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SEMMLER-WOLFF AROMATIZATION OF 4-HYDROXYIMINO-4,5,6,7-TETRAHYDRO-[2,1,3]BENZOXADIAZOLE AND 4-HYDROXYIMINO-4,5,6,7-TETRAHYDRO[2,1,3]BENZOXADIAZOLE 1-OXIDE AND SOME PROPERTIES OF THE OBTAINED AMINES

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The Semmler-Wolff aromatization of 4-hydroxyimino-4,5,6,7-tetrahydro[2,1,3]benzoxadiazole and its 1-oxide derivative in sulfuric acid and in acetic anhydride gave 4-amino[2,1,3]benzoxadiazole and 4-acetamido[2,1,3]benzoxadiazole 1-oxide. Some reactions of the resultant amines were studied.

Keywords: 4-amino[2,1,3]benzoxadiazole, 4-acetamido[2,1,3]benzoxadiazole 1-oxide, oximes, Semmler-Wolff reaction, ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy, ^{15}N NMR spectroscopy.

The rearrangement of oxides of α,β-unsaturated cyclic ketones and ketone oximes within condensed systems to give aromatic amines by the action of acid reagents has long been known and has been studied in detail by a whole series of workers [1-3]. However, there is still no completely clear understanding of all the transformation steps leading from oximes to amines and the effect of the reagents and reaction conditions. The Semmler-Wolff reaction and Beckmann rearrangement are carried out under the same conditions. The conditions for these reactions are usually optimized experimentally.

We have already shown that 4-hydroxyimino-4,5,6,7-tetrahydro[2,1,3]benzodiazole (**1**) and 4-hydroxyimino-4,5,6,7-tetrahydro[2,1,3]benzodiazole 1-oxide (**2**), may be obtained in good yield [4]. In the present work, we examined the feasibility of converting these compounds into amino derivatives of [2,1,3]benzoxadiazole and [2,1,3]benzoxadiazole 1-oxide using the Semmler-Wolff aromatization.

Oxime **1** is an 8:1 mixture of derivatives with *syn* and *anti* configuration of the oxime group [4]. The starting oxime must be in the *anti* configuration for the aromatization [1]. We have found that isomerization

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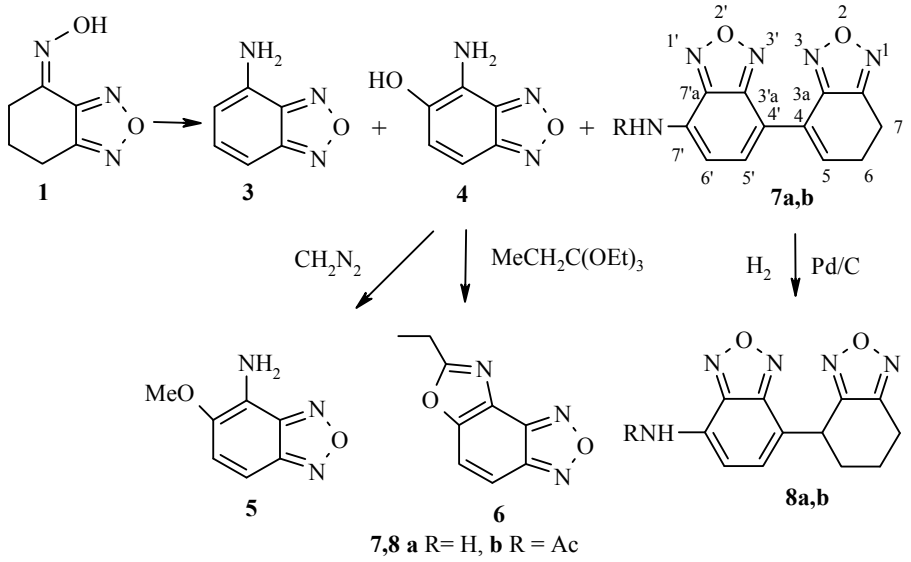
occurs upon dissolving the *syn* isomer in sulfuric acid and a mixture of both isomers is formed in the resultant solution. Thus, we would expect that the oxime configuration will not have great significance in the aromatization in acids. The authors of work [3] came to the same conclusion.

Three major products were isolated following heating oxime **1** in sulfuric acid at 123-125°C. 4-Amino[2,1,3]benzoxadiazole (**3**) was isolated in 34% yield. Better results were obtained using PPA. The product obtained was similar to 4-amino[2,1,3]benzoxadiazole described by Uchiyama et al. [5].

The second product isolated in 13% yield was 4-amino-5-hydroxy-2,1,3-benzoxadiazole (**4**). The structure of this compound was established using analytical and spectral data and also by its conversion into 4-amino-5-methoxy[2,1,3]benzoxadiazole (**5**) by treatment with diazomethane and comparison of these data with literature results [6]. 7-Ethyloxazolo[4,5-*e*][2,1,3]benzoxadiazole (**6**) was obtained smoothly in the reaction of benzoxadiazole **4** with triethyl orthopropionate, which supports the assignment of the structure of **4**.

A previously unreported product, **7a**, was obtained in 8% yield in addition to the above products. The IR spectrum of compound **7a** shows NH_2 group stretching bands at 3230, 3350, and 3480 cm^{-1}, and a C=N stretching band at 1630 cm^{-1}. The ^1H NMR spectrum in $CDCl_3$ shows a multiplet for four protons at 2.77-3.16 ppm, a broad singlet for the NH_2 group protons at 4.73 ppm, doublet for one proton at 6.42 ppm, triplet for one proton at 7.67 ppm, and doublet for one proton at 8.25 ppm. The ^{13}C NMR spectrum shows signals for CH_2 group carbon atoms at 16.90 and 23.30 ppm, for CH group carbon atoms at 104.04, 134.35, and 136.17 ppm, and signals at 107.48, 123.02, 137.34, 144.87, 148.29, 149.19, and 152.71 ppm for carbon atoms not bound to hydrogen. The mass spectrum of compound **7a** shows a molecular ion peak at *m/z* 255. Treating **7a** with acetic anhydride gives acetyl derivative **7b**. In the presence of palladium on carbon black as a catalyst, compounds **7a**,**b** readily add a molecule of hydrogen to give compounds **8a**,**b**. These data and the results obtained from two-dimensional ^1H-^{13}C, ^{13}C-^{13}C, and ^1H-^{15}N NMR correlations for direct and long-range coupling constants (see Experimental) permitted us to assign the structure of 7'-amino-6,7-dihydro-4,4'-di[2,1,3]benzoxadiazole to product **7a**.



