Göbel, Dominik; Rusch, Pascal; Duvinage, Daniel; Stauch, Tim; Bigall, Nadja; Nachtsheim, Boris

Substitution Effect on 2-(Oxazolinyl)-phenols and 1,2,5-Chalcogenadiazole-Annulated Derivatives: Emission-Color-Tunable, Minimalistic Excited-State Intramolecular Proton Transfer (ESIPT)-Based Luminophores

Journal Article as: peer-reviewed accepted version (Postprint)

DOI of this document*(secondary publication): https://doi.org/10.26092/elib/3684

Publication date of this document: 17/02/2025

* for better findability or for reliable citation

Recommended Citation (primary publication/Version of Record) incl. DOI:

Substitution Effect on 2-(Oxazolinyl)-phenols and 1,2,5-Chalcogenadiazole-Annulated Derivatives: Emission-Color-Tunable, Minimalistic Excited-State Intramolecular Proton Transfer (ESIPT)-Based Luminophores
Dominik Göbel, Pascal Rusch, Daniel Duvinage, Tim Stauch, Nadja-C. Bigall, and Boris J. Nachtsheim
The Journal of Organic Chemistry 2021 86 (21), 14333-14355
DOI: 10.1021/acs.joc.1c00846

Substitution Effect on 2-(Oxazolinyl)-phenols and 1,2,5-Chalcogenadiazole-Annulated Derivatives: Emission Color-Tunable, Minimalistic Excited-State Intramolecular Proton Transfer (ESIPT)-based Luminophores

Dominik Göbel,[†] Pascal Rusch,[‡,∥] Daniel Duvinage,[§] Tim Stauch,*[,⍰,∩,^] Nadja-C. Bigall*[,‡,∥] and Boris J. Nachtsheim*[,†]

[†] Institute for Organic and Analytical Chemistry, University of Bremen, 28359 Bremen, Germany

[‡] Leibniz Universität Hannover, Institute of Physical Chemistry and Electrochemistry, Callinstraße 3a, D-30167 Hannover, Germany

[∥] Cluster of Excellence PhoenixD (Photonics, Optics, and Engineering – Innovation Across Disciplines), Hannover, Germany

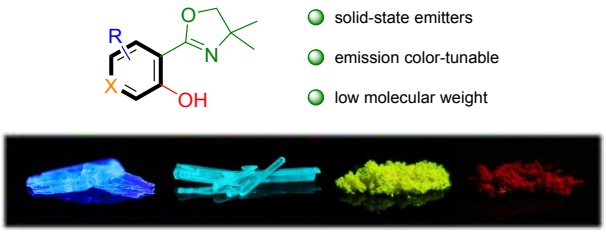
[§] Institute for Inorganic and Crystallographic Chemistry, University of Bremen, 28359 Bremen, Germany

[⍰] Institute for Physical and Theoretical Chemistry, University of Bremen, Leobener Straße NW2, D-28359 Bremen, Germany

[∩] Bremen Center for Computational Materials Science, University of Bremen, Am Fallturm 1, D-28359 Bremen, Germany

[^] MAPEX Center for Materials and Processes, University of Bremen, Bibliothekstraße 1, D-28359 Bremen, Germany

Supporting Information Placeholder



Minimalistic 2-(oxazolinyl)-phenols substituted with different electron-donating and -withdrawing groups as well as 1,2,5-chalcogenadiazole-annulated derivatives thereof were synthesized and investigated towards their emission behavior in solution as well as in the solid state. Depending on the nature of the incorporated substituent and its position, emission efficiencies were increased or diminished, resulting in AIE- or ACQ-characteristics. Single crystal analysis revealed J- and H-type packing motifs and a so far undescribed isolation of ESIPT-based fluorophores in the keto form.

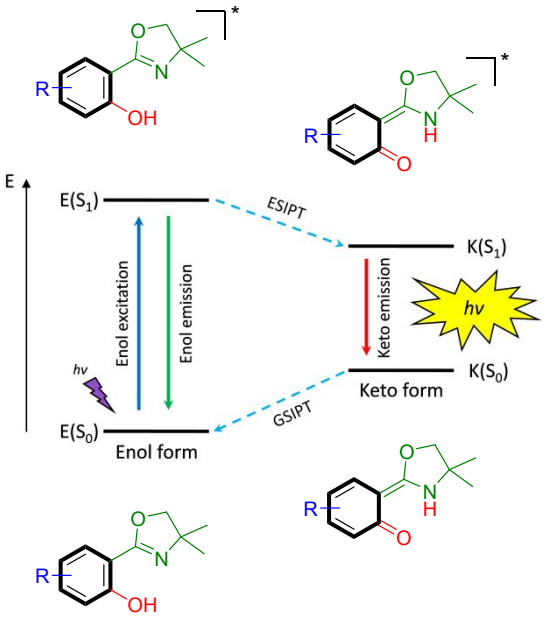
INTRODUCTION

The design of novel luminophores exhibiting outstanding emission properties in the solid state is of great interest due to their application in organic light-emitting diodes (OLEDs).[1] Excited-state intramolecular proton transfer (ESIPT)-based fluorophores which underlie a four level photocycle based on an enol-keto-tautomerism (Scheme 1) are of particular interest.[2] Within this cycle, excitation of the enol form is followed by a tautomerism on the subpicosecond timescale.[3] Emission of the so obtained keto form and ground-state intramolecular proton transfer (GSIPT) completes the photocycle. As a result, large Stokes shifted emission (up to 12,000 cm^{-1}) and, in respect of the phototautomerism, dual emission properties can be observed, which can result in the generation of white light.[4] Beside their extensive applications in biological imaging,[5] chemical sensing[6] and electroluminescent devices,[7] various special feature such as emission color-tuning,[7b,8] polymorph-dependent emission[9] and

crystallization-induced emission (CIE)[10] have been reported. In general, ESIPT-based luminophores consists of a proton donor in close vicinity to a proton acceptor. While phenols and *N*-substituted anilines are used as proton donor functionality, a wide variety of proton acceptors have been reported so far.

Commonly, organic molecules exhibiting bright luminescence comprise either a π-expanded or a π-conjugated aromatic system,[11] whereas single-benzene emitters showing high quantum yields in the solid state are still a peripheral phenomenon. Recent efforts in this research field resulted in the development of tetrasubstituted X-shaped structures bearing donor and acceptor substituents as displayed by the examples of Shimizu[12] and Katagiri (Figure 1).[13] Due to their design, such luminophores suffer from strong inter- and intramolecular hydrogen-bonds (H-bonds) and a highly substituted benzene core.

Scheme 1: Schematic representation of the ESIPT-process.

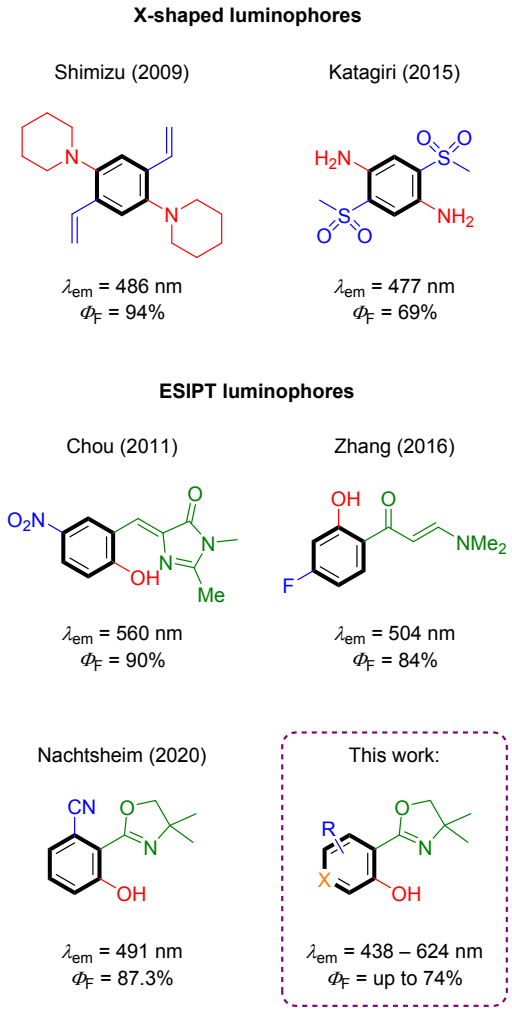


Hence, further derivatization and emission boosting might be complicated. ESIPT-based luminophores are another class of solid state single-benzene emitter with rare literature examples. While Chou and coworkers[8b] reported an ESIPT based analogue of the green fluorescent protein chromophore, Zhang *et al.*[14] presented powerful (2-hydroxyphenyl)propenone derivatives showing remarkable high quantum yields in the solid state. During our research towards minimalistic luminophores we discovered the aerobic C(sp²)–H hydroxylation of magnesiated 2-aryloxazolines using sustainable oxygen sources.[15] The obtained phenols exhibited powerful ESIPT fluorescence and emission colors were covering the whole visible spectrum. We also reported nitrile-substituted 2-(oxazolinyl)-phenols as minimalistic, benzene-based fluorophores with remarkable high quantum yields (up to 87.3%) in the solid state.[16] Very recently, we investigated oxazolinyl- and arylchalcogenazolyl-substituted hydroxyfluorenes as emission color-tunable luminophores.[17] Reasoned by these findings we implemented the oxazoline group as a highly efficient proton acceptor in ESIPT-based luminophores and extended their usage as a protecting and directed metalation group (DMG).[18] Moreover, not only the oxazoline group, but the entire 2-(oxazolinyl)-phenol motif is found in several natural products like spoxazomicins and tetroazolemycins, making the study of such structural motifs of greater importance.[19]

However, up to now there is no systematic investigation of diverse substituted 2-(oxazolinyl)-phenols towards their emission properties. Owing to this, we were intended to synthesize 2-(oxazolinyl)-phenols bearing various electron-donating and -withdrawing groups and examine them in respect of their photophysical properties in solution as well as in the solid state.[20]

RESULTS AND DISCUSSION

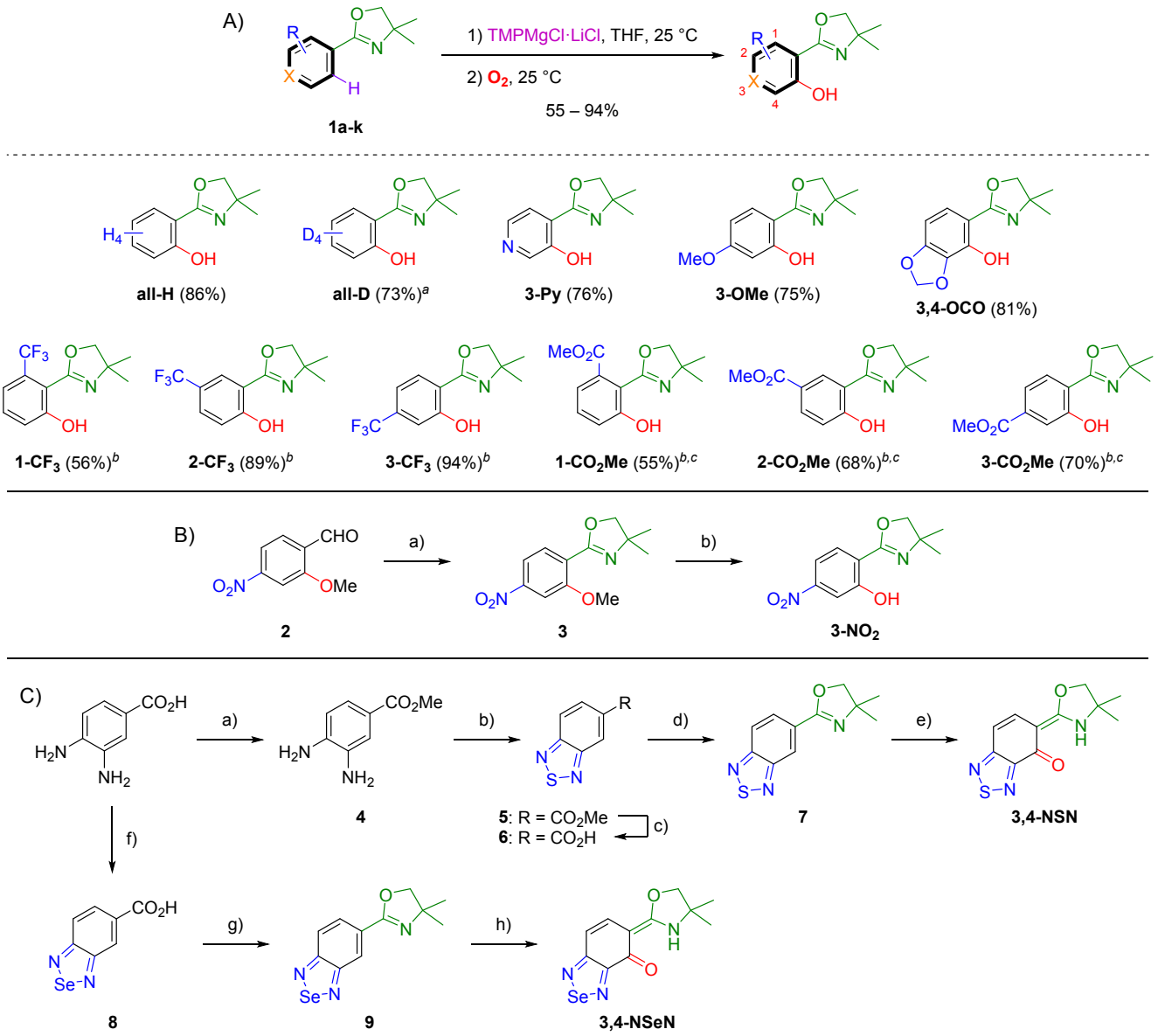
2-(Oxazolinyl)-phenols were achieved by applying our recently established C(sp²)–H hydroxylation method of 2-aryloxazolines.[15b] In an initial step, the corresponding benzaldehydes[21] or benzoic acids[22] were transformed to 2-aryloxazolines (**1a-k**) in good to excellent yields. Phenol formation was succeeded by a directed C(sp²)–magnesiation using TMPMgCl·LiCl and subsequent oxidation with molecular oxygen providing phenols in good yields (Scheme 2A). Noteworthily, phenols bearing -CF_3 or -CO_2Me groups in position 4 of the benzene core were not achieved, due to the great regioselectivity of the hydroxylation protocol and steric hindrance of the substituents during the metalation step. Since nitro-substituted 2-aryloxazoline was not accessible via this hydroxylation method, another synthetic pathway was implemented (Scheme 2B).



Scheme 2: Synthesis of 2-(Oxazolinyl)-phenols.

Figure 1: Single-benzene solid state emitters.

Benzaldehyde **2** was achieved by a bromination/hydrolysis[23] or an acetoxylation/hydrolysis[24] protocol and converted to the corresponding oxazoline **3** by using the implemented two step procedure. Unveiling of the phenolic hydroxy group using BBr_3 provided the nitro-substituted 2-(oxazolinyl)-phenol **3-NO₂** in excellent yield.[25] Attachment of very strong electron-withdrawing groups, *i.e.* thiadiazole and selenadiazole, was achieved starting from commercially available 3,4-diaminobenzoic acid (Scheme 2C). In case of thiadiazole, esterification[26] followed by sulfur incorporation[27] and saponification[28] afforded benzoic acid **6**. Oxazoline formation and subsequent oxidation provided ketone **3,4-NSN**. A similar procedure was applied for selenadiazole including selenium incorporation,[29] oxazoline formation and oxidation to ketone **3,4-NSeN**. To our surprise, during oxazoline formation to selenadiazole **9** a partial selenium-sulfur-exchange has taken place, yielding **7** in moderate yield. Similar findings were already discussed in literature.[30]



A) Reaction conditions: 2-aryloxazoline (1 eq.), TMPMgCl·LiCl (3 eq.), THF (0.4 M) at 25 °C for 1 to 6 h under N_2. Then, the reaction vessel was flushed with molecular oxygen at 25 °C and stirring was continued for another 24 h. Yields of isolated compounds are given in parentheses. [a] 5% Protonation occurred on position 1 of the benzene ring during reaction. [b] Metalated for 2 h. [c] Metalation performed at 0 °C and warming to 25 °C while oxidation. B) a) (1) 2-amino-2-methylpropan-1-ol, 4 Å MS, CH_2Cl_2, 25 °C, 18 h; (2) NBS, CH_2Cl_2, 25 °C, 4 h, 78%; b) BBr_3, CH_2Cl_2, –78 °C to –30 °C, 5 h, 65%. C) a) $SOCl_2$, MeOH, 0 °C to 25 °C, 14 h, 93%; b) $SOCl_2$, NEt_3, CH_2Cl_2, 0 °C; then 80 °C, 6 h, 87%; c) NaOH (1.0 M), 1,4-dioxane, 25 °C, 16 h, 88%; d) (1) $SOCl_2$, 80 °C, 3 h; (2) 2-amino-2-methylpropan-1-ol, CH_2Cl_2, 0 °C to 25 °C, 3 h; (3) $SOCl_2$, 25 °C, 40 min, 94%; e) (1) TMPMgCl·LiCl, THF, 25 °C, 3 h; (2) O_2, 25 °C, 24 h, 71%; f) SeO_2, HCl (1.0 M), 80 °C, 3 h, 98%; g) (1) $SOCl_2$, 80 °C, 3 h; (2) 2-amino-2-methylpropan-1-ol, CH_2Cl_2, 0 °C to 25 °C, 3 h; (3) $SOCl_2$, 25 °C, 40 min, 58% (+ **7** in 36% yield); h) (1) TMPMgCl·LiCl, THF, 25 °C, 3 h; (2) O_2, 25 °C, 24 h, 34%.

Interestingly, chalcogenadiazoles were functionalized in the final oxidation step with perfect regioselectivity between both substituents, which is similar to **3,4-OCO** and reasoned by a double coordination effect. Moreover, both chalcogenadiazoles showed unique behavior, since they were found to exist in the keto form and not in the full-aromatic enol form. The molecular structure of both chalcogenadiazoles could be verified by X-ray diffraction (XRD).

With all 2-(oxazolinyl)-phenols and 1,2,5-chalcogenadiazole-annulated derivatives in hand, we started to examine their emission properties (Table S1). UV-vis absorption spectra were measured in solvents differing in their degree of polarity, *i.e.* methanol (MeOH), dichloromethane (DCM) and cyclohexane (CH). Luminophores bearing strong electron withdrawing groups (**3-NO_2**, **3,4-NSN** and **3,4-NSeN**) were analyzed in additional solvents, since their absorption/emission features are more complex. In general, the absorption

properties of the respective ESIPT-based luminophore are solvent independent with the exception of chalcogenadiazoles **3,4-NSN** and **3,4-NSeN**, whose absorptions bands are found to be significantly more resolved in nonpolar solvents. In DCM solution, absorption features below 300 nm are specific for π-π* transitions and are associated with the single benzene unit (Figure 2). Maxima of broad and unstructured absorption features are detected between λ_{abs} 300 nm (**3-OMe**) and 349 nm (**3-NO_2**) with extinction coefficients ranging from 3050 to 8670 mol L^{-1} cm^{-1}. Generally, the stronger the electron-withdrawing ability of the respective substituent, the more red-shifted the broadened absorption maximum. This red-shifted trend of absorption maxima is the result of a smaller HOMO–LUMO gap, reasoned by the stronger stabilization of the LUMO than of the HOMO.[31]

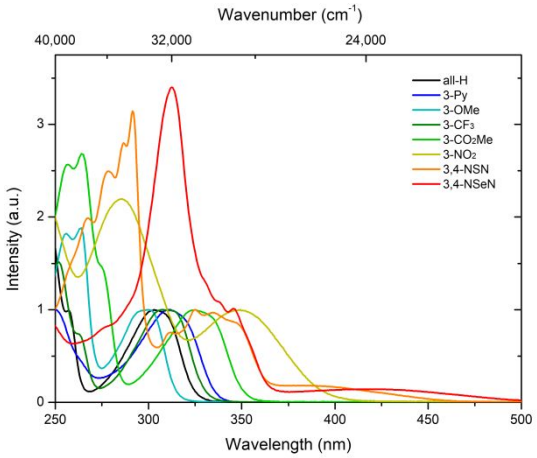


Figure 2: Normalized UV-vis absorption spectra of selected 2-(oxazolinyl)-phenols and 1,2,5-chalcogenadiazole-annulated derivatives in CH_2Cl_2 solution.

In contrast, **3,4-NSN** and **3,4-NSeN** show broad and intense absorption characteristics between 290 and 350 nm. Broad bands are detected above 380 nm, which were attributed to a n-π* transition of the carbonyl group. Fluorescence properties of all 2-(oxazolinyl)-phenols and 1,2,5-chalcogenadiazole-annulated derivatives were analyzed in the same solvents as absorption measurements. Results obtained in dichloromethane are listed in Table 1 and displayed in Figure 3a/b. Diluted solutions of luminophores were excited in the respective unstructured and broad absorption maxima resulted in emission colors ranging from blue to red. The only exception represents **3,4-OCO**, which is non-fluorescent in solution as well as in the solid (crystalline) state. Dual emission characteristics, which could be observed for such fluorophores, were only detected to a reduced extent for **1-CO_2Me** (see Figure S59). All other luminophores emit exclusively from the keto form demonstrating the great efficiency of proton transfer in the excited state. As common for ESIPT-based emitters, red-shifted emission is observed in nonpolar solvents, while spectra were blue-shifted in protic solvents. Here, phenol coordination can occur. Due to large Stokes' shifted emission for all luminophores (up to 13,870 cm^{-1} for **3,4-NSN** in MeOH), baseline separated absorption and emission spectra were obtained.

Interestingly, **3-NO_2** is the exclusive minimalistic 2-(oxazolinyl)-phenol, which exhibits strong positive solvatochromism as investigated for 12 solvents with distinctive dipole moments.

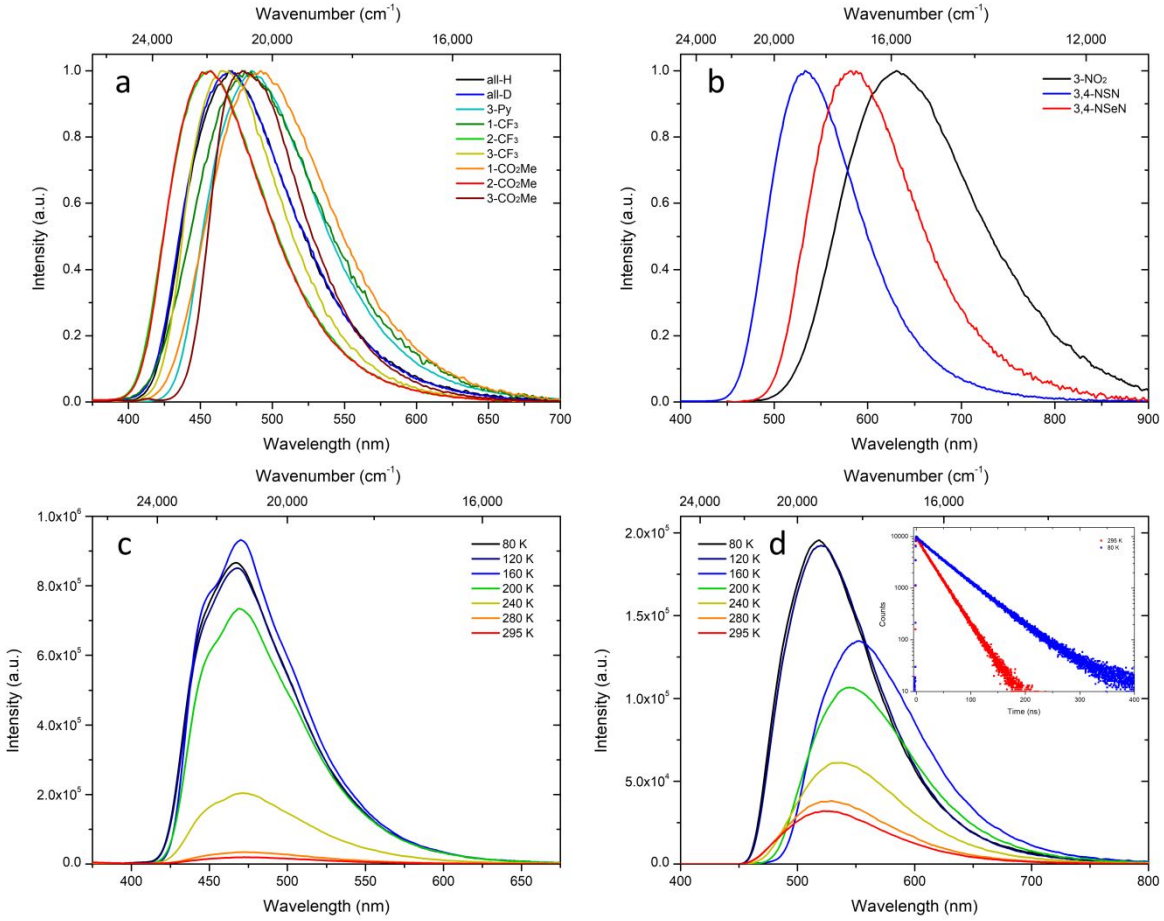


Figure 3: (a,b) Normalized emission spectra of 2-(oxazolinyl)-phenols and ketones in CH_2Cl_2 solution. (c,d) Temperature-dependent emission spectra of **all-H** (c) and **3,4-NSN** (d) in deaerated 2-MeTHF during heating from 80 K to 295 K with excitation at 303 and 345 nm, respectively. Inset in (d) displays time resolved emission decay curves of **3,4-NSN** in deaerated 2-MeTHF at 295 K (red dots) and 80 K (blue dots).

