Synthesis of imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]difuroxanes

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A method for the synthesis of imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]difuroxanes, potential nitric oxide donors, has been developed. The synthesized compounds were characterized by IR and NMR spectroscopy, high resolution mass spectrometry, and elemental analysis.

Key words: 3.5-dibromophenylene-1,2-diamine, carboxylic acids, acyl chlorides, benzimidazoles, nitration, azidation, thermal cyclization, imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]difuroxanes.

Nitric oxide, being one of the universal regulators of the functions of cellular metabolism, is involved, among other things, in the regulation of the tone of blood vessels.[1] The therapeutic effect of known vasodilators is due to the processes of decomposition of these substances *in vivo* with the release of NO.[2,3] Compounds having in the structure a furoxane ring can be considered as potential nitric oxide donors.[4—11] It has been found that, as vasodilators, furoxanes are distinguished by the absence of nitrate tolerance and the slow transformation, which reduces the risk of hypotensive conditions, one of the most serious problems of antihypertensive therapy.[12] It was also noted that furoxanes possess antiinflammatory[13] and cytotoxic[14] activity. Thus, it can be concluded that compounds with a furoxane ring are promising objects for the study in pharmaceutics. At the present time, the studies are carried out for both the linear heterocyclic assembles based on furoxanes and the fused systems. Among the latter, a certain interest is caused by benzodifuroxanes,[15—17] compounds with two furoxane rings in the structure.

From the multitude of annulated systems with a furoxane ring, a relatively new type based on imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]difuroxane requires special attention. Imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]difuroxane derivatives are nitric oxide generators,[18] possess vasodilator,[18] spasmolytic,[18] hypotensive[18] effect and inhibit platelet aggregation.[18—23]

An example of the synthesis of imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]difuroxane from 4,7-diiodo-5,6-dinitrobenzimidazole was described recently.[24]

In the present work, we consider a general approach to the synthesis of imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]difuroxanes, representatives of a new class of NO-generating compounds.

Results and Discussion

The condensation of 3,5-dibromophenylene-1,2-diamine (**1**) with carboxylic acids leads to the corresponding benzimidazoles **2a**—**e**. Compound **2f** was obtained by the reaction of **1** with valeroyl chloride in the presence of pyridine (Scheme 1).

The nitration of compounds **2a**—**f** with a mixture of concentrated HNO_3 and H_2SO_4 at 90—95 °C gave the corresponding dinitroderivatives **3a**—**f** (Scheme 2).

Treatment of compounds **3a**—**f** with NaN_3 in DMF at room temperature led to the formation of the corresponding diazido derivatives **4a**—**f** (Scheme 3).

Because of a potentially high sensitivity to mechanical impacts, compounds **4a**—**f** after the azidation reaction were precipitated from DMF with water and subject-

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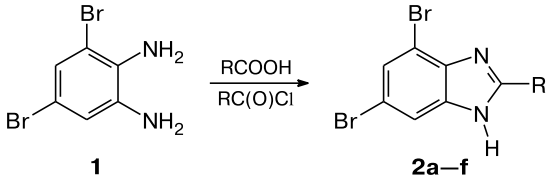
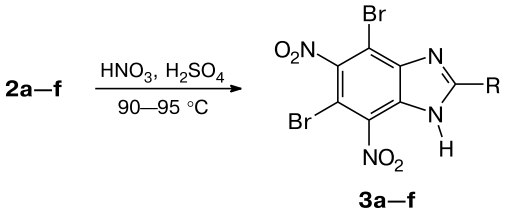
Scheme 1



1 **2a—f**

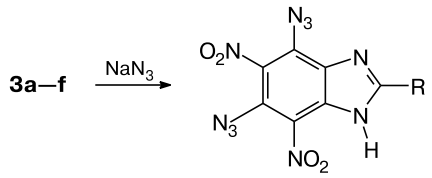
R = H (**a**), Me (**b**), Et (**c**), Pr (**d**), Pr^{i} (**e**), Bu (**f**)

Scheme 2



3a—f

Scheme 3

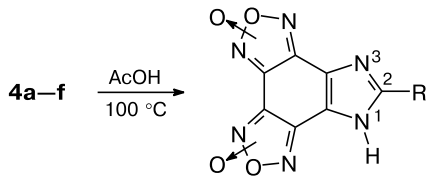


4a—f

ed to thermal cyclization without preliminary purification and drying.