The formation of compounds **3** and **4** can be explained on the basis of the reported schemes for the Semmler-Wolff reaction. The oxime initially undergoes isomerization leading to an azirine, which, upon protonation gives carbocation **A**. Then, this intermediate is stabilized by the loss of a proton to give amine **3** or adds water to give amino alcohol **B**, which is oxidized to give aminophenol **4**. We should note that the formation of aminophenols has not been noted previously in studies of the Semmler-Wolff reaction.

TABLE 1. Characteristics of Compounds Synthesized

Compound	Empirical formula	Found, % / Calculated, %			mp, °C*	Yield, %
		C	H	N		
4	$C_6H_5N_3O_2$	47.78 / 47.68	3.25 / 3.34	27.90 / 27.81	147-149	13
6	$C_9H_7N_3O_2$	57.20 / 57.14	3.55 / 3.70	22.08 / 22.22	145-147	71
7a	$C_{12}H_9N_5O_2$	56.48 / 56.47	3.48 / 3.55	27.60 / 27.44	212-214	8*[2]
7b	$C_{14}H_{11}N_5O_3$	56.47 / 56.56	3.40 / 3.73	23.50 / 23.56	230-232	83
8a	$C_{12}H_{11}N_5O_2$	56.12 / 56.02	4.28 / 4.31	27.08 / 27.23	173-175	80
8b	$C_{14}H_{13}N_5O_3$	56.26 / 56.18	4.32 / 4.38	23.31 / 23.40	157-159	83
11	$C_{12}H_7N_5O_2$	57.12 / 56.91	2.78 / 2.79	27.71 / 27.66	207-208	6.7
12a	$C_{12}H_9N_3O$	68.12 / 68.23	4.15 / 4.30	19.72 / 19.90	78-80	68
12b	$C_{13}H_{11}N_3O$	69.11 / 69.32	4.88 / 4.92	18.59 / 18.66	82-84	45.6
12c	$C_{13}H_{11}N_3O$	69.36 / 69.32	4.90 / 4.92	18.52 / 18.66	93-95	51
12d	$C_{13}H_{11}N_3O$	69.38 / 69.32	4.93 / 4.92	18.45 / 18.66	75-77	49
12e	$C_{13}H_{11}N_3O_2$	64.70 / 64.72	4.60 / 4.60	17.34 / 17.42	93-94	64
12f	$C_{13}H_{11}N_3O_2$	64.65 / 64.72	4.48 / 4.60	17.48 / 17.42	102-103	72
14	$C_8H_7N_3O_3$	50.00 / 49.74	3.80 / 3.65	21.68 / 21.76	131-133	8.8
16	$C_{12}H_{13}N_3O_3$	58.11 / 58.29	5.24 / 5.30	17.12 / 17.00	240-242	61
17	$C_{11}H_{13}N_3O_3$	56.22 / 56.16	5.50 / 5.57	17.79 / 17.86	165-168 (dec.)	65.7
18	$C_8H_7N_3O_3$	49.83 / 49.74	3.60 / 3.65	21.69 / 21.76	185-187 (dec.)	2.0*[3]
19	$C_8H_7N_3O_2$	54.32 / 54.23	3.65 / 3.98	23.68 / 23.72	98-100	8.8

* Recrystallization solvents: compounds **7a**,**b**, **8a**,**b**, **11, 16-18** – ethanol, compounds **12a**,**c-f** – hexane, compound **12b** – pentane, compound **4** – ethyl acetate, compounds – **6**, **14**, **19** 1:3 ethyl acetate–hexane.

*[2] The yield of compound **7a** obtained from amine **3** and ketone **9** was 29.6%.

*[3] The yield of compound **18** upon the acylation of compound **4** using acetic anhydride was 74%.

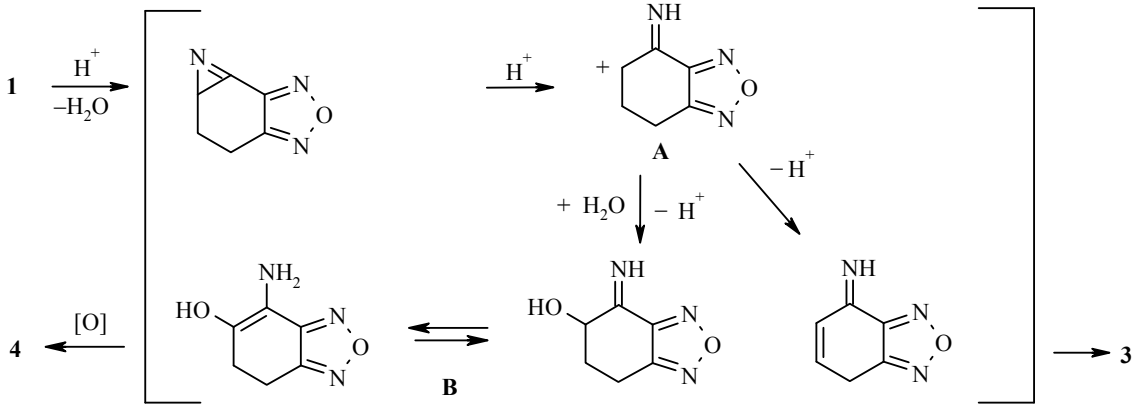


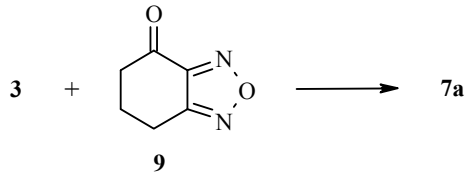
TABLE 2. Spectral Characteristics of Products