Table 1: Photophysical data of investigated luminophores in CH_2Cl_2 solution at 295 K.[1]

Compd	λ_{abs} [nm][2]	λ_{em} [nm]	$\Delta\nu$ [cm^{-1}]	Φ_F [%]	τ [ns] (Rel %)[4]	k_r [10^8 s^{-1}][5]	k_{nr} [10^8 s^{-1}][5]
all-H	303	470	11,730	1.1	<0.2	–	–
all-D	303	472	11,930	1.1	0.25 (20.8); 1.78 (43.5); 5.72 (35.7)	0.04	3.45
3-Py	311	486	11,580	9.1	1.50 (84.8); 5.45 (15.2)	0.43	4.33
3-OMe	300	464	11,780	<0.2	<0.2	–	–
1-CF_3	312	481	11,260	<0.2	<0.2	–	–
2-CF_3	298	457	11,680	17.1	2.29	0.75	3.62
3-CF_3	307	466	11,110	37.5	4.65	0.81	1.34
1-CO_2Me	312	492	11,730	1.6	<0.2	–	–
2-CO_2Me	308	457	10,590	12.9	1.78	0.72	4.89
3-CO_2Me	325	479	9,890	62.6	8.91	0.70	0.42
3-NO_2	349	631	12,810	0.6	0.58	0.10	17.3
3,4-NSN	325 (384)[3]	536	12,110 (7,390)[3]	27.8	32.4 (37.7)[6]	0.09	0.22
3,4-NSeN	346	582	11,720	2.8	4.00	0.07	2.43

	(420)[3]	(6,630)[3]

[1] Additional spectroscopic data is given in the supporting information. [2] Absorption maxima for π-π*-transitions are given. [3] Absorption maxima for n-π*-transitions and the respective Stokes shifts are given in parentheses. [4] Intensity-weighted relative ratios of the two/three decay components are given in parentheses if a bi/tri-exponential fit was used. [5] k_r and k_{nr} were calculated using the equations $k_r = \Phi_F/\tau$ and $k_{nr} = (1-\Phi_F)/\tau$. [6] Lifetime were measured after bubbling with argon for 30 minutes.

While blue-cyan emission is detected in nonpolar solvents (λ_{em} = 495 nm for CH), red emission is obtained in polar solvents (λ_{em} = 631 nm for acetone). This strong solvatochromism can arise from an intramolecular charge transfer (ICT) mechanism, reasoned by the donor-(hydroxy group) acceptor (nitro group) substitution pattern.[32] A similar emission behavior in respect of the Stokes shifts in a respective solvent is observed for chalcogenadiazoles **3,4-NSN** and **3,4-NSeN**. Blue-shifted emission in toluene is opposed a strong red-shifted emission in methanol. This unusual ESIPT performance can be explained by the existence of the keto form for chalcogenadiazoles and thus, positive solvatochromism is detected. Quantum yields (Φ_F) in solvents differing in their degree of polarity are found to be very low (Φ_F < 5%) for the derivatives **all-H**, **all-D**, **3-OMe**, **1-CF$_3$**, **1-CO$_2$Me** and **3,4-NSeN**. Moderate Φ_F (up to 20%) in solution are detected for **3-Py**, **2-CF$_3$**, **2-CO$_2$Me** and **3-NO$_2$**, while high Φ_F (up to 63%) are observed for **3-CF$_3$**, **3-CO$_2$Me** and **3,4-NSN**. Based on these findings, a significant tendency can be seen in which neutral and electron-rich 2-(oxazolinyl)-phenols exhibit very low quantum efficiencies in solution.

Table 2: Photophysical data of investigated luminophores in the solid state at 295 K.[1]

Compd	λ_{exc} [nm][4]	λ_{em} [nm][4]	$\Delta\nu$ [cm^{-1}][4]	Φ_F [%]	τ [ns] (Rel %)[5]	k_r [10^8 s^{-1}][6]	k_{nr} [10^8 s^{-1}][6]	x;y (CIE 1931)
all-H[2]	328	469	9,170	48.2	5.80	0.83	0.89	0.160; 0.200
all-D[3]	333	466	8,570	50.2	5.85	0.86	0.85	0.162; 0.200
3-Py[2]	343	485	8,540	17.8	2.40	0.74	3.43	0.180; 0.318
3-OMe[3]	311	438	9,320	28.5	0.86 (14.4); 3.45 (85.6)	0.93	2.32	0.154; 0.082
1-CF$_3$[3]	339	463	7,900	12.9	1.79	0.72	4.88	0.162; 0.198
2-CF$_3$[3]	369	445	4,630	37.4	5.33	0.70	1.18	0.154; 0.110
3-CF$_3$[3]	334	466	8,480	57.0	7.62	0.75	0.56	0.151; 0.175
1-CO$_2$Me[3]	386	478	5,000	7.9	0.64 (36.1); 7.52 (63.9)	0.27	3.20	0.179; 0.283
2-CO$_2$Me[3]	316	446	9,220	54.9	5.36	1.02	0.84	0.154; 0.106
3-CO$_2$Me[2]	355	477	7,210	74.0	9.07	0.82	0.29	0.155; 0.294
3,4-NSN[2]	466	546	3,140	5.6	7.53	0.07	1.25	0.402; 0.577
3,4-NSeN[2]	500	624	3,970	<0.2	<0.2	–	–	0.587; 0.401

[1] Additional spectroscopic data is given in the supporting information. [2] Investigated in the crystalline state. [3] Investigated in the amorphous state. [4] Excitation spectra of the crystalline samples were used for evaluation of the stokes shift. [5] Intensity-weighted relative ratios of the two decay components are given in parentheses if a bi-exponential fit was used. [6] k_r and k_{nr} were calculated using the equations $k_r = \Phi_F/\tau$ and $k_{nr} = (1-\Phi_F)/\tau$.

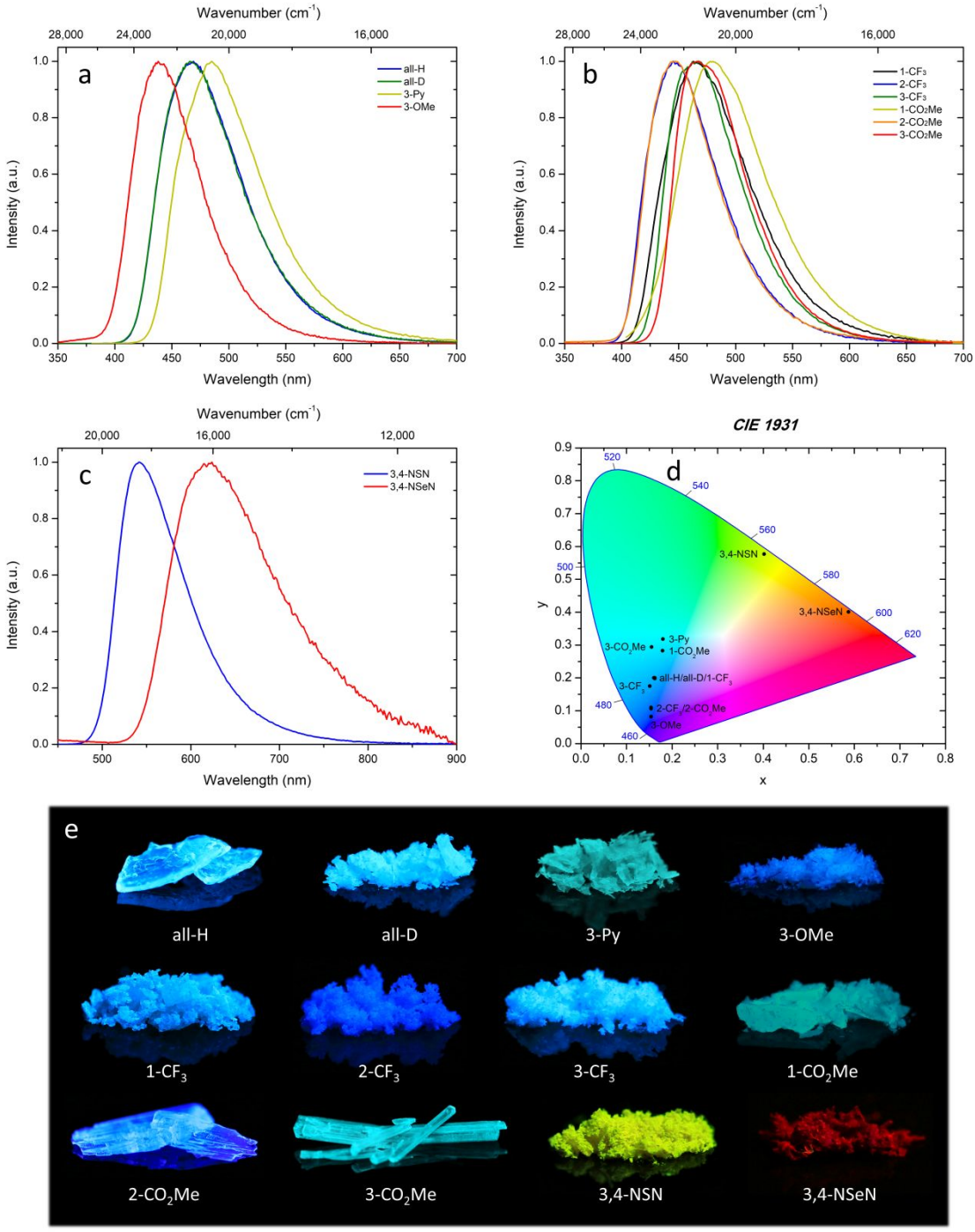


Figure 4: (a-c) Normalized emission spectra of 2-(oxazolinyl)-phenols and ketones measured in the solid state (see footnotes of Table 2). (d) CIE 1931 chromaticity plot with emission color coordinates of presented luminophores in the solid state. (e) Representative images of investigated fluorophores in the solid state under 366 nm irradiation.

Furthermore, the position of incorporation of the electron-withdrawing group is of great importance, since Φ_F increases with the migration of the accepting groups from position 1 with the lowest to position 3 showing the highest Φ_F. In this context, **3,4-NSeN** owns an outstanding position, due to the heavy atom effect of selenium on the luminescence properties.[33] Fluorescence lifetimes (τ) of excited states were determined by time-correlated single photon counting (TCSPC) at ambient temperature. Lifetimes for almost all fluorophores are varying between < 0.2 ns and 7 ns, with exception of **3-CO_2Me**, **3-NO_2** and **3,4-NSN**. While **3-CO_2Me** and **3-NO_2** show lifetimes of up to 8.9 (DCM) and 14.2 ns (Et_2O), , a significant increase was detected for **3,4-NSN** with lifetimes of up to 32.4 ns (DCM). Due to its very high fluorescence lifetimes in aerated media, diluted solutions of **3,4-NSN** were bubbled with argon for ten minutes and measured again. Prolonged lifetimes were observed in several solvents with the

largest increase in EtOAc by a factor of 1.7 from 22.4 ns in aerated to 38.0 ns in deaerated solution.

In addition, temperature-dependent emission behavior was investigated in deaerated 2-MeTHF solution for **all-H**, **3-NO_2**, **3,4-NSN** and **3,4-NSeN** (Table S2). Temperature maps were created by measuring in 40 K intervals starting from 80 K up to 295 K. For **all-H** a drastic increase in emission intensity is observed for 160 K (factor of 48 compared to 295 K) followed by a decrease in intensity at 120 and 80 K (Figure 3c). Upon cooling of the luminophore solution, the degrees of freedom are limited and non-radiative relaxation processes become restricted. This results in an increase of emission intensity. If the temperature drops below a certain level the crucial proton transfer is hindered, thus, less emission intensity is observed at very low temperatures for ESIPT-based luminophores.[16,34] Differently, for **3,4-NSN** we observed a steady increase in emission intensity, which could be explained by its non-ESIPT behavior, since no suppression of the proton transfer can take place. Also, no significant shift in emission maximum wavelength was detected. Different to **all-H**, maximum emission efficiency was measured at 80 K for all electron-poor structures with a growth in intensity for **3-NO_2**, **3,4-NSN** and **3,4-NSeN** by factor 5.8, 6.1 and 2.7, compared to 295 K. Another similarity of those emitters is the initial red-shifted emission until 160 K and the following strong blue shift at lower temperatures. Fluorescence lifetimes (τ) of the excited states at 80 K were measured in deaerated 2-MeTHF. Lifetimes were significantly prolonged for all investigated emitters with a maximum of 50.9 ns for **3,4-NSN** (Figure 3d). Despite the elongation of fluorescence at deep temperatures, neither phosphorescence nor thermally activated delayed fluorescence (TADF) was observed during our investigations.

Almost all luminophores, with the exception of **3,4-OCO** and **3-NO_2**, show bright emission in the solid state, which is clearly visible to the naked eye by irradiation with a 366 nm UV-handlamp (Figure 4e). Hence, investigation of their photophysical properties were performed for either crystalline or amorphous samples (see footnotes of Table 2). In this context, crystalline is exclusively attributed to luminophores whose molecular structure has been verified by XRD. In general, large Stokes' shifts are detected for all investigated solids, which is caused by efficient proton transfer in the excited state (Table 2). Thus, emission bands are attributed to the keto form (Figure 4a-d). Contrary to their weak or non-existing emission in solution, **all-H**, **all-D**, **3-OMe**, **1-CF_3** and **1-CO_2Me** showed remarkable quantum efficiencies (up to 50.2% for **all-D**) in the solid state with emission maxima in the blue-(cyan) region. Compared to the Φ_F in DCM solution, an increase in the quantum yield by a factor of at least 142 for **3-OMe** is detected, which is why these five minimalistic structures represent aggregation-induced emission (AIE) luminophores. Noteworthily, with the incorporation of heavier isotopes we were intended to boost the quantum efficiency by suppressing the non-radiative decay processes and increasing the vibronic coupling strength.[35] However, only a slight improvement of Φ_F was detected for **all-D** compared to **all-H**. **3-Py**, **2-CF_3**, and **2-CO_2Me** showed moderate Φ_F in DCM solution, however, their emission efficiencies increased in the solid state (up to 54.9% for **2-CO_2Me**). Similar to previously discussed fluorophores, emission maxima are located in the blue-(cyan) region. Based on these findings, these three 2-(oxazolinyl)-phenols are typical aggregation-induced emission enhancement (AIEE) representatives. Strong fluorescence properties were already observed for **3-CF_3** and **3-CO_2Me** in solution and again, high Φ_F (up to 74.0% for **3-CO_2Me**) were determined in the solid state with emission maxima in the blue-(cyan) range. Thus, these two structures represent dual state emission (DSE) luminophores. In contrast, for chalcogenadiazoles **3,4-NSN** and **3,4-NSeN**, which showed already exceptional emission behavior in solution due to their preferred existence in the keto form, a reduction of Φ_F in the solid state compared to those in solution was indicated. Owing to this, they demonstrate aggregation-caused quenching (ACQ) character with yellow and red emission colors. Interestingly, both chalcogenadiazoles exhibit strong bathochromic shifted emission compared to previously described luminophores with yellow (**3,4-NSN**) and red (**3,4-NSeN**) emission colors. Despite their significantly red-shifted emission both chalcogenadiazoles evince relatively small Stokes shifts, which is reasoned by their preferred keto form existence. This is also indicated by a strong red-shifted absorption in the solid state. Thus, they must be attributed to the non-ESIPT luminophores. To generalize these results, the quantum efficiency in the solid state increases continuously with migration of the electron-withdrawing group from position 1 to position 3. Neutral and electron-rich 2-(oxazolinyl)-phenols showed tremendously increased Φ_F in the solid state compared to solution, which is characteristic for AIE-luminophores. Importantly, no crystallization-induced emission enhancement (CIEE) was observed for crystalline samples, which is coincident with our previous observation for 2-(oxazolinyl)-phenols.[16] Anyhow, electron-deficient 2-(oxazolinyl)-phenols outperform neutral and electron-rich structures in any matter, but an electron-poor arene core (**3-Py**) does not seem to increase quantum efficiency significantly. If the strength of electron-accepting groups exceeds a certain limit the emission efficiency in the solid state drops for **3,4-NSN** and **3,4-NSeN**, or is quenched as observed for **3-NO_2**. The presented fluorophores differ strongly in their emission color ranging from blue to red, thus covering the whole visible spectrum. In this context the unique behavior of nitrile-substituted 2-(oxazolinyl)-phenol **1-CN** appears to be even more extraordinary, since other luminophores bearing substituents in position 1 do not show any approximate performance.[16]

To gain a better understanding of the results achieved from solid state emission investigation, suitable single crystals of seven 2-(oxazolinyl)-phenols and ketones (**all-H**, **3-Py**, **3,4-OCO**, **3-CO_2Me**, **3-NO_2**, **3,4-NSN** and **3,4-NSeN**) were grown and analyzed in respect of their molecular conformation as well as their crystal structure lattice (Figure 5 and Table S46). Two of those crystals – **3,4-OCO** and **3-NO_2** – showed no emission. For **3,4-OCO**

this could be due to a highly unordered crystal lattice and a relatively high dihedral angle (7.0°) between the arene and the oxazoline, hence, inhibiting efficient proton transfer in the excited state. Contrary, **3-NO_2** exhibits a very low dihedral angle (0.8°) and a short H-bond (1.763 Å) including a large H-bond angle (152.37°), which should facilitate proton transfer upon excitation. Strong intermolecular π-π-interactions lead to the formation of H-aggregates with a slip angle of 76.8° and a plane distance of 3.438 Å, which could cause the non-existing solid state emission. In general, it is well known that intense π-π-interactions result in the decrease or complete disappearance of emission and only a small number of luminophores exhibit powerful emission despite the formation of H-aggregates.[36] Single crystals of **all-H** and **3-Py** exhibiting two molecules in the asymmetric unit with distinct H-bond lengths ranging between 1.784 and 1.879 Å and angles ranging from 144.09 to 151.76°. Also, moderate dihedral angles with a maximum of |3.5°| were detected. Both ESIPT fluorophores show dimeric π-π-interactions with slip angles of 33.2° for **all-H** and 45.3° for **3-Py**, which is representative for J-type aggregates. A significant difference between both luminophores is hidden in the plane distance including the corresponding centroid-centroid distance. While **all-H** shows a greater plane distance with 4.822 Å and a centroid-centroid distance of 8.800 Å, the corresponding values (3.459 and 4.867 Å) are significantly shorter for **3-Py**, demonstrating that stronger π-π-interactions exists in the **3-Py** crystal lattice. With **3-CO_2Me** being the most powerful crystallized luminophore, average values were determined for the H-bond length (1.843 Å) and angle (147.39°) and for the dihedral angle (|1.8°|).

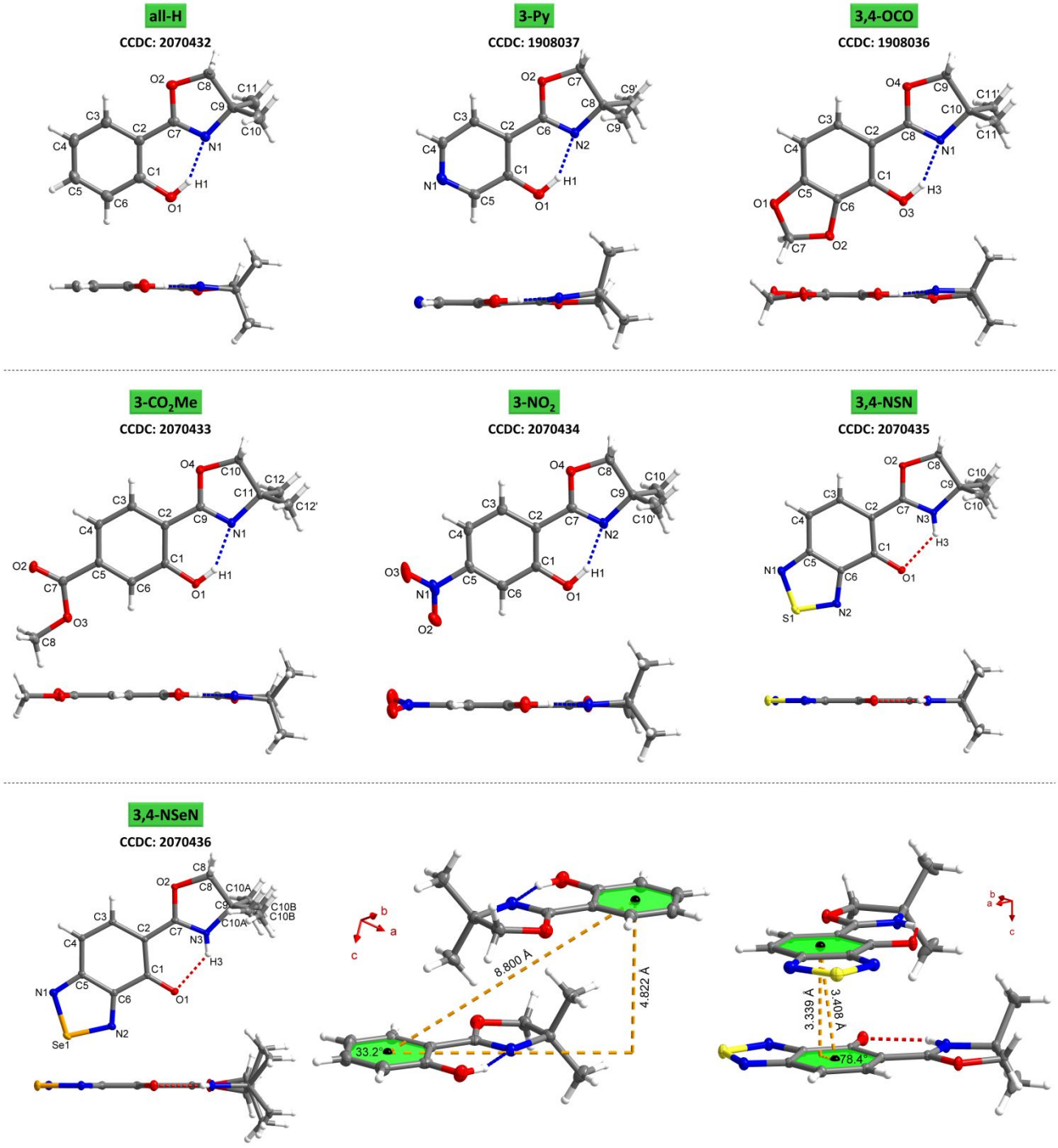


Figure 5: Molecular structures showing 50% probability ellipsoids, including top view and side view of the single structure. Upper row: **all-H** (left), **3-Py** (center), **3,4-OCO** (right); central row: **3-CO2Me** (left), **3-NO2** (center), **3,4-NSN** (right); lower row: **3,4NSeN** (left), intermolecular π-π-interactions of **all-H** (center) and **3,4-NSN** (right) demonstrating the J-type (**all-H**) and H-type (**3,4-NSN**) aggregates in the respective crystal lattice.

Again, typical for J-type packing motifs, intermolecular π-π-interactions were detected with slip angles of 37.6 and 48.8°, respectively, including short plane distances (3.258 and 3.335 Å) and larger centroid-centroid distances up to 5.339 Å. The high quantum efficiency is explained by the observation that 2-(oxazolinyl)-phenols bearing carbonyl-related functionalities such as nitriles exhibit brighter emission than those emitters that do not bear them. As a result, ester substituted 2-(oxazolinyl)-phenols exhibit stronger emission than for example trifluoromethyl-substituted derivatives.

