Synthesis of Substituted Benzoxazolinones by the Curtius Rearrangement: Crystal Structures of Intermediates and By-Products

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3-Substituted salicyloyl chlorides were converted to salicyloyl azides (R = Br, NO_2) which underwent thermal rearrangement and intramolecular cyclization to benzoxazolinones. The crystal structures of 7-substituted benz[*d*]oxazolin-2-ones (R = Br, NH_2), intermediate salicyloyl azides and by-products, *i. e.* 3-(2-hydroxy-3-nitrophenyl)-8-nitrobenz[*e*][1,3]oxazine-2,4-dione and 2-hydroxy-*N*-(2-hydroxy-3-nitrophenyl)-3-nitrobenzamide, have been determined. 7-Aminobenzoxazolinone was obtained by catalytic hydrogenation of the nitro compound as the hemihydrate or in anhydrous form, depending on the temperature of the crystallization.

Key words: Acyl Azide, Benzoxazolinone, Crystal Structure, Curtius Rearrangement

Introduction

For the synthesis of bifeprunox (Fig. 1) [1], an experimental drug for the treatment of psychic disorders such as schizophrenia, the need for a convenient supply of some benzoxazolinones arose. In particular, we needed suitable procedures for 7-bromo- and 7-aminobenzoxazolinones (and the 7-nitro precursor) as building blocks for 7-piperazinobenzoxazolinones. These compounds are usually accessed by treatment of the respective aminophenols with carbonyldiimidazole [1, 2], phosgene [3], or urea [4]. However, the aminophenols are not readily available. Therefore, we considered the appropriate salicylic acid derivatives as inexpensive starting materials. The Curtius reaction was envisioned as a pathway towards the title compounds. A published one-pot procedure [5], however, did not give satisfactory results when applied to 3-nitrosalicylic acid. Hence, we opted for a more conventional step-by-step approach: acyl chlorides were converted to acyl azides which underwent Curtius rearrangement with subsequent ring closure. This endeavor not only provided the desired benzoxazolinones in good yield and purity but also gave us the opportunity to study the intermediate salicyloyl azides in crystalline form. Moreover, the 3-nitro series yielded several unexpected by-products which were also characterized by spectroscopy and X-ray crystallography.

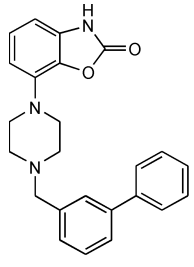
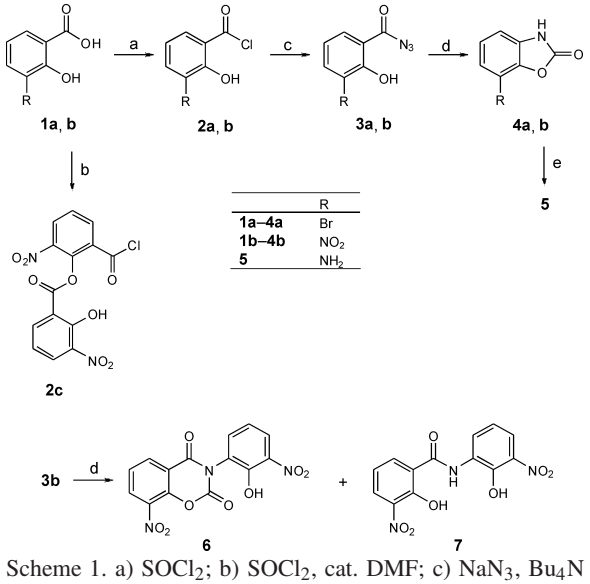


Fig. 1. Molecular structure of bifeprunox.

Results and Discussion

The synthesis of the acyl chlorides **2a**,**b** (Scheme 1) was deemed a straightforward venture. 3-Nitrosalicyloyl chloride has been described several times in the literature [6, 7], *e. g.* as a precursor of antimycin [8], whereas the 3-bromosalicyloyl chloride has not yet been reported. Several methods involving phosphorus pentachloride [6], thionyl chloride [7], and thionyl chloride in the presence of dimethylformamide (DMF) [8] have been disclosed. However, depending on the conditions, varying amounts of an unknown by-product were observed with the 3-nitro compound.



Scheme 1. a) $SOCl_2$; b) $SOCl_2$, cat. DMF; c) NaN_3, Bu_4N Br, acetone; d) 60 °C, acetone or toluene; e) 4 bar H_2, Pd/C, EtOH.