Com-pound	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max} (log ε)	^{1}H NMR spectrum, δ, ppm (*J*, Hz)*
4	1636 (C=N), 3263, 3325, 3370, 3415 (NH_2, OH)	426 (4.14)	5.28 (2H, br. s, NH_2); 7.10, 7.28 (each 1H, both d, *J* = 10.0, H arom); 9.56 (1H, br. s, OH)
6	1548 (C=N), 1573, 1639	235 (4.09), 329 (3.54)	1.46 (3H, t, *J* = 7.8, CH_3); 3.03 (2H, q, *J* = 7.5, CH_2); 7.67, 7.72 (each 1H, both d, *J* = 9.6, H arom)
7a*[2]	1634 (C=N), 3227, 3354, 3480 (NH_2)	278 (3.96), 445 (3.60)	2.77-2.89 (2H, m, CH_2); 3.05-3.16 (2H, m, CH_2); 4.73 (2H, br. s, NH_2); 6.42, 8.25 (each 1H, both d, *J* = 7.2, H arom); 7.67 (1H, t, *J* = 4.8, CH)
7b	1703 (C=O), 3312 (NH)	266 (4.11), 390 (3.85)	2.18 (3H, s, CH_3); 2.63-2.87 (2H, m, CH_2); 2.98-3.13 (2H, m, CH_2); 7.48 (1H, t, *J* = 3.5, CH); 7.92-8.05 (2H, m, 2CH arom); 10.61 (1H, s, NH)
8a	1641 (C=N), 3230, 3342, 3430 (NH_2)	415 (3.48)	1.67-2.21 (4H, m, $2CH_2$); 2.75-3.10 (2H, m, CH_2); 4.46-4.55 (1H, m, CH); 6.26, 7.14 (each 1H, both d, *J* = 7.5, H arom); 6.49 (2H, br. s, NH_2)
8b	1691 (C=O), 3321 (NH)	235 (4.11), 359 (3.77)	2.20 (3H, s, CH_3); 1.78-2.31 (4H, m, $2CH_2$); 2.80-3.40 (2H, m, CH_2); 4.67-4.75 (1H, m, CH); 7.43, 8.06 (each 1H, both d, *J* = 7.7, H arom); 10.69 (1H, s, NH)
11	1622 (C=N), 3303 (NH)	418 (3.41)	7.05 (2H, d, *J* = 6.9, H arom); 7.48-7.56 (2H, m, H arom); 7.61 (2H, d, *J* = 9.0, H arom); 9.87 (1H, s, NH)
12a	1595 (C=N), 3307 (NH)	268 (4.04), 423 (3.79)	6.80 (1H, br. s, NH); 6.83 (1H, d, *J* = 7.4, H arom); 7.08-7.43 (7H, m, H arom)
12b	1616 (C=N), 3391 (NH)	412 (3.65)	4.53 (2H, d, *J* = 5.6, CH_2); 5.44 (1H, br. s, NH); 6.11, 7.21 (each 1H, both d, *J* = 7.2, H arom); 7.05 (1H, d, *J* = 9.1, H arom); 7.24-7.45 (5H, m, H arom)
12c	1610 (C=N), 3403 (NH)	428 (4.34), 268 (4.62), 233 (4.78)	2.35 (3H, s, CH_3); 6.71 (1H, d, *J* = 7.1, H arom); 6.75 (1H, br. s, NH); 7.11 (1H, d, *J* = 8.7, H arom); 7.18 (4H, s, H arom); 7.19-7.24 (1H, m, H arom)
12d	1584 (C=N), 3403 (NH)	422 (4.61)	2.30 (3H, s, CH_3); 6.35 (1H, d, *J* = 7.2, H arom); 6.51 (1H, br. s, NH); 7.08-7.42 (6H, m, H arom)
12e	1594 (C=N), 3357 (NH)	265 (3.80), 430 (3.86)	3.84 (3H, s, OCH_3); 6.56 (1H, d, *J* = 7.4, H arom); 6.72 (1H, br. s, NH); 6.96, 7.26 (each 2H, d, *J* = 8.8, H arom); 7.08-7.22 (2H, m, H arom)
12f	1623 (C=N), 3409 (NH)	263 (4.73), 425 (4.96)	3.91 (3H, s, OCH_3); 6.95-7.30 (7H, m, NH, H arom); 7.51 (1H, dd, J_1 = 7.6, J_2 = 1.8, H arom)
13	1621 (C=N), 1685 (C=O), 3348 (NH)	382 (3.32)	2.19 (3H, s, CH_3); 7.16 (1H, d, *J* = 8.5, H arom); 7.25-7.33 (1H, m, H arom); 8.1 (1H, d, *J* = 7.1, H arom); 10.56 (1H, s, NH)
14	1625, 1647 (C=N)	280 (3.88)	2.51 (3H, s, CH_3); 3.00-3.09 (2H, m, CH_2); 3.11-3.19 (2H, m, CH_2)
16	1678 (C=O), 3112 (NH)	262 (4.64), 390 (4.54)	2.19 (3H, s, CH_3); 2.56 (3H, s, CH_3); 2.59 (3H, s, CH_3); 7.73-7.83 (1H, m, H arom); 8.12 (1H, d, *J* = 8.4, H arom); 8.89 (1H, d, *J* = 7.9, H arom); 13.79 (1H, s, NH)
17	1693 (C=O), 3062 (NH)	251 (4.92), 520 (4.46)	1.68 (6H, s, $2CH_3$); 2.18 (3H, s, CH_3); 6.77-6.84 (2H, m, H arom); 7.80-7.85 (1H, m, H arom); 10.40 (1H, s, NH)
18	1643 (C=O), 3320 (NH)	355 (3.14)	2.09 (3H, s, CH_3); 5.68 (1H, br. s, OH); 7.54, 7.81 (each 1H, both d, *J* = 9.3, H arom); 9.76 (1H, br. s, NH)
19	1656 (C=N)	263 (3.83)	2.49 (3H, s, CH_3); 3.09-3.17 (2H, m, CH_2); 3.24-3.32 (2H, m, CH_2)