Last but not least, both chalcogenadiazoles **3,4-NSN** and **3,4-NSeN** were crystallized and similar properties were identified. As a structural feature, **3,4-NSeN** exhibits a

disorder in the oxazoline backbone resulting in a twist above and underneath the molecular plane with an identical dihedral angle of |13.8°|. The essential dihedral angles between the former arene and the oxazolidine are equal to zero for both chalcogenadiazoles. Very intensive intermolecular π-π-interactions were detected with slip angles of 78.4° and 80.2° including plane distances of 3.332 and 3.339 Å, respectively, indicating the formation of strong H-aggregates. Such intense interaction could cause the diminished quantum yield in the solid state compared to those in solution.

With the crystallographic data in hand we were prompted to analyze the bonding situation in chalcogenadiazoles **3,4-NSN** and **3,4-NSeN** with respect to the distribution of single and double bonds. For this, natural bond orbital (NBO)[37] analysis was performed at the PBE[38]/cc-pVDZ[39] level of theory. The calculations revealed for both chalcogenadiazoles that the respective C1–O1 bond has full double bond character. This is confirmed through the shortened bond lengths of 1.2608 Å (**3,4-NSN**) and 1.2554 Å (**3,4-NSeN**) compared to phenols with C1–O1 lengths ranging from 1.3433 (**3-Py**) to 1.3558 Å (**all-H**), respectively. In addition, for chalcogenadiazoles, C1–C2 as well as C7–N3 are attributed to be single bonds. Interestingly, the benzene-oxazoline bond connecting C2–C7 exhibits only a partial double bond character. In **3,4-NSN**, the σ bond is occupied with 1.96 electrons, while the π-bond comprises only 1.62 electrons, which is similar to **3,4-NSeN** with an occupied σ bond of 1.96 electrons and 1.63 electrons in the π bond. Due to the identically twisted oxazoline backbone, both disorders resulted in almost the same occupation numbers.

SUMMARY

In summary, minimalistic 2-(oxazolinyl)-phenols bearing various substituents acting as ESIPT-based luminophores have been successfully synthesized and examined towards their photophysical properties in solution as well as in the solid state. To our surprise, isolated thiadiazole and selenadiazole bearing fluorophores exist preferentially not in the full-aromatic enol form, but in the corresponding keto form. Emission characteristics strongly depend on the nature and the position of the substitution. Electron-neutral and -rich phenols showed significant increased quantum yields in the solid state compared to solution (up to factor 142), thus representing AIE-luminophores. In contrast, electron-deficient single-benzenes exhibit high emission efficiencies in solution as well as the solid state (up to $\Phi_F = 74.0\%$). Strong electron-poor derivatives including the nitro- and chalcogenadiazole-substituted ones showed strong solvatochromism or ACQ characteristics. Through varying of the substitution pattern, full-color emission was achieved. Carful single crystal analysis revealed J-type packing features for powerful emitters, while H-type packing was observed for derivatives with decreased emission efficiencies. With crystallographic data in hand we were able to determine the unique bonding situation in chalcogenadiazoles, verifying the existence of the keto form. With the knowledge gained from the substitution effect on the ESIPT properties of 2-(oxazolinyl)-phenols future design strategies based on the judicious combination of selected substituents will be expediently.

EXPERIMENTAL SECTION

General Experimental Procedures. Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere using standard *Schlenk* techniques. All chemicals were purchased from commercial suppliers and either used as received or purified according to *Purification of Common Laboratory Chemicals*.[40] Anhydrous tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), diethylether (Et_2O) and pentane were obtained from an *inert* PS-MD-6 solvent purification system. All other solvents were dried using standard methods.[40] Low temperature reactions (−78 °C or −30 °C) were cooled using a *Julabo* FT902 cryostat. If not otherwise noted, solvents were removed on a *Büchi* Rotavapor R-300 with 40 °C water bath temperature. Yields refer to isolated yields of compounds estimated to be > 95% pure as determined by ^{1}H-NMR spectroscopy.

Chromatography. Thin layer chromatography was performed on fluorescence indicator marked precoated silica gel 60 plates (*Macherey-Nagel*, ALUGRAM Xtra SIL G/UV_{254}) and visualized by UV light (254 nm/366 nm). Flash column chromatography was performed on silica gel (0.040 – 0.063 mm) with the solvents given in the procedures. Abbreviations for solvents used: CH = cyclohexane, EA = ethyl acetate. Retention factors were determined at chamber saturation at 25 °C. Developments were carried out between 3.0 – 3.5 cm.

NMR Spectroscopy. NMR spectra were recorded on a *Bruker* Avance 360WB spectrometer, a *Bruker* Avance Neo 600 MHz spectrometer with BBO probe head and a *Bruker* Avance Neo 600 MHz spectrometer with TXI probe head at 23 °C. Chemical shifts for ^{1}H-NMR spectra are reported as δ (parts per million) relative to the residual proton signal of $CDCl_3$ at 7.26 ppm (s) or DMSO-d_6 at 2.50 ppm (quin). Chemical shifts for ^{13}C-NMR spectra are reported as δ (parts per million) relative to the signal of $CDCl_3$ at 77.0 ppm (t) or DMSO-d_6 at 39.5 ppm (sept). Chemical shifts for ^{19}F-NMR spectra are reported as δ (parts per million) relative to the signal of $Si(CH_3)_4$ at 0.0 ppm. Chemical shifts for ^{77}Se-NMR spectra are reported as δ (parts per million) relative to the signal of $Se(CH_3)_2$ at 0.0 ppm The following abbreviations are used to describe splitting patterns: br. = broad, s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublet of doublets, t = triplet, td = triplet of doublets, q = quartet, p = pentet, m = multiplet. Coupling constants *J* are given in Hertz.

Mass Spectrometry. ESI and APCI mass spectra were recorded on an *Advion* Expression CMS^L *via* ASAP probe or direct inlet. High resolution (HR) EI mass spectra were recorded on a double focusing mass spectrometer ThermoQuest MAT 95 XL from *Finnigan MAT*. HR-ESI and HR-APCI mass spectra were recorded on a *Bruker* Impact II. All Signals are reported with the quotient from mass to charge m/z.

Infrared Spectroscopy. IR spectra were recorded on a *Nicolet* Thermo iS10 scientific spectrometer with a diamond ATR unit. The absorption bands are reported in cm^{-1} with indicated relative intensities: s (strong, 0 – 33% T); m (medium, 34 – 66% T), w (weak, 67 – 100% T), and br (broad).

Melting Points. Melting points of solids, compounds that solidified after chromatography, were measured on a *Büchi* M-5600 Melting Point apparatus and are uncorrected. The measurements were performed with a heating rate of 5 °C/min and the melting points are reported in °C.

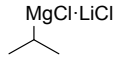
Photoluminescence Spectroscopy. Absorption measurements were performed using a *Shimadzu* UV-2700 UV-vis spectrophotometer. Excitation spectra were recorded by detection of the emission at the respective emission maximum of the sample. Emission measurements were performed using an *Edinburgh Instruments* FLS 1000 photoluminescence spectrometer. The excitation wavelength was chosen to be at the respective absorption maximum of the sample. Absolute quantum yields were measured using an *Edinburgh* integrating sphere. TCSPC measurements were performed using a fast response MCP-PMT detector on the FLS 1000 and a 376 nm *Edinburgh* EPL Laser as excitation source with 10 – 20 MHz repetition rate and 80 ps pulse width. Low-temperature measurements were performed in the same *Edinburgh Instruments* spectrometer coupled with an *Oxford Intruments* OptistatCF optical cryostat cooled with liquid nitrogen. Furthermore, TCSPC measurements were performed using the *Horiba* FluoroHub coupled with the *Horiba* Fluoromax-4 spectrometer. A NanoLED by *Horiba* was used as excitation source with 254 nm wavelength with 5 MHz repetition rate and pulse width of 1.2 ns. All measurements were performed at 23 °C room temperature in Quartz Cuvettes with 10 mm path length by *Hellma Analytics*.

Crystallography. Single crystals were grown as described in the procedures below. Intensity data of suitable crystals were collected on a *Bruker* Venture D8 diffractometer at 100 K with Mo-Kα (0.71073 Å) radiation. All structures were solved by direct methods and refined based on F^2 by use of the SHELX program package as implemented in Olex2.[41] All non-hydrogen atoms were refined using anisotropic displacement parameters. Hydrogen atoms attached to carbon atoms were included in geometrically calculated positions using a rigid model. Crystal and refinement data are collected in Tables S3-46. Figures were created using *Crystal Impact's* DIAMOND Version 4.6.3. All molecular structures represented in these figures are showing 50% probability ellipsoids.

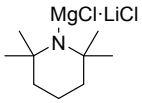
Computational Details. Natural Bond Orbital (NBO) analysis[37b] was carried out at the PBE[38]/cc-pVDZ[39] level of theory using the geometries of the crystal structure as input. The calculations were run with the Q-Chem 5.2 program package[42] and NBO 5.0.[37a]

Photographs. Photographs of vials containing diluted solutions were taken with a *Canon* EOS 700D and a *Canon* EFS 18–55 mm lens. For close-up photographs of solid samples, a *Sigma* 105 mm F2.8 EX DG OS HSM lens was used.

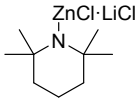
Experimental Procedures. Preparation of Metalation Agents.



Preparation of the Reagent iPrMgCl·LiCl. A slightly modified literature procedure was used.[43] LiCl (4.24 g, 100 mmol, 1.00 eq) was placed in a heat gun-dried and nitrogen-flushed *Schlenk* flask and heated *in vacuo* at 140 °C by heat gun for five hours. Magnesium turnings (2.67 g, 110 mmol, 1.10 eq) were placed in another heat gun-dried and nitrogen-flushed *Schlenk* flask and the dried LiCl and anhydrous THF (50 mL) were added. 2-Chloropropane (9.14 mL, 100 mmol, 1.00 eq) in anhydrous THF (50 mL) was slowly added at 25 °C through a dropping funnel. After approximately 1/5 of addition the mixture was slightly warmed with a heat gun until the reaction started (within ten minutes). When the reaction started the remaining solution was added dropwise and stirring was continued for 18 hours. After complete addition the temperature of the mixture rose until it started to boil. To remove excess of magnesium the grey solution was cannulated to another heat gun-dried and nitrogen-flushed *Schlenk* flask. The Grignard reagent was titrated[44] prior to use against I_2 (0.50 – 0.60 mmol) in anhydrous THF (2 mL) at 0 °C which resulted in a conversion of 92 – 96%. Color change from dark violet to pale brown indicated the end of the titration.



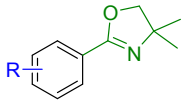
Preparation of the Reagent TMPMgCl·LiCl. A slightly modified literature procedure was used.[45] A heat gun-dried and nitrogen-flushed *Schlenk* flask was charged with freshly titrated *i*PrMgCl·LiCl (75.0 mL, 90.0 mmol, 1.00 eq, 1.20 M). Freshly distilled TMP (16.0 mL, 94.5 mmol, 1.05 eq) was added through a rubber septum to the vigorously stirred Grignard solution *via* syringe pump (0.5 mL/min) at 25 °C. The reaction mixture was stirred at 25 °C for 48 hours, while the solution turned dark green. The base was titrated[46] prior to use against benzoic acid (122 mg, 1.00 mmol) using (4-phenylazo)diphenylamine (3 mg) as indicator in anhydrous THF (2.00 mL) at 0 °C which resulted in a conversion of 96 – 99%. Color change from orange to dark violet indicated the end of the titration.



Preparation of the Reagent TMPZnCl·LiCl. A literature procedure was used.[47] A heat gun-dried and nitrogen-flushed *Schlenk* flask was charged with freshly distilled TMP (6.81 mL, 40.0 mmol, 1.00 eq) and anhydrous THF (40 mL) was added. The colorless solution was cooled to −40 °C and *n*BuLi (16.0 mL, 40.0 mmol, 1.00 eq, 2.50 M) was added dropwise *via* syringe pump (0.5 mL/min). After complete addition, the yellow solution was allowed to

warm slowly to −10 °C within one hour. $ZnCl_2$ (44.0 mL, 44.0 mmol, 1.10 eq, 1.00 M in THF) was added dropwise *via* syringe pump (0.8 mL/min) through the rubber septum and the resulting mixture was stirred for 30 minutes at −10 °C and then for 30 minutes at 25 °C. All volatile components were removed under reduced pressure using oil pump vacuum providing a yellow/slightly brown solid. Anhydrous THF (25 mL) was slowly added under vigorous stirring until all solids were dissolved providing freshly prepared TMPZnCl·LiCl. The base was titrated[46] prior to use against benzoic acid (122 mg, 1.00 mmol) using (4-phenylazo)diphenylamine (3 mg) as indicator in anhydrous THF (2.00 mL) at 0 °C. Color change from orange to bright red indicated the end of the titration and resulted in a concentration of c = 1.05 M.

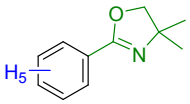
General Procedures for Oxazoline Syntheses.



*General Procedure for the Oxazoline Synthesis from the corresponding Aldehyde (**GP 1**).* A modified literature procedure was used.[21] A round bottom flask, equipped with a magnetic stirring bar and a rubber septum, was charged with aldehyde (1.00 eq) and CH_2Cl_2 (0.25 – 0.4 M). Then 2-amino-2-methylpropan-1-ol (1.50 eq) and 4 Å MS (1.0 g/1.0 – 3.0 mmol aldehyde) were added successively. Due to the waxy nature of the 2-amino-2-methylpropan-1-ol at 25 °C and for a better handling, the bottle containing 2-amino-2-methylpropan-1-ol was placed in a 40 °C water bath until the reagent was melted and simple transfer *via* syringe was possible. After slowly stirring (100 – 200 rpm) for the indicated time at 25 °C NBS[(1)] (1.50 eq) was added in one portion and rapid stirring was continued for the indicated time at 25 °C. Then all solids were filtered off and washed with CH_2Cl_2. The organic phase was subjected to aqueous workup, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification of the crude product was conducted by flash column chromatography using the given eluent. [(1)] In case of electron rich compounds DDQ was used instead of NBS.

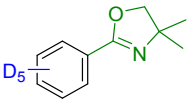
*General Procedure for the Oxazoline Synthesis from the corresponding Carboxylic Acid (**GP 2**).* A modified literature procedure was used.[22] A heat gun-dried and nitrogen-flushed *Schlenk* flask, equipped with a magnetic stirring bar and a reflux condenser on top, was charged with carboxylic acid (1.00 eq) and thionyl chloride (10.0 eq). The mixture was heated to 60 °C and stirred for the indicated time to give a yellow solution. Upon cooling to 25 °C, all volatile components were removed under reduced pressure and collected in a cooling trap. A second heat gun-dried and nitrogen-flushed *Schlenk* flask was charged with 2-amino-2-methylpropan-1-ol (2.00 eq) in anhydrous CH_2Cl_2 (1.0 M). The oily crude acid chloride was dissolved in CH_2Cl_2 (2.0 M) and added *via* syringe pump (0.5 mL/min) at 0 °C to the amino alcohol mixture. After stirring for the indicated time, while the mixture was allowed to warm to 25 °C, the mixture was concentrated *in vacuo* using a cooling trap. The oily crude amide was redissolved in thionyl chloride (10.0 eq) and stirred for the indicated time at 25 °C. All volatile components were removed *in vacuo* and collected in a cooling trap. The crude oil was subjected to aqueous workup, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification of the crude product was conducted by flash column chromatography using the given eluent.

Preparation of Oxazolines.



1a

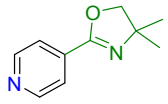
*4,4-Dimethyl-2-phenyl-4,5-dihydrooxazole (**1a**).* Prepared according to **GP 1** from freshly distilled benzaldehyde (2.12 g, 2.03 mL, 20.0 mmol, 1.00 eq) in CH_2Cl_2 (50 mL, 0.4 M) and 2-amino-2-methylpropan-1-ol (2.67 g, 2.86 mL, 30.0 mmol, 1.50 eq) and 4 Å MS (10.0 g). Stirring for 20 h and addition of NBS (5.34 g, 30.0 mmol, 1.50 eq) was followed by stirring for four more hours. After filtration the organic phase was washed with saturated $NaHCO_3$ solution (3 × 50 mL). The combined aqueous phases were extracted with CH_2Cl_2 (2 × 50 mL). All organic phases were washed with saturated NaS_2O_3 solution (50 mL) and the aqueous phase was extracted with CH_2Cl_2 (20 mL). Purification by flash column chromatography (SiO_2, CH:EA 5:1 v:v) afforded **1a** (3.34 g, 19.1 mmol, 95%) as a pale brown liquid. Data for **1a**: R_f = 0.31 (SiO_2, CH:EA 5:1 v:v). ^{1}H-NMR (360 MHz, $CDCl_3$): δ = 7.97 – 7.91 (m, 2H), 7.49 – 7.43 (m, 1H), 7.42 – 7.36 (m, 2H), 4.10 (s, 2H), 1.38 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (91 MHz, $CDCl_3$): δ = 162.2, 131.3, 128.4 (2x), 128.3 (2x), 128.2, 79.2, 67.7, 28.5 (2x) ppm. IR (ATR, neat): ν = 2966 (w), 2928 (w), 2892 (w), 1648 (s), 1603 (w), 1580 (w), 1494 (w), 1462 (w), 1450 (m), 1384 (w), 1351 (m), 1319 (m), 1297 (m), 1248 (w), 1214 (w), 1189 (m), 1077 (m), 1059 (s), 1025 (m), 1002 (w), 989 (w), 965 (m), 921 (m), 870 (w), 818 (w), 780 (m), 694 (s) cm^{-1}. MS (APCI): m/z = 176.0 $[C_{11}H_{13}NO+H]^+$. The analytical data are in accordance with the literature.[48]



1b

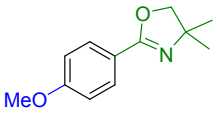
*4,4-Dimethyl-2-(phenyl-d5)-4,5-dihydrooxazole (**1b**).* A slightly modified literature procedure was used.[49] A heat gun-dried and nitrogen-flushed *Schlenk* flask was charged with 4,4-dimethyl-2-oxazoline (198 mg, 211 µL, 2.00 mmol, 1.20 eq) and anhydrous THF (1.67 mL, 1.0 M). The colorless solution was cooled to 0 °C and freshly prepared TMPZnCl·LiCl (2.22 mL, 2.33 mmol, 1.40 eq, 1.05 M in THF) was added *via* syringe pump (0.4 mL/min) to the vigorously stirred mixture. After complete addition stirring was continued for one more hour under the same conditions to give a red/brown solution. Then

bromobenzene-d_5 (270 mg, 1.67 mmol, 1.00 eq), Pd_2dba_3 (30.5 mg, 33.3 µmol, 0.02 eq) and SPhos (41.0 mg, 100 µmol, 0.06 eq) were added and the mixture was heated to 50 °C. After six hours of heating the reaction was cooled to 25 °C and terminated by the addition of saturated NH_4Cl solution (20 mL) and water (20 mL). CH_2Cl_2 (20 mL) was added, the phases were separated and the aqueous layer was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification by flash column chromatography (SiO_2, CH:EA 6:1 v:v) afforded **1b** (239 mg, 1.33 mmol, 80%) as a colorless liquid. Data for **1b**: R_f = 0.19 (SiO_2, CH:EA 6:1 v:v). ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 4.11 (s, 2H), 1.38 (s, 6H) ppm. $^{13}C\{^1H\}$-NMR (151 MHz, $CDCl_3$): δ = 162.2, 130.76 (t, $^1J_{CD}$ = 24.5 Hz), 128.0, 127.93 (t, $^1J_{CD}$ = 24.9 Hz, 2x), 127.88 (t, $^1J_{CD}$ = 24.5 Hz, 2x), 79.2, 67.7, 28.6 (2x) ppm. IR (ATR, neat): ν = 2966 (w), 2928 (w), 2892 (w), 1646 (s), 1569 (w), 1542 (w), 1461 (w), 1400 (m), 1364 (w), 1345 (m), 1328 (m), 1272 (s), 1248 (w), 1202 (s), 1049 (s), 1032 (s), 987 (m), 967 (m), 955 (m), 919 (m), 875 (w), 858 (w), 842 (w), 812 (m), 705 (m), 655 (m) cm^{-1}. MS (APCI): m/z = 181.1 $[C_{11}H_8D_5NO+H]^+$. HRMS (ESI) m/z: $[M+H]^+$ calcd for $[C_{11}H_9D_5NO^+]$: 181.1384; Found: 181.1383. $[M+Na]^+$ calcd for $[C_{11}H_8D_5NNaO^+]$: 203.1203; Found: 203.1203. The analytical data are in accordance with the literature.[15b]



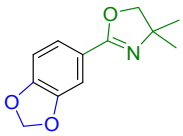
1c

*4,4-Dimethyl-2-(pyridin-4-yl)-4,5-dihydrooxazole (**1c**).* Prepared according to **GP 1** from isonicotinaldehyde (1.07 g, 942 µL, 10.0 mmol, 1.00 eq) in CH_2Cl_2 (40 mL, 0.25 M) and 2-amino-2-methylpropan-1-ol (1.34 g, 1.43 mL, 15.0 mmol, 1.50 eq) and 4 Å MS (10.0 g). Stirring for 20 h and addition of NBS (2.67 g, 15.0 mmol, 1.50 eq) was followed by stirring for four more hours. After filtration the organic phase was washed with saturated $NaHCO_3$ solution (3 × 50 mL). The combined aqueous phases were extracted with CH_2Cl_2 (2 × 50 mL). All organic phases were washed with saturated NaS_2O_3 solution (50 mL) and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). Purification by flash column chromatography (SiO_2, CH:EA 2:1 v:v) afforded **1c** (1.56 g, 8.85 mmol, 89%) as a colorless liquid. Data for **1c**: R_f = 0.10 (SiO_2, CH:EA 2:1 v:v). ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 8.68 (d, $^3J_{HH}$ = 5.4 Hz, 2H), 7.75 (d, $^3J_{HH}$ = 5.4 Hz, 2H), 4.12 (s, 2H), 1.37 (s, 6H) ppm. $^{13}C\{^1H\}$-NMR (151 MHz, $CDCl_3$): δ = 160.5, 150.3 (2x), 135.5, 122.1 (2x), 79.5, 68.2, 28.4 (2x) ppm. IR (ATR, neat): ν = 3050 (w), 2983 (w), 2965 (m), 2928 (w), 2898 (w), 2865 (w), 1732 (w), 1651 (s), 1600 (m), 1552 (m), 1496 (w), 1476 (w), 1464 (w), 1443 (w), 1409 (m), 1380 (w), 1360 (m), 1334 (m), 1303 (s), 1253 (w), 1220 (m), 1183 (m), 1091 (m), 1079 (m), 1072 (m), 1061 (m), 1013 (w), 993 (m), 967 (s), 923 (m), 894 (w), 871 (m), 844 (s), 819 (m), 747 (m), 689 (s), 684 (s), 666 (m) cm^{-1}. MS (APCI): m/z = 277.1 $[M+H]^+$. HRMS (ESI) m/z: $[M+H]^+$ calcd for $[C_{10}H_{13}N_2O^+]$: 177.1022; Found: 177.1022. The analytical data are in accordance with the literature.[50]