In particular, the amount of DMF added as catalyst was found to be crucial: more DMF caused more by-product. Inspection of the NMR spectra led us to suspect the 'dimer' **2c**. In the literature, salicyl salicylates ('salsalates') have been reported as by-products from other salicyloyl chlorides as dimers, oligomers and polymers, although under more forceful conditions [9]. High-resolution mass spectrometry of the mixture confirmed our assumption. Unfortunately, no single crystals could be obtained due to the hydrolytic lability of this compound. This by-product has not been mentioned by the authors who used DMF as a catalyst [8]. Anyway, the problem could be avoided by not using DMF but, instead, refluxing the acid **1b** with thionyl chloride in diethyl ether [7] to give a quantitative yield of **2b**. No such by-product was observed with the 3-bromo compound, even after the twentyfold reaction time. In contrast, the DMF-free procedure yielded only oily products when applied to the 3-bromo compound, but a crystalline acid chloride **2a** was obtained when a catalytic amount of DMF was used.

The next step necessitated the optimization of the synthesis of the respective salicyloyl azides. Different conditions were tested, such as sodium azide/acetone or trimethylsilyl azide/toluene with or without the presence of catalytic amounts of 4-(dimethylamino)-pyridine (DMAP). However, although the crystalline products were pure, the yields were disappointing. Finally, the system sodium azide/acetone/tetrabutylammonium bromide gave satisfactory yields. To our delight, crude dimer **2c** gave the same yield and purity of **3b** as obtained from pure acid chloride **2b**.

The Curtius rearrangement of salicyloyl azides was conducted with or without prior isolation of the azide. In general, better results were obtained with isolated azides compared to one-pot reactions. As expected, the isocyanates as the primary products of the reaction could not be isolated due to subsequent intramolecular cyclization to the desired title compounds **4a**,**b**. The pure azide **3a** was observed to undergo Curtius rearrangement upon heating by thermomicroscopy and differential scanning calorimetry (DSC) after endothermic melting at 79 °C and slow exothermic crystallization between 110 and 130 °C, whereas DSC of azide **3b** showed a sharp exothermic conversion at 110 °C (Fig. 2). However, in solution a temperature of 60 °C was sufficient for the reaction to proceed. Furthermore, we observed that higher yields were obtained when the reaction was carried out in dilute solution, as expected.

Interesting by-products resulted from intermolecular reactions of the intermediate isocyanate and residual acyl azide during the thermal rearrangement. Thus, benz[*e*][1,3]oxazine-2,4-dione (**6**) and 3-nitrobenzamide (**7**) (Scheme 1) were isolated from the reaction mixture. Although feasible, the formation of a product with a five-membered ring was not observed.

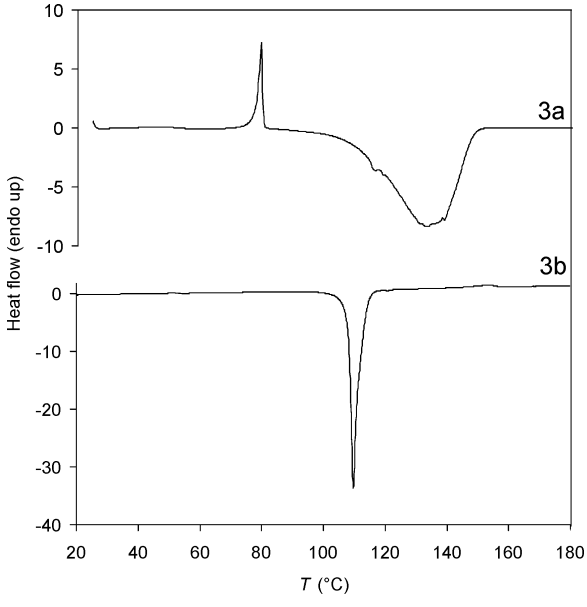


Fig. 2. Differential scanning calorimetry of the azides **3a** and **3b**.

Table 1. Crystal data and structure refinement details.