*The ^{1}H NMR spectra were taken in DMSO-d_6 (**4**, **7b**, **8b**, **11**, **13**, **14**, **16,** and **18**) and in $CDCl_3$ (**6**, **7a**, **8a**, **12a-f**, **17**, and **19**).

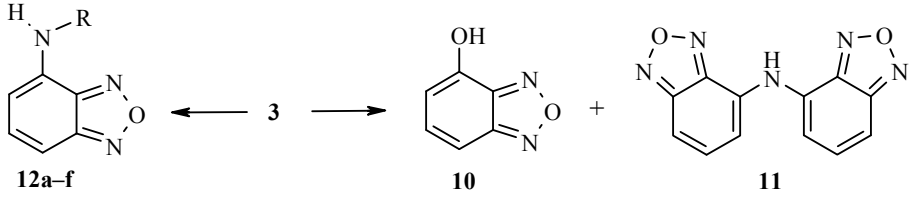
*[2] For the complete assignment of the signals in the ^{1}H NMR spectrum of amine **7a**, see Experimental.

The formation of product **7a** does not follow from the generally accepted mechanisms of the Semmler-Wolff reaction. Amine **7a** may be formed in the reaction of amine **3** with ketone **9**, which, in turn, can be formed from oxime **1** under acid conditions. Indeed, the reaction of amine **3** with previously synthesized 4-oxo-4,5,6,7-tetrahydro-[2,1,3]benzoxadiazole (**9**) [4] under the conditions of the aromatization reaction gave product **7a** in about 30% yield.



The alkylation of amine **3** by ketone **9** apparently occurs in this case. We might have assumed that amine **7a** would also form during work-up of the reaction mixture. However, 4-hydroxy[2,1,3]benzoxadiazole (**10**), whose structure was established using spectral and analytical data and by comparison with the published data for this compound [7], was obtained upon heating amine **3** with aqueous sulfuric acid. Di[2,1,3]benzoxadiazol-4-yl)amine (**11**) was also isolated from the reaction mixture. The structure of this product is in accord with its spectral and analytical data.

The formation of compounds **10** and **11** is attributed to the ease of the replacement of the amino group in amine **3**. Indeed, the action of anilines or benzylamine on amine **3** gives 4-arylamino[2,1,3]benzoxadiazoles **12a** and **12c-f** and 4-benzylamino[2,1,3]benzoxadiazole (**12b**).



12a R = Ph, **b** R = CH_2Ph, **c** R = *p*-MeC_6H_4, **d** R = *o*-MeC_6H_4, **e** R = *p*-$MeOC_6H_4$, **f** R = *o*-$MeOC_6H_4$

We used the Semmler-Wolff aromatization in an attempt to obtain 4-amino[2,1,3]benzoxadiazole 1-oxide from oxime **2**. Under the conditions for the preparation of amine **3**, oxime **2** decomposes. However, changing the reaction conditions and using acetic anhydride in the previously presence of sulfuric acid gave 4-acetylamido[2,1,3]benzoxadiazole 1-oxide (**13**), described previously [8], in about 30% yield. The reaction mixture also yielded 7-methyl-4,5-dihydrooxazolo[4,5-*e*][2,1,3]benzoxadiazole 3-oxide (**14**) and 4-acetamido-[2,1,3]benzoxa-diazole (**15**). The structures of these products are in accord with their spectral and analytical data (see Experimental, Tables 1-4).

