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Synthesis of 4(3*H*)Quinazolinimines by Reaction of (*E*)-*N*-(Aryl)-Acetimidoyl or -benzimidoyl chloride with Amines

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ABSTRACT

An efficient one-step access to 4(3*H*)quinazolinimines by reaction of phenylchloroimines with 2-aminobenzonitrile is described. The reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride with substituted anilines that yields a number of their corresponding C2, N3-substituted quinazoliniminium chloride or the neutral products is also reported. These methods provide a direct and flexible access to diverse substituted iminoquinazolines substituted at the C2, N3-positions. All new compounds are fully characterized and six examples are given with their single-crystal X-ray structure.

INTRODUCTION

Fused heterocyclic compounds are of particular interest and significant importance in the search for new bioactive scaffolds in the agrochemical and pharmaceutical industries. In particular, nitrogen-containing heterocycles exhibit diverse biological and pharmacological activities due in part to their structural relationship with many natural and synthetic compounds with known biological activities.[1] Among these kinds of molecules, the quinazolinimines[2-7] (Figure 1a) have been studied due to their extensive therapeutic potential[2] and also because of the possibility of using them as starting materials in the synthesis of quinazolinone (Figure 1b).[7a, 8] Another class of

N-heterocyclic compounds of interest are the imidazoquinazolines [9, 10] (Figure 1c), because they introduce in their framework biologically valuable moieties like imidazole and quinazoline.[9]

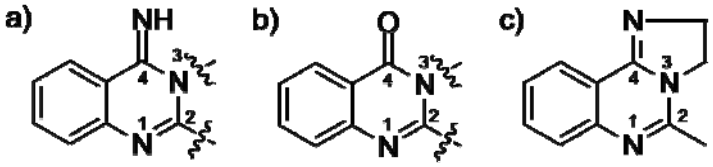


Figure 1. General structures of **(a)** quinazolinimines, **(b)** quinazolinone, and **(c)** imidazoquinazolines.

Several methods for synthesizing the class of compounds shown in Figure 1 have been reported.[2 - 10] However, only a few of them have been optimized in terms of their scope to construct functionalized quinazolinimines in a general way.[3] For example, quinazolinimines are commonly synthesized by reaction of anthranylonitriles with isocyanates, to give the corresponding ureas which further undergo cyclization under basic catalytic conditions.[4] To avoid the use of isocyanate, a modification of the amino group in anthranylonitrile has been carried out with different reagents such as diaryliodonium salts,[3a] triphenylphosphine bromide,[3b] phenyl chloroformate,[4a] orthoester,[5a] formic acid[5c] and lactams.[2c-g,6] In general, some of the existing protocols require long reaction times,[5c] high temperature,[6] special setup and workup conditions,[2f, g] and they have low yields.[2e]

At present, the goals in this area are directed towards the synthesis of new quinazolinimines structurally related to bioactive products, by means of new and effective synthetic routes, which may be quicker, more efficient and more versatile than the current methods. Based on this background, we designed a serie of substituted 2-(phenyl or methyl)-3-aryl-4(3*H*)-quinazoliniminium chlorides containing diverse substituents around the heterocycle through two alternative pathways. The first procedure is based on the reaction of (*E*)-*N*-(2,6-diisopropylphenyl)benzimidoyl chloride or (*E*)-*N*-(2,6-diisopropylphenyl)acetimidoyl chloride with

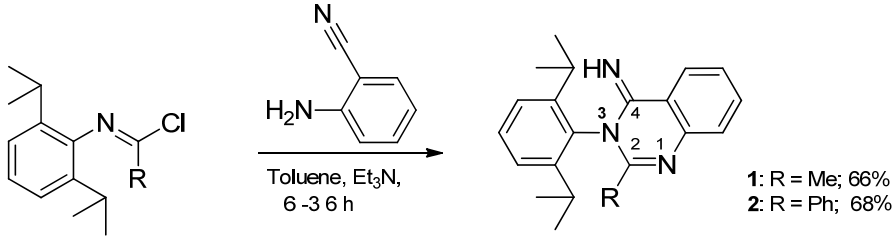
2-aminobenzonitrile, while the second one used the reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride with substituted anilines, chiral amines, or ethylenediamine, getting fused quinazoliniminium heterocyclic compounds under mild reaction conditions.

This synthetic routes were proposed considering that searching new methods to synthesize different diimine species,[11] we observe that a cyclization reaction takes place forming a 4(3*H*)-quinazolinimine framework. Due to the interest of these types of heterocycles, we focused our efforts on finding a new easy and efficient route to get these types of compounds.

RESULTS AND DISCUSSION

The compounds 3-(2,6-diisopropylphenyl)-2-methylquinazolin-4(3*H*)-imine (**1**) and 3-(2,6-diisopropylphenyl)-2-phenylquinazolin-4(3*H*)-imine (**2**) were synthesized by reacting (*E*)-*N*-(2,6-diisopropylphenyl)acetimidoyl chloride[12] and (*E*)-*N*-(2,6-diisopropylphenyl)benzimidoyl chloride[13] with stoichiometric amounts of 2-aminobenzonitrile in toluene under reflux. Work up of the reaction mixture produced compounds **1** and **2** in 66 and 68% yields, respectively (Scheme 1).