Compounds **5a**—**f** were obtained by heating diazido derivatives **4a**—**f** in glacial AcOH at 100 °C (Scheme 4).

Scheme 4

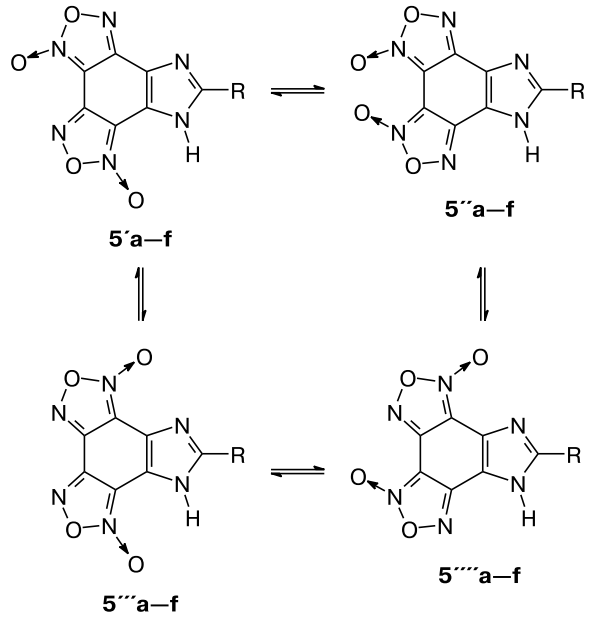


5a—f

The furoxane ring in the molecule of benzofuroxane derivatives possesses an ability to tautomerize to the second form containing an N-oxide group on the other side of the ring.[17,25,26] This isomerization is reversible, and in solutions both tautomers exist in equilibrium. Compounds **5a**—**f** theoretically can exist in four tautomeric forms **5´a**—**f**—**5´´´´a**—**f** (Scheme 5).

We used the density functional theory (DFT) with the exchange-correlation functional B3LYP[27—30] in the valence-split basis 6-311++G(d,p)[31,32] to calculate for compound **5a** (as an example) the relative thermodynamic

Scheme 5



5´a—f **5´´a—f** **5´´´a—f** **5´´´´a—f**

stabilities of tautomers **5´a**—**5´´´´a** in the gas phase and in DMSO (Table 1).

The computational results given in Table 1 indicate that tautomer **5´´a** has the lowest thermodynamic stability in the gas phase and in solution of DMSO in comparison with other tautomers. However, the comparative thermodynamic preference of different tautomers of compound **5a** was found to be very insignificant, namely, near the limit of the permissible error of calculation (~0.5 kcal mol^{-1}).[33]

The tautomerism of compound **5a** in solution of DMSO-d_6 at room temperature was confirmed by the presence in the ^{1}H NMR spectrum a triple set of signals for the C—H proton of the imidazole ring: δ 8.35 s, 8.40 s, 8.45 s in the ratio of 1 : 0.25 : 0.13 (Table 2). An evidence of tautomerism of compounds **5a**—**f** was the appearance in their ^{13}C NMR spectra of additional signals for the carbon atoms of the aromatic ring bonded to the N-oxide nitrogen atom (**5a**—**d**) and the oxazole nitrogen atom (**5c**); the imidazole carbon atom C(2) (**5e**); the carbon atom of the alkyl substituent CH_2—C= (**5f**) (see Table 2).

Compounds **5a**—**f** are yellowish crystalline substances, insoluble in water, but soluble in acetone and ethyl acetate. The compounds decompose upon heating without melting; they can be purified by recrystallization from ethanol or acetic acid. Compounds **5a**—**f** can give complexes with solvents. Thus, for example, compound **5a** forms 2 : 1 complex with acetic acid, which decomposes upon heating in water.