Compound	**3a**	**3b**	**4a**	**5** $^1/_2$ H_2O	**5**	**6**	**7**
CCDC no.	783667	783668	783669	783670	783671	783672	783673
Chemical formula	$C_7H_4BrN_3O_2$	$C_7H_4N_4O_4$	$C_7H_4BrNO_2$	$2(C_7H_6N_2O_2)\cdot H_2O$	$C_7H_6N_2O_2$	$C_{14}H_7N_3O_8$	$C_{13}H_9N_3O_7$
M_r	242.04	208.14	214.02	318.29	150.14	345.23	319.23
Crystal shape, color	thin plate, colorless	rhomb-shaped, yellow	thin plate, colorless	fragment, colorless	prism, colorless	prism, pale yellow	plate, yellow
Crystal size, mm^3	$0.59\times0.18\times0.03$	$0.4\times0.28\times0.28$	$0.28\times0.20\times0.02$	$0.30\times0.30\times0.20$	$0.22\times0.12\times0.04$	$0.44\times0.08\times0.08$	$0.36\times0.25\times0.08$
Crystal system	monoclinic	monoclinic	monoclinic	monoclinic	orthorhombic	monoclinic	monoclinic
Space group	Pc	$P2_1/n$	$P2_1$	$C2/c$	$P2_12_12_1$	$P2_1/a$	$P2_1/n$
a, Å	3.8688(9)	7.5244(8)	3.9447(18)	11.2960(5)	3.8487(2)	7.8824(11)	12.1497(13)
b, Å	11.3738(21)	11.6472(13)	5.967(3)	8.2133(3)	7.6750(5)	13.463(2)	7.9237(10)
c, Å	9.6954(20)	9.3965(12)	15.091(7)	15.5995(6)	22.122(2)	13.015(2)	14.0805(15)
β, deg	97.805(17)	97.572(10)	93.523(5)	106.659(4)	90	99.537(12)	111.624(8)
V, $Å^3$	422.67(15)	816.31(16)	354.5(3)	1386.54(10)	653.46(8)	1362.1(4)	1260.1(3)
Z	2	4	2	4	4	4	4
D_{calcd}, $g\,cm^{-3}$	1.90	1.69	2.01	1.53	1.53	1.68	1.68
μ, mm^{-1}	4.8	0.1	5.7	0.1	0.1	0.1	0.1
$F(000)$, e	236	424	208	664	312	704	656
Diffractometer	Stoe IPDS 2	Oxford Diffraction Gemini Ultra	Stoe IPDS 2	Oxford Diffraction Gemini Ultra	Nonius KappaCCD	Stoe IPDS 2	Stoe IPDS 2
Data collection method	rotation method	ω scans	rotation method	ω scans	ϕ and ω scans	rotation method	rotation method
Temperature, K	173(2)	173(2)	173(2)	173(2)	233(2)	173(2)	173(2)
θ_{max}, deg	24.6	25.3	24.6	25.3	25.0	24.8	24.6
h,k,l range	±4, $-12\rightarrow13$, $-11\rightarrow10$	$-8\rightarrow9$, $-13\rightarrow14$, $-8\rightarrow11$	±4, ±6, $-17\rightarrow16$	±13, $-6\rightarrow9$, $-15\rightarrow18$	±4, $-8\rightarrow9$, $-25\rightarrow26$	$-9\rightarrow8$, ±15, ±15	$-14\rightarrow13$, $-9\rightarrow8$, ±16
Absorption correction	multi-scan	multi-scan	analytical	multi-scan	none	none	none
Measured reflections	2396	4935	1789	4225	3313	8044	7081
Independent reflections / R_{int}	1287 / 0.045	1481 / 0.024	1175 / 0.049	1268 / 0.025	1141 / 0.058	2169 / 0.063	2099 / 0.047
Observed reflections $[I\geq2\sigma(I)]$	1131	1095	1084	1010	857	1633	1743
Data / restraints / parameters	1287 / 2 / 123	1481 / 1 / 139	1175 / 1 / 104	1268 / 0 / 121	1141 / 3 / 113	2169 / 0 / 228	2099 / 0 / 220
R_1 / wR_2 $[I\geq2\sigma(I)]$	0.044 / 0.098	0.031 / 0.082	0.040 / 0.096	0.033 / 0.079	0.043 / 0.082	0.067 / 0.144	0.037 / 0.085
R_1 / wR_2 (all data)	0.054 / 0.103	0.045 / 0.086	0.046 / 0.099	0.042 / 0.081	0.072 / 0.090	0.092 / 0.156	0.050 / 0.090
Goodness of fit	1.03	1.00	1.11	0.99	1.02	1.11	1.05
Flack parameter	0.14(3)	–	0.00(3)	–	2(2)	–	–
$\Delta\rho_{max\,/\,min}$, $e\,Å^{-3}$	0.50 / −0.67	0.19 / −0.21	0.59 / −0.82	0.22 / −0.23	0.14 / −0.15	0.47 / −0.39	0.18 / −0.16

