New Access to Oxazolopyridines via Hydroxyamidine Derivatives; Application to Quinolines

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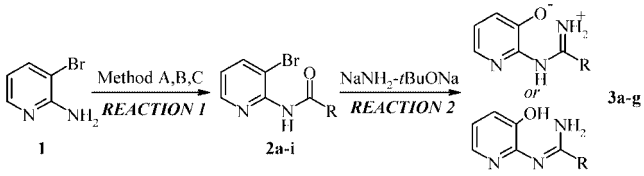
Abstract: Several 2-aryl and 2-heteroaryloxazolo[4,5-*b*]pyridines were synthesised in high yields from zwitterion or hydroxyamidine derivatives by heating in dimethylacetamide. These intermediates were generated via hetarynic reaction with the complex base $NaNH_2$–*t*-BuONa (5:2). The same reactions were possible with quinoline derivatives.

Key words: cyclizations, heterocycles, zwitterions, pyridines, quinolines

We previously showed that, in the presence of the complex base[1] $NaNH_2$–*t*-BuONa (2:1) (CB), 2-alkylamino-3-bromopyridines led to dipyridopyrazines[2] via intramolecular hetarynic cyclisations. In continuation of this program aiming at the hetarynic synthesis of polynuclear heterocycles, we investigated the behaviour of 2-aminopyridine derivatives **2** under analogous conditions. Curiously, in place of the usual hetarynic cyclisation, **2** led to an interesting while unexpected reaction, which we report herein. Moreover, a new synthesis of oxazolopyridines was also evidenced, as a consequence of this previously unknown reaction.

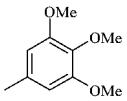
When non-enolisable amides were submitted to react with the CB, none of the expected dipyridopyrazines were detected. Nevertheless, zwitterions or hydroxyamidines **3a**–**g** were isolated in relation to the nature of the substituent R used in the reaction 2 (Scheme 1, Table 1).



Scheme 1

To get further insight into this reaction and determine its scope and limitations, we synthesised various representative amides **2** by three methods. The first one (Method A) involved the treatment of **1** with acyl chlorides in pyridine.[3] When acyl chlorides were not easily available we used a transfunctionalisation with esters in the presence of trimethylaluminium in toluene[4] (Method B). Finally, in Method C[5] the corresponding anhydride was preferred to acyl chloride for the preparation of **2h**.

Table 1 Synthesis of **3** from **1**

Compd	R	Reaction 1 Method[a] (Yield, %)[b]	Reaction 2 Time (h)	Yield of **3** (%) [b]
2a	*t*-Bu	A (80)	6	80
2b		B (65)	18	70
2c		A (88)	4	72
2d		A (81)	5	81
2e		A (91)	30	50
2f		A (89)	48	45
2g		B (89)	15	65
2h	Me[5]	C (98)	20	degradation
2i		A (80)	12	degradation

[a] Method A: RCOCl (1 equiv), pyridine, 1 h, 10 °C; Method B: RCOOEt (1 equiv), $AlMe_3$ (1 equiv), toluene, 9 h, reflux; Method C: Ac_2O, reflux, 12 h.
[b] Yield of pure, isolated products.

Concerning the formation of **3**, we required the usual 2 equivalents of CB to generate the hetarynes,[6] and an extra equivalent for deprotonation of the amides. The structure of these compounds was established by X-ray diffraction, when crystals were available (Figures 1, 2 and 3).

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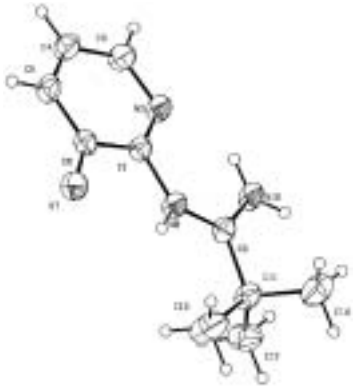


Figure 1 ORTEP diagram of compound **3a**

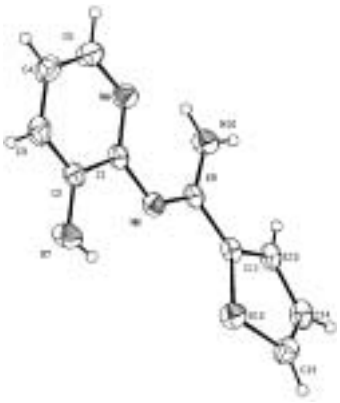


Figure 2 ORTEP diagram of compound **3f**

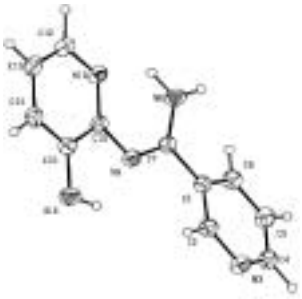


Figure 3 ORTEP diagram of compound **3g**

Thus, the zwitterionic form was obtained when R was non-aromatic, whereas only hydroxyamidines were obtained when R was aromatic. These results were enlightened by the determination of X-Ray structures for **3a**, **3f** and **3g** (Figures 1, 2, 3).

In **3a** two hydrogens located on N(10) were assigned from the study of the difference electron-density maps. The first one H(10A) is also bound to N(2), generating a pseudo cycle [H(10A)–N(2) is 2.01(2) Å] whereas H(10B) is bound to the O(7) of another molecule [$H(10B_I)$–$O(7_{II})$ is 1.80(2) Å]. Moreover, as depicted in Table 2, the two bond lengths C(9)–N(10) and C(9)–N(8) illustrate the sp^2 character of N(10) in **3a**. For **3f** (Figure 2), the corresponding bond lengths (Table 2) indicate that the hybridisation state of N(10) was intermediate between sp^2 and sp^3. Moreover, the two hydrogens H(10A) and H(10B) in **3f** are implicated in a chelate with N(6) and in a hydrogen bond with O(7) of another molecule, respectively. Similar results were observed for **3g** concerning the hybridisation state of N(8) and the bonding of the two hydrogens H(8A) and H(8B) (Table 2).

Additional arguments in favour of the proposed structures were obtained from the study of the pyridyl ring moiety. No hydrogen was located on O(7) in **3a**. Moreover, the bond length C(6)–O(7) = 1.296(3) Å is shorter than the corresponding C(2)–O(7) in **3f** or C(15)–O(16) in **3g**, which almost comparable to a usual phenolic bond. On the other hand, in **3a** O(7) participates in a chelate O(7)---H(8)–N(8), with O(7)–H(8) = 2.20 Å and and O(7)–N(8) = 2.621(2) Å (angle = 109.8°). Conversely, in **3f**, O(7) bound to H(7) established a chelate with N(8) with O(7)–N(8) = 2.664(4) Å and H(7)–N(8) = 2.19 Å (angle = 116.5°). The same phenomenon was found for O(16) in **3g**: O(16) bound to H(16) established a chelate with N(9) with O(16)–N(9) = 2.612(2) Å and H(16)–N(9) = 2.00 Å (angle 127°).