In conclusion, we have developed a general method for the synthesis of imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]-difuroxanes by the condensation of 3,5-dibromophenylene-1,2-diamine with carboxylic acids or their

Table 1. Relative thermodynamic stabilities of tautomers of imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*′]-difuroxane (**5a**) in the gas phase and in DMSO calculated by DFT B3LYP/6-311++G(d,p)

Compound	Gas phase		DMSO	
	$(E + ZPE)$ /at.u.	RTS * /kcal mol^{-1}	$(E_{DMSO} + ZPE)$ /at.u.	RTS* /kcal mol^{-1}
5′a	−897.186886	0	−897.207080	0.1
5″a	−897.184042	1.8	−897.205472	1.1
5‴a	−897.185713	0.7	−897.205662	1.0
5⁗a	−897.186042	0.5	−897.207285	0

* Relative thermodynamic stabilities (RTS) of tautomers were calculated in the gas phase using the following formula $[(E + ZPE)_x - (E + ZPE)_y] \cdot 627.5$ kcal mol^{-1} (see Ref. 34) (E is the total energy, ZPE is the correction for the zero-point energy of vibrations, x is the data for compound **5′a**, y is the data for all other compounds), in DMSO using the following formula $[(E_{DMSO} + ZPE)_x - (E_{DMSO} + ZPE)_y] \cdot 627.5$ kcal mol^{-1} (E_{DMSO} is the total energy in the solvent, ZPE is the correction for the zero-point energy of vibrations, x is the data for compoundя **5⁗a**, y is the data for all other compounds).

Table 2. Spectral characteristics of the synthesized compounds

Compound	IR, ν/cm^{-1}	NMR (δ, *J*/Hz)	
		^{1}H	^{13}C
2a	3160, 1615, 1556, 1547, 1486, 1387, 1343, 1314, 1280, 1197, 1142, 987, 936, 822, 806, 753, 703, 625, 588, 469	7.54 (s, 1 H, CH); 7.80 (s, 1 H, CH); 8.36 (s, 1 H, C(2)H)	110.5, 114.2, 116.3, 126.4, 137.7, 138.5 (—C=); 144.0 (N—<u>C</u>H=N)
2b*	3400, 2921, 2850, 1619, 1539, 1517, 1393, 1335, 1297, 1257, 1234, 1183, 1071, 1019, 958, 833, 757, 742, 660, 581, 570, 513	2.50 (s, Me);** 7.45 (s, 1 H, CH); 7.64 (s, 1 H, CH); 12.75 (s, 1 H, NH)	14.7 (CH_3); 113.5, 125.8 (—C=); 153.9 (<u>C</u>—CH_3)
2c*	3437, 2973, 2929, 1619, 1571, 1541, 1454, 1424, 1411, 1315, 1292, 1265, 1245, 1185, 1076, 1059, 1030, 949, 839	1.29 (t, 3 H, Me, ^3J = 7.62); 2.84 (q, 2 H, CH_2, ^3J = 7.62); 7.43 (s, 1 H, CH); 7.64 (s, 1 H, CH); 12.74 (s, 1 H, NH)	1.4 (CH_3); 22.1 (<u>C</u>H_2CH_3); 1113.6, 124.8, 127.1 (—C=); 158.7 (<u>C</u>—CH_2)
2d*	3400, 2956, 2871, 1619, 1570, 1537, 1470, 1411, 1359, 1321, 1298, 1260, 1236, 1183, 1071, 1012, 960, 836, 806, 758, 733, 662, 582	0.92 (t, 3 H, Me, ^3J = 7.35); 1.78 (m, 2 H, CH_2); 2.80 (t, 2 H, CH_2, ^3J = 7.35); 7.49 (s, 1 H, CH); 7.63 (s, 1H, CH); 12.71 (s, 1 H, NH)	13.7 (CH_3); 21.0 (<u>C</u>H_2CH_3); 30.4 (<u>C</u>$H_2CH_2CH_3$); 113.7, 121.0, 125.8 (—C=)
2e*	3450, 2969, 2926, 1615, 1568, 1533, 1461, 1410, 1392, 1338, 1307, 1287, 1233, 1184, 1070, 1006, 956, 839, 759, 728, 659, 610, 583	1.34 (d, 6 H, Me, ^3J = 7.35); 3.18 (m, 1 H, CH); 7.51 (s, 1 H, CH); 7.62 (s, 1 H, CH); 12.71 (s, 1 H, NH)	21.2 (CH_3); 28.5 (CH); 113.6, 115.4, 126.0, 138.5 (—C=); 162.3 (C—CH)
2f	3318, 2960, 2929, 2858, 1611, 1568, 1474, 1410, 1320, 1288, 1255, 1225, 1191, 1071, 958, 846, 768, 739, 684, 583	0.92 (t, 3 H, Me, ^3J = 7.04); 1.37 (m, 2 H, CH_2Me); 1.79 (m, 2 H, CH_2CH_2Me); 2.95 (t, 2 H, CH_2 $(CH_2)_2$Me, ^3J = 7.50); 7.40 (s, 1 H, CH); 7.73 (s, 1 H, CH)	13.5 (CH_3); 21.7 (<u>C</u>H_2CH_3); 27.1 (<u>C</u>$H_2CH_2CH_3$); 29.2 (<u>C</u>$H_2(CH_2)_2CH_3$); 115.7, 118.2, 124.5, 128.1, 132.8, 135.6 (—C=); 157.3(=<u>C</u>—CH_2)
3a*	3131, 1613, 1549, 1479, 1385, 1339, 1315, 1278, 1196, 1127, 939, 805, 752, 701, 628	8.79 (s, CH)	149.1 (CH)
3b	3370, 1615, 1561, 1546, 1518, 1448, 1384, 1360, 1335, 1302, 1276, 1196, 906, 818, 766, 660	2.50 (s, Me)**	15.0 (CH_3); 99.3, 104.7, 132.6, 135.7, 140.6; 146.2 (—C=); 160.4 (=<u>C</u>—CH_3)

