) was added, and the mixture was stirred for an additional 1—2 h at ~20 °C. Ether (60 mL) and then powdered $MgSO_4$ (1 g) were added, and the mixture was stirred for 10 min and filtered. The filtrate was concentrated using a rotary evaporator to afford a reduction product, which was additionally purified by recrystallization or reprecipitation in those cases where it was a solid.

3-(1-Hydroxyethyl)-4-nitrofuroxan (2j). A 90% solution of H_2O_2 (4.0 mL) was added to anhydrous CH_2Cl_2 (60 mL), and at a temperature of no more than 20 °C, trifluoroacetic anhydride (25 mL) was added dropwise. At ~20 °C, 4-amino-3-(1-hydroxethyl)furoxan **2c** (2.9 g, 20 mmol) was added in one portion to the resulting solution. The reaction mixture was stirred for 2 h at 20 °C, diluted with water (50 mL), and extracted with CH_2Cl_2 (3×50 mL). The extracts were washed with water (3×100 mL) and dried with $MgSO_4$. Evaporation on a rotary evaporator gave compound **2j**.

3-Hydroxymethyl-4-nitrofuroxan (2k). 4-Amino-3-hydroxymethylfuroxan **2h** (1.0 g, 7.6 mmol) was added in one portion to a mixture of 90% H_2O_2 (7 mL) and conc. H_2SO_4 (7 mL), while the temperature was maintained below 18 °C. The mixture was stirred for 1 h at 20 °C. Then water (33 mL) was added dropwise at a temperature of no more than 10 °C. The mixture was extracted with EtOAc (3×25 mL), and the extracts were washed with water (2×50 mL) and dried with $MgSO_4$. Evaporation on a rotary evaporator gave compound **2k**.

3-Methyl-4-nitroxymethylfuroxan (3i). 4-Methyl-3-hydroxymethylfuroxan (**2i**) (1.0 g, 7.7 mmol) was added dropwise over a period of 5 min to a mixture of fuming HNO_3 (2 mL) and conc. H_2SO_4 (2 mL), while the temperature was maintained below 0 °C. The reaction mixture was stirred for 15 min at 5 °C, and water (20 mL) was added dropwise at a temperature of no more than 10 °C. The reaction mixture was extracted with $CHCl_3$ (3×10 mL), and the extracts were washed with water (3×20 mL) and dried with $MgSO_4$. Evaporation on a rotary evaporator gave compound **3i**.

General procedure for the preparation of chloro-derivatives by the replacement of the hydroxyl groups in furoxan and furazan derivatives (4a—c, f—k). A hydroxy-derivative (4 mmol of compounds **2a—2c**, **2f**, or **2g**, 9 mmol of compounds **2i—2k**, or 12 mmol of compound **2h**) was added with stirring and cooling with ice (at a temperature of no more than 12—15 °C) to a solution of pyridine (2.43 mL, 30 mmol) and $SOCl_2$ (2.16 mL, 30 mmol) in 15 mL of dry CH_2Cl_2 (compounds **2a**, **2b**, **2i**, **2j**, and **2k**) or in 15 mL of dry dioxane (compounds **2c**, **2f**, **2g**, and **2h**). The reaction mixture was stirred for 15 min, and 0.5 mL of water (compounds **2c**, **2f—2k**; method A) or 15 mL of water (compounds **2a**, **2b**; method B) was added dropwise with stirring. In method A, the reaction mixture was concentrated on a rotary evaporator to a small volume, and the residue was extracted with EtOAc (6×20 mL) and filtered through a thin SiO_2 layer. Evaporation on a rotary evaporator afforded a chloro-derivative, which, in some cases, was additionally purified by recrystallization. In method B, the organic layer was separated, washed with 15 mL of water, dried with $MgSO_4$, and concentrated on a rotary evaporator. The residue was dissolved in a 1 : 1 petroleum ether—benzene mixture and then the product was isolated as in method A.

4-Iodomethyl-3-methylfuroxan (5i). 4-Methyl-3-chloromethylfuroxan **4i** (0.30 g, 2 mmol) was added with stirring to a solution of NaI (0.60 g, 4 mmol) in anhydrous acetone (4 mL). The reaction mixture was stirred for 30 min and concentrated on a rotary evaporator. The residue was washed with ether (2×10 mL) on a filter, and the ethereal layer was filtered through a thin SiO_2 layer. Evaporation on a rotary evaporator gave compound **5i**.

General procedure for the preparation of azido-derivatives of furoxan and furazan (6c, 6f). Sodium azide (1.95 g, 30 mmol) was added to a solution of 1-chloroethyl derivatives **4c** and **4f** (10 mmol) in MeCN (40 mL). The reaction mixture was stirred for 10 h at 65—70 °C and poured into 60 mL of water. Extraction with $CHCl_3$ (4×45 mL), drying with $MgSO_4$, and evaporation of the solvent on a rotary evaporator gave the azido-derivatives.

4-Amino-3-[α-(phenylamino)benzyl]furazan (7g). Aniline (0.37 g, 4 mmol) was added to a solution of 4-amino-3-(α-chlorobenzyl)furazan (**4g**) (0.42 g, 2 mmol) in benzene (5 mL). The mixture was stirred for 72 h at 20 °C until **4g** disappeared, according to TLC and concentrated on a rotary evaporator. The residue was treated with water and allowed to stand until the oil crystallized. The solid product was filtered off, washed with water, triturated with hexane on a filter, and dried in air.

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