Finally, the three molecules are quite planar. As an example, the atoms of the pyridyl ring and of the lateral chain belong to a single plane. The maximum deviation to previous plane and the implicated atom are reported in Table 3.

Table 2 Selected Bond Lengths (Å)

	3a	**3f**	**3g**
C(9)–N(10)	1.302(2)	1.337(4)	
C(9)–N(8)	1.334(2)	1.316(4)	
C(7)–N(8)			1.341(2)
C(7)–N(9)			1.304(2)
C(6)–O(7)	1.296(3)		
C(2)–O(7)		1.358(4)	
C(15)–O(16)			1.360(2)

Table 3 Maximum Deviations to Previous Plane (Å) and Implicated Atom

Plane	**3a**	**3f**	**3g**
N(10), C(9), N(8), C(1), N(2)	+0.0248, C(9)		
N(10), C(9), N(8), C(1), N(6)		–0.0456, C(1)	
N(8), C(7), N(9), C(10), N(11)			+0.0012, C(7)

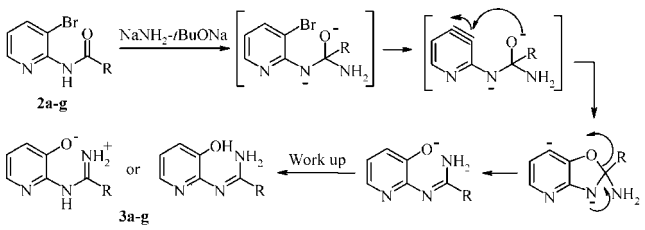
Interestingly, it appeared that zwitterions possessed a large and strong absorption band between 3500–2200 cm^{-1} while with hydroxyamidines a broad sharp absorption between 3500–3000 cm^{-1} was observed. A more de-

tailed IR study was made with diluted solutions of these different compounds: thus, an increasingly diluted solution of **3a** showed a decreasing of the 3400 cm^{-1} bond (intermolecular association) with simultaneous increasing of the 2961 cm^{-1} bond (intramolecular chelation), according to that which is expected for zwitterions. In contrast, with **3f** and **3g**, increasing dilution gave a decrease of the 3500–3300 cm^{-1} bond (intermolecular association) with simultaneous appearance of a narrow bond at 3590 cm^{-1} (free hydroxyl group).

As a consequence, when crystals could not be obtained (in spite of the fact that these compounds were solid) we used IR spectra to establish the structures.

Finally it appeared that such reactions were limited to non-enolisable amides: the presence of acidic protons on the R group, such as methyl and even cyclopropyl (Table 1, entry **2h** and **2i**), which is generally unfavourable to enolisation, only led to degradation and tars.

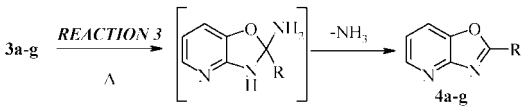
We have previously shown[6] that under the conditions presently used, dihydropyridines were formed. So the mechanism reported in Scheme 2 is suggested to account for the observed reactions. The protonation of the anionic intermediate formed during the cyclisation step must be due, as usual, to proton abstraction from the solvent and/or from the formed NH_3. This latter, as previously shown,[7] substantially remains in solution.



Scheme 2

At first we thought that oxazolopyridines such as **4** (vide infra) could be an intermediate in these reactions. However, when **4** were submitted to the action of the CB under the reaction conditions used to obtain **3**, these latter compounds were never formed. Thus we suggest that amide anion attacks **2** before the hetaryne formation.

Finally, we reasoned that it ought to be possible to prepare oxazolopyridines **4** (Scheme 3) from **3** by intramolecular cyclisation and NH_3 elimination. This methodology is a new access to oxazolopyridine derivatives.[8] We guessed that such reactions could be performed by classical warming or with the help of microwave irradiation.[9] According to our hypothesis, compounds **4** were obtained in very good yields as reported in Table 4. The cyclisations were performed in dimethylacetamide, a solvent usually used for microwave irradiations. The main interest of the latter is to greatly shorten the reaction time.



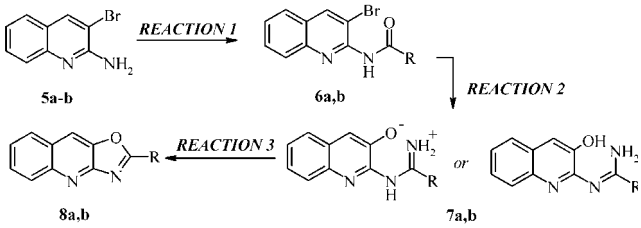
Scheme 3

Table 4 Synthesis of **4** from **3** by Warming or Microwave Irradiation

Compd	Time (h)	(Yield, %)[a]	Mp (°C)[d]	Molecular formular	MS (IS)
	Classical[b]	Microwave[c]			
4a	5 (88)	0.5 (88)	72–73	$C_{10}H_{12}N_2O$	177.0 (M + 1)
4b	12 (88)	3 (85)	82–83	$C_{10}H_{12}N_2O$	175.0 (M + 1)
4c	6 (83)	3 (85)	126–127[e]	$C_{12}H_8N_2O$	197.0 (M + 1)
4d	10 (85)	3 (74)	139–140	$C_{15}H_{14}N_2O_4$	287.0 (M + 1)
4e	15 (70)	7 (70)	oil	$C_{10}H_6N_2O_2$	187.0 (M + 1)
4f	12 (70)	4 (68)	142–143	$C_{10}H_6N_2OS$	203.0 (M + 1)
4g	10 (55)	3 (65)	oil	$C_{11}H_7N_3O$	198.0 (M + 1)

[a] Yield of pure isolated products.
[b] Warming: dimethylacetamide, 170 °C in an oil bath.
[c] Microwave irradiations dimethylacetamide, 165 °C under 150 W with a quartz reactor.
[d] Uncorrected.
[e] Lit.[8a] mp 127–127.5°C

As an extension of the reactions described above, we briefly studied the behaviour of two quinoline derivatives (Scheme 4).



Scheme 4

We chose *tert*-butyl and phenyl groups as examples of aliphatic and aromatic substituents, respectively. The compounds **7** were obtained from **5** under the same conditions as described before (Table 5).

Table 5 Synthesis of **7** from **5**

Compd	R	Reaction 1[a] Yield of **6** (%)	Reaction 2 Time (h)	Yield of **7** (%)
6a	*t*-Bu	81[b]	24	87[d]
6b		–[c]	24	53[e]

[a] Acyl chloride (1 equiv), pyridine, 1 h, 10 °C.
[b] Yield of pure, isolated product **6a** based on **5**.
[c] Partially soluble, sufficiantly pure to be directly used in the next reaction.
[d] Yield of pure, isolated product **7a** based on **6a**.
[e] Yield of pure, isolated product **7b** based on **5**.