(*to be continued*)

Table 2 (*continued*)

Compound	IR, ν/cm^{-1}	NMR (δ, *J*/Hz)	
		^{1}H	^{13}C
3c*	3430, 2991, 2945, 1614, 1553, 1538, 1513, 1457, 1400, 1379, 1359, 1340, 1315, 1299, 1208, 1187, 1076, 991, 905, 823, 806	1.32 (t, 3 H, Me, ^3J = 7.54); 2.93 (q, 2 H, CH_2, ^3J = 7.56); 13.65 (br.s, 1 H, NH)	11.7 (CH_3); 22.0 ($\underline{C}H_2CH_3$); 164.4 (=$\underline{C}$—CH_2)
3d	3450, 2966, 1618, 1553, 1405, 1356, 1303, 1206, 1092, 992, 807, 716	0.95 (t, 3 H, Me, ^3J = 6.99); 1.81 (m, 2 H, CH_2); 2.91 (t, 2 H, CH_2, ^3J = 7.35); 13.67 (br.s, 1 H, NH)	13.6 (CH_3); 20.9 ($\underline{C}H_2CH_3$); 30.3 ($\underline{C}H_2CH_2CH_3$); 99.1, 104.5, 132.3, 135.5, 140.5, 145.9 (—C=); 163.4 (=$\underline{C}$—CH_2)
3e	3449, 2974, 2934, 1619, 1551, 1537, 1462, 1421, 1358, 1310, 1209, 1094, 991, 806, 716	1.36 (d, 6 H, Me, ^3J = 7.32) 3.31 (m, 1 H, CH); 13.80 (br.s, 1 H, NH)	21.0 (CH_3); 28.6 (CH); 99.0, 104.8, 132.2, 135.8, 140.1, 145.9 (—C=); 168.0 (=C—CH_2)
3f	3450, 2958, 2930, 2860, 1615, 1552, 1403, 1355, 1300, 1221, 907, 808	0.91 (t, 3 H, Me, ^3J = 7.32); 1.36 (m, 2 H, CH_2Me); 1.76 (m, 2 H, CH_2CH_2Me); 2.90 (m, 2 H, $CH_2(CH_2)_2$Me)	13.6 (CH_3); 21.8 ($\underline{C}H_2CH_3$); 28.2 ($\underline{C}H_2CH_2CH_3$); 29.5 ($\underline{C}H_2(CH_2)_2CH_3$); 99.2, 104.7, 132.3, 135.7, 140.3, 145.9 (—C=); 163.6 (=$\underline{C}$—CH_2)
5a	3130, 1654, 1607, 1563, 1534, 1498, 1461, 1416, 1391, 1262, 1064, 997, 965, 887, 811, 772, 656, 641, 456	8.35 s; 8.40 s; 8.45 s (CH) d for the mixture of four isomers in the ratio 1 : 0.25 : 0.13	101.4, 103.7, 105.2, 106.3 ($\underline{C}$=N(O)O, =$\underline{C}$—N=C, =$\underline{C}$—NH—C); 141.4, 143.8, 145.7 (CH и $\underline{C}$=NO)