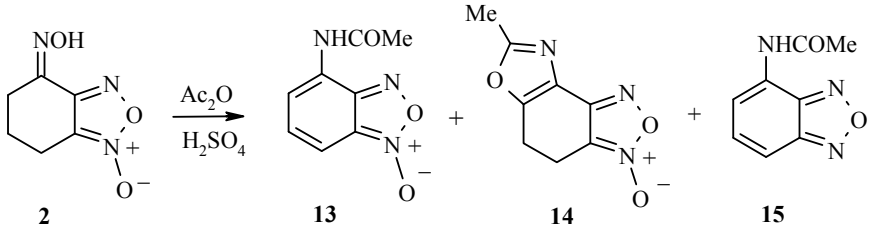


TABLE 3. ^{13}C NMR Spectra of Compounds Synthesized

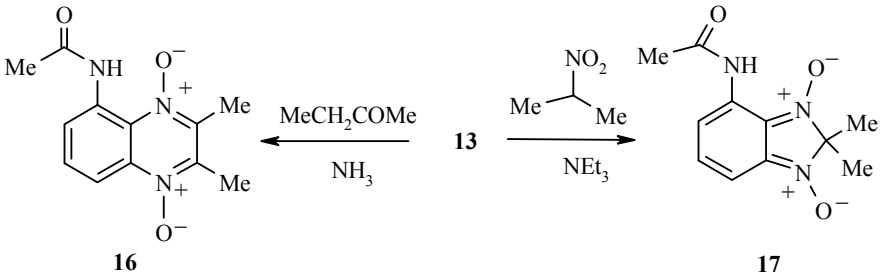
Com-pound	^{13}C NMR spectra, δ, ppm*		
	C=N	C–H	Other signals
3	144.69, 149.85	103.51, 106.23, 133.41	134.92
4	137.99, 145.25	101.94, 129.56	117.93, 146.96 (C-5)
5	140.26, 144.56	103.83, 124.16	57.27 (OCH_3), 120.63, 146.93 (C-5)
6	142.97, 148.97, 151.06, 169.25	113.09, 118.88	10.80 (CH_3), 22.04 (CH_2), 126.95
7a*[2]	144.87, 148.29, 149.19, 152.71	104.04, 134.35, 136.17	16.90 (CH_2), 23.30, 107.48, 123.02, 137.34
7b	144.79, 147.45, 148.55, 152.34	116.29, 132.20, 140.46	16.57, 23.52 (CH_2), 23.83 (CH_3), 116.36, 122.18, 126.41, 169.87 (C=O)
8a	145.04, 148.46, 152.49, 154.54	35.32, 104.10, 133.32	19.48, 20.58, 29.29 (CH_2), 113.53, 136.24
8b	145.25, 148.06, 152.46, 153.91	131.97, 117.56, 35.44	19.42, 20.52, 23.80 (CH_3), 29.10 (CH_2), 123.41, 125.80, 169.81 (C=O)
10	145.18, 146.22	105.35, 109.41, 134.39	150.58
11	145.25, 150.04	108.03, 115.41, 130.93	130.40
12a	145.25, 149.91	104.29, 104.46, 121.05, 123.90, 129.48, 133.49	132.56, 139.44
12b	144.47, 149.54	101.32, 101.89, 127.01, 127.35, 128.45, 133.60	47.26 (CH_2), 135.63, 136.91
12c	146.06, 149.90	103.62, 103.82, 121.60, 129.98, 133.85	20.73 (CH_3), 133.11, 133.59, 136.65
12d*[3]	144.76, 149.69	103.46, 103.65, 123.58, 125.20, 126.62, 130.97, 133.31	17.35 (CH_3), 132.04, 137.08
12e	144.72, 149.66	102.68, 103.05, 114.40, 124.15, 133.42	55.10 (OCH_3), 131.70, 133.85, 156.46 (C–OCH_3)
12f	145.39, 149.69	104.23, 104.32, 110.58, 118.44, 120.28, 122.87, 133.28	55.29 (OCH_3), 128.88, 131.76, 149.46 (C–OCH_3),
13	114.62, 148.28	106.26, 118.43, 131.10	23.87 (OCH_3), 127.79, 169.96 (C=O)
14	111.11, 149.11, 155.46, 163.13		13.63 (CH_3), 16.92, 18.35 (CH_2), 123.94
15	144.53, 149.12	109.35, 116.59, 133.07	23.97 (CH_3), 126.57 (C-4), 169.95 (C=O)
16		112.50, 118.30, 131.34	13.91, 14.23, 25.80 (CH_3); 125.51, 133.94, 136.60, 141.39, 142.69, 168.32 (C=O)
17		108.43, 115.02, 132.03	23.58, 24.50 (CH_3), 96.51 (C_2), 129.97, 130.64, 135.96, 168.67 (C=O)
18	146.81, 148.50	114.82, 130.96	22.68 (CH_3), 104.58, 153.50 (C–O), 169.37 (C=O),
19	150.50, 152.90, 162.90		13.59 (CH_3), 17.64, 19.15 (CH_2), 124.69, 145.32

*The ^{13}C NMR spectra were taken in DMSO-d_6 (**4**, **7b**, **8b**, **9**, **10**, **13**, **14**, **16**, and **18**) and in $CDCl_3$ (**3**, **5**, **6**, **7a**, **8a**, **11a-f**, **15**, **17**, and **19**).

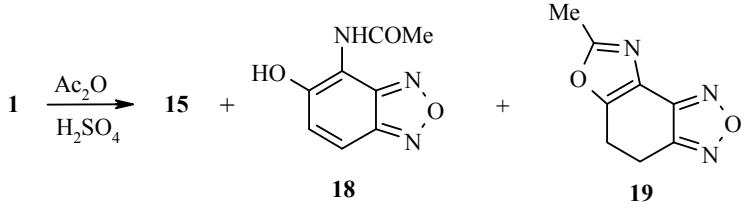
*[2] The complete assignment of the signals in the ^{13}C NMR spectrum of compound **7a** is given in the Experimental.

*[3] Overlap of signals in the ^{13}C NMR spectrum.

Oxide **13** undergoes the usual reactions of [2,1,3]benzoxadiazole 1-oxides [9]. This oxide reacts with 2-butanone in the presence of ammonia to give quinoxaline di-N-oxide **16** and with 2-nitropropane to give 2H-benzimidazole 1,3-dioxide **17**. The structures of these products are in accord with their analytical and spectral data.



Under the conditions for the aromatization of oxide **2**, oxime **1** also gives a mixture of products.



The reaction mixture yielded 4-acetamido[2,1,3]benzoxadiazole (**15**), 4-acetamido-5-hydroxy[2,1,3]-benzoxadiazole (**18**), and 7-methyl-4,5-dihydrooxazolo[4,5-*e*][2,1,3]benzoxadiazole (**19**). The structures of these products are in accord with their analytical and spectral data.

Thus, we have shown that the Semmler-Wolff aromatization can be used to effect the facile conversion of oximes of tetrahydro[2,1,3]benzoxadiazole **1** and tetrahydro[2,1,3]benzoxadiazole 1-oxide **2** to amine derivatives of [2,1,3]benzoxadiazole and [2,1,3]benzoxadiazole 1-oxide.