Furthermore, as with pyridine derivatives, by classical heating or with microwave irradiation, the intramolecular cyclisation can be observed, and some oxazoles **8** have been isolated in good yields, as shown in Table 6.

Table 6 Synthesis of **8** from **7** by Warming or Microwave Irradiation

Compd	Time (h) (Yield, %)[d]		Mp (°C)[c]	Molecular formula	MS (IS)
	Classical [a]	Microwave [b]			
8a	5 (90)	1 h (94)	134–135	$C_{14}H_{14}N_2O$	227.0 (M + 1)
8b	5 (96)	1 h (85)	220–222	$C_{16}H_{10}N_2O$	247.0 (M + 1)

[a] Warming: dimethylacetamide, 170 °C in an oil bath.
[b] Microwave irradiations: dimethylacetamide, 165 °C under 150 W with a quartz reactor.
[c] Uncorrrected.
[d] Yields of pure, isolated product **8**.

Again under microwave irradiations the reaction times were significantly reduced without significantly affecting the yields.

In this work, non-enolisable amides were submitted to reaction in the presence of the complex base $NaNH_2$–*t*-BuONa, leading either to zwitterions or to hydroxyamidines. Furthermore, we have shown that zwitterions or hydroxyamidines **3** and **6** were good starting materials to generate corresponding oxazolo derivatives. Moreover, we have underlined the interest of using microwave irradiation to reduce reaction time and degradation.

Mps were determined on a Tottoli or a Kofler melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Bruker AM 400 or a Bruker 250 MHz spectrometer (Attached Proton Test Method, APT) or a Bruker instrument Avance DPX 250 at 250.131 and 62.9 MHz, respectively. Chemical Shifts (δ values) were reported in parts per million and coupling constants (*J* values) in Hz. TMS was the internal standard. Infrared spectra were recorded using NaCl films or KBr pellets techniques on a Perkin–Elmer 841 instrument. Elemental analyses were performed by CNRS laboratory (Vernaison). Mass spectra (MS) were recorded on a Perkin–Elmer mass spectrometer SCIEX API 300 by ion spray (IS). Mass HR spectra were recorded by 'peak matching' with a Finnigan MAT 95Q, BEQQ by the Institut de recherches Servier (Suresnes). TLC was performed with plates coated with Kieselgel G (Merck). The silica gel used for flash chromatography was Kieselgel of 0.04–0.063 mm particle size. Focused microwave irradiations were carried out with a Synthewave™ S402 Prolabo® microwave reactor (monomode system, 2450 MHz, 300 W) which has variable-speed rotation, visual control, irradiation monitored by PC computer, IR measurement and continuous feedback temperature control by PC.

Sodium amide powder was commercially available (Merck). Reagent-grade THF was first distilled from potassium hydroxide, then from sodium benzophenone ketyl and stored over sodium until used. Petroleum ether refers to the fraction with bp 40–60 ºC.

The 2-amino-3-bromopyridine (**1**) was prepared as described in the literature.[1c]

Amides 2a–g and 6a,b; General Procedure

Method A

Acyl chlorides (8.7 mmol) were added dropwise to a solution of 2-amino-3-bromopyridine (**1**) (1.5 g, 8.7 mmol) in pyridine (9 mL) at 10 °C. After 1 h at 10 °C, the reaction was poured into EtOAc (20 mL) and washed several times with H_2O (20 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The expected compounds were isolated after purification by chromatography (silica gel; EtOAc–hexane, 1:6 for pyridines; EtOAc–petroleum ether, 1:1 for quinolines).

Method B

Under argon, at r.t., a solution of $AlMe_3$ in toluene (2.0 M; 2.9 mL, 5.8 mmol) was added dropwise to a solution of 2-amino-3-bromopyridine (**1**) (1.0 g, 5.8 mmol) in toluene (30 mL). After 1 h at r.t., esters (5.8 mmol) were added to the previous mixture which was refluxed for 9 h. After cooling at 0 °C, the mixture was hydrolysed and filtered on Celite. The filtrate was extracted several times with CH_2Cl_2 and the combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. The expected compounds were isolated after purification by chromatography (silica gel; EtOAc–hexane, 1:6 for pyridines; EtOAc–petroleum ether, 1:1 for quinolines).

N-(3-Bromopyridin-2-yl)-2,2-dimethylpropanamide (2a)

Mp (Kofler) 136–137 °C (Lit.[10] mp 140–141 °C).

^1H NMR ($CDCl_3$): δ = 1.36 (s, 9 H, CH_3), 6.98 (dd, 1 H, *J* = 7.9, 4.9 Hz, H5), 7.87 (dd, 1 H, *J* = 7.9 Hz, *J* = 1.5 Hz, H4), 8.04 (br s, 1 H, NH), 8.44 (dd, 1 H, *J* = 4.9, 1.5 Hz, H6).

N-(3-Bromopyridin-2-yl)-1-methylcyclopropanacarboxamide (2b)

Mp (Tottoli) 71–72 °C.

IR (KBr): 1664, 3222–3015 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.71–0.75 (m, 2 H, CH_2), 1.37–1.41 (m, 2 H, CH_2), 1.53 (s, 3 H, CH_3), 6.98 (dd, 1 H, *J* = 7.9, 4.7 Hz, H5), 7.88 (dd, 1 H, *J* = 7.9, 1.2 Hz, H4), 8.24 (br s, 1 H, NH), 8.43 (dd, 1 H, *J* = 4.7, 1.2 Hz, H6).

^{13}C NMR ($CDCl_3$): δ = 17.2 (2 CH_2), 19.4 (CH_3), 20.3 (Cq), 111.8 (C3), 121.0 (C5), 141.1 (C4), 147.4 (C6), 148.4 (C2), 172.5 (C=O).

MS (IS): *m*/*z* = 255 (M + 1, ^{79}Br), 257 (M + 1, ^{81}Br).

Anal: Calcd for $C_{10}H_{11}N_2BrO$: C, 47.08; H, 4.35; N,10.98. Found: C, 47.46; H, 4.67; N, 11.20.

N-(3-Bromopyridin-2-yl)-2-benzamide (2c)

Mp (Tottoli) 89–90 °C.

IR (KBr): 1671, 3219 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.03 (dd, 1 H, *J* = 7.9, 4.8 Hz, H5), 7.46–7.61 (m, 3 H, H_{arom}), 7.92 (dd, 1 H, *J* = 7.9, 1.5 Hz, H4), 7.93–7.97 (m, 2 H, H_{arom}), 8.46 (dd, 1 H, *J* = 4.8,1.5 Hz, H6), 8.63 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 112.6 (C3), 121.5 (C5), 127.4 (2 C_{arom}), 128.8 (2 C_{arom}), 132.3 (C_{arom}), 134.1 (Cq), 141.4 (C4), 147.4 (C6), 148.7 (C2), 164.8 (C=O).