Scheme 1. Preparation of 3-(2,6-diisopropylphenyl)-2-methylquinazolin-4(3*H*)-imines (**1**) and 3-(2,6-diisopropylphenyl)-2-phenylquinazolin-4(3*H*)-imines (**2**).



It seems possible that the formation of 2-methyl or phenylquinazolinimines **1** and **2** proceeds *via* a two step sequence which involves first the nucleophilic substitution of a chlorine atom in the precursor induced by the arylamine to give an azaenamine intermediate, which by a subsequent 6-*exo-dig* ring-closure reaction[14] provides the *N*-heterocycles 4(3*H*)-quinazolinimines.

The FT-IR, ^{1}H and ^{13}C NMR spectra, and HRMS (ESI) analyses are consistent with the formation of a single isomer of the compounds. The NMR diagnostic peaks (in ppm) are shown in Table 1.

Table 1. Selected spectroscopic parameters of the quinazolinimine compounds **1** and **2**.

Compound	δ ^{13}C		δ ^{1}H		
	C_4=N	RC_2=N	C_4N-H	HC^{iPr}	Me^{iPr}
1	154.42	153.59	6.10	2.69	1.17, 1.11
2	154.95	154.87	6.33	2.86	1.14, 1.00

Compounds **1** and **2** were isolated in good yields as pure materials by crystallization, and the C_4N-H resonances are indicative of the molecular imine moiety.

As an additional confirmation of the structure assignment of both compounds, single crystals of **1** and **2** suitable for X-ray diffraction studies were obtained by slow evaporation of methanol (**1**) and ethyl acetate (**2**), and the resulting structures are shown in Figures 2. The crystallographic parameters are including in the supporting information.

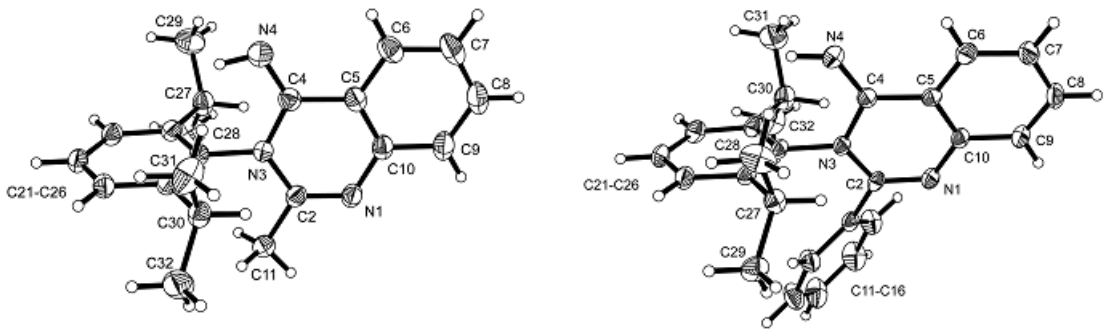


Figure 2. Molecular structure of compound **1** (Left) and compound **2** (Right).

The X-ray crystal structure of compound **1** (Figure 2, Left) shows that the heterocyclic fragment is orthogonal to the 2,6-*i*PrPh (aryl) fragment, similar to the previously reported 4(3H)-quinazolinimine.[3, 7b] In the hetero-atomic ring and the imine the C2-N1, C2-N3 and C4-N4, C4-N3 bond lengths are 1.290(2), 1.389(2) and 1.276(2), 1.408(2) Å, respectively, showing the double bond character of the cyclic and exocyclic imine fragment and the tertiary amine nitrogen (N3). In the heterocyclic ring, the C4-C5 bond length is the only one that fits a single bond (1.468(2) Å) indicating that the conjugation extends along the side of N3, probably associated with an sp^2 instead of sp^3 character of nitrogen. This is consistent with the planarity of the ring and the N3 bond angles (range 117.7(1)-122.5(1)°), very close to a perfect trigonal planar geometry (See Table S1 (Supporting Information)).

The crystal lattice of compound **1** presents hydrogen bond interactions involving the exocyclic imine moieties (N4A---H23B-C23B 2.552 Å; N4B---H23A-C23A 2.568 Å). These interactions lead to the formation of a "zig-zag" chain structure along the c-axis.

X-ray diffraction studies also confirm unequivocally the structure of compound **2** (Figure 2, right). The structures show the same rearranged to compound **1**, with the aryl group orthogonal to the fused ring. The bond lengths in the heterocyclic ring and the angles over the amine nitrogen atoms (N3) are equivalent to those shown above for compound **1**, See Figure 2. (For further detail see, Figure S2 and Table S1, Supporting Information).

The satisfactory results arising from the reaction of (*E*)-*N*-(2,6-diisopropylphenyl)acetimidoyl chloride and (*E*)-*N*-(2,6-diisopropylphenyl)benzimidoyl chloride with 2-aminobenzonitrile to get the quinazolinimine derivatives encourage us to study a convenient access to quinazolinimine derivatives by reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride[15] with anilines.