1d

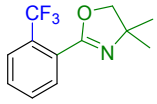
*2-(4-Methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (**1d**).* Prepared according to **GP 1** from 4-methoxybenzaldehyde (817 mg, 729 µL 6.00 mmol, 1.00 eq) in CH_2Cl_2 (15 mL, 0.4 M) and 2-amino-2-methylpropan-1-ol (802 mg, 859 µL, 9.00 mmol, 1.50 eq) and 4 Å MS (10.0 g). Stirring for 20 h and addition of DDQ (2.04 g, 9.00 mmol, 1.50 eq) was followed by stirring for two more hours. Saturated NH_4Cl solution (20 mL) and water (20 mL) were added and the mixture was stirred for 30 minutes. After filtration the aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL) and the combined organic phases were washed with water (20 mL). Purification by flash column chromatography (SiO_2, CH:EA 8:1 v:v) afforded **1d** (783 mg, 3.81 mmol, 64%) as a slightly yellow oil. Data for **1d**: R_f = 0.13 (SiO_2, CH:EA 8:1 v:v). ^{1}H-NMR (360 MHz, $CDCl_3$): δ = 7.92 – 7.84 (AA'XX', 2H), 6.95 – 6.85 (AA'XX', 2H), 4.08 (s, 2H), 3.84 (s, 3H), 1.37 (s, 6H) ppm. $^{13}C\{^1H\}$-NMR (91 MHz, $CDCl_3$): δ = 162.1, 162.0, 130.0 (2x), 120.7, 113.7 (2x), 79.1, 67.5, 55.5, 28.6 (2x) ppm. IR (ATR, neat): ν = 2964 (w), 2930 (w), 2893 (w), 1645 (s), 1609 (m), 1578 (w), 1512 (s), 1461 (w), 1443 (w), 1421 (w), 1384 (w), 1352 (m), 1307 (m), 1251 (s), 1215 (w), 1169 (s), 1113 (w), 1066 (s), 1029 (s), 1010 (m), 992 (m), 966 (m), 920 (w), 872 (w), 840 (s), 792 (m), 742 (m), 686 (m) cm^{-1}. MS (APCI): m/z = 206.1 $[C_{12}H_{15}NO_2+H]^+$. The analytical data are in accordance with the literature.[48]



1e

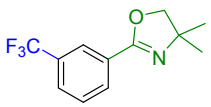
*2-(Benzo[d][1,3]dioxol-5-yl)-4,4-dimethyl-4,5-dihydrooxazole (**1e**).* Prepared according to **GP 2** from benzo[*d*][1,3]dioxole-5-carboxylic acid (1.66 g, 10.0 mmol, 1.00 eq) in $SOCl_2$ (7.25 mL, 100 mmol, 10.0 eq) and stirring for six hours. 2-Amino-2-methylpropan-1-ol (1.78 g, 1.91 mL, 20.0 mmol, 2.00 eq) was dissolved in CH_2Cl_2 (20 mL) and addition of the crude acid chloride in CH_2Cl_2 (5 mL) and stirring for three hours. The crude amide in $SOCl_2$ (7.25 mL, 100 mmol, 10.0 eq) was stirred for 60 minutes. After solvent evaporation the crude oil was dissolved in CH_2Cl_2 (50 mL) and water (40 mL) and aqueous NaOH (20%, 40 mL) were added. The phases were separated and the aqueous phase (pH > 9) was extracted with CH_2Cl_2 (3 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 3:1 v:v) afforded **1e** (1.82 g, 8.30 mmol, 83%) as a colorless oil. Data for **1e**: R_f = 0.27 (SiO_2, CH:EA 3:1 v:v). ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 7.48 (dd, $^3J_{HH}$ = 8.1 Hz, $^4J_{HH}$ = 1.7 Hz, 1H), 7.40 (d, $^4J_{HH}$ = 1.6 Hz, 1H), 6.81 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 6.00 (s, 2H), 4.07 (s, 2H), 1.36 (s, 6H) ppm. $^{13}C\{^1H\}$-NMR (151 MHz, $CDCl_3$): δ =

161.8, 150.2, 147.7, 123.2, 122.2, 108.6, 108.1, 101.6, 79.3, 67.6, 28.6 (2x) ppm. IR (ATR, neat): ν = 2965 (w), 2891 (w), 1647 (s), 1626 (w), 1606 (w), 1503 (m), 1492 (s), 1463 (m), 1449 (s), 1384 (w), 1366 (m), 1303 (s), 1257 (s), 1237 (s), 1188 (m), 1146 (w), 1102 (m), 1036 (s), 992 (m), 968 (m), 932 (m), 903 (m), 876 (m), 845 (m), 818 (m), 807 (m), 754 (m), 733 (s), 708 (s), 679 (m), 663 (w) cm^{-1}. MS (APCI): m/z = 220.2 [$C_{12}H_{13}NO_3$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{12}H_{14}NO_3^+$]: 220.0968; Found: 220.0966. [M+Na]$^+$ calcd for [$C_{12}H_{13}NNaO_3^+$]: 242.0788; Found: 242.0786. The analytical data are in accordance with the literature.[51]



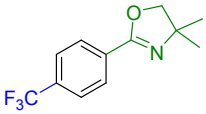
1f

*4,4-Dimethyl-2-(2-(trifluoromethyl)phenyl)-4,5-dihydrooxazole (**1f**).* Prepared according to **GP 1** from 2-(trifluoromethyl)benzaldehyde (1.74 g, 1.32 mL, 10.0 mmol, 1.00 eq) in CH_2Cl_2 (25 mL, 0.4 M) and 2-amino-2-methylpropan-1-ol (1.34 g, 1.43 mL, 15.0 mmol, 1.50 eq) and 4 Å MS (10.0 g). Stirring for 18 h and addition of NBS (2.67 g, 15.0 mmol, 1.50 eq) was followed by stirring for three more hours. After filtration the organic phase was washed with saturated $NaHCO_3$ solution (3 × 50 mL). The combined aqueous phases were extracted with CH_2Cl_2 (2 × 50 mL). All organic phases were washed with saturated NaS_2O_3 solution (50 mL) and the aqueous phase was extracted with CH_2Cl_2 (20 mL). Purification by flash column chromatography (SiO_2, CH:EA 4:1 v:v) afforded **1f** (1.42 g, 5.84 mmol, 58%) as a colorless liquid. Data for **1f**: R_f = 0.14 (SiO_2, CH:EA 4:1 v:v). ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 7.74 (d, $^3J_{HH}$ = 7.3 Hz, 1H), 7.72 (d, $^3J_{HH}$ = 7.2 Hz, 1H), 7.56 (p, $^3J_{HH}$ = 7.2 Hz, 2H), 4.15 (s, 2H), 1.39 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 161.7, 131.7, 131.2, 130.5, 129.21 (q, $^2J_{CF}$ = 32.0 Hz), 127.99 (d, $^3J_{CF}$ = 2.3 Hz), 126.62 (q, $^3J_{CF}$ = 5.2 Hz), 123.68 (q, $^1J_{CF}$ = 273.5 Hz), 80.2, 68.1, 28.2 (2x) ppm. ^{19}F-NMR (565 MHz, $CDCl_3$): δ = −59.7 (s) ppm. IR (ATR, neat): ν = 2970 (w), 2931 (w), 2894 (w), 1662 (w), 1606 (w), 1579 (w), 1496 (w), 1463 (w), 1451 (w), 1385 (w), 1353 (w), 1309 (s), 1269 (m), 1215 (w), 1163 (s), 1136 (s), 1112 (s), 1085 (s), 1034 (s), 987 (w), 962 (m), 921 (w), 870 (w), 819 (w), 769 (s), 705 (m), 690 (m) cm^{-1}. MS (APCI): m/z = 244.0 [$C_{12}H_{12}F_3NO$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{12}H_{13}F_3NO^+$]: 244.0944; Found: 244.0940. [M+Na]$^+$ calcd for [$C_{12}H_{13}F_3NNaO^+$]: 266.0763; Found: 266.0760. [M+K]$^+$ calcd for [$C_{12}H_{13}F_3KNO^+$]: 282.0503; Found: 282.0499. [2M+Na]$^+$ calcd for [$C_{24}H_{24}F_6N_2NaO_2^+$]: 509.1634; Found: 509.1627. The analytical data are in accordance with the literature.[15b]



1g

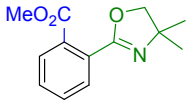
*4,4-Dimethyl-2-(3-(trifluoromethyl)phenyl)-4,5-dihydrooxazole (**1g**).* Prepared according to **GP 1** from 3-(trifluoromethyl)benzaldehyde (1.74 g, 1.34 mL, 10.0 mmol, 1.00 eq) in CH_2Cl_2 (40 mL, 0.25 M) and 2-amino-2-methylpropan-1-ol (1.34 g, 1.43 mL, 15.0 mmol, 1.50 eq) and 4 Å MS (10.0 g). Stirring for 20 h and addition of NBS (2.67 g, 15.0 mmol, 1.50 eq) was followed by stirring for four more hours. After filtration the organic phase was washed with saturated $NaHCO_3$ solution (3 × 50 mL). The combined aqueous phases were extracted with CH_2Cl_2 (2 × 50 mL). All organic phases were washed with saturated NaS_2O_3 solution (50 mL) and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). Purification by flash column chromatography (SiO_2, CH:EA 20:1 v:v) afforded **1g** (1.26 g, 5.18 mmol, 52%) as a pale yellow liquid. Data for **1g**: R_f = 0.15 (SiO_2, CH:EA 20:1 v:v). ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.21 (s, 1H), 8.11 (d, $^3J_{HH}$ = 7.9 Hz, 1H), 7.71 (d, $^3J_{HH}$ = 7.9 Hz, 1H), 7.52 (td, $^3J_{HH}$ = 7.9 Hz, $^4J_{HH}$ = 2.4 Hz, 1H), 4.13 (d, $^4J_{HH}$ = 2.2 Hz, 2H), 1.39 (d, $^4J_{HH}$ = 2.1 Hz, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 160.8, 131.4, 130.88 (q, $^2J_{CF}$ = 32.9 Hz), 129.0, 128.9, 127.72 (q, $^3J_{CF}$ = 3.8 Hz), 125.22 (q, $^3J_{CF}$ = 3.9 Hz), 123.79 (q, $^1J_{CF}$ = 272.4 Hz), 79.4, 67.9, 28.4 (2x) ppm. ^{19}F-NMR (565 MHz, $CDCl_3$): δ = −62.7 (s) ppm. IR (ATR, neat): ν = 2970 (w), 2931 (w), 2896 (w), 2871 (w), 1652 (m), 1618 (w), 1591 (w), 1487 (w), 1464 (w), 1434 (w), 1386 (w), 1360 (m), 1335 (s), 1298 (m), 1280 (s), 1211 (m), 1166 (m), 1124 (s), 1099 (m), 1062 (s), 1018 (w), 1001 (w), 990 (w), 968 (m), 918 (m), 888 (w), 880 (w), 855 (w), 809 (m), 789 (w), 756 (w), 720 (m), 697 (s), 653 (w) cm^{-1}. MS (APCI): m/z = 244.2 [$C_{12}H_{12}F_3NO$+H]$^+$. The analytical data are in accordance with the literature.[48]



1h

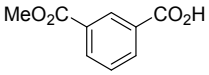
*4,4-Dimethyl-2-(4-(trifluoromethyl)phenyl)-4,5-dihydrooxazole (**1h**).* Prepared according to **GP 1** from 4-(trifluoromethyl)benzaldehyde (1.74 g, 1.36 mL, 10.0 mmol, 1.00 eq, 95% purity) in CH_2Cl_2 (40 mL, 0.25 M) and 2-amino-2-methylpropan-1-ol (1.34 g, 1.43 mL, 15.0 mmol, 1.50 eq) and 4 Å MS (10.0 g). Stirring for 20 h and addition of NBS (2.67 g, 15.0 mmol, 1.50 eq) was followed by stirring for four more hours. After filtration the organic phase was washed with saturated $NaHCO_3$ solution (3 × 50 mL). The combined aqueous phases were extracted with CH_2Cl_2 (2 × 50 mL). All organic phases were washed with saturated NaS_2O_3 solution (50 mL) and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). Further purification was not necessary and **1h** (2.40 g, 9.86 mmol, 99%) was obtained as a colorless solid. Data for **1h**: R_f = 0.10 (SiO_2, CH:EA 20:1 v:v). Mp: 100 – 102 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 8.05 (d, $^3J_{HH}$ = 8.2 Hz, 2H), 7.66 (d, $^3J_{HH}$ = 8.1 Hz, 2H), 4.14 (s, 2H), 1.39 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 161.0, 132.91 (q, $^2J_{CF}$ = 32.6 Hz, 2x), 131.6, 128.7, 125.39 (q, $^3J_{CF}$ = 3.6 Hz, 2x), 123.95 (q, $^1J_{CF}$ = 272.5 Hz), 79.5, 68.1, 28.5 (2x) ppm. ^{19}F-NMR (565 MHz, $CDCl_3$): δ = −62.9 (s) ppm. IR (ATR, neat): ν = 2972 (w), 2932 (w), 2898 (w), 1942 (w), 1651 (m), 1619 (w), 1581 (w), 1520 (w), 1464 (w), 1411 (m), 1369 (w), 1356 (w), 1322 (s), 1298 (m), 1250 (w), 1217 (w),

1166 (s), 1128 (m), 1106 (s), 1069 (s), 1060 (s), 1016 (s), 988 (w), 963 (m), 921 (w), 871 (w), 852 (s), 818 (w), 775 (w), 755 (m), 692 (m), 686 (s) cm^{-1}. MS (APCI): m/z = 244.2 $[C_{12}H_{12}F_3NO+H]^+$. The analytical data are in accordance with the literature.[48]



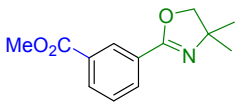
1i

*Methyl 2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)benzoate (**1i**).* A modified literature procedure was used.[52] A heat gun-dried and nitrogen-flushed *Schlenk* flask, equipped with a magnetic stirring bar was charged with 2-(methoxycarbonyl)benzoic acid (1.80 g, 10.0 mmol, 1.00 eq) in non-anhydrous CH_2Cl_2 (12.5 mL, 0.8 M). Catalytic amounts of DMF (73.1 mg, 77.4 µL, 1.00 mmol, 0.10 eq) were added and the mixture was cooled to 0 °C. Oxalyl chloride (1.90 g, 1.29 mL, 15.0 mmol, 1.50 eq) was added *via* syringe pump (0.5 mL/min) to the vigorously stirred solution. Upon complete addition, the cooling bath was removed and the mixture was stirred at 25 °C for two hours. Then all volatile components were removed under reduced pressure using a cooling trap. A second heat gun-dried and nitrogen-flushed *Schlenk* flask was charged with 2-amino-2-methylpropan-1-ol (1.78 g, 1.91 mL, 20.0 mmol, 2.00 eq) and NEt_3 (2.02 g, 2.79 mL, 20.0 mmol, 2.00 eq) in non-anhydrous CH_2Cl_2 (10.0 mL, 1.0 M). The crude acid chloride, suspended in non-anhydrous CH_2Cl_2 (10.0 mL, 1.0 M), was added *via* syringe pump (1.0 mL/min) at 0 °C. Stirring for three hours, while the mixture was allowed to warm to 25 °C, was followed by removing of all volatile components under reduced pressure using a cooling trap. The crude amide was redissolved in non-anhydrous CH_2Cl_2 (20.0 mL, 0.5 M) and cooled to 0 °C. $SOCl_2$ (2.90 mL, 40.0 mmol, 4.00 eq) was added *via* syringe pump (0.5 mL/min) and the mixture was stirred for three hours, while the mixture was allowed to warm slowly to 25 °C. All volatile components were removed *in vacuo* to give an oily residue, which was dissolved in CH_2Cl_2 (50 mL). Water (50 mL) and saturated $NaHCO_3$ solution (50 mL) were added to adjust a pH value of 9. Then the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (5 × 40 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification by flash column chromatography (SiO_2, CH:EA 3:1 to 2:1 v:v) afforded **1i** (1.76 g, 7.55 mmol, 76%) as a slightly yellow oil. Data for **1i**: R_f = 0.08 (SiO_2, CH:EA 3:1 v:v). R_f = 0.20 (SiO_2, CH:EA 2:1 v:v). ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 7.75 – 7.70 (AA'XX', 2H), 7.54 – 7.45 (AA'XX', 2H), 4.09 (s, 2H), 3.87 (s, 3H), 1.39 (s, 6H) ppm. $^{13}C\{^1H\}$-NMR (151 MHz, $CDCl_3$): δ = 168.2, 162.3, 132.1, 131.2, 130.4, 129.9, 129.2, 128.8, 80.0, 68.2, 52.5, 28.3 (2x) ppm. IR (ATR, neat): ν = 2967 (w), 2930 (w), 2892 (w), 1729 (s), 1655 (m), 1598 (w), 1577 (w), 1488 (w), 1447 (w), 1432 (m), 1384 (w), 1364 (w), 1352 (m), 1290 (s), 1271 (s), 1214 (w), 1189 (m), 1126 (m), 1099 (m), 1049 (m), 1033 (m), 988 (w), 962 (m), 921 (m), 872 (w), 826 (w), 770 (m), 731 (m), 702 (m), 690 (m) cm^{-1}. MS (APCI): m/z = 234.0 $[C_{13}H_{15}NO_3+H]^+$. HRMS (ESI) m/z: $[M+H]^+$ calcd for $[C_{13}H_{16}NO_3^+]$: 234.1125; Found: 234.1124. $[M+Na]^+$: calcd for $[C_{13}H_{15}NNaO_3^+]$: 256.0944; Found: 256.0944. $[2M+Na]^+$ calcd for $[C_{26}H_{30}N_2NaO_6^+]$: 489.1996; Found: 489.1991. The analytical data are in accordance with the literature.[52]



S1

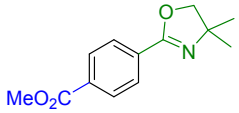
*3-(Methoxycarbonyl)benzoic acid (**S1**).* A modified literature procedure was used.[53] Dimethyl isophthalate (3.88 g, 20.0 mmol, 1.00 eq) was dissolved in acetone (50.0 mL, 0.4 M) and a solution of NaOH (840 mg, 21.0 mmol, 1.05 eq) in methanol (8.0 mL) was added using a *Pasteur* pipette over a time period of two minutes at 25 °C. During addition of the alkaline solution a colorless solid start to precipitate. The mixture was stirred for nine hours, while the stirring rate was increased to 1400 rpm to ensure efficient miscibility owing to enormous precipitation. All volatile components were removed *in vacuo* on a rotary evaporator and the colorless solid was dissolved in saturated $NaHCO_3$ solution (100 mL). The aqueous phase was extracted with CH_2Cl_2 (4 × 30 mL) to remove remaining starting material. Acidification using concentrated hydrochloric acid was conducted until a pH of 1 was adjusted – during addition a colorless solid precipitated. Filtration was followed by washing with water (3 × 50 mL) and drying *in vacuo* to obtain **S1** (3.24 g, 18.0 mmol, 90%) as a colorless solid. Data for **S1**: R_f = 0.13 (SiO_2, CH:EA 3:1 v:v). R_f = 0.32 (SiO_2, CH:EA 1:1 v:v). Mp.: 187 – 189 °C. ^{1}H-NMR (601 MHz, DMSO-d_6): δ = 13.32 (br. s, 1H), 8.48 (s, 1H), 8.21 – 8.16 (m, 2H), 7.67 (t, $^3J_{HH}$ = 7.7 Hz, 1H), 3.89 (s, 3H) ppm. $^{13}C\{^1H\}$-NMR (151 MHz, DMSO-d_6): δ = 166.5, 165.6, 133.8, 133.2, 131.4, 130.1, 129.8, 129.4, 52.4 ppm. IR (ATR, neat): ν = 2966 (w), 2823 (w), 2548 (br), 1727 (s), 1674 (s), 1609 (m), 1586 (w), 1486 (w), 1457 (w), 1432 (m), 1316 (m), 1294 (s), 1265 (s), 1190 (m), 1161 (m), 1142 (m), 1094 (s), 1075 (s), 1001 (w), 961 (m), 928 (m), 881 (m), 830 (m), 785 (w), 723 (s), 705 (s), 671 (m), 657 (m) cm^{-1}. MS (APCI): m/z = 181.0 $[C_9H_8O_4+H]^+$. HRMS (ESI) m/z: $[M+H]^+$ calcd for $[C_9H_9O_4^+]$: 181.0495; Found: 181.0495. $[M+Na]^+$ calcd for $[C_9H_8NaO_4^+]$: 203.0315; Found: 203.0315. $[2M+Na]^+$ calcd for $[C_{18}H_{16}NaO_8^+]$: 383.0737; Found: 383.0735. $[M-H]^-$ calcd for $[C_9H_7O_4^-]$: 179.0350; Found: 179.0348. $[2(M-H)+Na]^-$ calcd for $[C_{18}H_{14}NaO_8^-]$: 381.0592; Found: 381.0592. The analytical data are in accordance with the literature.[54]



1j

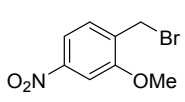
*Methyl 3-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)benzoate (**1j**).* A modified literature procedure was used.[52] A heat gun-dried and nitrogen-flushed *Schlenk* flask, equipped with a magnetic stirring bar was charged with **S1** (1.80 g, 10.0 mmol, 1.00 eq) in non-anhydrous CH_2Cl_2 (12.5 mL,

0.8 M). Catalytic amounts of DMF (73.1 mg, 77.4 µL, 1.00 mmol, 0.10 eq) were added and the mixture was cooled to 0 °C. Oxalyl chloride (1.90 g, 1.29 mL, 15.0 mmol, 1.50 eq) was added *via* syringe pump (0.5 mL/min) to the vigorously stirred solution. Upon complete addition, the cooling bath was removed and the mixture was stirred at 25 °C for two hours. Then all volatile components were removed under reduced pressure using a cooling trap. A second heat gun-dried and nitrogen-flushed *Schlenk* flask was charged with 2-amino-2-methylpropan-1-ol (1.78 g, 1.91 mL, 20.0 mmol, 2.00 eq) and NEt_3 (2.02 g, 2.79 mL, 20.0 mmol, 2.00 eq) in non-anhydrous CH_2Cl_2 (10.0 mL, 1.0 M). The crude acid chloride, suspended in non-anhydrous CH_2Cl_2 (10.0 mL, 1.0 M), was added *via* syringe pump (1.0 mL/min) at 0 °C. Stirring for three hours, while the mixture was allowed to warm to 25 °C, was followed by removing of all volatile components under reduced pressure using a cooling trap. The crude amide was redissolved in non-anhydrous CH_2Cl_2 (20.0 mL, 0.5 M) and cooled to 0 °C. $SOCl_2$ (2.90 mL, 40.0 mmol, 4.00 eq) was added *via* syringe pump (0.5 mL/min) and the mixture was stirred for three hours, while the mixture was allowed to warm slowly to 25 °C. All volatile components were removed *in vacuo* to give an oily residue, which was dissolved in CH_2Cl_2 (50 mL). Water (50 mL) and saturated $NaHCO_3$ solution (50 mL) were added to adjust a pH value of 9. Then the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (5 × 40 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification by flash column chromatography (SiO_2, CH:EA 2:1 v:v) afforded **1j** (2.07 g, 8.87 mmol, 89%) as a colorless oil, which slowly solidified upon standing at 25 °C to give a colorless solid. Data for **1j**: R_f = 0.31 (SiO_2, CH:EA 2:1 v:v). Mp.: 54 – 56 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 8.58 (t, $^4J_{HH}$ = 1.7 Hz, 1H), 8.16 – 8.10 (m, 2H), 7.48 (t, $^3J_{HH}$ = 7.8 Hz, 1H), 4.13 (s, 2H), 3.92 (s, 3H), 1.39 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 166.6, 161.4, 132.6, 132.3, 130.6, 129.5, 128.7, 128.6, 79.4, 68.0, 52.3, 28.5 (2x) ppm. IR (ATR, neat): ν = 2968 (w), 2934 (w), 2903 (w), 1716 (s), 1645 (m), 1601 (w), 1436 (m), 1388 (w), 1380 (w), 1358 (m), 1323 (s), 1297 (s), 1251 (m), 1211 (m), 1193 (m), 1176 (w), 1164 (w), 1114 (s), 1098 (m), 1082 (w), 1060 (s), 1013 (w), 1002 (w), 975 (m), 962 (m), 929 (m), 915 (m), 822 (m), 765 (m), 724 (m), 704 (s), 657 (w) cm^{-1}. MS (APCI): m/z = 234.1 [$C_{13}H_{15}NO_3$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{13}H_{16}NO_3^+$]: 234.1125; Found: 234.1124. [M+Na]$^+$ calcd for [$C_{13}H_{15}NNaO_3^+$]: 256.0944; Found: 256.0943. [2M+Na]$^+$ calcd for [$C_{26}H_{30}N_2NaO_6^+$]: 489.1996; Found: 489.1994. The analytical data are in accordance with the literature.[55]