MS (IS): *m*/*z* = 277 (M + 1, ^{79}Br), 279 (M + 1, ^{81}Br).

Anal: Calcd for $C_{12}H_9N_2BrO$: C, 52.01; H, 3.27; N, 10.11. Found: C, 52.10; H, 3.32; N, 9.85.

***N*-(3-Bromopyridin-2-yl)-3,4,5-trimethoxybenzamide (2d)**
Mp (Tottoli) 154–155 °C.

IR (KBr): 1651, 3186 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.92 (s, 6 H, 2 CH_3), 3.93 (s, 3 H, CH_3), 7.05 (dd, 1 H, *J* = 7.9 Hz, *J* = 4.6 Hz, H5), 7.17 (br s, 2 H, H_{arom}), 7.94 (dd, 1 H, *J* = 7.9, 1.5 Hz, H4), 8.45–8.47 (m, 2 H, H6, NH).

^{13}C NMR ($CDCl_3$): δ = 56.3 (2 CH_3), 60.9 (CH_3), 104.9 (2 C_{arom}), 121.6 (C5), 129.4 (Cq), 141.5, 141.7, (C3, C4), 147.5 (C6), 148.7 (C2), 153.3 (2 C_q), 164.7 (C=O).

MS (IS): *m*/*z* = 367 (M + 1, ^{79}Br), 369 (M + 1, ^{81}Br).

Anal: Calcd for $C_{15}H_{15}N_2BrO_4$: C, 49.06; H, 4.12; N, 7.63. Found: C, 49.18; H, 4.12; N, 7.61.

***N*-(3-Bromopyridin-2-yl)-2-furamide (2e)**
Mp, gum.

IR (KBr): 1733, 3250 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 6.58 (dd, 1 H, *J* = 1.5, 3.3 Hz, =CH), 7.07 (dd, 1 H, *J* = 7.9, 4.8 Hz, H5), 7.28 (dd, 1 H, *J* = 3.3, 0.9 Hz, =CH), 7.56 (m, 1 H, =CH), 7.96 (dd, 1 H, *J* = 7.9, 1.5 Hz, H4), 8.47 (dd, 1 H, *J* = 4.8, 1.5 Hz, H6), 8.85 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 111.6 (C3), 112.6 (=CH), 116.2 (=CH), 121.2 (C5), 141.2 (C4), 144.6 (=CH), 147.2 (Cq), 147.3 (C6), 147.9 (C2), 154.8 (C=O).

MS (IS): *m*/*z* = 267 (M + 1, ^{79}Br), 269 (M + 1, ^{81}Br).

Anal: Calcd for $C_{10}H_7N_2BrO_2$: C, 44.97; H, 2.64; N, 10.49. Found: C, 44.88; H, 2.66; N, 10.32.

***N*-(3-Bromopyridin-2-yl)-2-thienamide (2f)**
Mp (Tottoli) 100–101 °C.

IR (KBr): 1662, 3258 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.03 (dd, 1 H, *J* = 8.2, 4.7 Hz, H5), 7.14 (dd, 1 H, *J* = 5.0, 3.8 Hz, =CH), 7.59 (dd, 1 H, *J* = 5.0, 1.1 Hz, =CH), 7.72 (dd, 1 H, *J* = 3.8, 1.1 Hz, =CH), 7.92 (dd, 1 H, *J* = 8.2, 1.3 Hz, H4), 8.44 (dd, 1 H, *J* = 4.7, 1.3 Hz, H6), 8.53 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 112.5 (C3), 121.5 (C5), 127.9 (=CH), 129.5 (=CH), 131.7 (=CH), 138.5 (Cq), 141.5 (C4), 147.4 (C6), 156,7 (C2), 157.8 (C=O).

MS (IS): *m*/*z* = 283 (M + 1, ^{79}Br), 285 (M + 1, ^{81}Br).

Anal: Calcd for $C_{10}H_7N_2BrOS$: C, 42.42; H, 2.49; N, 9.89. Found: C, 42.56; H, 2.54; N, 9.75.

***N*-(3-Bromopyridin-2-yl)nicotinamide (2g)**
Mp, gum.

IR (KBr): 1681, 3232 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.07 (dd, 1 H, *J* = 8.2, 4.8 Hz, H5), 7.43 (m, 1 H, H_{pyr}), 7.95 (dd, 1 H, *J* = 8.2, 1.8 Hz, H4), 8.26 (ddd, 1 H, *J* = 7.9, 1.8, 1.5 Hz, H_{pyr}), 8.42–8.43 (m, 1 H, H_{pyr}), 8.78 (dd, 1 H, *J* = 4.8, 1.8 Hz, H6), 8.99 (br s, 1 H, NH), 9.16 (d, 1 H, *J* = 1.5 Hz, H_{pyr}).

^{13}C NMR ($CDCl_3$): δ = 114.7 (C3), 122.3 (C5), 123.3 (C_{pyr}), 129.7 (Cq), 135.6 (Cq), 141.7 (C4), 147.1 (C_{pyr}), 148,4 (C_{pyr}), 152.3 (C6), 155,8 (C2), 164.0 (C=O).

MS (IS): *m*/*z* = 278 (M + 1, ^{79}Br), 280 (M + 1, ^{81}Br).

Anal: Calcd for $C_{11}H_8N_3BrO$: C, 47.51; H, 2.90; N, 15.11. Found: C, 47.72; H, 3.18; N, 14.71.

***N*-(3-Bromopyridin-2-yl)cyclopropanecarboxamide (2i)**
Mp (Tottoli) 136–137 °C.

IR (KBr): 1664, 3227 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.88–0.96 (m, 2 H, CH_2), 1.15–1.21 (m, 2 H, CH_2), 2.15–2.25 (m, 1 H, CH), 6.96 (dd, 1 H, *J* = 7.9, 4.7 Hz, H5), 7.87 (dd, 1 H, *J* = 7.9, 1.5 Hz, H4), 8.08 (br s, 1 H, NH), 8.36 (dd, 1 H, *J* = 4.7, 1.5 Hz, H6).

^{13}C NMR ($CDCl_3$): δ = 9.1 (2 CH_2), 14.7 (CH), 110.9 (C3), 120.7 (C5), 141.3 (C4), 147.0 (C6), 148.6 (C2), 173.0 (C=O).

MS (IS): *m*/*z* = 241 (M + 1, ^{79}Br), 243 (M + 1, ^{81}Br).

Anal: Calcd for $C_9H_9N_2BrO$: C, 44.84; H, 3.76; N, 11.62. Found: C, 45.10; H, 3.68; N, 11.60.