5b*	3021, 2888, 1653, 1575, 1561, 1522, 1472, 1450, 1383, 1286, 1227, 1114, 1069, 1023, 894, 870, 828, 816, 773, 750, 715, 659	2.55 (s, Me); 14.20 (br.s, 1 H, NH)	14.0 (CH_3); 100.7, 103.1, 104.6 ($\underline{C}$=N(O)O, =$\underline{C}$—N=C, =$\underline{C}$—NH—C); 140.9, 143.2 (C=NO); 153.7 ($\underline{C}$—CH_3)
5c	2852, 1650, 1608, 1564, 1541, 1520, 1469, 1450, 1392, 1367, 1269, 1232, 1070, 1034, 998, 968, 925, 813, 771, 750	1.29 (t, 3 H, Me, ^3J = 7.70); 2.80 (q, 2 H, CH_2, ^3J = 7.70); 14.15 (br.s, 1 H, NH)	12.2 (CH_3); 21.8 (CH_2); 101.0, 103.3, 104.8, 105.9 ($\underline{C}$=N(O)O, =$\underline{C}$—N=C, =$\underline{C}$—NH—C); 141.1, 143.5, 144.7, 145.2 ($\underline{C}$=NO); 158.6 ($\underline{C}$—CH_2)
5d*	3430, 2961, 2873, 1676, 1649, 1604, 1562, 1537, 1510, 1446, 1407, 1332, 1259, 1067, 1015, 996, 969, 923, 817, 769, 650	0.96 (t, 3 H, Me, ^3J = 6.99); 1.76 (m, 2 H, CH_2); 2.75 (q, 2 H, CH_2, ^3J = 7.35); 14.19 (br.s, 1 H, NH)	13.6 (CH_3); 21.0 ($\underline{C}H_2CH_3$); 30.1 ($\underline{C}H_2CH_2CH_3$); 100.9; 103.2; 104.8 (C=N(O)O, =$\underline{C}$—N=C, =$\underline{C}$—NH—C); 141.0, 143.4 ($\underline{C}$=NO); 157.6 (=$\underline{C}$—CH_2)
5e*	3430, 2972, 1649, 1606, 1560, 1518, 1448, 1384, 1236, 1092, 1063, 997, 967, 924, 806, 769, 741, 648	1.36 (d, 6 H, Me, ^3J = 6.62); 3.20 (m, 1 H, CH); 14.19 (br.s, 1 H, NH)	21.1 (CH_3); 28.4 (CH); 101.1, 103.4 ($\underline{C}$=N(O)O, =$\underline{C}$—N=C, =$\underline{C}$—NH—C); 141.2 ($\underline{C}$=NO); 162.1, 162.3, 162.4 ($\underline{C}$—CH)
5f*	3448, 2956, 2874, 1681, 1647, 1607, 1557, 1519, 1450, 1393, 1266, 1096, 1065, 1024, 997, 971, 924, 811, 770, 651, 650	0.94 (t, 3 H, Me, ^3J = 7.35); 1.36 (m, 2 H, CH_2); 1.73 (m, 2 H, CH_2); 2.82 (t, 2 H, CH_2, ^3J = 7.35); 14.23 (br.s, 1 H, NH)	13.6 (CH_3); 21.7 ($\underline{C}H_2CH_3$); 27.8 ($\underline{C}H_2$—CH_2—CH_3); 29.5, 29.7, 29.8 ($\underline{C}H_2$—C=); 103.4 ($\underline{C}$=N(O)O); 141.2 ($\underline{C}$=NO);157.6 ($\underline{C}$—CH_3)