Compound	Interaction	D–H	H···A	D···A	D–H···A	Symmetry code (A)
3a	O1–H···O2	0.91(11)	1.8(1)	2.609(9)	146(11)	–
3b	O1–H···O2	0.890(14)	1.718(15)	2.5603(15)	156.7(18)	–
4a	N1–H···O2	0.88(2)	1.95(3)	2.803(9)	162(8)	$2-x, 1/2+y, 1-z$
5 $\cdot 1/2\,H_2O$	O3–H···N2	0.892(18)	2.009(18)	2.8913(14)	169.9(17)	–
	N1–H···O3	0.874(17)	2.016(17)	2.8752(15)	167.3(15)	$1-x, -y, 1-z$
5	N1–H···O1	0.89(3)	1.99(3)	2.858(3)	164(3)	$1-x, -1/2+y, 3/2-z$
6	O4–H···O5	0.840(2)	1.867(3)	2.572(3)	140.7(2)	–
7	O3–H···O1	0.86(3)	1.84(3)	2.584(2)	143(3)	–
	O4–H···O5	0.93(3)	1.85(4)	2.613(2)	138(3)	–

Table 2. Hydrogen bonding geometries (Å, deg) with estimated standard deviations in parentheses.

The oxazine **6** was a very minor by-product. However, compound **7** was prepared intentionally in acceptable yield, using a higher concentration of the azide which favored the bimolecular reaction and aqueous workup. To our knowledge, no such by-products of the Curtius reaction have been reported so far. However, these by-products were found only in the nitro series. Notably, while by-products **2c** and **6** are due to the presence of the *ortho*-hydroxy group, the formation of **7** must of course have a different reason. The respective benzamide (identical with an authentic sample [10]) was in fact also observed in a model reaction of 3-nitrobenzoyl azide [11] with 3-nitrophenyl isocyanate [12], which corroborates the alleged mechanism. It is evident that formation of **7** is caused by the activating effect of the nitro group.

It is noteworthy that the reported alternative synthesis of 7-bromobenzoxazolinone **4a** from 7-aminobenzoxazolinone **5** *via* the diazonium salt [13] gave only a very poor yield. In addition, numerous experiments to prepare the 7-iodo compound *via* diazonium salts were futile.

Catalytic hydrogenation of 7-nitrobenzoxazolinone **4b** was straightforward and afforded 7-aminobenz-[*d*]oxazolinone **5** in excellent yield [14]. Surprisingly, the 7-amino compound was obtained as the hemihydrate or in an anhydrous form, depending on the temperature of the crystallization. Thermogravimetry and DSC of the hemihydrate crystallized at 0 °C showed the theoretical loss of weight (5.7 %) between 75 and 100 °C. The powder X-ray diffractogram (PXRD) of the bulk material was identical to the one calculated from single crystal data of the hemihydrate. Crystallization at −20 °C, however, gave the anhydrous product.

Fortunately, most of the compounds reported herein gave crystals suitable for X-ray diffraction. Crystal data and refinement details are summarized in Table 1. Hydrogen bonding parameters are shown in Table 2. Some crystal structures of benzoyl azides have previ-

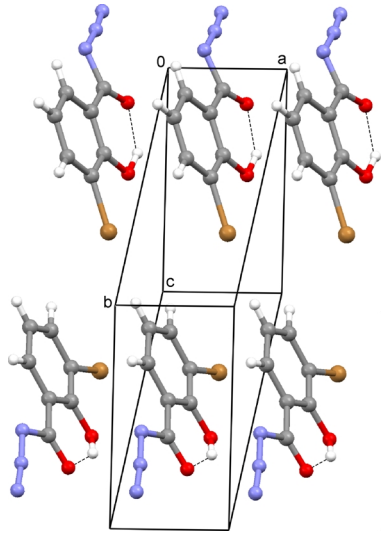


Fig. 3. Arrangement of the molecules of **3a** in the crystal.

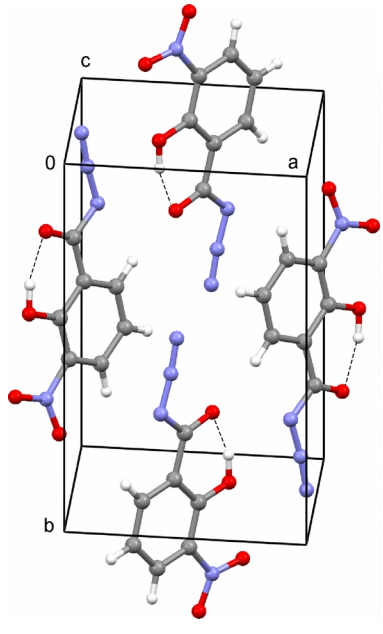


Fig. 4. Arrangement of the molecules of **3b** in the crystal.