***N*-(3-Bromo-2-quinolyl)-2,2-dimethylpropanamide (6a)**
Mp (Tottoli) 133–135 °C.

IR (KBr): 1657, 3464 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.41 (9 H, s, 3 CH_3), 7.48 (1 H, ddd, *J* = 6.9, 1.1, 7.5 Hz, H6), 7.67 (1 H, dd, *J* = 7.5, 1.2 Hz, H5), 7.69 (1 H, ddd, *J* = 6.9, 1.2, 8.0 Hz, H7), 8.04 (1 H, dd, *J* = 1.1, 8.0 Hz, H8), 8.35 (1 H, s, H4), 8.41 (1 H, br s, NH).

^{13}C NMR ($CDCl_3$): δ = 27.7 (3 CH_3), 40.6 (Cq), 110.9 (C3), 126.5 (C6), 126.6 (C4′), 127.1 (C8), 128.9 (C5), 130.4 (C4), 140.5 (C7), 146.0 (C8′), 146.7 (C_2), 176.1 (C=O).

MS (IS): *m*/*z* = 307.0 (M + 1, ^{79}Br), 309.0 (M + 1, ^{81}Br).

Anal: Calcd for $C_{15}H_{15}N_2BrO$: C, 54.74; H, 4.92; N, 9.12. Found: C, 54.44; H, 5.02; N, 9.39.

***N*-(3-Bromo-2-quinolinyl)benzamide (6b)**
An analytical sample was obtained by purification on column chromatography, in order to obtain physical and spectroscopic data.

Mp (Tottoli) 173–174 °C.

IR (KBr): 1659, 3206 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.49–7.63 (5 H, m, H_{arom}), 7.69–7.74 (2 H, m, H6, H7), 7.99–8.07 (2 H, m, H8, H5), 8.41 (1 H, s, H4), 8.79 (1 H, br s, NH).

^{13}C NMR ($CDCl_3$): δ = 101.4 (C_3), 123.5 (C_6), 16.9 (C_4′), 127.3 (2 $C_{arom.}$), 128.9 (2 C_{arom}), 129.1 (C8), 130.7 (C_{arom}), 131.6 (C5), 132.4 (Cq), 133.5 (C4), 136.4 (C7), 144.4 (C8′), 155.1 (C2), 175.8 (C=O).

MS (IS): *m*/*z* = 327.0 (M + 1, ^{79}Br), 329.0 (M + 1, ^{81}Br).

Anal: Calcd for $C_{16}H_{11}N_2BrO$: C, 52.01; H, 3.27; N, 10.11. Found: C, 52.10; H, 3.32; N, 9.85.

Formation of Zwitterions or Hydroxyamidines 3a–g and 7a,b; General Procedure

Preparation of the Complex Base

Under argon, to a suspension of sodium amide (529 mg, 13.6 mmol) in THF (2 mL) was added fresh distilled *t*-BuOH (0.37 mL, 3.88 mmol) in THF (0.5 mL). The mixture was warmed to 45 °C over 2 h, then cooled to 0 °C with a vigorous stream of argon.

Reaction with The Complex Base

Under argon, a solution of the desired amides **2** or **6** (500 mg, 1.94 mmol) in THF (10 mL) was added dropwise on the complex base.

The mixture was stirred at r.t. and stopped when the starting material disappeared (TLC). The mixture was hydrolysed at 0 °C and extracted with EtOAc. The combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. After purification by chromatography (silica gel; EtOAc–hexane, 1:1), the expected compounds **3** or **7** were isolated.

2-[(1-Iminio-2,2-dimethylpropyl)amino]pyridin-3-olate (3a)
Mp (Tottoli) 113–114 °C.

IR (KBr): 1645, 2400–3400 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.32 (s, 9 H, 3 CH_3), 5.69 (sl, 2 H, NH_2), 6.81 (dd, 1 H, *J* = 7.9, 5.2 Hz, H5), 7.11 (dd, 1 H, *J* = 7.9, 1.5 Hz, H4), 7.75 (dd, 1 H, *J* = 5.2, 1.5 Hz, H6), 10.65 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 28.4 (3 CH_3), 37.9 (Cq), 118.1 (C5), 118.4 (C6), 135.8 (C4), 147.4 (C3), 151.2 (C2), 169.8 (C=N).

MS (IS): *m*/*z* = 194 (M + 1).

Anal: Calcd for $C_{10}H_{15}N_3O$: C, 62.15; H, 7.82; N, 21.74. Found: C, 62.20; H, 7.77; N, 21.71.

2-{[Iminio-(1-methylcyclopropyl)methyl]amino}pyridin-3-olate (3b)
Mp (Tottoli) 113–114 °C.

IR (KBr): 1624, 2250–3250 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.75 (q, 2 H, *J* = 3.8 Hz, CH_2), 1.28 (q, 2 H, *J* = 3.8 Hz, CH_2), 1.41 (s, 3 H, CH_3), 5.77 (br s, 2 H, NH_2), 6.78 (dd, 1 H, *J* = 7.9, 5.2 Hz, H5), 7.08 (dd, 1 H, *J* = 7.9, 1.5 Hz, H4), 7.73 (dd, 1 H, *J* = 5.2, 1.5 Hz, H6), 10.70 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 17.1 (2 CH_2), 19.6 (Cq), 20.3 (CH_3), 117.9, 118.0 (C5, C6), 135.9 (C4), 146.9 (C3), 151.2 (C2), 166.8 (C=N).

MS (IS): *m*/*z* = 192 (M + 1).

Anal: Calcd for $C_{10}H_{13}N_3O$: C, 62.81; H, 6.85; N, 21.97. Found: C, 62.53; H, 6.79; N, 21.84.

***N*′-(3-Hydroxypyridin-2-yl)benzenecarboximidamide (3c)**
Mp (Tottoli) 149–150 °C.

IR (KBr): 1642, 2700–3150 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.55–6.00 (m, 2 H, NH_2), 6.87 (dd, 1 H, *J* = 7.9, 5.0 Hz, H5), 7.19 (dd, 1 H, *J* = 7.9, 1.5 Hz, H4), 7.33–7.51 (m, 3 H, H_{arom}), 7.73 (dd, 1 H, *J* = 5.0, 1.5 Hz, H6), 7.82–8.07 (m, 2 H, H_{arom}.), 8.69 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 119.3, 119.5 (C4, C5), 126.7 (2 C_{arom}), 128.7 (2 C_{arom}), 131.2 (C_{arom}), 135.6 (Cq), 136.0 (C6), 147.7 (C3), 150.1 (C2), 158.7 (CNH_2).

MS (IS): *m*/*z* = 214 (M + 1).

Anal: Calcd for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.29; H, 5.34; N, 19.86.