* Low intensity and broadening of signals in the ^{13}C NMR spectra of compounds **2b**,**c**,**d**,**f**, **3a**,**c**, and **5b**,**d**,**e**,**f** lead to a decrease in the number of signals for aromatic carbon atoms.
** Overlapped with the signal of the solvent DMSO-d_6.

chlorides, nitration of 4,6-dibromobenzimidazoles, azidation of 4,6-dibromo-5,7-dinitrobenzimidazoles, and thermal cyclization of 4,6-diazido-5,7-dinitrobenzimidazoles.

Experimental

Melting points were determined on a Boetius microscope heating stage. Electrospray ionization high resolution mass

spectra (ESI-MS) were recorded on a Q Exactive in a positive ion mode; capillary potential 3500 V, range of scanning masses 90—900 Da. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300; ^{1}H and ^{13}C NMR chemical shift were measured relative to the signal of solvent (DMSO-d_6, δ_H 2.5; δ_C 39.5). IR spectra were recorded on a Vector 22 spectrometer in KBr pellets.

Quantum chemical calculations were carried out by DFT B3LYP in the basis 6-311++G(d,p) using the GAUSSIAN 09 software[35] with full optimization of geometrical parameters of structure without any restriction of the symmetry. After optimization of geometry, the frequencies of normal vibration of these compounds were calculated. The absence of imaginary values of frequency in the vibrational spectrum indicated that the optimized structures correspond to the minima on the potential energy surface (PES), rather than to the transition states.

Synthesis of 2-R-4,6-dibromobenzimidazoles (2a—e) (general procedure). A solution of **1** (1.0 g, 3.76 mmol) in RCOOH (2 mL) was refluxed for 2 h and cooled to 20 °C. Then, a 10% aqueous solution of NaOH was added to make the reaction mixture weakly basic, a precipitate formed was collected by filtration, washed with water, dried, and recrystallized from a mixture of EtOH—H_2O. Characteristics of compounds **2a—e** are summarized in Tables 2 and 3.

Synthesis of 2-butyl-4,6-dibromobenzimidazole (2f). A mixture of compound **1** (1.7 g, 6.39 mmol) and valeroyl chloride (2.0 g, 16.53 mmol) in pyridine (4 mL) was refluxed for 2 h, cooled to 50 °C, and poured into water (15 mL), a precipitate formed was collected by filtration, washed with water, dried, and recrystallized from a mixture of EtOH—H_2O. Characteristics of compound **2f** are summarized in Tables 2 and 3.

Synthesis of 2-R-4,6-dibromo-5,7-dinitrobenzimidazoles (3a—f) (general procedure). Nitric acid (1 mL, d = 1.50 g cm^{-3}) was added dropwise to compounds **2a—f** (3.62 mmol) in H_2SO_4 (7 mL) (d = 1.84 g cm^{-3}) at 0—5 °C with stirring. The temperature was increased to 90—95 °C and the mixture was stirred for