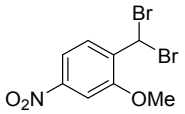


1k

*Methyl 4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)benzoate (**1k**).* Prepared according to **GP 1** from methyl 4-formylbenzoate (1.64 g, 10.0 mmol, 1.00 eq) in CH_2Cl_2 (25 mL, 0.4 M) and 2-amino-2-methylpropan-1-ol (1.34 g, 1.43 mL, 15.0 mmol, 1.50 eq) and 4 Å MS (10.0 g). Stirring for 20 h and addition of NBS (2.67 g, 15.0 mmol, 1.50 eq) was followed by stirring for four more hours. After filtration the organic phase was washed with saturated $NaHCO_3$ solution (3 × 50 mL). The combined aqueous phases were extracted with CH_2Cl_2 (2 × 50 mL). All organic phases were washed with saturated NaS_2O_3 solution (50 mL) and the aqueous phase was extracted with CH_2Cl_2 (20 mL). Further purification was not necessary and **1k** (2.28 g, 9.77 mmol, 98%) was obtained as a colorless solid. Data for **1k**: R_f = 0.15 (SiO_2, CH:EA 6:1 v:v). Mp.: 68 – 70 °C. ^{1}H-NMR (360 MHz, $CDCl_3$): δ = 8.09 – 8.03 (AA'XX', 2H), 8.03 – 7.96 (AA'XX', 2H), 4.13 (s, 2H), 3.92 (s, 3H), 1.39 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (91 MHz, $CDCl_3$): δ = 166.6, 161.4, 132.4, 132.3, 129.6 (2x), 128.3 (2x), 79.4, 68.0, 52.5, 28.5 (2x) ppm. IR (ATR, neat): ν = 2960 (w), 2927 (w), 2894 (w), 1718 (s), 1645 (m), 1612 (w), 1509 (w), 1439 (m), 1408 (m), 1380 (w), 1363 (w), 1354 (w), 1315 (m), 1299 (w), 1271 (s), 1216 (w), 1195 (m), 1179 (m), 1114 (m), 1104 (s), 1064 (s), 1015 (m), 993 (w), 966 (m), 916 (m), 868 (m), 851 (w), 842 (w), 824 (m), 780 (m), 707 (s), 676 (m) cm^{-1}. MS (APCI): m/z = 234.1 [$C_{13}H_{15}NO_3$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{13}H_{16}NO_3^+$]: 234.1125; Found: 234.1124. [M+Na]$^+$ calcd for [$C_{13}H_{15}NNaO_3^+$]: 256.0944; Found: 256.0945. The analytical data are in accordance with the literature.[15b]



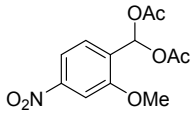
S2



S3

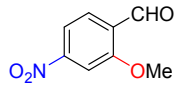
*1-(Bromomethyl)-2-methoxy-4-nitrobenzene (**S2**) & 1-(Dibromomethyl)-2-methoxy-4-nitrobenzene (**S3**).* A slightly modified literature procedure was used.[23b] 2-Methoxy-1-methyl-4-nitrobenzene (3.34 g, 20.0 mmol, 1.00 eq) was dissolved in CCl_4 (40 mL, 0.5 M) and NBS (10.7 g, 60.0 mmol, 3.00 eq) and AIBN (328 mg, 2.00 mmol, 0.10 eq) were added successively. The mixture was heated to 95 °C (oil bath temperature) and stirred for 24 hours at this temperature. After cooling to ambient temperature, the mixture was filtered over a plug of Celite® and washed with ethyl acetate (~50 mL). Concentration under reduced pressure on a rotary evaporator afforded a colorless solid (4.68 g, 15.7 mmol, 79%). A mixture of mono- **S2** (1.32 g, 5.37 mmol, 27%) and dibrominated species **S3** (3.36 g, 10.3 mmol, 52%) was obtained as determined by ^{1}H-NMR (ratio: 0.52:1.00). The crude was used without further purification. Data for **S2**: R_f = 0.47 (SiO_2, CH:EA 6:1 v:v). ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 7.82 (dd, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 2.0 Hz, 1H, H–5), 7.73 (d, $^4J_{HH}$ = 1.7 Hz, 1H, H–3), 7.49 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H–6), 4.54 (s, 2H, CH_2Br), 4.00 (s, 3H, OCH_3) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 157.8 (C–2), 149.1 (C–4), 133.4 (C–1), 131.2 (C–6), 116.1 (C–5), 106.0 (C–3), 56.4 (OCH_3), 26.5 (CH_2Br) ppm. MS (EI, 70 eV): m/z = 166.1 [$C_8H_8NO_3$–Br]$^{+\cdot}$. HRMS (EI, 70 eV) m/z: [M–Br]$^{+\cdot}$ calcd for [$C_8H_8NO_3^{+\cdot}$]: 166.0499; Found: 166.0499. Data for **S3**: R_f = 0.53 (SiO_2, CH:EA 6:1 v:v). ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 8.03 (d, $^3J_{HH}$ = 8.6 Hz, 1H, H–6), 7.91 (dd, $^3J_{HH}$ =

8.6 Hz, $^4J_{HH}$ = 1.9 Hz, 1H, H–5), 7.71 (d, $^4J_{HH}$ = 1.8 Hz, 1H, H–3), 7.07 (s, 1H, C*H*Br$_2$), 4.02 (s, 3H, OC*H*$_3$) ppm. ^{13}C{^{1}H}-NMR (151 MHz, CDCl$_3$): δ = 154.0 (C–2), 149.4 (C–4), 136.5 (C–1), 131.2 (C–6), 116.5 (C–5), 106.1 (C–3), 56.7 (OC*H*$_3$), 32.9 (C*H*Br$_2$) ppm. MS (EI, 70 eV): m/z = 244.0 [$C_8H_7{}^{79}BrNO_3$–Br]$^{+\cdot}$. HRMS (EI, 70 eV) m/z: [M–Br]$^{+\cdot}$ calcd for [$C_8H_7{}^{79}BrNO_3{}^{+\cdot}$]: 243.9604; Found: 243.9605. Data for mixture of **S2** and **S3**: Mp.: 89 – 109 °C. IR (ATR, neat): ν = 3111 (w), 3085 (w), 3036 (w), 2980 (w), 2941 (w), 2840 (w), 1616 (w), 1589 (w), 1511 (s), 1487 (m), 1455 (m), 1409 (m), 1342 (s), 1276 (m), 1251 (s), 1223 (m), 1185 (m), 1163 (m), 1113 (m), 1085 (m), 1026 (s), 925 (w), 871 (s), 828 (m), 812 (s), 791 (m), 749 (m), 727 (s), 673 (m) cm^{-1}.



S4

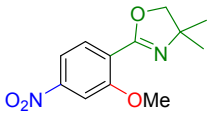
*(2-Methoxy-4-nitrophenyl)methylene diacetate (**S4**).* A slightly modified literature procedure was used.[24] 2-Methoxy-1-methyl-4-nitrobenzene (5.01 g, 30.0 mmol, 1.00 eq) was dissolved in acetic acid (43 mL, 0.7 M) and acetic anhydride (43 mL, 0.7 M) and cooled to 0 °C. Concentrated H_2SO_4 (7.20 mL, 135 mmol, 4.50 eq, 98% in H_2O) was added dropwise within 5 minutes *via Pasteur* pipette to the open flask reaction. Upon complete addition, CrO_3 (9.00 g, 90.0 mmol, 3.00 eq) was added in small portions over 60 minutes, while the reaction temperature was kept below 5 °C. In the course of the reaction, the color turned from pale yellow to dark green. Thereafter, the mixture was stirred for an additional 30 minutes at 0 °C and then poured carefully into a beaker filled with ice (400 mL). After the ice was melted the precipitated material was collected *via* filtration and washed with cool water (2 × 40 mL). Purification by flash column chromatography (SiO_2, CH:EA 4:1 v:v) afforded **S4** (4.93 g, 17.4 mmol, 58%) as a pale yellow solid. If necessary, the product can be washed with small amounts of cyclohexane to remove yellow impurities. Data for **S4**: R_f = 0.21 (SiO_2, CH:EA 4:1 v:v). Mp.: 136 – 140 °C. ^{1}H-NMR (601 MHz, CDCl$_3$): δ = 8.00 (s, 1H), 7.87 (dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.9 Hz, 1H), 7.75 (d, $^4J_{HH}$ = 1.9 Hz, 1H), 7.64 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 3.96 (s, 3H), 2.13 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, CDCl$_3$): δ = 168.4 (2x), 157.6, 149.8, 130.7, 127.9, 115.8, 106.2, 84.7, 56.5, 20.9 (2x) ppm. IR (ATR, neat): ν = 3124 (w), 3094 (w), 3064 (w), 2961 (w), 1754 (s), 1623 (w), 1595 (w), 1527 (m), 1495 (m), 1470 (w), 1420 (w), 1373 (m), 1352 (m), 1313 (m), 1282 (w), 1261 (m), 1232 (s), 1196 (s), 1127 (m), 1094 (w), 1059 (m), 1014 (s), 991 (s), 970 (s), 949 (s), 908 (m), 877 (s), 833 (m), 802 (s), 743 (m), 731 (m), 681 (w), 657 (m) cm^{-1}. MS (EI, 70 eV): m/z = 283.1 [$C_{12}H_{13}NO_7$]$^{+\cdot}$. HRMS (ESI) m/z: [M+Na]$^+$ calcd for [$C_{12}H_{13}NNaO_7{}^+$]: 306.0584; Found: 306.0583. [2M+Na]$^+$ calcd for [$C_{24}H_{26}N_2NaO_{14}{}^+$]: 589.1276; Found: 589.1275. The analytical data are in accordance with the literature.[56]



2

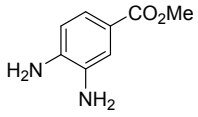
*2-Methoxy-4-nitrobenzaldehyde (**2**).* A slightly modified literature procedure was used.[23a] A mixture (4.47 g, 15.0 mmol, 1.00 eq) of mono- **S2** (1.26 g, 5.13 mmol) and dibrominated species **S3** (3.21 g, 9.87 mmol) was suspended in EtOH:H_2O (15 mL, 1:1 v:v, 1.0 M) and hexamethylenetetramine (6.31 g, 45.0 mmol, 3.00 eq) was added in one portion. Heating for three hours at 100 °C (oil bath temperature), while the solid slowly dissolved, was followed by the addition of concentrated hydrochloric acid (2.48 mL, 30.0 mmol, 2.00 eq). After stirring for another 30 minutes at 100 °C (oil bath temperature) the mixture was cooled to ambient temperature. Ethanol was removed under reduced pressure by rotary evaporation and water (30 mL) and CH_2Cl_2 (30 mL) were added. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification by flash column chromatography (SiO_2, CH:EA 6:1 v:v) afforded **2** (780 mg, 4.31 mmol, 29%) as a colorless solid.

*2-Methoxy-4-nitrobenzaldehyde (**2**).* A slightly modified literature procedure was used.[24] **S4** (1.42 g, 5.00 mmol, 1.00 eq) was dissolved in 1,4-dioxane (5.00 mL, 1.0 M) and concentrated hydrochloric acid (1.00 mL, 37% in H_2O) was added in one portion. The mixture was heated to 105 °C (oil bath temperature) and stirred under these conditions for 12 hours. After cooling to ambient temperature no solids precipitated, that is why the reaction mixture was subjected to aqueous workup. Saturated $NaHCO_3$ solution was added until no more bubbling was observed and a pH value of approximately 8 was adjusted. The aqueous phase was extracted with ethyl acetate (3 × 10 mL) and the combined organic phases were washed with water (20 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator to afford **2** (885 mg, 4.89 mmol, 98%) as a bright yellow solid. Data for **2**: R_f = 0.29 (SiO_2, CH:EA 4:1 v:v). Mp.: 118 – 120 °C. ^{1}H-NMR (601 MHz, CDCl$_3$): δ = 10.51 (s, 1H), 7.98 (d, $^4J_{HH}$ = 8.3 Hz, 1H), 7.89 – 7.85 (m, 2H), 4.06 (s, 3H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, CDCl$_3$): δ = 188.4, 161.9, 152.4, 129.7, 128.7, 115.7, 107.3, 56.6 ppm. IR (ATR, neat): ν = 3113 (w), 3047 (w), 2959 (w), 2884 (w), 1683 (s), 1612 (m), 1583 (m), 1515 (s), 1483 (m), 1465 (m), 1413 (m), 1393 (m), 1347 (s), 1310 (m), 1254 (s), 1191 (m), 1179 (s), 1114 (m), 1088 (m), 1012 (s), 880 (s), 836 (m), 811 (s), 740 (s), 711 (m), 676 (m) cm^{-1}. MS (EI, 70 eV): m/z = 181.0 [$C_8H_7NO_4$]$^{+\cdot}$. HRMS (EI, 70 eV) m/z: [M]$^{+\cdot}$ calcd for [$C_8H_7NO_4{}^{+\cdot}$]: 181.0370; Found: 181.0371. The analytical data are in accordance with the literature.[56]



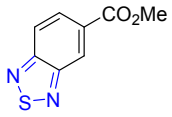
3

*2-(2-Methoxy-4-nitrophenyl)-4,4-dimethyl-4,5-dihydrooxazole (**3**).* Prepared according to **GP 1** from **2** (181 mg, 1.00 mmol, 1.00 eq) in CH_2Cl_2 (2.50 mL, 0.4 M) and 2-amino-2-methylpropan-1-ol (178 mg, 191 µL, 2.00 mmol, 2.00 eq) and 4 Å MS (2.0 g). Stirring for 18 h and addition of NBS (356 mg, 2.00 mmol, 2.00 eq) was followed by stirring for four more hours. After filtration the organic phase was washed with saturated $NaHCO_3$ solution (3 × 30 mL). The combined aqueous phases were extracted with CH_2Cl_2 (2 × 30 mL). All organic phases were washed with saturated NaS_2O_3 solution (30 mL) and the aqueous phase was extracted with CH_2Cl_2 (20 mL). Purification by flash column chromatography (SiO_2, CH:EA 2:1 v:v) afforded **3** (196 mg, 783 µmol, 78%) as a pale yellow solid. Data for **3**: R_f = 0.17 (SiO_2, CH:EA 2:1 v:v). Mp.: 65 – 67 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 7.89 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.83 (dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 2.1 Hz, 1H), 7.79 (d, $^4J_{HH}$ = 2.0 Hz, 1H), 4.12 (s, 2H), 3.99 (s, 3H), 1.41 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 159.6, 159.0, 150.3, 132.3, 124.0, 115.3, 106.8, 79.3, 68.2, 56.8, 28.5 (2x) ppm. IR (ATR, neat): ν = 2965 (w), 2930 (w), 2898 (w), 2868 (w), 1640 (m), 1607 (w), 1589 (w), 1520 (s), 1494 (m), 1463 (m), 1408 (m), 1343 (s), 1284 (m), 1260 (s), 1210 (m), 1181 (m), 1136 (w), 1123 (w), 1102 (m), 1065 (w), 1038 (s), 1025 (s), 988 (m), 965 (s), 915 (m), 858 (s), 819 (w), 803 (s), 756 (w), 731 (s), 672 (m) cm^{-1}. MS (APCI): m/z = 251.1 [$C_{12}H_{14}N_2O_4$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{12}H_{15}N_2O_4^+$]: 251.1026; Found: 251.1027. [M+Na]$^+$ calcd for [$C_{12}H_{14}N_2NaO_4^+$]: 273.0846; Found: 273.0845. [2M+Na]$^+$ calcd for [$C_{24}H_{28}N_4NaO_8^+$]: 523.1799; Found: 523.1796.



4

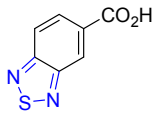
*Methyl 3,4-diaminobenzoate (**4**).* A slightly modified literature procedure was used.[26] A two-necked round bottom flask equipped with a reflux condenser and a gas line leading into a gas washing bottle filled with half saturated $NaHCO_3$ solution was charged with 3,4-diaminobenzoic acid (2.28 g, 15.0 mmol, 1.00 eq). Methanol (50 mL, 0.3 M) was added and the solution was cooled to 0 °C. $SOCl_2$ (4.35 mL, 60.0 mmol, 4.00 eq) was added *via* syringe pump (0.2 mL/min) through a rubber septum – with every drop hitting the reaction mixture a little pop was audible. After complete addition the mixture was allowed to warm slowly to 25 °C and stirred for 14 hours in all. All volatile components were removed under reduced pressure using a cooling trap and water (40 mL) and saturated $NaHCO_3$ solution (60 mL) were added to adjust a pH value of approximately 8. The aqueous layer was extracted with ethyl acetate (4 × 40 mL). and the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Recrystallization from a hot cyclohexane/ethyl acetate solution afforded **4** (2.31 g, 13.9 mmol, 93%) as a fluffy pale brown solid. Data for **4**: R_f = 0.17 (SiO_2, CH:EA 1:1 v:v). Mp.: 106 – 108 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 7.46 (dd, $^3J_{HH}$ = 8.1 Hz, $^4J_{HH}$ = 1.9 Hz, 1H), 7.41 (d, $^4J_{HH}$ = 1.9 Hz, 1H), 6.67 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 3.85 (s, 3H), 3.80 (br. s, 2H), 3.35 (br. s, 2H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 167.5, 140.5, 133.2, 123.4, 121.3, 118.5, 115.0, 51.8 ppm. IR (ATR, neat): ν = 3434 (w), 3361 (w), 3193 (br), 2942 (w), 1689 (m), 1663 (m), 1625 (m), 1586 (m), 1513 (m), 1449 (m), 1426 (m), 1315 (s), 1293 (s), 1235 (s), 1188 (m), 1154 (m), 1102 (m), 1064 (m), 991 (m), 891 (m), 806 (m), 765 (s), 712 (s) cm^{-1}. MS (APCI): m/z = 167.1 [$C_8H_{10}N_2O_2$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$: calcd for [$C_8H_{11}N_2O_2^+$]: 167.0815; Found: 167.0814. [M+Na]$^+$ calcd for [$C_8H_{10}N_2NaO_2^+$]: 189.0635; Found: 189.0634. The analytical data are in accordance with the literature.[57]



5

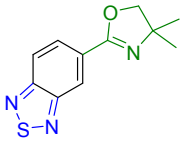
*Methyl benzo[c][1,2,5]thiadiazole-5-carboxylate (**5**).* A slightly modified literature procedure was used.[27] A two-necked round bottom flask equipped with a reflux condenser and a gas line leading into a gas washing bottle filled with half saturated $NaHCO_3$ solution was charged with **4** (997 mg, 6.00 mmol, 1.00 eq). CH_2Cl_2 (30 mL, 0.2 M) and NEt_3 (2.43 g, 3.35 mL, 24.0 mmol, 4.00 eq) were added and the solution was cooled to 0 °C. $SOCl_2$ (870 µL, 12.0 mmol, 2.00 eq) was added *via* syringe pump (0.2 mL/min) through a rubber septum. After complete addition the mixture was heated to 80 °C (oil bath temperature) and stirred for six hours under these conditions. The mixture was allowed to cool to ambient temperature and all volatile components were removed under reduced pressure using a cooling trap. Water (30 mL) and half concentrated hydrochloric acid (2 mL) were added to adjust a pH value of approximately 2. The aqueous layer was extracted with CH_2Cl_2 (4 × 30 mL) and the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification by flash column chromatography (SiO_2, CH:EA 5:1 v:v) afforded **5** (1.01 g, 5.20 mmol, 87%)as a beige solid. Data for **5**: R_f = 0.52 (SiO_2, CH:EA 5:1 v:v). Mp.: 90 – 92 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 8.74 (dd, $^4J_{HH}$ = 1.4 Hz, $^5J_{HH}$ = 0.7 Hz, 1H), 8.20 (dd, $^3J_{HH}$ = 9.2 Hz, $^4J_{HH}$ = 1.6 Hz, 1H), 8.04 (dd, $^3J_{HH}$ = 9.1 Hz, $^5J_{HH}$ = 0.6 Hz, 1H), 4.00 (s, 3H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 166.3, 156.5, 154.4, 131.3, 128.9, 124.5, 121.6, 52.9 ppm. IR (ATR, neat): ν = 3099 (w), 3021 (w), 2962 (w), 1717 (s), 1611 (w), 1525 (w), 1436 (m), 1319 (m), 1306 (m), 1290 (m), 1221 (s), 1189 (m), 1135 (m), 1089 (s), 964 (m), 944 (m), 913 (m), 862 (m), 841 (m), 833 (m), 822 (m), 804 (m), 774 (m), 747 (s), 663 (m) cm^{-1}. MS (EI, 70 eV): m/z = 194.0 [$C_8H_6N_2O_2S$]$^{+\cdot}$. MS (APCI): m/z = 195.0 [$C_8H_6N_2O_2S$+H]$^+$. HRMS (EI, 70 eV) m/z: [M]$^{+\cdot}$ calcd for

$[C_8H_6N_2O_2S^{+\cdot}]$: 194.0145; Found: 194.0146. The analytical data are in accordance with the literature.[27]



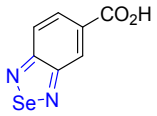
6

*Benzo[c][1,2,5]thiadiazole-5-carboxylic acid (**6**).* A slightly modified literature procedure was used.[28] **5** (77.7 mg, 400 µmol, 1.00 eq) was dissolved in 1,4-dioxane (4.0 mL, 0.1 M) and NaOH solution (0.4 mL, 1.0 M in H_2O) was added at 25 °C. The slightly yellow solution was stirred for 16 hours under the same conditions while the yellow color became more intensive. Carefully addition of hydrochloric acid (~6 mL, 1.0 M) resulted in precipitation of the carboxylic acid. The solid was filtered off, washed with water (3 × 5 mL) and dried *in vacuo* to afford **6** (63.5 mg, 352 µmol, 88%) as an off-white solid. Data for **6**: R_f = 0.06 (SiO_2, CH:EA 4:1 v:v). Mp.: 232 – 234 °C. ^{1}H-NMR (601 MHz, DMSO-d_6): δ = 13.55 (br. s, 1H), 8.62 (dd, $^4J_{HH}$ = 1.4 Hz, $^5J_{HH}$ = 0.9 Hz, 1H), 8.17 (dd, $^3J_{HH}$ = 9.1 Hz, $^5J_{HH}$ = 0.8 Hz, 1H), 8.14 (dd, $^3J_{HH}$ = 9.1 Hz, $^4J_{HH}$ = 1.5 Hz, 1H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, DMSO-d_6): δ = 166.7, 155.8, 153.8, 132.0, 128.9, 123.3, 121.5 ppm. IR (ATR, neat): ν = 2807 (br), 2507 (br), 1682 (s), 1608 (m), 1520 (w), 1475 (w), 1438 (m), 1414 (m), 1370 (w), 1327 (m), 1294 (m), 1242 (m), 1223 (s), 1137 (m), 1089 (m), 920 (m), 892 (m), 867 (m), 857 (s), 837 (s), 821 (m), 785 (m), 772 (s), 749 (s), 670 (m), 657 (m) cm^{-1}. MS (APCI): m/z = 181.1 $[C_7H_4N_2O_2S+H]^+$. HRMS (ESI) m/z: $[M-H]^-$ calcd for $[C_7H_3N_2O_2S^-]$: 178.9921; Found: 178.9919.



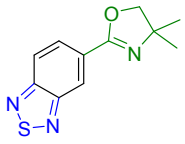
7

*2-(Benzo[c][1,2,5]thiadiazol-5-yl)-4,4-dimethyl-4,5-dihydrooxazole (**7**).* Prepared by analogy to **GP 2** from **6** (180 mg, 1.00 mmol, 1.00 eq) in $SOCl_2$ (725 µL, 10.0 mmol, 10.0 eq) and stirring for three hours at 80 °C (oil bath temperature). 2-Amino-2-methylpropan-1-ol (267 mg, 286 µL, 10.0 mmol, 3.00 eq) was dissolved in CH_2Cl_2 (5.0 mL) and addition of the crude acid chloride in CH_2Cl_2 (30 mL) *via* syringe pump (1.5 mL/min) at 0 °C was followed by stirring for three hours. The crude amide in $SOCl_2$ (725 µL, 10.0 mmol, 10.0 eq) was stirred for 40 minutes. After solvent evaporation the crude oil was dissolved in CH_2Cl_2 (50 mL) and water (50 mL) and aqueous NaOH (20%, 50 mL) were added. The phases were separated and the aqueous phase – a pH value of approximately 9 was adjusted – was extracted with CH_2Cl_2 (4 × 30 mL). Purification by flash column chromatography (SiO_2, CH:EA 10:1 v:v) afforded **7** (220 mg, 943 µmol, 94%) as an off-white solid. Data for **7**: R_f = 0.16 (SiO_2, CH:EA 10:1 v:v). R_f = 0.27 (SiO_2, CH:EA 6:1 v:v). Mp.: 73 – 75 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 8.51 (dd, $^4J_{HH}$ = 1.5 Hz, $^5J_{HH}$ = 0.8 Hz, 1H), 8.21 (dd, $^3J_{HH}$ = 9.2 Hz, $^4J_{HH}$ = 1.6 Hz, 1H), 7.99 (dd, $^3J_{HH}$ = 9.2 Hz, $^5J_{HH}$ = 0.8 Hz, 1H), 4.18 (s, 2H), 1.42 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 161.3, 155.9, 154.6, 129.5, 129.2, 121.9, 121.4, 79.6, 68.3, 28.5 (2x) ppm. IR (ATR, neat): ν = 2969 (w), 2926 (w), 2898 (w), 1651 (m), 1608 (w), 1522 (w), 1476 (w), 1461 (m), 1442 (w), 1389 (w), 1368 (w), 1357 (m), 1328 (m), 1305 (w), 1238 (w), 1197 (s), 1125 (w), 1045 (s), 990 (w), 968 (s), 918 (m), 878 (w), 857 (w), 845 (w), 826 (s), 818 (s), 708 (s), 673 (m) cm^{-1}. MS (APCI): m/z = 234.1 $[C_{11}H_{11}N_3OS+H]^+$. HRMS (ESI) m/z: $[M+H]^+$ calcd for $[C_{11}H_{12}N_3OS^+]$: 234.0696; Found: 234.0695.