***N*′-(3-Hydroxypyridin-2-yl)-3,4,5-trimethoxybenzenecarboximidamide (3d)**
Mp (Tottoli) 135–136 °C.

IR (KBr): 1648, 2500–3200 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.92 (s, 6 H, 2 CH_3), 3.93 (s, 3 H, CH_3), 5.99 (sl, 2 H, NH_2), 7.05 (dd, 1 H, *J* = 7.9, 4.6 Hz, H5), 7.17 (br s, 2 H, H_{arom}), 7.94 (dd, 1 H, *J* = 7.9,1.5 Hz, H4), 8.45–8.47 (m, 2 H, H6, OH).

^{13}C NMR ($CDCl_3$): δ = 56.3 (2 CH_3), 60.9 (CH_3), 104.1 (2 C_{arom}), 104.9 (C5), 129.4 (Cq), 141.5 (C4), 141.6 (Cq), 147.5 (C6), 148.7 (C2), 153.3 (2 Cq), 164.7 (C=N).

MS (IS): *m*/*z* = 304 (M + 1).

Anal: Calcd for $C_{15}H_{17}N_3O_4$: C, 59.40; H, 5.65; N, 13.85. Found: C, 59.05; H, 5.57; N, 13.79.

***N*′-(3-Hydroxypyridin-2-yl)furan-2-carboximidamide (3e)**
Mp (Tottoli) 108–109 °C.

IR (KBr): 1599, 2900–3500 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.30–6.30 (m, 2 H, NH_2), 6.54 (dd, 1 H, *J* = 3.3, 1.5 Hz, =CH), 6.85 (dd, 1 H, *J* = 7.9, 5.2 Hz, H5), 7.13–7.16 (m, 2 H, H_{arom}), 7.51–7.52 (m, 1 H, H_{arom}), 7.81 (dd, 1 H, *J* = 5.2, 1.2 Hz, H6), 10.58 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 111.9, 112.4, 118.6, 136.5, 143.9 (CH_{arom}), 147.3 (C3), 149.2 (C2), 149.7 (C=N), 141.2 (C4), 151.2 (C_{arom}).

MS (IS): *m*/*z* = 204 (M + 1).

Anal: Calcd for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.96; N, 20.68. Found: C, 59.27; H, 4.46; N, 20.25.

***N*′-(3-Hydroxypyridin-2-yl)thienyl-2-carboximidamide (3f)**
Mp (Tottoli) 142–143 °C.

IR (KBr): 1618, 3300–3500 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.90–6.70 (m, 2 H, NH_2), 6.86 (dd, 1 H, *J* = 7.8, 5.0 Hz, H5), 7.08 (dd, 1 H, *J* = 5.0, 3.8 Hz, =CH), 7.16 (dd, 1 H, *J* = 7.8, 1.6 Hz, H4), 7.44–7.46 (m, 2 H, =CH), 7.81 (dd, 1 H, *J* = 5.0, 1.6 Hz, H6), 10.63 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 118.8, 119.1 (C5, =CH), 126.0, 127.6, 129.7 (C4, C6, =CH), 136.5 (=CH), 141.1 (Cq), 147.5 (C3), 150.7 (C2), 153.0 (C=N).

MS (IS): *m*/*z* = 220 (M + 1).

Anal: Calcd for $C_{10}H_9N_3OS$: C, 54.78; H, 4.14; N, 19.16. Found: C, 54.55; H, 4.13; N, 18.84.

***N*′-(3-Hydroxypyridin-2-yl)pyridin-3-carboximidamide (3g)**
Mp (Tottoli): 134–135 °C.

IR (KBr): 1643, 3000–3400 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.15 (sl, 2 H, NH_2), 6.92 (dd, 1 H, *J* = 7.8, 5.0 Hz, H5), 7.20 (dd, 1 H, *J* = 7.8, 1.5 Hz, H4), 7.41 (ddd, 1 H, *J* = 0.6, 7.8, 4.7 Hz, H_{pyr}), 7.86 (dd, 1 H, *J* = 4.7, 1.6 Hz, H_{pyr}), 8.20 (ddd, 1 H, *J* = 1.8, 7.8, 1.6 Hz, H_{pyr}), 8.73 (dd, 1 H, *J* = 5.0, 1.5 Hz, H6), 9.13 (d, 1 H, *J* = 1.8 Hz, H_{pyr}), 10.92 (br s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 119.2, 119.7 (C5, C6), 123.3 (C9), 132.2 (C11), 134.4 (C4), 136.4 (C10), 147.8 (C2), 148.0 (C12), 150.6 (C3), 151.6 (C8), 156.2 (C=N).

MS (IS): *m*/*z* = 215 (M + 1).

Anal: Calcd for $C_{11}H_{10}N_4O$: C, 61.67; H, 4.25; N, 26.28. Found: C, 61.94; H, 4.21; N, 26.30.

2-[(1-Iminio-2,2-dimethylpropyl)amino]quinolin-3-olate (7a)
Mp (Tottoli) 139–140 °C.

IR (KBr): 1654, 2750–3300 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.37 (9 H, s, 3 CH_3), 6.08 (2 H, br s, NH_2), 7.32 (1 H, ddd, *J* = 7.9 Hz, *J* = 7.0, 1.2 Hz, H6), 7.35 (1 H, s, H4), 7.40 1 H, ddd, *J* = 1.5, 7.9, 7.0 Hz, H7), 7.59 (1 H, dd, *J* = 7.9, 1.5 Hz, H5), 7.71 (1 H, dd, *J* = 7.9, 1.2 Hz, H8), 11.61 (1 H, br s, NH).

^{13}C NMR ($CDCl_3$): δ = 28.6 (CH_3), 38.4 (Cq), 112.3 (C4), 124.8 (C4′), 125.8 (C5), 126.2 (C6), 126.9 (C8), 127.2 (C7), 140.6 (C3), 145.5 (C8′), 151.7 (C2), 157.2 (C=N).

MS (IS): *m*/*z* = 244.0 (M + 1).

Anal: Calcd for $C_{15}H_{17}N_2O$: C, 69.11; H, 7.04; N, 17.27. Found: C, 68.87; H, 7.17; N, 17.00.

***N′*-(3-Hydroxyquinolyn-2-yl)benzenecarboximidamide (7b)**
Mp (Tottoli) 159–162 °C.

IR (KBr): 1659, 3000–3350 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.38 (2 H, br s, NH_2), 7.33–7.64 (8 H, m, 5 H_{arom}, H4, H6, H7), 7.80 (1 H, d, *J* = 7.9 Hz, H5), 7.95 (1 H, d, *J* = 8.1 Hz, H8), 11.77 (1 H, br s, OH).