TABLE 4. Mass Spectra of Compounds Synthesized

Compounds	*m/z* (I_{rel}, %)
4	151 $[M]^+$ (100), 134 (38), 107 (16), 80 (69)
5	165 $[M]^+$ (82), 150 (100), 120 (18), 96 (14), 92 (26), 80 (45). Found: *m/z* 165.0532. $C_7H_7N_3O_2$. Calculated: M = 165.0533
6	189 $[M]^+$ (54), 104 (68), 76 (28)
7a	255 $[M]^+$ (100), 225 (29), 215 (79), 208 (25), 199 (36), 185 (53), 169 (55)
7b	297 $[M]^+$ (16), 255 (100), 225 (16), 215 (38), 199 (15), 185 (17), 169 (17)
8a	257 $[M]^+$ (100), 240 (16), 189 (33), 173 (19), 169 (17), 143 (15), 169 (55)
8b	299 $[M]^+$ (10), 257 (100), 189 (10)
11	253 $[M]^+$ (100), 223 (73), 206 (21), 193 (44)
12a	211 $[M]^+$ (100), 194 (29), 181 (85), 154 (18)
12b	225 $[M]^+$ (37)
12c	225 $[M]^+$ (100), 210 (22), 208 (27), 195 (44), 193 (20), 180 (87)
12d	225 $[M]^+$ (91), 210 (32), 208 (14), 195 (47), 193 (24), 180 (100)
12e	241 $[M]^+$ (100), 226 (16), 211 (40), 196 (52), 180 (28). 168 (17)
12f	241 $[M]^+$ (100), 226 (14), 210 (18), 196 (37), 193 (22), 180 (34)
13	193 $[M]^+$ (37), 151 (100), 133 (19), 91 (40)
14	193$[M]^+$ (60)
16	247 $[M]^+$ (100), 231 (16), 205 (30), 188 (51), 171 (90)
17	235 $[M]^+$ (100), 193 (44), 176 (18), 162 (12), 146 (11), 135 (49), 117 (14)
18	193 $[M]^+$ (25), 151 (100), 134 (15)
19	177 $[M]^+$ (36), 137 (100)

EXPERIMENTAL

The IR spectra were taken on a Bruker Vector spectrometer for KBr pellets (c = 0.25%). The strongest absorption bands in the spectra are given. The ^{1}H and ^{13}C NMR spectra were taken on a Bruker AM 400 spectrometer at 400 and 100 MHz, respectively, and on a Bruker Avance DRX-500 spectrometer at 500 and 125 MHz, respectively, in $CDCl_3$ and DMSO-d_6 for 10% solutions at 25°C. The chemical shifts were measured relative to the residual solvent signals: $CHCl_3$ (δ 7.24 and 76.90 ppm, respectively), and δ 2.50 and 39.50 ppm, respectively, for DMSO-d_6. The multiplicity of the signals in the ^{13}C NMR spectra was determined in JMOD and using the ^{13}C-H correlations.

The ^{1}H, ^{13}C, and ^{15}N NMR spectra for compound **7a** were recorded on a Bruker Avance-III 600 spectrometer at 600, 150, and 61 MHz, respectively in DMSO-d_6. The chemical shifts of the hydrogen and carbon atoms in the ^{1}H and ^{13}C NMR spectra were determined relative to the residual signals of the DMSO-d_6 solvent (δ 2.50 and 39.50 ppm, respectively) and the chemical shifts of the nitrogen atoms in the ^{15}N NMR spectra were determined relative to ammonia as an external standard. The establishment of the structure of compound **7a** and the assignment of the signals in the ^{1}H and ^{13}C NMR spectra were carried out using two-dimensional ^{1}H-^{13}C inverse correlations for the direct (HSQC [10-12]) and long-range coupling constants (HMBC [13]) and ^{13}C-^{13}C correlations with detection relative to ^{1}H (1,1-ADEQUATE [14]). The $^{1}J_{CH}$ coupling constants were determined from the ^{13}C NMR spectrum without proton decoupling. The assignment of the signals in the ^{15}N NMR spectrum was carried out relative to the two-dimensional ^{1}H-^{15}N inverse correlation for long-range coupling constants (HMBC). The chemical shifts of the signals in the ^{15}N NMR spectrum and the $^{1}J_{NH}$ coupling constants were obtained from the two-dimensional HMBC spectrum. (The spectral data for the two-dimensional NMR spectra for compound **7a** may be obtained from the authors upon request).

The mass spectra were taken on a Thermo-Scientific DFS mass spectrometer with direct sample inlet. The ionizing electron energy was 70 eV and the ion source temperature was 180°C. The reaction course and purity of the compounds were monitored by thin-layer chromatography on Sorbfil UV-254 plates. The chromatograms were developed by UV light and iodine vapor. Products **1**, **2**, and **9** were prepared according to our reported procedures [4]. The melting points were determined on a Koefler microheating block. The elemental analysis was carried out in the Microanalysis Laboratory at the Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences.

We used a sample of PPA prepared by the evaporation of orthophosphoric acid in vacuum at 15 mm Hg at 150°C and also by dissolving P_2O_5 in heated orthophosphoric acid until the total P_2O_5 content in the mixture was 80%. In the syntheses, we used chemically-pure grade sulfuric acid State Standard 4204-66.

The identification of previously described compounds was carried out by comparison of their IR spectra and melting points.

Isomerization of Oximes. *syn*-Isomer of compound **1** (0.5 g, 3 mmol) was added to concentrated sulfuric acid (5 ml) and the mixture was stirred for 2 h at 60°C. The reaction mixture was poured into 20 g crushed ice and extracted with three 20-ml portions of ethyl acetate. The combined extract was washed with two 20-ml portions of saturated aqueous NaCl and dried over $MgSO_4$. The solvent was evaporated and the residue was subjected to chromatography on silica gel using 1:1 ethyl acetate–hexane as the eluent to give 0.28 g starting oxime and 0.15 g *anti*-isomer.