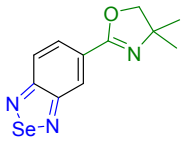


8

*Benzo[c][1,2,5]selenadiazole-5-carboxylic acid (**8**).* A slightly modified literature procedure was used.[29] 3,4-Diaminobenzoic acid (1.22 g, 8.00 mmol, 1.00 eq) was dissolved in hydrochloric acid (26.7 mL, 0.3 M, 1.0 M in H_2O) and heated to 80 °C (oil bath temperature). To the brownish solution was added a solution of SeO_2 (1.78 g, 16.0 mmol, 2.00 eq), dissolved in water (12 mL), *via Pasteur* pipette within one minute. The mixture was stirred under the same conditions for three hours while a pale brown solid precipitated. Filtration of the precipitate was followed by washing with water (3 × 20 mL) and drying *in vacuo* to afford **8** (1.78 g, 7.84 mmol, 98%) as a beige solid. Data for **8**: R_f = 0.17 (SiO_2, CH:EA 1:5 v:v). Mp.: 292 – 294 °C. ^{1}H-NMR (601 MHz, DMSO-d_6): δ = 13.26 (br. s, 1H), 8.41 (dd, $^4J_{HH}$ = 1.4 Hz, $^5J_{HH}$ = 0.9 Hz, 1H), 7.96 (dd, $^3J_{HH}$ = 9.3 Hz, $^4J_{HH}$ = 1.6 Hz, 1H), 7.91 (dd, $^3J_{HH}$ = 9.3 Hz, $^5J_{HH}$ = 0.9 Hz, 1H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, DMSO-d_6): δ = 166.9, 160.7, 159.2, 131.2, 127.9, 125.4, 123.3 ppm. ^{77}Se-NMR (115 MHz, DMSO-d_6): δ = 1564.9 (s) ppm. IR (ATR, neat): ν = 2809 (br), 2528 (br), 1678 (s), 1608 (m), 1505 (m), 1482 (w), 1441 (m), 1408 (m), 1327 (m), 1296 (m), 1274 (m), 1252 (s), 1242 (s), 1220 (s), 1136 (m), 1087 (w), 916 (m), 893 (s), 835 (m), 778 (m), 767 (s), 747 (s), 725 (s) cm^{-1}. MS (APCI): m/z = 228.9 $[C_7H_4N_2O_2{}^{80}Se+H]^+$. HRMS (ESI) m/z: $[M-H]^-$ calcd for $[C_7H_3N_2O_2{}^{80}Se^-]$: 226.9365; Found: 226.9363. The analytical data are in accordance with the literature.[29]



7

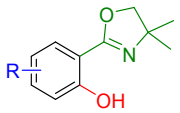


9

2-(Benzo[c][1,2,5]selenadiazol-5-yl)-4,4-dimethyl-4,5-dihydrooxazole (**9**) & 2-(Benzo[c][1,2,5]thiadiazol-5-yl)-4,4-dimethyl-4,5-dihydrooxazole (**7**). Prepared by analogy to **GP 2** from **8** (908 mg, 4.00 mmol, 1.00 eq) in $SOCl_2$ (2.90 mL, 40.0 mmol, 10.0 eq) and stirring for three hours at 80 °C (oil bath temperature). 2-Amino-2-methylpropan-1-ol (1.07 g, 1.15 mL, 12.0 mmol, 3.00 eq) was dissolved in CH_2Cl_2 (20 mL) and addition of the crude acid chloride in

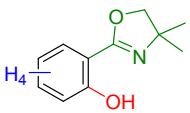
CH_2Cl_2 (30 mL) via syringe pump (1.5 mL/min) at 0 °C was followed by stirring for three hours. The crude amide in $SOCl_2$ (2.90 mL, 40.0 mmol, 10.0 eq) was stirred for 40 minutes. After solvent evaporation the crude oil was dissolved in CH_2Cl_2 (50 mL) and water (50 mL) and aqueous NaOH (20%, 50 mL) were added. The phases were separated and the aqueous phase – a pH value of approximately 9 was adjusted – was extracted with CH_2Cl_2 (4 × 30 mL). Purification by flash column chromatography (SiO_2, CH:EA 10:1 to 6:1 v:v) provided first **7** (339 mg, 1.45 mmol, 36%) as an off-white solid and then **9** (648 mg, 2.31 mmol, 58%) as a beige solid. Data for **9**: R_f = 0.07 (SiO_2, CH:EA 10:1 v:v). R_f = 0.14 (SiO_2, CH:EA 6:1 v:v). Mp.: 105 – 107 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 8.34 (s, 1H), 8.08 (d, $^3J_{HH}$ = 9.2 Hz, 1H), 7.81 (d, $^3J_{HH}$ = 9.3 Hz, 1H), 4.18 (s, 2H), 1.42 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 161.3, 161.2, 160.3, 129.5, 129.1, 123.7, 123.2, 79.6, 68.4, 28.5 (2x) ppm. ^{77}Se-NMR (115 MHz, $CDCl_3$): δ = 1534.2 (s) ppm. IR (ATR, neat): ν = 2969 (w), 2959 (w), 2923 (w), 2898 (w), 1640 (m), 1601 (m), 1506 (w), 1457 (m), 1446 (m), 1382 (w), 1355 (m), 1327 (m), 1315 (m), 1261 (m), 1249 (m), 1201 (s), 1175 (m), 1129 (m), 1043 (s), 992 (m), 968 (s), 913 (m), 886 (s), 861 (m), 820 (s), 762 (s), 725 (m), 712 (s) cm^{-1}. MS (APCI): m/z = 282.0 [$C_{11}H_{11}N_3O^{80}Se$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{11}H_{12}N_3O^{80}Se^+$]: 282.0140; Found: 282.0139. [M+Na]$^+$ calcd for [$C_{11}H_{11}N_3NaO^{80}Se^+$]: 303.9960; Found: 303.9960.

General Procedure for ortho-Hydroxylations.



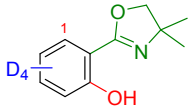
*General Procedure for the ortho-Hydroxylation of 2-Aryloxazolines using O_2 (**GP 3**).* A literature method was used.[15b] A heat gun-dried and nitrogen-flushed *Schlenk* tube, equipped with a magnetic stirring bar and a rubber septum, was charged with 2-aryloxazoline (1.00 eq) and anhydrous THF (0.2 – 0.4 M) was added. Dropwise addition of TMPMgCl·LiCl (3.00 eq) *via* syringe through the rubber septum, if not otherwise noted at 25 °C, was followed by stirring for the indicated time under the same conditions, while the mixture discolored pale red to dark red/brown, depending on the substrate. Then the nitrogen atmosphere was replaced by an oxygen atmosphere by flushing the reaction system using an oxygen filled balloon and the mixture was stirred for an additional 24 hours, if not otherwise noted at 25 °C. The clear, pale red to yellow, mixture was subjected to aqueous workup and the organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification of the crude product was conducted by flash column chromatography using the given eluent.

Preparation of ortho-hydroxylated 2-Aryloxazolines.



all-H

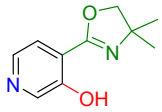
*2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)phenol (**all-H**).* Prepared according to **GP 3** from **1a** (87.6 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M) and TMPMgCl·LiCl (1.30 mL, 1.50 mmol, 3.00 eq, 1.15 M in THF). Stirring for six hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 20:1 v:v) afforded **all-H** (82.3 mg, 430 µmol, 86%) as a colorless liquid. **1a** (9.7 mg, 55.4 µmol, 11%) was recovered. Upon standing at 25 °C, the liquid solidified to form a colorless solid. Single crystals suitable for X-ray analysis were grown from hexane solution at 5 °C without solvent evaporation. Data for **all-H**: R_f = 0.36 (SiO_2, CH:EA 20:1 v:v). Mp.: 47 – 49 °C. ^{1}H-NMR (360 MHz, $CDCl_3$): δ = 12.21 (s, 1H), 7.63 (ddd, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.8 Hz, $^5J_{HH}$ = 0.5 Hz, 1H), 7.36 (ddd, $^3J_{HH}$ = 8.3 Hz, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 1.7 Hz, 1H), 1H), 7.00 (ddd, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 1.1 Hz, $^5J_{HH}$ = 0.4 Hz, 1H), 6.86 (ddd, $^3J_{HH}$ = 7.8 Hz, $^3J_{HH}$ = 7.3 Hz, $^4J_{HH}$ = 1.1 Hz, 1H), 4.10 (s, 2H), 1.40 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (91 MHz, $CDCl_3$): δ = 163.6, 160.0, 133.3, 128.0, 118.7, 116.8, 111.0, 78.5, 67.2, 28.6 (2x) ppm. IR (ATR, neat): ν = 2969 (w), 2929 (w), 2896 (w), 1639 (s), 1617 (m), 1581 (w), 1491 (m), 1462 (w), 1423 (w), 1384 (w), 1360 (s), 1328 (w), 1308 (m), 1259 (s), 1209 (m), 1190 (m), 1154 (m), 1125 (m), 1061 (s), 1033 (m), 961 (s), 940 (m), 877 (m), 828 (m), 792 (m), 754 (s), 691 (m), 664 (m) cm^{-1}. MS (APCI): m/z = 192.1 [$C_{11}H_{13}NO_2$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{11}H_{14}NO_2^+$]: 192.1019; Found: 192.1022. The analytical data are in accordance with the literature.[58]



all-D

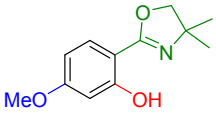
*2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)phen-3,4,5,6-d4-ol (**all-D**).* Prepared according to **GP 3** from **1b** (72.1 mg, 400 µmol, 1.00 eq) in THF (1.00 mL, 0.4 M) and TMPMgCl·LiCl (984 µL, 1.20 mmol, 3.00 eq, 1.22 M in THF). Stirring for six hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 20:1 v:v) afforded **all-D** (57.3 mg, 293 µmol, 73%) as a colorless liquid. As indicated by ^{1}H-NMR the product contains 5% of C–1 protonated byproduct. Upon standing for several months the liquid solidified to form a colorless solid. Data for **all-D**: R_f = 0.36 (SiO_2, CH:EA 20:1 v:v). Mp.: 47 – 49 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 12.19 (s, 1H), 4.10 (s, 2H), 1.40 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (91 MHz, $CDCl_3$): δ = 163.6, 159.9, 144.2, 127.7, 119.8, 117.1, 108.4, 78.4, 67.1, 28.7 (2x) ppm. IR (ATR, neat): ν = 2968 (w), 2929 (w), 2901 (w), 1632 (s), 1604 (m), 1555 (m), 1462 (w), 1441 (w), 1418 (s), 1385 (w), 1368 (s), 1318 (w), 1261 (s), 1212 (m), 1184 (s), 1138 (w), 1058 (s), 1009 (m), 958 (m), 938 (m), 884 (w), 867

(w), 817 (m), 787 (m), 770 (s), 699 (w) cm^{-1}. MS (APCI): m/z = 196.2 $[C_{11}H_9D_4NO_2+H]^+$. HRMS (ESI) m/z: $[M+H]^+$ calcd for $[C_{11}H_{10}D_4NO_2^+]$: 196.1270; Found: 196.1268. $[M+Na]^+$ calcd for $[C_{11}H_9D_4NNaO_2^+]$: 218.1090; Found: 218.1088. The analytical data are in accordance with the literature.[15b]



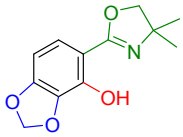
3-Py

*4-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)pyridin-3-ol (**3-Py**).* Prepared according to **GP 3** from **1c** (88.1 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M) and TMPMgCl·LiCl (1.23 mL, 1.50 mmol, 3.00 eq, 1.22 M in THF). Stirring for six hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 4:1 v:v) afforded **3-Py** (73.0 mg, 380 µmol, 76%) as a colorless solid. Single crystals suitable for X-ray analysis were grown during $CHCl_3$ evaporation on a rotary evaporator by sublimation at 40 °C bath temperature and 3 mbar pressure. Data for **3-Py**: R_f = 0.11 (SiO_2, CH:EA 4:1 v:v). Mp.: 74 – 76 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 11.82 (br. s, 1H), 8.46 (d, $^4J_{HH}$ = 0.7 Hz, 1H), 8.17 (d, $^3J_{HH}$ = 5.0 Hz, 1H), 7.43 (dd, $^3J_{HH}$ = 5.0 Hz, $^4J_{HH}$ = 0.7 Hz, 1H), 4.14 (s, 2H), 1.41 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 162.3, 154.6, 140.6, 140.1, 120.3, 116.6, 78.9, 67.8, 28.5 (2x) ppm. IR (ATR, neat): ν = 2972 (w), 2930 (w), 1639 (m), 1612 (m), 1556 (w), 1492 (m), 1465 (m), 1403 (m), 1382 (m), 1356 (s), 1326 (s), 1302 (s), 1250 (m), 1225 (s), 1214 (s), 1189 (m), 1167 (s), 1088 (s), 1054 (m), 1021 (w), 986 (w), 956 (s), 943 (s), 911 (w), 881 (m), 843 (m), 831 (m), 792 (s), 767 (m), 696 (s), 671 (s) cm^{-1}. MS (APCI): m/z = 193.1 $[C_{10}H_{12}N_2O_2+H]^+$. HRMS (EI, 70 eV) m/z: $[M]^{+\cdot}$ calcd for $[C_{10}H_{12}N_2O_2^{+\cdot}]$: 192.0893; Found: 192.0895. The analytical data are in accordance with the literature.[50]



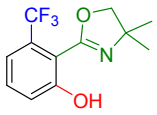
3-OMe

*2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-5-methoxyphenol (**3-OMe**).* Prepared according to **GP 3** from **1d** (41.0 mg, 200 µmol, 1.00 eq) in THF (500 µL, 0.4 M) and TMPMgCl·LiCl (500 µL, 600 µmol, 3.00 eq, 1.20 M in THF). Stirring for six hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (5 mL), water (5 mL) and CH_2Cl_2 (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 10 mL). Purification by flash column chromatography (SiO_2, CH:EA 20:1 v:v) afforded **3-OMe** (33.2 mg, 150 µmol, 75%) as a colorless liquid, which slowly solidified upon standing at 25 °C to form a colorless solid. Data for **3-OMe**: R_f = 0.19 (SiO_2, CH:EA 20:1 v:v). Mp.: 58 – 60 °C. ^{1}H-NMR (360 MHz, $CDCl_3$): δ = 12.41 (br. s, 1H), 7.52 (d, $^3J_{HH}$ = 8.7 Hz, 1H), 6.51 (d, $^4J_{HH}$ = 2.3 Hz, 1H), 6.43 (dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.5 Hz, 1H), 4.06 (s, 2H), 3.81 (s, 3H), 1.38 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (91 MHz, $CDCl_3$): δ = 163.8, 163.6, 161.8, 129.0, 106.5, 104.2, 100.8, 78.4, 66.9, 55.5, 28.7 (2x) ppm. IR (ATR, neat): ν = 2967 (w), 2930 (w), 2898 (w), 2841 (w), 1634 (s), 1579 (m), 1511 (m), 1462 (w), 1442 (m), 1403 (w), 1383 (w), 1364 (s), 1334 (w), 1312 (w), 1291 (m), 1270 (s), 1248 (w), 1205 (s), 1190 (s), 1165 (s), 1141 (m), 1124 (s), 1066 (s), 1028 (s), 966 (s), 955 (s), 869 (w), 834 (m), 796 (m), 735 (w), 690 (w) cm^{-1}. MS (APCI): m/z = 222.1 $[C_{12}H_{15}NO_3+H]^+$. HRMS (ESI) m/z: $[M+H]^+$ calcd for $[C_{12}H_{16}NO_3^+]$: 222.1125; Found: 222.1127. The analytical data are in accordance with the literature.[15b]



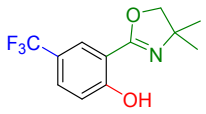
3,4-OCO

*5-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)benzo[d][1,3]dioxol-4-ol (**3,4-OCO**).* Prepared according to **GP 3** from **1e** (110 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M) and TMPMgCl·LiCl (1.23 mL, 1.50 mmol, 3.00 eq, 1.22 M in THF). Stirring for six hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 6:1 v:v) afforded **3,4-OCO** (95.4 mg, 406 µmol, 81%) as an off-white solid. Single crystals suitable for X-ray analysis were grown from CH_2Cl_2 solution by slow solvent evaporation. Data for **3,4-OCO**: R_f = 0.25 (SiO_2, CH:EA 6:1 v:v). Mp.: 99 – 101 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 12.46 (br. s, 1H, O*H*), 7.22 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H–5), 6.44 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H–6), 6.03 (s, 2H, O–C*H*$_2$–O), 4.07 (s, 2H, C*H*$_2$), 1.38 (s, 6H, C(C*H*$_3$)$_2$) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 163.5 (C=N), 151.7 (C–1), 144.6 (C–3), 134.2 (C–2), 122.4 (C–5), 107.4 (C–4), 102.0 (O–*C*H$_2$–O), 100.3 (C–6), 78.4 (*C*H$_2$), 67.0 (*C*(CH$_3$)$_2$), 28.6 (2x, C(*C*H$_3$)$_2$) ppm. IR (ATR, neat): ν = 2981 (w), 2905 (w), 2794 (w), 1652 (m), 1622 (m), 1490 (m), 1471 (s), 1428 (m), 1407 (m), 1383 (m), 1365 (m), 1343 (s), 1322 (s), 1297 (m), 1278 (m), 1254 (m), 1235 (m), 1222 (m), 1188 (m), 1146 (w), 1113 (m), 1069 (s), 1023 (s), 974 (s), 946 (m), 925 (m), 905 (s), 846 (m), 799 (s), 789 (s), 752 (s), 703 (m), 667 (m) cm^{-1}. MS (APCI): m/z = 236.2 $[C_{12}H_{13}NO_4+H]^+$. HRMS (ESI) m/z: $[M+H]^+$ calcd for $[C_{12}H_{14}NO_4^+]$: 236.0917; Found: 236.0916. $[M+Na]^+$ calcd for $[C_{12}H_{13}NNaO_4^+]$: 258.0737; Found: 258.0736. $[M+K]^+$ calcd for $[C_{12}H_{13}KNO_4^+]$: 274.0476; Found: 274.0475. The analytical data are in accordance with the literature.[15b]



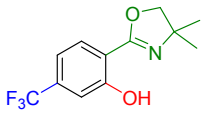
1-CF$_3$

*2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-3-(trifluoromethyl)phenol (**1-CF$_3$**).* Prepared according to **GP 3** from **1f** (122 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M) and TMPMgCl·LiCl (1.23 mL, 1.50 mmol, 3.00 eq, 1.22 M in THF). Stirring for two hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 20:1 v:v) afforded **1-CF$_3$** (72.6 mg, 280 µmol, 56%) as a colorless liquid. Upon standing for several months the liquid solidified to form a colorless solid. Data for **1-CF$_3$**: R_f = 0.24 (SiO_2, CH:EA 20:1 v:v). Mp.: 33 – 35 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 13.31 (s, 1H), 7.40 (t, $^3J_{HH}$ = 8.1 Hz, 1H), 7.27 (d, $^3J_{HH}$ = 7.2 Hz, 1H), 7.22 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 4.17 (s, 2H), 1.43 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 163.3, 161.6, 132.1, 129.3 (q, $^2J_{CF}$ = 32.2 Hz), 123.6 (q, $^1J_{CF}$ = 273.3 Hz), 121.7, 117.9 (q, $^3J_{CF}$ = 6.9 Hz), 107.9, 79.0, 66.2, 28.4 (2x) ppm. ^{19}F-NMR (565 MHz, $CDCl_3$): δ = –58.3 (s) ppm. IR (ATR, neat): ν = 2972 (w), 2933 (w), 2900 (w), 1625 (m), 1579 (w), 1492 (w), 1456 (m), 1384 (w), 1354 (m), 1329 (m), 1296 (s), 1253 (m), 1187 (m), 1130 (s), 1085 (m), 1058 (m), 963 (m), 915 (s), 876 (m), 833 (m), 809 (s), 758 (m), 698 (m), 689 (m) cm^{-1}. MS (APCI): m/z = 260.0 [$C_{12}H_{12}F_3NO_2$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{12}H_{13}F_3NO_2^+$]: 260.0893; Found: 260.0893. The analytical data are in accordance with the literature.[15b]



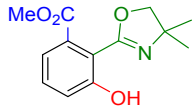
2-CF$_3$

*2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-4-(trifluoromethyl)phenol (**2-CF$_3$**).* Prepared according to **GP 3** from **1g** (122 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M) and TMPMgCl·LiCl (1.23 mL, 1.50 mmol, 3.00 eq, 1.22 M in THF). Stirring for two hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 20:1 v:v) afforded **2-CF$_3$** (115 mg, 444 µmol, 89%) as a colorless liquid. Upon standing for several months the liquid solidified to form a colorless solid. Data for **2-CF$_3$**: R_f = 0.36 (SiO_2, CH:EA 20:1 v:v). Mp.: 34 – 36 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 12.64 (s, 1H), 7.92 (d, $^4J_{HH}$ = 2.4 Hz, 1H), 7.59 (ddd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.3 Hz, $^5J_{HH}$ = 0.8 Hz, 1H), 7.07 (dd, $^3J_{HH}$ = 8.8 Hz, $^5J_{HH}$ = 0.9 Hz, 1H), 4.14 (s, 2H), 1.41 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 162.9, 162.5, 130.0 (q, $^3J_{CF}$ = 3.6 Hz), 125.8 (q, $^3J_{CF}$ = 4.0 Hz), 124.3 (q, $^1J_{CF}$ = 271.0 Hz), 121.1 (q, $^2J_{CF}$ = 33.2 Hz), 117.4, 111.0, 78.8, 67.6, 28.6 (2x) ppm. ^{19}F-NMR (565 MHz, $CDCl_3$): δ = –61.6 (s) ppm. IR (ATR, neat): ν = 2973 (w), 2933 (w), 2903 (w), 1648 (s), 1624 (w), 1599 (w), 1503 (m), 1465 (w), 1388 (w), 1367 (m), 1336 (s), 1318 (m), 1292 (s), 1270 (s), 1241 (m), 1205 (s), 1162 (m), 1115 (s), 1078 (s), 1060 (s), 964 (s), 945 (m), 912 (m), 901 (m), 831 (m), 800 (m), 762 (m), 690 (s) cm^{-1}. MS (APCI): m/z = 260.1 [$C_{12}H_{12}F_3NO_2$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{12}H_{13}F_3NO_2^+$]: 260.0893; Found: 260.0887. The analytical data are in accordance with the literature.[15b]