^{13}C NMR ($CDCl_3$): δ = 113.0 (C5), 125.1 (C4′), 126.0 (Cq), 126.3 (C4), 127.0 (2 C_{arom}), 127.1 (C6), 127.5 (C8), 128.9 (2 C_{arom}), 129.2 ($C_{arom.}$), 131.6 (C3), 136.1 (C2), 140.7 (C7), 146.7 (C8′), 153.6 (C=N).

MS (IS): *m*/*z* = 264.0 (M + 1).

Anal: Calcd for $C_{16}H_{13}N_2O$: C, 72.99; H, 4.98; N, 15.96. Found: C, 72.81; H, 5.01; N, 15.93.

Oxazolopyridines 4a–g and 8a,b; General Procedure
The zwitterions or hydroxyamidines **3** or **7** were diluted in dimethylacetamide (2 mL) and the mixture was heated either by classical means to 170 °C in an oil bath (for 200 mg of starting material) or by microwaves in a quartz reactor (for 50 mg). When the reaction was finished, the mixture was co-evaporated with toluene in vacuo and the oil was purified by chromatography (silica gel; EtOAc–hexane, 1:6 for pyridines; EtOAc–petroleum ether 1:9 for quinolines).

2-(*tert*-Butyl)[1,3]oxazolo[4,5-*b*]pyridine (4a)
IR (KBr): 1670, 3182 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.52 (s, 9 H, CH_3), 7.24 (dd, 1 H, *J* = 8.2, 4.9 Hz, H6), 7.77 (dd, 1 H, *J* = 8.2, 1.2 Hz, H7), 7.52 (dd, 1 H, *J* = 4.9, 1.2 Hz, H5).

^{13}C NMR ($CDCl_3$): δ = 28.2 (3 CH_3), 34.5 [$C(CH_3)$], 117.7 (C5), 119.4 (C3), 142.9 (C4), 145.9 (C6), 155.9 (C2), 176.5 (C=O).

Anal: Calcd for $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.27; H, 6.70; N, 15.54.

2-(1-Methylcyclopropyl)[1,3]oxazolo[4,5-*b*]pyridine (4b)
^1H NMR ($CDCl_3$): δ = 1.04 (q, 2 H, *J* = 4.3 Hz, CH_2), 1.54 (q, 2 H, *J* = 4.3 Hz, CH_2), 1.65 (s, 3 H, CH_3), 7.18 (dd, 1 H, *J* = 7.9, 4.8 Hz, H6), 7.69 (dd, 1 H, *J* = 7.9, 1.2 Hz, H7), 8.47 (dd, 1 H, *J* = 4.8, 1.2 Hz, H5).

^{13}C NMR ($CDCl_3$): δ = 15.5 (Cq), 18.1 (2 CH_2), 20.0 (CH_3), 117.2, 118.9 (C6, C7), 142.7 (Cq), 145.8 (C5), 156.4, 173.9 (2 Cq).

Anal: Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 68.91; H, 5.81; N, 16.04.

2-Phenyl[1,3]oxazolo[4,5-*b*]pyridine (4c)
^1H NMR ($CDCl_3$): δ = 7.29 (dd, 1 H, *J* = 8.2, 4.9 Hz, H6), 7.50–7.59 (m, 3 H, H_{arom}), 7.86 (dd, 1 H, *J* = 8.2, 1.6 Hz, H7), 8.30–8.34 (m, 2 H, H_{arom}), 8.58 (dd, 1 H, *J* = 4.9, 1.6 Hz, H5).

2-(3,4,5-Trimethoxyphenyl)[1,3]oxazolo[4,5-*b*]pyridine (4d)
^1H NMR ($CDCl_3$): δ = 3.95 (s, 3 H, OCH_3), 3.99 (s, 6 H, 2 OCH_3), 7.29 (dd, 1 H, *J* = 8.2, 4.8, H6), 7.57 (s, 2 H, H_{arom}), 7.86 (dd, 1 H, *J* = 8.2, 1.3 Hz, H7), 8.58 (dd, 1 H, *J* = 4.9, 1.3 Hz, H5).

^{13}C NMR ($CDCl_3$): δ = 118.1 (C7), 120.0 (C6), 126.4 (Cq), 128.0 (2 C_{arom}), 128.9 (2 C_{arom}), 132.4 (C_{arom}), 143.0 (C7a), 146.6 (C5), 156.3 (C3a), 165.5 (C2).

Anal: Calcd for $C_{12}H_8N_2O$: C, 62.93; H, 4.93; N, 9.78. Found: C, 62.76; H, 5.16; N, 9.75.

2-(2-Furyl)[1,3]oxazolo[4,5-*b*]pyridine (4e)
^1H NMR ($CDCl_3$): δ = 6.66 (dd, 1 H, *J* = 3.3, 1.3 Hz, =CH), 7.30 (dd, 1 H, *J* = 8.2, 4.9 Hz, H6), 7.42 (d, 1 H, *J* = 3.3 Hz, =CH), 7.73 (d, 1 H, *J* = 1.3 Hz, =CH), 7.85 (dd, 1 H, *J* = 8.2, *J* = 1.5 Hz, H7), 8.59 (dd, 1 H, *J* = 4.9, 1.5 Hz, H5).

^{13}C NMR ($CDCl_3$): δ = 112.6 (=CH), 116.2 (=CH), 118.1 (C7), 120.1 (C6), 141.9, 142.4 (2 Cq), 146.6, 146.9 (C5, =CH), 155.8, 157.5 (2 C_q).

Anal: Calcd for $C_{10}H_6N_2O_2$: C, 64.52; H, 3.25; N, 15.05. Found: C, 64.56; H, 3.32; N, 14.94.

2-(2-Thienyl)[1,3]oxazolo[4,5-*b*]pyridine (4f)
^1H NMR ($CDCl_3$): δ = 7.22 (dd, 1 H, *J* = 5.0, 3.8 Hz, =CH), 7.28 (dd, 1 H, *J* = 8., 5.0 Hz, H6), 7.65 (dd, 1 H, *J* = 5.0, 1.3 Hz, =CH), 7.82 (dd, 1 H, *J* = 8.0, 1.2 Hz, H7), 8.02 (dd, 1 H, *J* = 3.8, 1.3 Hz, =CH), 8.56 (dd, 1 H, *J* = 5.0, 1.2 Hz, H5).

^{13}C NMR ($CDCl_3$): δ = 117.8 (=CH), 119.9 (C7), 128.4 (C6), 128.9 (Cq), 131.2, 131.8 (2 =CH), 142.7 (Cq), 146.7 (C5), 156.3 (C3a), 161.5 (C2).

Anal: Calcd for $C_{10}H_6N_2OS$: C, 59.39; H, 2.99; N, 13.85. Found: C, 58.43; H, 2.91; N, 13.50.