Table 3. Physicochemical characteristics of synthesized compounds

Compound	Yield (%)	M.p./°C	Found / Calculated (%)				Molecular formula	m/z [M + H]$^+$ found / calculated
			C	H	N	Br		
2a	95	230—232	30.53	1.48	10.23	58.05	$C_7H_4Br_2N_2$	276.8790
		(Ref. 36: 223—225)	30.43	1.45	10.14	57.97		276.8794
2b	81	216—218	33.26	2.15	9.22	55.23	$C_8H_6Br_2N_2$	290.8942
		(Ref. 36: 212—215)	33.10	2.07	9.66	55.17		290.8950
2c	78	179—181	35.56	2.65	9.22	52.68	$C_9H_8Br_2N_2$	304.9099
			35.53	2.63	9.21	52.63		304.9107
2d	85	225—227	37.81	3.17	8.83	50.33	$C_{10}H_{10}Br_2N_2$	318.9256
			37.74	3.14	8.81	50.31		318.9263
2e	80	226—228	37.79	3.16	8.85	50.38	$C_{10}H_{10}Br_2N_2$	318.9255
			37.74	3.14	8.81	50.31		318.9263
2f	83	181—183	39.80	3.64	8.51	48.34	$C_{11}H_{12}Br_2N_2$	332.9414
			39.76	3.61	8.43	48.19		332.9420
3a	90	303—305	23.02	0.41	15.21	43.85	$C_7H_2Br_2N_4O_4$	366.8488
			22.95	0.55	15.30	43.72		366.8495
3b	86	306—308	25.45	1.18	14.53	42.26	$C_8H_4Br_2N_4O_4$	380.8643
			25.26	1.05	14.74	42.11		380.8652
3c	75	287—289	27.44	1.54	14.22	40.85	$C_9H_6Br_2N_4O_4$	394.8799
			27.41	1.52	14.21	40.61		394.8808
3d	70	272—274	29.53	2.01	13.82	39.30	$C_{10}H_8Br_2N_4O_4$	408.8957
			29.41	1.96	13.73	39.22		408.8965
3e	53	275—277	29.43	1.98	13.75	39.41	$C_{10}H_8Br_2N_4O_4$	408.8958
			29.41	1.96	13.73	39.22		408.8965
3f	37	254—256	31.34	2.43	13.31	38.04	$C_{11}H_{10}Br_2N_4O_4$	422.9114
			31.27	2.37	13.27	37.91		422.9121
5a	80	220 (decomp.)	35.94	0.75	35.80	—	$C_7H_2N_6O_4$	235.0206
			35.90	0.85	35.90			235.0210
5b	40	190 (decomp.)	38.56	1.43	33.69	—	$C_8H_4N_6O_4$	249.0360
			38.71	1.61	33.87			249.0367
5c	70	211 (decomp.)	41.23	2.31	32.06	—	$C_9H_6N_6O_4$	263.0517
			41.22	2.29	32.06			263.0523
5d	70	200 (decomp.)	43.55	2.96	30.48	—	$C_{10}H_8N_6O_4$	277.0673
			43.48	2.90	30.43			277.0680
5e	80	195 (decomp.)	43.58	2.98	30.52	—	$C_{10}H_8N_6O_4$	277.0674
			43.48	2.90	30.43			277.0680
5f	72	195 (decomp.)	45.61	3.52	29.04	—	$C_{11}H_{10}N_6O_4$	291.0830
			45.52	3.45	28.97			291.08367

3 h, cooled to 20 °C, and poured onto ice. A precipitate formed was collected by filtration, washed with water, and dried. Characteristics of compounds **3a—f** are summarized in Tables 2 and 3.

Synthesis of 2-R-imidazo[4,5-*e*]benzo[1,2-*c*;3,4-*c*´]difuroxanes 5a—f (general procedure). A mixture of compounds **3a—f** (2.63 mmol) and NaN_3 (0.45 g, 6.92 mmol) in DMF (5 mL) was stirred at 20 °C until the starting compound disappeared (TLC monitoring). After addition of water (100 mL), a precipitate formed (**4a—f**) was collected by filtration, transferred into AcOH (3 mL), heated for 2 h at 100 °C, and cooled to 20 °C. A precipitate formed was collected by filtration, washed with water, heated in water (10 mL) for 0.5 h at 100 °C, cooled to 20 °C, filtered, and dried. Characteristics of compounds **5a—f** are summarized in Tables 2 and 3.

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