3-CF$_3$

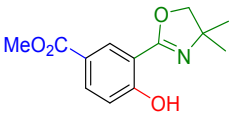
*2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-5-(trifluoromethyl)phenol (**3-CF$_3$**).* Prepared according to **GP 3** from **1h** (122 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M) and TMPMgCl·LiCl (1.23 mL, 1.50 mmol, 3.00 eq, 1.22 M in THF). Stirring for two hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 20:1 v:v) afforded **3-CF$_3$** (122 mg, 471 µmol, 94%) as a colorless solid. Data for **3-CF$_3$**: R_f = 0.33 (SiO_2, CH:EA 20:1 v:v). Mp.: 55 – 57 °C. ^{1}H-NMR (600 MHz, $CDCl_3$): δ = 12.43 (s, 1H), 7.73 (dd, $^3J_{HH}$ = 8.1 Hz, 1H), 7.26 – 7.25 (m, 1H), 7.10 (dd, $^3J_{HH}$ = 8.0 Hz, $^5J_{HH}$ = 1.0 Hz, 1H), 4.14 (s, 2H), 1.41 (s, 6H) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 162.9, 160.0, 134.8 (q, $^2J_{CF}$ = 32.6 Hz), 128.7, 123.7 (q, $^1J_{CF}$ = 272.7 Hz), 115.1 (q, $^3J_{CF}$ = 3.8 Hz), 114.1 (q, $^3J_{CF}$ = 4.0 Hz), 113.8, 78.8, 67.6, 28.6 (2x) ppm. ^{19}F-NMR (565 MHz, $CDCl_3$): δ = –63.3 (s) ppm. IR (ATR, neat): ν = 2975 (w), 2932 (w), 1641 (m), 1620 (w), 1582 (w), 1513 (w), 1461 (w), 1401 (m), 1384 (w), 1368 (m), 1329 (s), 1301 (m), 1237 (m), 1211 (w), 1163 (s), 1121 (s), 1074 (s), 1017 (w), 956 (m), 945 (m), 916 (s), 883 (m), 867 (m), 834 (m), 820 (s), 747 (m), 695 (s), 679 (m), 662 (w) cm^{-1}. MS (APCI): m/z = 260.2 [$C_{12}H_{12}F_3NO_2$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{12}H_{13}F_3NO_2^+$]: 260.0893; Found: 260.0891. The analytical data are in accordance with the literature.[15b]



1-CO$_2$Me

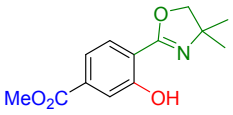
*Methyl 2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3-hydroxybenzoate (**1-CO$_2$Me**).* Prepared according to **GP 3** from **1i** (117 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M). The mixture was cooled to 0 °C and TMPMgCl·LiCl (1.20 mL, 1.50 mmol, 3.00 eq, 1.25 M in THF) was added. Stirring for two hours and slowly warming of the mixture to 10 °C, was followed by flushing with oxygen and stirring for another 24 hours, while the mixture was allowed to warm slowly to 25 °C. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column

chromatography (SiO_2, CH:EA 10:1 v:v) afforded **1-CO_2Me** (68.2 mg, 274 µmol, 55%) as a colorless oil, which very slowly solidified over four months while standing at 0 °C to give a colorless solid. Data for **1-CO_2Me**: R_f = 0.11 (SiO_2, CH:EA 10:1 v:v). Mp.: 35 – 37 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 12.56 (s, 1H, O*H*), 7.36 (dd, $^3J_{HH}$ = 8.4 Hz, $^3J_{HH}$ = 7.5 Hz, 1H, H–5), 7.08 (dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.1 Hz, 1H, H–4), 6.91 (dd, $^3J_{HH}$ = 7.4 Hz, $^4J_{HH}$ = 1.1 Hz, 1H, H–6), 4.08 (s, 2H, CH_2), 3.87 (s, 3H, CH_3), 1.39 (s, 6H, C(CH_3)$_2$) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 169.8 (*C*=O), 162.8 (*C*=N), 160.2 (C–3), 134.2 (C–1), 132.6 (C–5), 119.0 (C–4), 118.2 (C–6), 107.7 (C–2), 79.0 (CH_2), 67.0 (*C*(CH$_3$)$_2$), 52.7 (*C*H$_3$), 28.4 (2x, C(*C*H$_3$)$_2$) ppm. IR (ATR, neat): ν = 2969 (w), 2930 (w), 2897 (w), 2645 (br), 1732 (s), 1631 (s), 1575 (w), 1490 (w), 1455 (m), 1432 (m), 1383 (w), 1367 (w), 1350 (w), 1316 (m), 1282 (s), 1251 (m), 1193 (s), 1176 (s), 1142 (s), 1088 (m), 1056 (m), 1006 (s), 984 (m), 957 (m), 921 (m), 875 (m), 829 (m), 812 (m), 798 (s), 759 (s), 703 (m), 693 (m) cm^{-1}. MS (APCI): m/z = 250.1 [$C_{13}H_{15}NO_4$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{13}H_{16}NO_4^+$]: 250.1074; Found: 250.1074. [M+Na]$^+$ calcd for [$C_{13}H_{15}NNaO_4^+$]: 272.0893; Found: 272.0892. [2M+Na]$^+$ calcd for [$C_{26}H_{30}N_2NaO_8^+$]: 521.1894; Found: 521.1890.



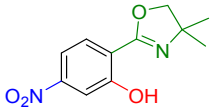
2-CO_2Me

*Methyl 3-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-4-hydroxybenzoate (**2-CO_2Me**).* Prepared according to **GP 3** from **1j** (117 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M). The mixture was cooled to 0 °C and TMPMgCl·LiCl (1.20 mL, 1.50 mmol, 3.00 eq, 1.25 M in THF) was added. Stirring for two hours and slowly warming of the mixture to 10 °C, was followed by flushing with oxygen and stirring for another 24 hours, while the mixture was allowed to warm slowly to 25 °C. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 10:1 v:v) afforded **2-CO_2Me** (84.4 mg, 339 µmol, 68%) as a colorless solid. Data for **2-CO_2Me**: R_f = 0.16 (SiO_2, CH:EA 10:1 v:v). Mp.: 110 – 112 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 12.79 (s, 1H, O*H*), 8.36 (d, $^4J_{HH}$ = 2.2 Hz, 1H, H–2), 8.04 (dd, $^3J_{HH}$ = 8.7 Hz, $^4J_{HH}$ = 2.2 Hz, 1H, H–6), 7.02 (d, $^3J_{HH}$ = 8.7 Hz, 1H, H–5), 4.14 (s, 2H, CH_2), 3.89 (s, 3H, CH_3), 1.41 (s, 6H, C(CH_3)$_2$) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 166.5 (*C*=O), 163.8 (C–4), 163.2 (*C*=N), 134.6 (C–6), 130.5 (C–2), 120.8 (C–1), 116.9 (C–5), 110.8 (C–3), 78.7 (CH_2), 67.4 (*C*(CH$_3$)$_2$), 52.0 (*C*H$_3$), 28.6 (2x, C(*C*H$_3$)$_2$) ppm. IR (ATR, neat): ν = 2975 (w), 2958 (w), 2908 (w), 2557 (br), 1709 (m), 1640 (m), 1604 (m), 1590 (w), 1495 (m), 1470 (w), 1433 (m), 1415 (w), 1388 (w), 1367 (s), 1308 (m), 1282 (s), 1229 (m), 1205 (m), 1189 (s), 1134 (m), 1106 (s), 1061 (s), 978 (m), 963 (s), 944 (s), 915 (m), 827 (s), 804 (m), 764 (s), 700 (s), 690 (s) cm^{-1}. MS (APCI): m/z = 250.1 [$C_{13}H_{15}NO_4$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{13}H_{16}NO_4^+$]: 250.1074; Found: 250.1073. [M+Na]$^+$ calcd for [$C_{13}H_{15}NNaO_4^+$]: 272.0893; Found: 272.0892.



3-CO_2Me

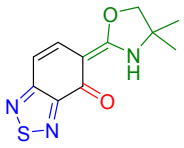
*Methyl 4-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3-hydroxybenzoate (**3-CO_2Me**).* Prepared according to **GP 3** from **1k** (117 mg, 500 µmol, 1.00 eq) in THF (1.25 mL, 0.4 M). The mixture was cooled to 0 °C and TMPMgCl·LiCl (1.23 mL, 1.50 mmol, 3.00 eq, 1.22 M in THF) was added. Stirring for two hours at 0 °C was followed by flushing with oxygen and stirring for another 24 hours, while the mixture was allowed to warm slowly to 25 °C. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 6:1 v:v) afforded **3-CO_2Me** (86.7 mg, 348 µmol, 70%) as a colorless solid. Single crystals suitable for X-ray analysis were grown from methanol solution by slow solvent evaporation. Data for **3-CO_2Me**: R_f = 0.29 (SiO_2, CH:EA 6:1 v:v). Mp.: 102 – 104 °C. ^{1}H-NMR (360 MHz, $CDCl_3$): δ = 12.26 (s, 1H, O*H*), 7.69 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H–5), 7.66 (d, $^4J_{HH}$ = 1.6 Hz, 1H, H–2), 7.52 (dd, $^3J_{HH}$ = 8.1 Hz, $^4J_{HH}$ = 1.6 Hz, 1H, H–6), 4.13 (s, 2H, CH_2), 3.92 (s, 3H, CH_3), 1.41 (s, 6H, C(CH_3)$_2$) ppm. ^{13}C{^{1}H}-NMR (91 MHz, $CDCl_3$): δ = 166.5 (*C*=O), 163.0 (*C*=N), 159.7 (C–3), 134.2 (C–1), 128.0 (C–5), 119.4 (C–6), 117.9 (C–2), 114.5 (C–4), 78.6 (CH_2), 67.4 (*C*(CH$_3$)$_2$), 52.4 (*C*H$_3$), 28.5 (2x, C(*C*H$_3$)$_2$) ppm. IR (ATR, neat): ν = 2973 (w), 1711 (s), 1621 (m), 1574 (m), 1506 (m), 1481 (w), 1465 (w), 1449 (m), 1435 (m), 1404 (m), 1380 (m), 1370 (m), 1362 (m), 1330 (w), 1306 (s), 1241 (m), 1220 (s), 1209 (s), 1190 (s), 1100 (s), 1062 (s), 984 (m), 953 (m), 946 (m), 928 (m), 902 (m), 893 (m), 869 (m), 827 (s), 795 (s), 771 (s), 746 (s), 685 (s) cm^{-1}. MS (APCI): m/z = 250.2 [$C_{13}H_{15}NO_4$+H]$^+$. HRMS (EI, 70 eV) m/z: [M]$^{+\cdot}$ calcd for [$C_{13}H_{15}NO_4^{+\cdot}$]: 249.0996; Found: 249.0995. The analytical data are in accordance with the literature.[15b]



3-NO_2

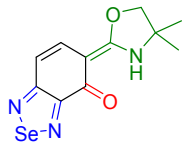
*2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-5-nitrophenol (**3-NO_2**).* A slightly modified literature procedure was used.[25] A heat gun-dried and nitrogen-flushed *Schlenk*-tube was charged with **3** (62.6 mg, 250 µmol, 1.00 eq), anhydrous CH_2Cl_2 (2.50 mL, 0.1 M) was added and the yellow solution was cooled to –78 °C. BBr_3 (81.4 mg, 325 µL, 325 µmol, 1.30 eq, 1.0 M in CH_2Cl_2) was added *via* syringe pump (0.1 mL/min) through a rubber septum to the cooled solution. With every drop the mixture turned intensively red whereupon the color immediately disappeared. The yellow mixture was stirred for one hour at –78 °C and then for additional four hours while it was allowed to warm slowly to –30 °C. The cooling bath was removed and CH_2Cl_2

(5 mL) and saturated NH_4Cl solution (5 mL) were added. The phases were separated and the aqueous phase extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure on a rotary evaporator. Purification by column chromatography (CH:EA 10:1 v:v) afforded **3-NO$_2$** (38.5 mg, 163 µmol, 65%) as a pale yellow solid. Single crystals suitable for X-ray analysis were grown from CH_2Cl_2 solution by slow solvent evaporation. Data for **3-NO$_2$**: R_f = 0.20 (SiO_2, CH:EA 10:1 v:v). Mp.: 123 – 125 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 12.59 (s, 1H, O*H*), 7.83 (d, $^4J_{HH}$ = 2.2 Hz, 1H, H–6), 7.78 (d, $^3J_{HH}$ = 8.6 Hz, 1H, H–3), 7.70 (dd, $^3J_{HH}$ = 8.6 Hz, $^4J_{HH}$ = 2.2 Hz, 1H, H–4), 4.17 (s, 2H, CH_2), 1.43 (s, 6H, C(CH_3)$_2$) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 162.6 (*C*=N), 160.5 (C–1), 150.8 (C–5), 129.0 (C–3), 116.2 (C–2), 113.3 (C–4), 112.1 (C–6), 78.9 (*C*H$_2$), 67.8 (*C*(CH$_3$)$_2$), 28.5 (2x, C(*C*H$_3$)$_2$) ppm. IR (ATR, neat): ν = 2977 (w), 2930 (w), 2587 (br), 1644 (m), 1598 (w), 1520 (s), 1463 (w), 1414 (w), 1382 (w), 1368 (m), 1349 (m), 1330 (m), 1294 (s), 1262 (m), 1234 (m), 1207 (m), 1183 (m), 1130 (m), 1084 (m), 1060 (s), 962 (m), 943 (m), 886 (m), 834 (w), 823 (m), 812 (s), 758 (m), 732 (s), 689 (m), 679 (s) cm^{-1}. MS (APCI): m/z = 237.1 [$C_{11}H_{12}N_2O_4$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{11}H_{13}N_2O_4^+$]: 237.0870; Found: 237.0869. [M+Na]$^+$ calcd for [$C_{11}H_{12}N_2NaO_4^+$]: 259.0689; Found: 259.0690.



3,4-NSN

5-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)benzo[c][1,2,5]thiadiazol-4-ol ***(3,4-NSN)****.* Prepared according to **GP 3** from **7** (93.3 mg, 400 µmol, 1.00 eq) in THF (1.00 mL, 0.4 M) and TMPMgCl·LiCl (968 µL, 1.20 mmol, 3.00 eq, 1.24 M in THF). Stirring for three hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (6 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 2:1 v:v) afforded **3,4-NSN** (71.1 mg, 285 µmol, 71%) as a yellow solid. Single crystals suitable for X-ray analysis were grown from CH_2Cl_2 solution by slow solvent evaporation. Data for **3,4-NSN**: R_f = 0.11 (SiO_2, CH:EA 2:1 v:v). R_f = 0.19 (SiO_2, CH:EA 1:1 v:v). Mp.: 245 – 247 °C. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 12.97 (s, 1H, N*H*), 7.62 (d, $^3J_{HH}$ = 9.2 Hz, 1H, H–3), 7.12 (d, $^3J_{HH}$ = 9.2 Hz, 1H, H–4), 4.32 (s, 2H, CH_2), 1.51 (s, 6H, C(CH_3)$_2$) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 166.9 (*C*–N), 164.4 (*C*=O), 159.3 (C–5), 150.9 (C–6), 128.4 (C–3), 108.5 (C–4), 101.0 (C–2), 79.8 (*C*H$_2$), 63.5 (*C*(CH$_3$)$_2$), 28.0 (2x, C(*C*H$_3$)$_2$) ppm. IR (ATR, neat): ν = 2974 (w), 2930 (w), 2873 (w), 2628 (br), 1636 (s), 1578 (m), 1528 (s), 1480 (s), 1461 (s), 1381 (m), 1361 (m), 1352 (m), 1305 (m), 1259 (m), 1234 (m), 1201 (m), 1169 (m), 1109 (m), 1092 (s), 992 (s), 926 (m), 875 (m), 836 (m), 819 (s), 804 (s), 774 (m), 714 (s), 672 (s) cm^{-1}. MS (APCI): m/z = 250.1 [$C_{11}H_{11}N_3O_2S$+H]$^+$. HRMS (ESI) m/z: [M+H]$^+$ calcd for [$C_{11}H_{12}N_3O_2S^+$]: 250.0645; Found: 250.0645. [M+Na]$^+$ calcd for [$C_{11}H_{11}N_3NaO_2S^+$]: 272.0464; Found: 272.0463. [2M+Na]$^+$ calcd for [$C_{22}H_{22}N_6NaO_4S_2^+$]: 521.1036; Found: 521.1034.



3,4-NSeN

5-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)benzo[c][1,2,5]selenadiazol-4-ol ***(3,4-NSeN)****.* Prepared according to **GP 3** from **9** (112 mg, 400 µmol, 1.00 eq) in THF (1.00 mL, 0.4 M) and TMPMgCl·LiCl (968 µL, 1.20 mmol, 3.00 eq, 1.24 M in THF). Stirring for three hours was followed by flushing with oxygen and stirring for another 24 hours. Saturated NH_4Cl solution (10 mL), water (10 mL) and CH_2Cl_2 (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (6 × 20 mL). Purification by flash column chromatography (SiO_2, CH:EA 1:2 v:v) afforded **3,4-NSeN** (39.7 mg, 134 µmol, 34%) as a red solid. Single crystals suitable for X-ray analysis were grown from CH_2Cl_2 solution by slow solvent evaporation. Data for **3,4-NSeN**: R_f = 0.04 (SiO_2, CH:EA 1:1 v:v). R_f = 0.07 (SiO_2, CH:EA 1:2 v:v). Mp.: 222 °C decomp. ^{1}H-NMR (601 MHz, $CDCl_3$): δ = 12.32 (s, 1H, N–*H*), 7.50 (d, $^3J_{HH}$ = 9.4 Hz, 1H, H–3), 6.90 (d, $^3J_{HH}$ = 9.5 Hz, 1H, H–4), 4.35 (s, 2H, CH_2), 1.53 (s, 6H, C(CH_3)$_2$) ppm. ^{13}C{^{1}H}-NMR (151 MHz, $CDCl_3$): δ = 169.2 (*C*=O), 167.6 (*C*–N), 164.3 (C–5), 158.1 (C–6), 128.6 (C–3), 110.1 (C–4), 98.1 (C–2), 80.1 (*C*H$_2$), 62.2 (*C*(CH$_3$)$_2$), 27.8 (2x, C(*C*H$_3$)$_2$) ppm. ^{77}Se-NMR (115 MHz, $CDCl_3$): δ = 1507.2 (s) ppm. IR (ATR, neat): ν = 2971 (w), 2926 (w), 2871 (w), 2628 (br), 1634 (m), 1576 (m), 1533 (m), 1478 (m), 1460 (m), 1381 (m), 1362 (m), 1308 (m), 1260 (m), 1232 (m), 1199 (m), 1108 (m), 1090 (m), 984 (s), 919 (m), 805 (m), 770 (m), 758 (m), 738 (m), 711 (s), 656 (s) cm^{-1}. MS (APCI): m/z = 298.0 [$C_{11}H_{11}N_3O_2{}^{80}$Se+H]$^+$. HRMS (ESI) m/z: [M+Na]$^+$ calcd for [$C_{11}H_{11}N_3NaO_2{}^{80}Se^+$]: 319.9909; Found: 319.9907. [2M+Na]$^+$ calcd for [$C_{22}H_{22}N_6NaO_4{}^{80}Se_2^+$]: 616.9930; Found: 616.9925.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Photophysical spectra for the target molecules, crystallographic coordinates and structural factors for **all-H**, **3-Py**, **3,4-OCO**, **3-CO$_2$Me**, **3-NO$_2$**, **3,4-NSN** and **3,4-NSeN** along with ^{1}H and ^{13}C NMR spectra for all compounds and ^{77}Se NMR for selenium containing compounds
Complete optimization table, detailed experimental procedures, characterization data, X-ray crystallographic data, photophysical properties and copies of NMR spectra

CCDC 1908036, 1908037 and 2070432–2070436 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via

www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: nachtsheim@uni-bremen.de
*E-mail: tstauch@uni-bremen.de
*E-mail: nadja.bigall@pci.uni-hannover.de

Notes

The authors declare no competing financial interest.

ACKNOWLEDGEMENTS

N.-C. B. and P. R. thank the DFG for partial funding under Germany's Excellence Strategy within the Cluster of Excellence PhoenixD (EXC 2122, Project ID 390833453) and the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement no. 714429).

REFERENCES

(1) a) Yersin, H. *Highly Efficient OLEDs with Phosphorescent Materials;* Wiley-VCH, Hoboken, 2008; b) Müllen, K.; Scherf, U. *Organic Light-Emitting Devices*: Synthesis, Properties, and Applications; Wiley-VCH, Weinheim, 2006;

(2) a) Sedgwick, A. C.; Wu, L.; Han, H.-H.; Bull, S. D.; He, X.-P.; James, T. D.; Sessler, J. L.; Tang, B. Z.; Tian, H.; Yoon, J. Excited-state intramolecular proton-transfer (ESIPT) based fluorescence sensors and imaging agents. *Chem. Soc. Rev.* **2018**, *47*, 8842–8880; b) Padalkar, V. S.; Seki, S. Excited-state intramolecular proton-transfer (ESIPT)-inspired solid state emitters. *Chem. Soc. Rev.* **2016**, *45*, 169–202; c) Demchenko, A. P.; Tang, K.-C.; Chou, P.-T. Excited-state proton coupled charge transfer modulated by molecular structure and media polarization. *Chem. Soc. Rev.* **2013**, *42*, 1379–1408; d) Kwon, J. E.; Park, S. Y. Advanced organic optoelectronic materials. *Adv. Mater.* **2011**, *23*, 3615–3642;

(3) Barbara, P. F.; Walsh, P. K.; Brus, L. E. Picosecond kinetic and vibrationally resolved spectroscopic studies of intramolecular excited-state hydrogen atom transfer. *J. Phys. Chem.* **1989**, *93*, 29–34.