4-Amino[2,1,3]benzoxadiazole (3). A. A solution of oxime **1** (70.0 g, 460 mmol) in concentrated sulfuric acid (150 ml) was added dropwise with stirring to 80 ml concentrated sulfuric acid heated to 125°C over about 90 min maintaining the temperature at 123-128°C. The reaction mixture was maintained for 30 min at 125°C, cooled, and poured over 500 g crushed ice. The mixture was brought to pH 10 by adding 25% ammonium hydroxide. The precipitate was filtered off, washed with water, dried, and placed in a steam distillation apparatus, and distilled. Pure 4-amino[2,1,3]benzoxadiazole was steam distilled. The yield of amine **3** was 21.0 g (34%); mp 110-111°C (benzene) (mp 110-111°C [7]). The residue after the steam distillation

was subjected to chromatography on silica gel using 5:1 CCl_4–$CHCl_3$ as the eluent to give 9.3 g compound **7a**. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.01 ((1H, d, $J_{6,5}$ = 7.8, H-5'); 7.40 (1H, m, H-5); 6.82 (2H, s, NH_2); 6.35 (1H, d, $J_{5,6}$ = 7.8, H-6'); 3.06 (2H, m, H-7); 2.76 (2H, m, H-6). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 152.59 (C-7a), 149.10 (C-3a), 148.23 (C-3'a), 144.82 (C-7'a), 137.33 (C-7'), 136.03 ($^1J_{CH}$ = 162.0, C-5), 134.24 ($^1J_{CH}$ = 159.0, C-5'), 122.98 (C-4), 107.53 (C-4'), 104.04 ($^1J_{CH}$ = 162.0, C-6'), 23.26 ($^1J_{CH}$ = 131.0, C-6), 16.85 ($^1J_{CH}$ = 134.0, C-7). ^{15}N NMR spectrum, δ, ppm (*J*, Hz): 410.6 (N-1'), 409.3 (N-3'), 395.7 (N-3), 393.8 (N-1). 70.1 ($^1J_{NH}$ = 88.8, NH_2).

The aqueous solution obtained after filtration of the precipitate was brought to pH 3 and extracted with three 100-ml portions of ethyl acetate. The extract was washed with three 50-ml portions of saturated aqueous NaCl and dried over magnesium sulfate, filtered, and evaporated. The residue was triturated with hexane to give 9.0 g amine **4**.

B. Oxime **1** (1.0 g, 6.5 mmol) was added in small portions with stirring to 5 ml PPA heated to 120°C at a rate such that the temperature of the reaction mixture remains in the range 120-130°C. After addition of the entire amount of oxime **1**, the reaction mixture was maintained at 125°C for 1 h, cooled, and poured onto 50 g ice. After decomposition, the reaction mixture was neutralized by adding 25% ammonium hydroxide and then extracted with four 20-ml portions of ethyl acetate. The combined extract was washed with saturated aqueous NaCl and dried over magnesium sulfate. The solvent was distilled off and the residue was steam distilled to give 0.41 g (50%) amine **3**, mp 110-111°C. The residue after steam distillation was subjected to chromatography on silica gel using 5:1 CCl_4–$CHCl_3$ as the eluent to give 0.1 g (5.9%) compound **7a**.

4-Amino-5-methoxy[2,1,3]benzoxadiazole (5). A solution of diazomethane obtained from nitroso-methylurea (1.0 g) in ether was added with stirring to amine **4** (0.5 g, 3.3 mmol) in 100 ml ethyl ether. The mixture was stirred for 4 h and the solvent was distilled off. The residue was subjected to chromatography on silica gel with 1:1 ethyl acetate–hexane as the eluent to give 0.34 g (62.3%) amine **5**; mp 85-88°C (ethanol) (mp 88°C [6]).

7-Ethyloxazolo[4,5-*e*][2,1,3]benzoxadiazole (6). Triethyl orthopropionate (8.0 g, 45 mmol) was added to amine **4** (1.0 g, 6.6 mmol). The mixture was boiled for 1h. The solvent was evaporated off. The residue was treated with 10 ml 5% aqueous NaOH and extracted with three 20-ml chloroform portions. The extract obtained was washed with three 20-ml water portions and dried over magnesium sulfate. The solvent was distilled off and the residue was subjected to chromatography on alumina using 1:3 ethyl acetate–hexane as the eluent to give 0.84 g benzoxadiazole **6**.

7'-Amino-6,7-dihydro-4,4'-di[2,1,3]benzoxadiazole (7a). Ketone **9** (1.1 g, 7.9 mmol) was added to a solution of amine **3** (1.0 g, 7.4 mmol) in concentrated sulfuric acid (10 ml) and the mixture was heated for 2 h at 125-128°C. The reaction mixture was cooled and poured over 100 g crushed ice. The mixture was brought to pH 8 by adding ammonium hydroxide and the product was extracted with three 50-ml portions of ethyl acetate. The combined extract was washed with saturated aqueous NaCl and dried over magnesium chloride. The solvent was evaporated off and the residue was subjected to chromatography on silica gel using CCl_4 as the eluent to give 0.39 g (39%) starting amine **3** and 0.34 g (29.6% relative to reacted amine) amine **7a**.

7'-Acetamido-6,7-dihydro-4,4'-di[2,1,3]benzoxadiazole (7b). Amine **7a** (3.8 g, 15 mmol) was added to acetic anhydride (20 ml) and stirred for 1 h at room temperature. The acetamide precipitate formed was filtered off and dried to give 3.90 g compound **7b**.

7'-Amino-4,5,6,7-tetrahydro-4,4'-di[2,1,3]benzoxadiazole (8a). Palladium (4%) on activated charcoal (0.3 g) was added to a solution of amine **7a** (1.0 g, 3.9 mmol) and the mixture was hydrogenated in a hydrogenation apparatus at atmospheric pressure and room temperature. The catalyst was filtered off and the solvent was evaporated off. The residue was suspended in hexane and filtered to give 0.8 g amine **8a**.