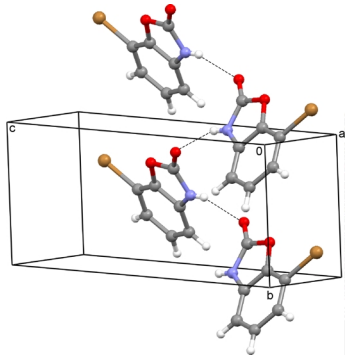


Fig. 5. Hydrogen bonding in the crystal structure of **4a**.

ously been published [15], but structures of salicyloyl azides are definitely new. These molecules are almost planar. It is noteworthy that the nitro group in 2-hydroxy-3-nitrobenzoyl azide **3b** adopts an in-plane conformation, which is in contrast to the known structure of 2-nitrobenzoyl azide [15] where the nitro group is twisted considerably out of the phenyl plane. The azide groups deviate from linearity with N–N–N angles of 174.4° (**3a**) and 173.9° (**3b**). The atoms of the azide group are located slightly out of the plane of the phenyl ring (terminal N by 0.28 Å in **3a**, 0.20 Å in **3b**). In addition, intramolecular OH···O=C hydrogen bonding is observed in **3a** and **3b** (Figs. 3 and 4).

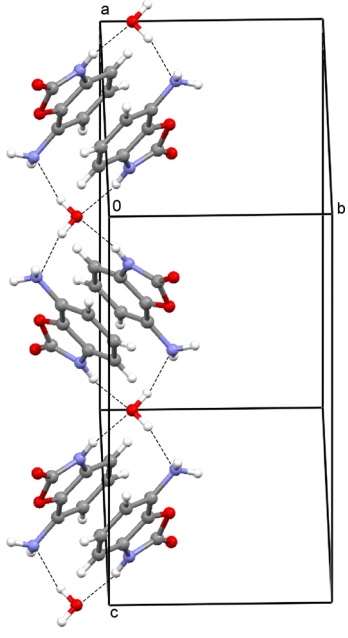


Fig. 6. Hydrogen bonding in the crystal structure of **5** $\cdot 1/2\,H_2O$.

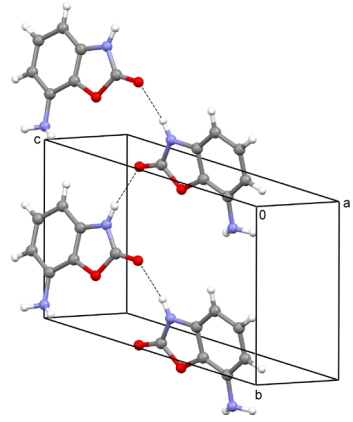


Fig. 7. Hydrogen bonding in the crystal structure of **5**.

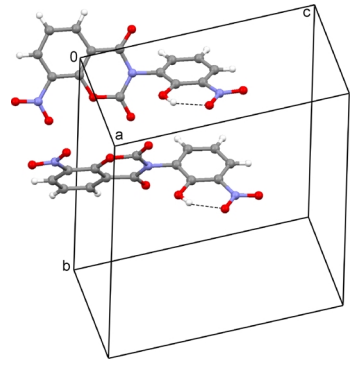


Fig. 8. Arrangement of two symmetry-related molecules of **6** in the crystal.

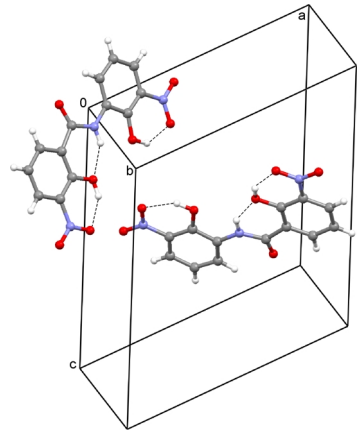


Fig. 9. Arrangement of two symmetry-related molecules of **7** in the crystal.

In the bromo compound **4a**, intermolecular hydrogen bonds (amide NH···O=C) are found (Fig. 5). Interestingly, benzoxazolinones **4a** and anhydrous **5** crystallize

in non-centrosymmetric space groups. In both cases hydrogen-bonded molecules are arranged along a two-fold screw axis in the direction of the crystallographic *b* axis. In the hemihydrate of **5**, one water molecule coordinates to four oxazolinone molecules (Fig. 6), exhibiting amide NH···OH_2 and OH (water)···amino N hydrogen bonds, whereas anhydrous **5** again shows amide NH···O=C contacts (Fig. 7). In crystals of compound **6** the benzoxazinedione and phenyl planes are twisted by 65.5°, whereas the benzamide molecules **7** are planar. Intramolecular hydrogen bonds between the hydroxy and nitro groups are observed in the crystal structures of **6** and **7** (Figs. 8 and 9). In addition, compound **7** displays an intramolecular hydrogen bond between the amide NH and the O atom of the hydroxy group.