(4) a) Sakai, K.; Tsuchiya, S.; Kikuchi, T.; Akutagawa, T. An ESIPT fluorophore with a switchable intramolecular hydrogen bond for applications in solid-state fluorochromism and white light generation. *J. Mater. Chem. C* **2016**, *4*, 2011–2016; b) Benelhadj, K.; Muzuzu, W.; Massue, J.; Retailleau, P.; Charaf-Eddin, A.; Laurent, A. D.; Jacquemin, D.; Ulrich, G.; Ziessel, R. White emitters by tuning the excited-state intramolecular proton-transfer fluorescence emission in 2-(2'-hydroxybenzofuran)benzoxazole dyes. *Chem. Eur. J.* **2014**, *20*, 12843–12857; c) Tang, K.-C.; Chang, M.-J.; Lin, T.-Y.; Pan, H.-A.; Fang, T.-C.; Chen, K.-Y.; Hung, W.-Y.; Hsu, Y.-H.; Chou, P.-T. Fine tuning the energetics of excited-state intramolecular proton transfer (ESIPT). *J. Am. Chem. Soc.* **2011**, *133*, 17738–17745; d) Park, S.; Kwon, J. E.; Kim, S. H.; Seo, J.; Chung, K.; Park, S.-Y.; Jang, D.-J.; Milián Medina, B.; Gierschner, J.; Park, S. Y. A white-light-emitting molecule. *J. Am. Chem. Soc.* **2009**, *131*, 14043–14049;

(5) a) Parthiban, C.; M., P.; L., V. K. R.; Sen, D.; S., M. S.; Singh, N. D. P. Visible-Light -Triggered Fluorescent Organic Nanoparticles for Chemo-Photodynamic Therapy with Real-Time Cellular Imaging. *ACS Appl. Nano Mater.* **2018**, *1*, 6281–6288; b) Biswas, S.; Das, J.; Barman, S.; Rao Pinninti, B.; K Maiti, T.; Singh, N. D. P. Environment Activatable Nanoprodrug. *ACS Appl. Mater. Interfaces* **2017**, *9*, 28180–28184; c) Chen, Q.; Jia, C.; Zhang, Y.; Du, W.; Wang, Y.; Huang, Y.; Yang, Q.; Zhang, Q. A novel fluorophore based on the coupling of AIE and ESIPT mechanisms and its application in biothiol imaging. *J. Mater. Chem. B* **2017**, *5*, 7736–7742; d) Kobayashi, H.; Ogawa, M.; Alford, R.; Choyke, P. L.; Urano, Y. New strategies for fluorescent probe design in medical diagnostic imaging. *Chem. Rev.* **2010**, *110*, 2620–2640;

(6) a) Liu, B.; Wang, J.; Zhang, G.; Bai, R.; Pang, Y. Flavone-based ESIPT ratiometric chemodosimeter for detection of cysteine in living cells. *ACS Appl. Mater. Interfaces* **2014**, *6*, 4402–4407; b) Wang, J.; Li, Y.; Patel, N. G.; Zhang, G.; Zhou, D.; Pang, Y. A single molecular probe for multi-analyte (Cr^{3+}, Al^{3+} and Fe^{3+}) detection in aqueous medium and its biological application. *Chem. Commun.* **2014**, *50*, 12258–12261; c) Yang, X.; Guo, Y.; Strongin, R. M. Conjugate addition/cyclization sequence enables selective and simultaneous fluorescence detection of cysteine and homocysteine. *Angew. Chem. Int. Ed.* **2011**, *50*, 10690–10693; d) Thomas, S. W.; Joly, G. D.; Swager, T. M. Chemical sensors based on amplifying fluorescent conjugated polymers. *Chem. Rev.* **2007**, *107*, 1339–1386;

(7) a) Mamada, M.; Inada, K.; Komino, T.; Potscavage, W. J.; Nakanotani, H.; Adachi, C. Highly Efficient Thermally Activated Delayed Fluorescence from an Excited-State Intramolecular Proton Transfer System. *ACS Cent. Sci.* **2017**, *3*, 769–777; b) Yao, D.; Zhao, S.; Guo, J.; Zhang, Z.; Zhang, H.; Liu, Y.; Wang, Y. Hydroxyphenyl-benzothiazole based full color organic emitting materials generated by facile molecular modification. *J. Mater. Chem.* **2011**, *21*, 3568; c) Tarkka, R. M.; Zhang, X.; Jenekhe, S. A. Electrically Generated Intramolecular Proton Transfer: Electroluminescence and Stimulated Emission from Polymers. *J. Am. Chem. Soc.* **1996**, *118*, 9438–9439;

(8) a) Park, S.; Kwon, J. E.; Park, S. Y. Strategic emission color tuning of highly fluorescent imidazole-based excited-state intramolecular proton transfer molecules. *Phys. Chem. Chem. Phys.* **2012**, *14*, 8878–8884; b) Chuang, W.-T.; Hsieh, C.-C.; Lai, C.-H.; Lai, C.-H.; Shih, C.-W.; Chen, K.-Y.; Hung, W.-Y.; Hsu, Y.-H.; Chou, P.-T. Excited-state intramolecular proton transfer molecules bearing o-hydroxy analogues of green fluorescent protein chromophore. *J. Org. Chem.* **2011**, *76*, 8189–8202;

(9) a) Mutai, T.; Shono, H.; Shigemitsu, Y.; Araki, K. Three-color polymorph-dependent luminescence. *CrystEngComm* **2014**, *16*, 3890–3895; b) Mutai, T.; Tomoda, H.; Ohkawa, T.; Yabe, Y.; Araki, K. Switching of polymorph-dependent ESIPT luminescence of an imidazo1,2-apyridine derivative. *Angew. Chem. Int. Ed.* **2008**, *47*, 9522–9524;

(10) a) Liu, H.; Cheng, X.; Zhang, H.; Wang, Y.; Zhang, H.; Yamaguchi, S. ESIPT-active organic compounds with white luminescence based on crystallization-induced keto emission (CIKE). *Chem. Commun.* **2017**, *53*, 7832–7835;

b) Park, S.; Kwon, J. E.; Park, S.-Y.; Kwon, O.-H.; Kim, J. K.; Yoon, S.-J.; Chung, J. W.; Whang, D. R.; Park, S. K.; Lee, D. K.; Jang, D.-J.; Gierschner, J.; Park, S. Y. Crystallization-Induced Emission Enhancement and Amplified Spontaneous Emission from a CF 3 -Containing Excited-State Intramolecular-Proton-Transfer Molecule. *Adv. Opt. Mater.* **2017**, *5*, 1700353;

(11) Shimizu, M.; Hiyama, T. Organic fluorophores exhibiting highly efficient photoluminescence in the solid state. *Chem. Asian. J.* **2010**, *5*, 1516–1531.

(12) Shimizu, M.; Takeda, Y.; Higashi, M.; Hiyama, T. 1,4-Bis(alkenyl)-2,5-dipiperidinobenzenes: minimal fluorophores exhibiting highly efficient emission in the solid state. *Angew. Chem. Int. Ed.* **2009**, *48*, 3653–3656.

(13) Beppu, T.; Tomiguchi, K.; Masuhara, A.; Pu, Y.-J.; Katagiri, H. Single Benzene Green Fluorophore. *Angew. Chem. Int. Ed.* **2015**, *54*, 7332–7335.

(14) Tang, B.; Liu, H.; Li, F.; Wang, Y.; Zhang, H. Single-benzene solid emitters with lasing properties based on aggregation-induced emissions. *Chem. Commun.* **2016**, *52*, 6577–6580.

(15) a) Göbel, D.; Friedrich, M.; Lork, E.; Nachtsheim, B. J. Clickable azide-functionalized bromoarylaldehydes – synthesis and photophysical characterization. *Beilstein J. Org. Chem.* **2020**, *16*, 1683–1692; b) Göbel, D.; Clamor, N.; Lork, E.; Nachtsheim, B. J. Aerobic C(sp2)-H Hydroxylations of 2-Aryloxazolines. *Org. Lett.* **2019**, *21*, 5373–5377; c) Göbel, D.; Clamor, N.; Nachtsheim, B. J. Regioselective ortho-functionalization of bromofluorenecarbaldehydes using TMPMgCl · LiCl. *Org. Biomol. Chem.* **2018**, *16*, 4071–4075;

(16) Göbel, D.; Duvinage, D.; Stauch, T.; Nachtsheim, B. J. Nitrile-substituted 2-(oxazolinyl)-phenols: minimalistic excited-state intramolecular proton transfer (ESIPT)-based fluorophores. *J. Mater. Chem. C* **2020**, *8*, 9213–9225.

(17) Göbel, D.; Rusch, P.; Duvinage, D.; Bigall, N. C.; Nachtsheim, B. J. Emission color-tunable oxazol(in)yl-substituted excited-state intramolecular proton transfer (ESIPT)-based luminophores. *Chem. Commun.* **2020**, *56*, 15430–15433.

(18) a) Reuman, M.; Meyers, A. I. The synthetic utility of oxazolines in aromatic substitution. *Tetrahedron* **1985**, *41*, 837–860; b) Meyers, A. I.; Mihelich, E. D. The Synthetic Utility of 2-Oxazolines. *Angew. Chem. Int. Ed.* **1976**, *15*, 270–281; c) Gschwend, H. W.; Hamdan, A. Ortho-lithiation of aryloxazolines. *J. Org. Chem.* **1975**, *40*, 2008–2009; d) Meyers, A. I.; Mihelich, E. D. Oxazolines. XVII. Regioselective metalation of 2-aryl oxazolines. Route to polydeuteriobenzoic acids. *J. Org. Chem.* **1975**, *40*, 3158–3159;

(19) a) Shaaban, K. A.; Saunders, M. A.; Zhang, Y.; Tran, T.; Elshahawi, S. I.; Ponomareva, L. V.; Wang, X.; Zhang, J.; Copley, G. C.; Sunkara, M.; Kharel, M. K.; Morris, A. J.; Hower, J. C.; Tremblay, M. S.; Prendergast, M. A.; Thorson, J. S. Spoxazomicin D and Oxachelin C, Potent Neuroprotective Carboxamides from the Appalachian Coal Fire-Associated Isolate Streptomyces sp. RM-14-6. *J. Nat. Prod.* **2017**, *80*, 2–11; b) Liu, N.; Shang, F.; Xi, L.; Huang, Y. Tetroazolemycins A and B, two new oxazole-thiazole siderophores from deep-sea Streptomyces olivaceus FXJ8.012. *Mar. Drugs* **2013**, *11*, 1524–1533; c) Inahashi, Y.; Iwatsuki, M.; Ishiyama, A.; Namatame, M.; Nishihara-Tsukashima, A.; Matsumoto, A.; Hirose, T.; Sunazuka, T.; Yamada, H.; Otoguro, K.; Takahashi, Y.; Omura, S.; Shiomi, K. Spoxazomicins A-C, novel antitrypanosomal alkaloids produced by an endophytic actinomycete, Streptosporangium oxazolinicum K07-0460(T). *J. Antibiot.* **2011**, *64*, 303–307;

(20) Göbel, D.; Rusch, P.; Duvinage, D.; Stauch, T.; Bigall, N. C.; Nachtsheim, B. J. Substitution Effect on 2-(Oxazolinyl)-phenols: Emission Color-Tunable, Minimalistic Excited-State Intramolecular Proton Transfer (ESIPT)-based Luminophores. *ChemRxiv* **2021**.

(21) Schwekendiek, K.; Glorius, F. Efficient Oxidative Synthesis of 2-Oxazolines. *Synthesis* **2006**, *2006*, 2996–3002.

(22) Meyers, A. I.; Gabel, R.; Mihelich, E. D. Nucleophilic aromatic substitution on (o-methoxyaryl)oxazolines. A convenient synthesis of o-alkyl-, o-alkenyl-, and o-arylbenzoic acids. *J. Org. Chem.* **1978**, *43*, 1372–1379.

(23) a) Newman, S. G.; Lautens, M. The role of reversible oxidative addition in selective palladium(0)-catalyzed intramolecular cross-couplings of polyhalogenated substrates. *J. Am. Chem. Soc.* **2010**, *132*, 11416–11417; b) Colletti, S. L.; Halterman, R. L. Asymmetric synthesis and metalation of a binaphthylcyclopentadiene, a C2-symmetric chiral cyclopentadiene. *Organometallics* **1991**, *10*, 3438–3448;

(24) Armistead, D. M.; Badia, M. C.; Bemis, G. W.; Bethiel, R. S.; Frank, C. A.; Novak, P. M.; Ronkin, S. M.; Saunders, J. O. Urea derivatives as inhibitors of impdh enzyme. WO 9740028, 1997.

(25) Nocentini, A.; Carta, F.; Tanc, M.; Selleri, S.; Supuran, C. T.; Bazzicalupi, C.; Gratteri, P. Deciphering the Mechanism of Human Carbonic Anhydrases Inhibition with Sulfocoumarins. *Chem. Eur. J.* **2018**, *24*, 7840–7844.

(26) Mitra, R.; Das, S.; Shinde, S. V.; Sinha, S.; Somasundaram, K.; Samuelson, A. G. Anticancer activity of hydrogen-bond-stabilized half-sandwich Ru(II) complexes with heterocycles. *Chem. Eur. J.* **2012**, *18*, 12278–12291.

(27) Macé, Y.; Bony, E.; Delvaux, D.; Pinto, A.; Mathieu, V.; Kiss, R.; Feron, O.; Quetin-Leclercq, J.; Riant, O. Cytotoxic activities and metabolic studies of new combretastatin analogues. *Med. Chem. Res.* **2015**, *24*, 3143–3156.

(28) Briehn, C. A.; Weyermann, P.; Dervan, P. B. Alternative heterocycles for DNA recognition. *Chem. Eur. J.* **2003**, *9*, 2110–2122.

(29) Ekambaram, R.; Enkvist, E.; Manoharan, G. b.; Ugandi, M.; Kasari, M.; Viht, K.; Knapp, S.; Issinger, O.-G.; Uri, A. Benzoselenadiazole-based responsive long-lifetime photoluminescent probes for protein kinases. *Chem. Commun.* **2014**, *50*, 4096–4098.

(30) a) Rakitin, O. A. Recent Developments in the Synthesis of 1,2,5-Thiadiazoles and 2,1,3-Benzothiadiazoles. *Synthesis* **2019**, *51*, 4338–4347; b) Konstantinova, L. S.; Knyazeva, E. A.; Rakitin, O. A. Direct Exchange of Oxygen and Selenium Atoms in the 1,2,5-Oxadiazoles and 1,2,5-Selenadiazoles by Action of Sulfur Monochloride. *Molecules* **2015**, *20*, 14522–14532; c) Smith, W. T.; Chen, W.-Y.; Linfield, M. Chloroalkyl-N-sulfinylamines. *J. Med. Chem.* **1965**, *8*, 718–719;

(31) Berens, H. R. V.; Mohammad, K.; Reiss, G. J.; Müller, T. J. J. 3,9-Disubstituted Bis[1]benzothieno[3,2-b;2',3'-e][1,4]thiazines with Low Oxidation Potentials and Enhanced Emission. *J. Org. Chem.* **2021**, *86*, 8000–8014.

(32) a) Kothavale, S.; Sekar, N. A New Series of Highly Fluorescent Blue-Green Emitting, Imidazole-Based ICT-ESIPT Compounds. *ChemistrySelect* **2017**, *2*, 7691–7700; b) Panja, S. K.; Dwivedi, N.; Saha, S. Tuning the intramolecular charge transfer (ICT) process in push–pull systems. *RSC Adv.* **2016**, *6*, 105786–105794;

(33) Lee, D. R.; Lee, K. H.; Shao, W.; Kim, C. L.; Kim, J.; Lee, J. Y. Heavy Atom Effect of Selenium for Metal-Free Phosphorescent Light-Emitting Diodes. *Chem. Mater.* **2020**, *32*, 2583–2592.

(34) Zhang, Y.; Yang, H.; Ma, H.; Bian, G.; Zang, Q.; Sun, J.; Zhang, C.; An, Z.; Wong, W.-Y. Excitation Wavelength Dependent Fluorescence of an ESIPT Triazole Derivative for Amine Sensing and Anti-Counterfeiting Applications. *Angew. Chem. Int. Ed.* **2019**, *58*, 8773–8778.

(35) a) Zhang, T.; Peng, Q.; Quan, C.; Nie, H.; Niu, Y.; Xie, Y.; Zhao, Z.; Tang, B. Z.; Shuai, Z. Using the isotope effect to probe an aggregation induced emission mechanism: theoretical prediction and experimental validation. *Chem. Sci.* **2016**, *7*, 5573–5580; b) Wright, M. R.; Frosch, R. P.; Robinson, G. W. Phosphorescence Lifetime of Benzene. An Intermolecular Heavy-Atom Effect, a Deuterium Effect, and a Temperature Effect. *J. Chem. Phys.* **1960**, *33*, 934–935;

(36) a) Hestand, N. J.; Spano, F. C. Expanded Theory of H- and J-Molecular Aggregates. *Chem. Rev.* **2018**, *118*, 7069–7163; b) Gierschner, J.; Lüer, L.; Milián-Medina, B.; Oelkrug, D.; Egelhaaf, H.-J. Highly Emissive H-Aggregates or Aggregation-Induced Emission Quenching? *J. Phys. Chem. Lett.* **2013**, *4*, 2686–2697; c) Yoon, S.-J.; Park, S. Polymorphic and mechanochromic luminescence modulation in the highly emissive dicyanodistyrylbenzene crystal. *J. Mater. Chem.* **2011**, *21*, 8338; d) Yoon, S.-J.; Chung, J. W.; Gierschner, J.; Kim, K. S.; Choi, M.-G.; Kim, D.; Park, S. Y. Multistimuli two-color luminescence switching via different slip-stacking of highly fluorescent molecular sheets. *J. Am. Chem. Soc.* **2010**, *132*, 13675–13683; e) Kabe, R.; Nakanotani, H.; Sakanoue, T.; Yahiro, M.; Adachi, C. Effect of Molecular Morphology on Amplified Spontaneous Emission of Bis-Styrylbenzene Derivatives. *Adv. Mater.* **2009**, *21*, 4034–4038;

(37) a) NBO 5.0. Glendening, E. D.; Badenhoop, J. K.; Reed, A. E.; Carpenter, J. E.; Bohmann, J. A.; Morales, C. M.; Weinhold, F.; Theoretical Chemistry Institute, University of Wisconsin, Madison, WI **2001**; b) Reed, A. E.; Curtiss, L. A.; Weinhold, F. Intermolecular interactions from a natural bond orbital, donor-acceptor viewpoint. *Chem. Rev.* **1988**, *88*, 899–926;

(38) Perdew, J. P.; Burke K.; Ernzerhof M. Generalized Gradient Approximation Made Simple. *Phys. Rev. Lett.* **1996**, *77*, 3865–3868.

(39) Dunning, T. H. Gaussian basis sets for use in correlated molecular calculations. I. The atoms boron through neon and hydrogen. *J. Chem. Phys.* **1989**, *90*, 1007–1023.

(40) Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals,* 6th ed.; Elsevier/BH, Oxford, 2009.

(41) a) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2. *J. Appl. Cryst.* **2009**, *42*, 339–341; b) Sheldrick, G. M. A short history of SHELX. *Acta Cryst. A* **2008**, *64*, 112–122;

(42) Shao, Y.; Gan, Z.; Epifanovsky, E.; Gilbert, A. T.; Wormit, M.; Kussmann, J.; Lange, A. W.; Behn, A.; Deng, J.; Feng, X.; Ghosh, D.; Goldey, M.; Horn, P. R.; Jacobson, L. D.; Kaliman, I.; Khaliullin, R. Z.; Kuś, T.; Landau, A.; Liu, J.; Proynov, E. I.; Rhee, Y. M.; Richard, R. M.; Rohrdanz, M. A.; Steele, R. P.; Sundstrom, E. J.; Woodcock, H. L.; Zimmerman, P. M.; Zuev, D.; Albrecht, B.; Alguire, E.; Austin, B.; Beran, G. J. O.; Bernard, Y. A.; Berquist, E.; Brandhorst, K.; Bravaya, K. B.; Brown, S. T.; Casanova, D.; Chang, C.-M.; Chen, Y.; Chien, S. H.; Closser, K. D.; Crittenden, D. L.; Diedenhofen, M.; DiStasio, R. A.; Do, H.; Dutoi, A. D.; Edgar, R. G.; Fatehi, S.; Fusti-Molnar, L.; an Ghysels; Golubeva-Zadorozhnaya, A.; Gomes, J.; Hanson-Heine, M. W.; Harbach, P. H.; Hauser, A. W.; Hohenstein, E. G.; Holden, Z. C.; Jagau, T.-C.; Ji, H.; Kaduk, B.; Khistyaev, K.; Kim, J.; Kim, J.; King, R. A.; Klunzinger, P.; Kosenkov, D.; Kowalczyk, T.; Krauter, C. M.; Lao, K. U.; Laurent, A. D.; Lawler, K. V.; Levchenko, S. V.; Lin, C. Y.; Liu, F.; Livshits, E.; Lochan, R. C.; Luenser, A.; Manohar, P.; Manzer, S. F.; Mao, S.-P.; Mardirossian, N.; Marenich, A. V.; Maurer, S. A.; Mayhall, N. J.; Neuscamman, E.; Oana, C. M.; Olivares-Amaya, R.; O'Neill, D. P.; Parkhill, J. A.; Perrine, T. M.; Peverati, R.; Prociuk, A.; Rehn, D. R.; Rosta, E.; Russ, N. J.; Sharada, S. M.; Sharma, S.; Small, D. W.; Sodt, A.; Stein, T.; Stück, D.; Su, Y.-C.; Thom, A. J.; Tsuchimochi, T.; Vanovschi, V.; Vogt, L.; Vydrov, O.; Wang, T.; Watson, M. A.; Wenzel, J.; White, A.; Williams, C. F.; Yang, J.; Yeganeh, S.; Yost, S. R.; You, Z.-Q.; Zhang, I. Y.; Zhang, X.; Zhao, Y.; Brooks, B. R.; Chan, G. K.; Chipman, D. M.; Cramer, C. J.; Goddard, W. A.; Gordon, M. S.; Hehre, W. J.; Klamt, A.; Schaefer, H. F.; Schmidt, M. W.; Sherrill, C. D.; Truhlar, D. G.; Warshel, A.; Xu, X.; Aspuru-Guzik, A.; Baer, R.; Bell, A. T.; Besley, N. A.; Chai, J.-D.; Dreuw, A.; Dunietz, B. D.; Furlani, T. R.; Gwaltney, S. R.; Hsu, C.-P.; Jung, Y.; Kong, J.; Lambrecht, D. S.; Liang, W.; Ochsenfeld, C.; Rassolov, V. A.; Slipchenko, L. V.; Subotnik, J. E.; van Voorhis, T.; Herbert, J. M.; Krylov, A. I.; Gill, P. M.; Head-Gordon, M. Advances in molecular quantum chemistry contained in the Q-Chem 4 program package. *Mol. Phys.* **2015**, *113*, 184–215.

(43) Krasovskiy, A.; Knochel, P. A LiCl-mediated Br/Mg exchange reaction for the preparation of functionalized aryl- and heteroarylmagnesium compounds from organic bromides. *Angew. Chem. Int. Ed.* **2004**, *43*, 3333–3336.

(44) Bodroux, F. On the method of converting monochlorinated and monobrominated derivatives into monoiodated derivatives. *C. R. Chim.* **1902**, *135*, 1350–1351.

(45) Krasovskiy, A.; Krasovskaya, V.; Knochel, P. Mixed Mg/Li amides of the type R2NMgCl.LiCl as highly efficient bases for the regioselective generation of functionalized aryl and heteroaryl magnesium compounds. *Angew. Chem. Int. Ed.* **2006**, *45*, 2958–2961.

(46) Hammett, L. P.; Walden, G. H.; Edmonds, S. M. New Indicators for Oxidimetry. *J. Am. Chem. Soc.* **1934**, *56*, 1092–1094.

(47) Mosrin, M.; Knochel, P. TMPZnCl.LiCl. *Org. Lett.* **2009**, *11*, 1837–1840.

(48) Ackermann, L.; Barfüsser, S.; Kornhaass, C.; Kapdi, A. R. C-H bond arylations and benzylations on oxazol(in)es with a palladium catalyst of a secondary phosphine oxide. *Org. Lett.* **2011**, *13*, 3082–3085.

(49) Haas, D.; Hofmayer, M. S.; Bresser, T.; Knochel, P. Zincation of 4,4-dimethyloxazoline using TMPZnCl·LiCl. A new preparation of 2-aryloxazolines. *Chem. Commun.* **2015**, *51*, 6415–6417.

(50) Meyers, A. I.; Gabel, R. A. Substitutions of pyridines activated by oxazolines via nucleophilic additions for metalation-alkylation. *J. Org. Chem.* **1982**, *47*, 2633–2637.
(51) Houlihan, W. J.; Kelly, L.; Pankuch, J.; Koletar, J.; Brand, L.; Janowsky, A.; Kopajtic, T. A. Mazindol Analogues as Potential Inhibitors of the Cocaine Binding Site at the Dopamine Transporter. *J. Med. Chem.* **2002**, *45*, 4097–4109.
(52) Iyori, Y.; Takahashi, K.; Yamazaki, K.; Ano, Y.; Chatani, N. Nickel-catalyzed reductive defunctionalization of esters in the absence of an external reductant. *Chem. Commun.* **2019**, *55*, 13610–13613.
(53) Chen, M. H.; Davidson, J. G.; Freisler, J. T.; Iakovleva, E.; Magano, J. AN EFFICIENT AND SCALABLE SYNTHESIS OF METHYL 3-HYDROXYMETHYLBENZOATE. *Org. Prep. Proced. Int.* **2000**, *32*, 381–384.
(54) Schneider, C.; Bierwisch, A.; Koller, M.; Worek, F.; Kubik, S. Detoxification of VX and Other V-Type Nerve Agents in Water at 37 ° C and pH 7.4 by Substituted Sulfonatocalix4arenes. *Angew. Chem. Int. Ed.* **2016**, *55*, 12668–12672.
(55) Bozzini, L. A.; Santos, T. D.; Murie, V. E.; Mello, M. B. M. de; Vessecchi, R.; Clososki, G. C. Regioselective Functionalization of Ester-, Amide-, Carbonate-, and Carbamate-Substituted 2-Phenyl-2-oxazolines with Mixed Lithium-Magnesium Amides. *J. Org. Chem.* **2021**, *86*, 1204–1215.
(56) Timothy, H.; Gregory, B. S.; Zulan, P.; Scott, P. E.; Murali, D. T. G. Use of compounds having an amine nucleus in manufacture of a medicament useful for treating factor viia-associated conditions. WO 2004000214, 2003.
(57) Lee, K.; Goo, J.-I.; Jung, H. Y.; Kim, M.; Boovanahalli, S. K.; Park, H. R.; Kim, M.-O.; Kim, D.-H.; Lee, H. S.; Choi, Y. Discovery of a novel series of benzimidazole derivatives as diacylglycerol acyltransferase inhibitors. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 7456–7460.
(58) Aspinall, H. C.; Bacsa, J.; Beckingham, O. D.; Eden, E. G. B.; Greeves, N.; Hobbs, M. D.; Potjewyd, F.; Schmidtmann, M.; Thomas, C. D. Adding the right (or left) twist to tris-chelate complexes--coordination chemistry of chiral oxazolylphenolates with M3+ ions (M = Al or lanthanide). *Dalton Trans.* **2014**, *43*, 1434–1442.