7'-Acetamido-4,5,6,7-tetrahydro-4,4'-di[2,1,3]benzoxadiazole (8b) was obtained from amine **7b** analogously to the preparation of acetamide **8a**.

4-Hydroxy[2,1,3]benzoxadiazole (10). Amine **3** (20 g, 148 mmol) was added to 200 ml 10% aqueous sulfuric acid and the mixture was heated on a water bath for 4 h. Then, the mixture was cooled and extracted with four 100-ml portions of ethyl acetate. The combined extract was extracted with four 60-ml portions of 20% aqueous potassium carbonate. The aqueous extract was carefully brought to pH 3 by adding 30% aqueous sulfuric acid and extracted with four 100-ml portions of ethyl acetate. The combined extract was washed once with saturated aqueous NaCl (200 ml) and dried over magnesium sulfate. The solvent was distilled off and the residue was subjected to chromatography on silica gel using 1:2 ether–hexane as the eluent to give about 12.0 g (60%) benzoxadiazole **10**; mp 148-150°C (mp 148-150°C [7]). The ethyl acetate extract obtained after extraction with 20% aqueous potassium carbonate was dried over magnesium sulfate, filtered, and evaporated. The residue was subjected to chromatography on silica gel using 1:3 ethyl acetate–hexane to give 2.5 g (6.7%) di[2,1,3]benzoxadiazol-4-yl)amine (**11**).

4-Phenylamino[2,1,3]benzoxadiazole (12a). Amine **3** (1.0 g, 7.4 mmol) and *p*-toluenesulfonic acid (0.05 g) were added to 10 ml aniline and the mixture was heated at reflux for 30 min. Excess aniline was distilled off in vacuum and the residue was subjected to chromatography on alumina with pentane as the eluent to give 1.06 g compound **12a**.

4-(4-Methylphenylamino)[1,2,3]benzoxadiazole (12c), 4-(2-Methylphenylamino)-2,1,3-benzoxadiazole (12d), 4-(4-Methoxyphenylamino)[2,1,3]benzoxadiazole (12e), and 4-(2-Methoxyphenylamino)[2,1,3]benzoxadiazole (12f) were obtained analogously to the preparation of compound **12a**.

4-Benzylamino[2,1,3]benzoxadiazole (12b). Amine **3** (0.5 g, 3.7 mmol) and *p*-toluenesulfonic acid (0.05 g) were added to benzylamine (5 ml) and the mixture was maintained for 6 h at 120°C. After cooling, 20 ml 1% hydrochloric acid was added and the product was extracted with three 20-ml portions of ethyl acetate. The combined extract was washed with two 10-ml portions of saturated aqueous NaCl, and dried over magnesium sulfate. The drying agent was filtered off and the solvent was evaporated off in vacuum. The residue was subjected to chromatography on silica gel with toluene as the eluent to give 0.38 g amine **12b**.

4-Acetamido[2,1,3]benzoxadiazole 1-Oxide (13), 7-Methyl-4,5-dihydrooxazolo[4,5-*e*][2,1,3]benzoxadiazole 3-oxide (14), and 4-acetamido-2,1,3-benzoxadiazole (15). Acetic anhydride (60 ml) was added to oxime **2** (12.0 g, 71 mmol). The reaction mixture was heated to 70°C and stirred until oxime **2** was completely dissolved. Then, concentrated sulfuric acid (1.5 ml) was added and the mixture was carefully heated to 100°C until the onset of an exothermal reaction. Heating was discontinued. The reaction mixture evolved heat spontaneously and reached reflux. After completion of the reaction, the mixture was cooled, poured into ice water (300 ml) and left stand for 4 h. The mixture was cautiously neutralized by adding dry sodium carbonate and extracted with four 75-ml portions of ethyl acetate. The combined extract was washed with saturated aqueous NaCl and dried over magnesium sulfate. The solvent was distilled off and the residue was subjected to chromatography on silica gel using 1:2 ethyl acetate–hexane as the eluent with the consecutive isolation of 3.95 g (28.8%) compound **13**; mp 168-170°C (3:1 ethyl acetate–hexane) (mp 162-163°C [8]), 1.2 g (8.8%) **14**, and 0.72 g (5.7%) compound **15**; mp 163-165°C (3:1 ethyl acetate–hexane) (mp 162-163°C [7]).

4-Acetamido-2,1,3-benzoxadiazole (15), 4-Acetamido-5-hydroxy[2,1,3]benzoxadiazole (18), and 7-Methyl-4,5-dihydrooxazolo[4,5-*e*][2,1,3]benzoxadiazole (19) were obtained analogously to compounds **13-15** from oxime **1** (10 g, 65 mmol). Chromatography on silica gel with 3:1 hexane–ethyl acetate led to the consecutive isolation of 4.40 g (38%) compound **15**, 0.25 g (2.0%) compound **18**, and 1.02 g (8.8%) compound **19**.

Benzoxadiazole 18 was also obtained from **4** analogously to the preparation of **7b**.

5-Acetamido-2,3-dimethylquinoxaline 1,4-Dioxide (16). A weak stream of ammonia was passed during 4 h through a solution of amine **13** (1.0 g, 5.2 mmol) in a mixture of 2-butanone (15 ml) and methanol (15 ml) at 50°C. The reaction mixture was left for 8 h at room temperature. The precipitate was filtered off to give 0. 78 g dioxide **16**.

4-Acetamido-2,3-dimethyl-2H-benzimidazole 1,3-Dioxide (17). 2-Nitropropane (0.6 g, 6.7 mmol) and triethylamine (0.6 g, 6 mmol) were added to a solution of amine **13** (0.4 g, 2.07 mmol) in chloroform (10 ml).

The reaction mixture was left stand at room temperature for 240 h. The solvent was distilled off and the residue was subjected to chromatography on alumina with ether as the eluent to give 0.32 g dark-red crystalline dioxide **17**.

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