Conclusion

The characterization of by-products is of increasing importance in medicinal chemistry. We successfully identified one by-product in the preparation of the acid chloride **2b** and two more of the Curtius rearrangement of the azide **3b**, all of them in the nitro series. The bromo compounds are obviously less prone to by-product formation. In addition, crystal structures of the intermediate salicyloyl azides **3a**,**b** were determined for the first time.

However, the projected synthesis of 'bifeprunox' met considerable obstacles. The planned Hartwig-Buchwald coupling of **4a** [13] or dialkylation of **5** [1] suffered from very unsatisfactory yields, at best. Therefore, a totally different pathway was chosen, involving a preformed phenylpiperazine scaffold in order to avoid the difficulty in the linking of these rings. These results will be published elsewhere.

Experimental Section

3-Bromosalicylic acid [16] and 3-nitrosalicylic acid [17] were prepared according to known procedures. NMR spectra were recorded using a Bruker AC 300 spectrometer. IR spectra were obtained with a Nicolet 5700 FT spectrometer in ATR mode (w = weak, m = medium, s = strong). DSC and TGA were recorded with Perkin-Elmer DSC 7 and TGA 7 instruments. The X-ray powder diffraction pattern (XRPD) was obtained with a X'Pert PRO diffractometer (PANalytical). High-resolution mass spectra were obtained with a Finnigan MAT 95 spectrometer. Elemental analyses were conducted at the University of Vienna, Austria.

*3-Bromo-2-hydroxybenzoyl chloride (**2a**)*

A mixture of 3-bromosalicylic acid **1a** (4.3 g, 20 mmol), thionyl chloride (20 mL) and DMF (1 drop) was stirred at room temperature until a clear solution was obtained. Excess thionyl chloride was evaporated, CH_2Cl_2 (2 mL) was added, and the volatiles were again removed. The residue crystallized on standing at r. t. Yield: 4.7 g (100 %). M. p. 51 °C. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.93 (t, J = 8.0 Hz, 1H), 7.86 (dd, J = 7.8 Hz, J = 1.5 Hz, 1H), 8.07 (dd, J = 8.2 Hz, J = 1.5 Hz, 1H), 10.27 (s, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.3, 118.6, 121.3, 133.6, 141.8, 158.2, 174.2. – IR (neat): ν = 3272 m, 1682 s, 1601 m, 1428 s, 1231 s, 1118 s, 930 s, 826 m, 735 s, 699 s, 665 s, 605 s cm^{-1}.

*2-Hydroxy-3-nitrobenzoyl chloride (**2b**)*

Prepared from 3-nitrosalicylic acid **1b** (3.7 g, 20 mmol) and thionyl chloride (20 mL) in Et_2O (40 mL) as previously described [7]. Yield: 4.0 g (98 %). M. p. 57 °C. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.16 (t, J = 8.2 Hz, 1H), 8.40 (m, 2H), 11.43 (s, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 119.7, 123.8, 132.2, 135.9, 141.3, 155.3, 165.6. – IR (neat): ν = 1767 m, 1693 m, 1606 m, 1585 m, 1533 s, 1441 s, 1345 m, 1266 s, 940 s, 674 s cm^{-1}.

*2-(2-Hydroxy-3-nitrobenzoyloxy)-3-nitrobenzoyl chloride (**2c**)*

A mixture of 3-nitrosalicylic acid **1b** (1.0 g, 5.5 mmol), thionyl chloride (5 mL) and DMF (7 drops) was stirred at r. t. for 2 d. Excess thionyl chloride was evaporated, CH_2Cl_2 (2 mL) was added, and the volatiles were again removed. The crude product mixture crystallized on standing at r. t. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.15 (t, J = 8.1 Hz, 1H), 7.71 (t, J = 8.2 Hz, 1H), 8.32 (dd, J = 1.6 Hz, J = 8.2 Hz, 1H), 8.40 (m, 2H), 8.55 (dd, J = 1.6 Hz, J = 8.0 Hz, 1H), 11.3 (br s, 1H). – HRMS (EI): m/z = 365.9995 and 367.9870 (calcd. 365.9885 and 367.9856 for $C_{14}H_7ClN_2O_8$, $[M]^+$).