2-Pyridin-3-yl[1,3]oxazolo[4,5-*b*]pyridine (4g)
^1H NMR ($CDCl_3$): δ = 7.36 (dd, 1 H, *J* = 8.0, 4.9 Hz, H6), 7.51 (dd, 1 H, *J* = 8.2, 5.0 Hz, H10), 7.93 (dd, 1 H, *J* = 8.0, 1.3 Hz, H7), 8.26 (dt, 1 H, *J* = 7.9, 1.8 Hz, H11), 8.63 (dd, 1 H, *J* = 5.0, 1.5 Hz, H9), 8.82 (dd, 1 H, *J* = 4.9, 1.3 Hz, H5), 9.53 (d, 1 H, *J* = 1.5, H13).

^{13}C NMR ($CDCl_3$): δ = 118.5 (C7), 120.6 (C6), 123.8 (C10), 135.3 (C11), 143.1 (Cq), 147.1 (C9), 149.0 (C13), 155.8 (C5), 155.9 (Cq), 163.4 (Cq).

Anal: Calcd for $C_{11}H_7N_3O$: C, 67.00; H, 3.58; N, 21.31. Found: C, 67.23; H, 3.44; N, 21.20.

2-(*tert*-Butyl)[1,3]oxazolo[4,5-*b*]quinoline (8a)
^1H NMR ($CDCl_3$): δ = 1.56 (9 H, s, CH_3), 7.55 (1 H, ddd, *J* = 8.2, 6.9, 1.3 Hz, H6), 7.71 (1 H, ddd, *J* = 1.4, 6.9, 8.5 Hz, H7), 7.93 (1 H, dd, *J* = 8.2, 1.4 Hz, H5), 8.11 (1 H, s, H4), 8.23 (1 H, dd, *J* = 1.3, 8.5 Hz, H8).

^{13}C NMR ($CDCl_3$): δ = 28.3 (3 CH_3), 38.0 (Cq), 114.5 (C4), 125.9 (C4′), 126.6 (C6), 128.0 (C5), 128.4 (C8), 129.7 (C7), 141.7 (C3), 146.6 (C8′), 157.5 (C2), 180.5 (C=N).

Anal: Calcd for $C_{14}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.12; H, 6.38; N, 12.47.

2-Phenyl[1,3]oxazolo[4,5-*b*]quinoline (8b)
^1H NMR ($CDCl_3$): δ = 7.54–7.68 (5 H, m, H_{arom}), 7.74 (1 H, ddd, *J* = 8.0, 7.2, 1.2 Hz, H6), 8.22 (1 H, ddd, *J* = 1.2, 7.2, 8.2 Hz, H7), 8.40–8.44 (2 H, m, H5, H8).

^{13}C NMR ($CDCl_3$): δ = 102.2 (C4), 125.6 (C4′), 126.1 (C_{arom}), 126.3 (C6), 126.9 (C5), 128.1 (C8), 129.2 (C_{arom}), 130.0 (C_{arom}), 133.3 (C7), 137.4 (=CH), 142.1 (C3), 149.4 (C8′), 162.0 (C2), 176.8 (C=N).

Anal: Calcd for $C_{16}H_{10}N_2O$: C, 78.03; H, 4.09; N, 11.38. Found: C, 77.99; H, 4.01; N, 11.29.

Crystal Structure Analysis of 3a
The crystal structure of compound **3a** has been determined by single-crystal X-ray diffraction techniques and refined by full-matrix least-squares procedures, to give a final R value of 0.04. The crystals are monoclinic, space group P $2_1/n$, with *a* = 7.699(1) Å, *b* = 11.326(2) Å, *c* = 12.300(1) Å, *b* = 91.96(1)°, and Z = 4. A crystal 0.25 × 0.40 × 0.50 mm was chosen.

The data were collected on a CAD4 Enraf–Nonius diffractometer with graphite monochromatized CuKα radiation. The cell parameters were determined by least-squares from the setting angles for 25 reflexions.

In the collection of intensities the θ/2θ scan method was used, and 1815 independent reflexions were collected in the region θ < 65°.

Correction was made for Lorentz and polarisation effects. 1582 reflexions with $I > 2\sigma$ (I) were considered observed and were used in the subsequent calculations. Semi-empirical method of absorption correction was applied. Full crystallographic results have been deposited at the Cambridge Crystallographic Data Centre (CCDC), UK, as Supplementary Materials.[11] The position of non-H atoms were determined by the program SHELXS[12] and the position of the H atoms were deduced from coordinates of the non-H atoms and confirmed by Fourier Synthesis. H atoms were included for structure factor calculations but not refined.

Crystal Structure Analysis of 3f

The crystal and molecular structure of **3f** has been determined by X-ray diffraction methods (CuKα) and refined to an R value of 0.032. A crystal $0.05 \times 0.15 \times 0.37$ mm was chosen. The crystal is orthorhombic, space group $Pna2_1$, with a = 10.690(1) Å, b = 16.646(1) Å, c = 5.686(1) Å, Z = 4.

The cell parameters were determined by least-squares from the settings angles for 25 reflexions. An empirical absorption correction was applied. The data were also corrected for Lorentz and polarization effect. In the collection of intensities the θ/20 scan method was used, and 958 independent reflexions were collected in the region $\theta < 65°$. The positions of non-H atoms were determined by the program SHELXS 86[12] and the position oh the H atoms were deduced from coordinates of the non-H atoms and confirmed by Fourier Synthesis. H atoms were included for structure factor calculations but not refined.

Full crystallographic results have been deposited at the Cambridge Ctystallographic Data Centre (CCDC), UK, as Supplementary Materials.[11]

Crystal Structure Analysis of 3g

The compound **3g** crystallizes in the monoclinic group $P\ 2_1/c$ with 8 molecules in a unit cell of dimension a = 13.567(1) Å, b = 13.150(2) Å, c = 12.656(6) Å, β = 116.44(2)° (two independent molecules). The intensities of the reflexions with $\theta < 65°$ were measured in in the ω/20 scan mode with a variable scan rate. 3430 independent reflexions were measured and 3180 of these with $I > 2\sigma$ (I) were used in the structure analysis. The reflexions were corrected for Lorentz and polarization factors and for absorption. The structure was solved by the program SHELXS 86[12] and refined by full-matrix least-squares procedures, to give a final R value of 0.036 for 3180 reflexions with reasonable intensities collected on a four-circle diffractometer. The position of the H atoms were deduced from coordinates of the non-H atoms and confirmed by Fourier Synthesis. H atoms were included for structure factor calculations but not refined.

There are two independent molecules A and B. The major difference between the two molecules are found in the dihedral angles concerning the cycles plans I ($C_1 \ldots C_6$), and II ($C_{10} \ldots C_{15}$): 19.0(1) for the A molecule; 26.9(1) for the B molecule.

Full crystallographic results have been deposited at the Cambridge Crystallographic Data Centre (CCDC), UK, as Supplementary Marerials.[11]

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