*General procedure for the preparation of compounds **3a**,**b***

A mixture of the respective salicyloyl chloride (10 mmol), sodium azide (0.71 g, 11 mmol), and tetrabutylammonium bromide (0.16 g, 0.5 mmol) in acetone (20 mL) was stirred at r. t. for 24 h. The solvent was removed at 20 °C, and the residue was partitioned between Et_2O (20 mL for **3a**, 150 mL for **3b**) and water (20 mL). The organic phase was washed with water (10 mL) and dried with anhydrous $MgSO_4$, and the solvent was evaporated at 20 °C. The residue crystallized on standing at r. t.

*3-Bromo-2-hydroxybenzoyl azide (**3a**)*

Single crystals were obtained by evaporation of the Et_2O solution. Yield: 2.0 g (83 %). M. p. 77 – 79 °C. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.80 (t, J = 7.9 Hz, 1H), 7.75 (dd,

J = 7.9 Hz, J = 1.6 Hz, 1H), 7.77 (dd, J = 7.9 Hz, J = 1.5 Hz, 1H), 11.44 (s, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 112.0, 114.9, 120.6, 129.6, 140.8, 158.9, 176.9. – IR (neat): ν = 2190 m, 2141 m, 1638 s, 1596 m, 1444 m, 1237 s, 1172 s, 1128 s, 835 m, 741 s, 712 s cm^{-1}.

*2-Hydroxy-3-nitrobenzoyl azide (**3b**)*

Single crystals were obtained from acetone/heptane solution. Yield: 2.0 g (96 %). M. p. 110 °C (dec.). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.03 (t, J = 8.1 Hz, 1H), 8.10 (dd, J = 7.9 Hz, J = 1.7 Hz, 1H), 8.22 (dd, J = 8.2 Hz, J = 1.7 Hz, 1H), 11.94 (br s, 1H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 117.2, 119.1, 132.9, 136.3, 138.3, 156.3, 175.8. – IR (neat): ν = 2211 m, 2149 m, 1650 m, 1587 m, 1522 s, 1341 s, 1258 s, 1157 s, 1036 s, 800 s, 746 s, 716 s cm^{-1}.

*7-Bromobenz[d]oxazolin-2-one (**4a**)*

A solution of azide **3a** (9.7 g, 40 mmol) in acetone (200 mL) was refluxed for 3 d. The solvent was evaporated, toluene (50 mL) was added, and the mixture was stirred at 0 °C. The crystalline product was collected by filtration, washed with toluene, and dried. Yield: 6.1 g (71 %). M. p. 244 °C. – ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 7.07 (d, J = 4.7 Hz, 2H), 7.26 (m, 1H), 11.94 (s, 1H). – ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 100.8, 109.2, 124.5, 125.3, 131.4, 141.2, 153.3. – IR (neat): ν = 3084 m, 3010 m, 2880 m, 2795 m, 2722 m, 2666 m, 1717 s, 1617 m, 1480 m, 1450 m, 1399 m, 1301 m, 1264 m, 1209 m, 1159 m, 1129 m, 1048 m, 959 m, 927 m, 866 m, 770 s, 726 s, 593 s, 527 s cm^{-1}. – $C_7H_4BrNO_2$ (214.02): calcd. C 39.28, H 1.88, N 6.54; found C 39.28, H 1.77, N 6.40.

*7-Nitrobenz[d]oxazolin-2-one (**4b**)*

A solution of azide **3b** (10.4 g, 50 mmol) in toluene (200 mL) was stirred at 60 °C for 8 h. The product was collected by filtration and dried to yield **4b** as fine yellow needles (5.7 g, 63 %). M. p. 233 °C. – ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 7.34 (dd, J = 8.5 Hz, J = 7.9 Hz, 1H), 7.48 (dd, J = 7.8 Hz, J = 1.0 Hz, 1H), 7.82 (dd, J = 8.6 Hz, J = 1.0 Hz, 1H), 12.3 (br s, 1H). – ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 115.9, 116.8, 123.9, 131.3, 133.3, 137.6, 153.6. – IR (neat): ν = 3276 w, 3236 w, 3085 w, 3066 w, 2887 w, 2807 w, 2740 w, 2653 w, 1777 m, 1741 m, 1526 s, 1483 m, 1466 m, 1347 s, 1327 m, 1295 m, 1258 m, 1222 m, 1148 m, 1062 m, 910 m, 868 m, 815 s, 736 s, 636 s, 595 s cm^{-1}. – $C_7H_4N_2O_4$ (180.12): calcd. C 46.68, H 2.24, N 15.55; found C 46.73, H 2.10, N 15.22.

*7-Aminobenz[d]oxazolin-2-one hemihydrate (**5** ·$^1/_2$ H_2O)*

A solution of the nitro compound **4b** (5.0 g, 23 mmol) in EtOH (250 mL) was hydrogenated at 60 °C/4 bar hydrogen pressure for 4 h using 5 % Pd/C (450 mg) as catalyst. The mixture was filtered and the solvent evaporated. The brown residue was redissolved in hot ethanol (10 mL), water (30 mL) was added, and the solution was cooled to 0 °C. The off-white precipitate was collected by filtration and dried in vacuum. Yield: 3.6 g (97 %). After treatment with charcoal and filtration, single crystals were obtained by slow evaporation of a solution in MeOH at r. t. The crystalline hemihydrate lost H_2O between 75 and 100 °C and was converted into the anhydrous form (see below). – ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 5.31 (s, 2H), 6.26 (d, J = 7.6 Hz, 1H), 6.37 (d, J = 8.1 Hz, 1H), 6.80 (t, J = 7.9 Hz, 1H), 11.3 (br s, 1H). – ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 97.6, 108.9, 124.1, 130.2, 130.6, 132.1, 154.6. – IR (neat): ν = 3368 m, 3292 w, 3183 m, 2814 w, 2740 w, 2665 w, 1744 s, 1650 m, 1510 m, 1475 m, 1409 m, 1288 m, 1201 m, 1137 m, 931 m, 866 m, 825 m, 768 m, 727 s, 634 m, 601 m, 576 m cm^{-1}.

*Anhydrous 7-aminobenz[d]oxazolin-2-one (**5**)*

Single crystals of the anhydrate **5** were obtained from a solution of the hemihydrate in MeOH at −20 °C. NMR spectra were identical to those of the hemihydrate. M. p. 185 °C. – IR (neat): ν = 3408 w, 3372 w, 3328 w, 3115 w, 2827 w, 2749 w, 2678 w, 1755 m, 1705 m, 1657 m, 1622 m, 1511 m, 1474 m, 1414 m, 1291 m, 1209 m, 1157 m, 1140 m, 936 m, 765 m, 631 s, 584 s cm^{-1}.

*3-(2-Hydroxy-3-nitrophenyl)-8-nitrobenz[e][1,3]oxazine-2,4-dione (**6**)*

Single crystals of **6** were obtained from the mother liquor of **4b**. M. p. 220 °C. – ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 7.14 (t, J = 8.1 Hz, 1H), 7.67 (dd, J = 7.8 Hz, J = 1.6 Hz, 1H), 7.68 (t, J = 7.9 Hz, 1H), 8.00 (dd, J = 8.2 Hz, J = 1.5 Hz, 1H), 8.36 (dd, J = 7.8 Hz, J = 1.4 Hz, 1H), 8.56 (dd, J = 8.1 Hz, J = 1.4 Hz, 1H), 11.1 (br s, 1H). – IR (neat): 1770 m, 1720 s, 1614 m, 1536 s, 1249 s cm^{-1}.

*2-Hydroxy-N-(2-hydroxy-3-nitrophenyl)-3-nitrobenzamide (**7**)*

A solution of azide **3b** (5.6 g, 27 mmol) in toluene (30 mL) was stirred at 60 °C for 48 h. The major product **4b** was removed by filtration, and the filtrate was taken to dryness. The oily residue was stirred with aqueous acetone (30 mL) to give yellow crystals of the benzamide **7**. Yield: 0.60 g (14 %). M. p. 246 °C. – ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 7.08 (t, J = 8.1 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 7.81 (d, J = 8.3 Hz, 1H), 8.13 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 9.0 Hz, 1H), 8.33 (d, J = 7.4 Hz, 1H), 11.06 (s, 1H). – ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 118.6, 119.3, 120.7, 121.5, 128.3, 129.4, 130.0, 135.0, 137.2, 138.7, 145.2, 153.0, 165.6. – IR (neat): ν = 3315 w, 3250 w, 3165 w, 1667 m, 1602 m, 1588 m, 1519 s, 1446 s, 1344 m, 1267 s,

1230 m, 1207 s, 1117 s, 1074 s, 941 s, 800 m, 727 m, 658 s, 527 s cm^{-1}.

Crystal structure determination

The crystal structures were determined using Oxford Diffraction Gemini-R Ultra, Stoe IPDS 2, and Nonius KappaCCD diffractometers with graphite-monochromatized MoK_α radiation (λ = 0.71073 Å) and refined on F^2. The crystal data and structure refinement details are listed in Table 1.

CCDC 783667 – 783673 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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