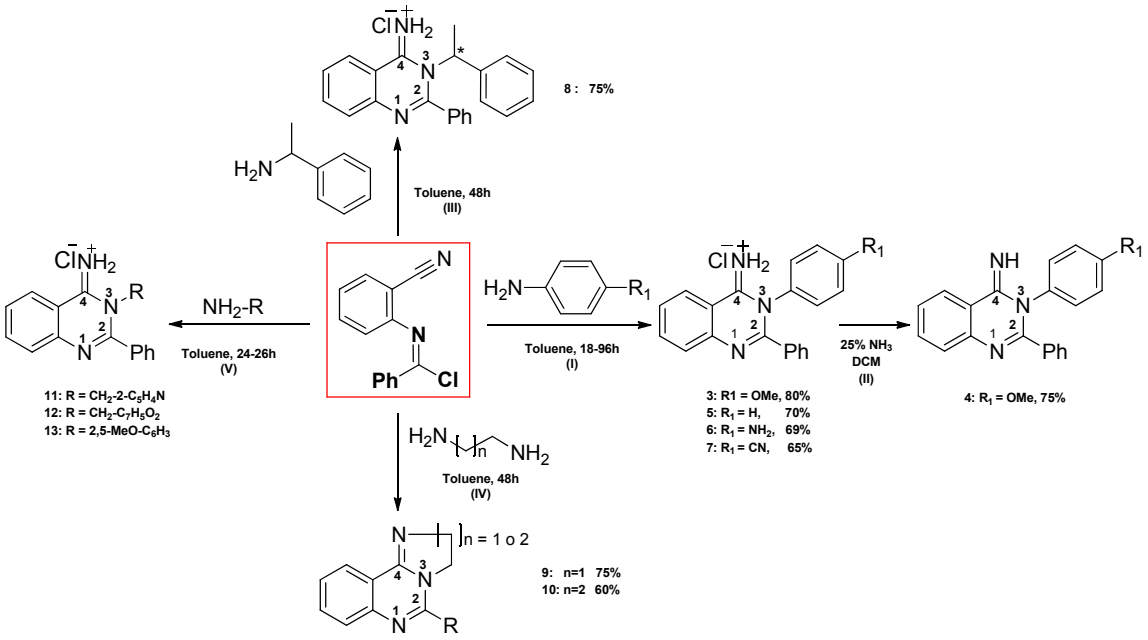
From benzimidoyl chloride, which contains a nitrile group in the ortho position, together with the wide range of commercially available primary amines (aliphatic and aromatic) it is possible to

prepare a large variety of quinazolinimines, Scheme 2. Furthermore, the preparation of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride is optimized using excess thionyl chloride instead of PCl_5 for the chlorination of *N*-(2-cyanophenyl)benzamide. Two important advantages are associated with this chlorinating agent. First, it is cheaper, and second, the purification of the chlorinated product is achieved, since the excess of thionyl chloride is recovered by distillation, reducing the generation of waste pollutants, and allowing isolation of the (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride in high purity. This new strategy is highly versatile and allows the building of quinazolinimine and/or its salt with rings and a variety of possibilities at "N3", which can be very important in the development of new drugs that would also be accessible by simple methods and in good yield. Scheme 2 (I) and (II) shows the two-step synthesis and the corresponding quinazolinimine salt with a 4-methoxy phenyl group as an option at N3.

Following similar procedure of **1** and **2**, the reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride with 4-methoxyaniline yields target compound **3** and **4** as colorless solids in 80% and 75% yields, respectively (Scheme 2 (I) and (II)).

The ^{1}H and ^{13}C NMR spectra of compound **3** in CD_3Cl/CD_3OD (97:3) feature C-H_5 signals as a doublet at δ 8.65 (^{13}C: 124.65 ppm) and a MeO singlet resonance at δ 3.83 (^{13}C: 55.6 ppm). The signal associated with the NH_2Cl proton was not seen, while the iminium carbon (C4) appears at δ 158.19 ppm. For further details see the Supporting Information. The IR (ν C=NH_2Cl) band of compound **3** was found at 3288 cm^{-1} and the HRMS analysis supports these results ($C_{21}H_{18}N_3O^+$: m/z calcd: 328.144, found: 328.144).

Scheme 2. Synthesis of 4(3H)Quinazolinimines by Reaction of (*E*)-N-(2-cyanophenyl)benzimidoyl chloride with Amines.



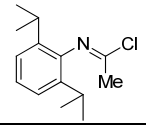
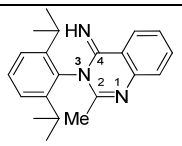
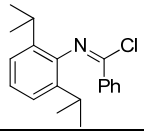
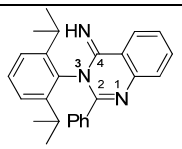
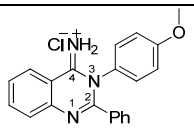
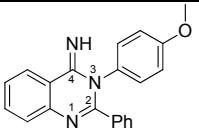
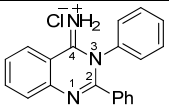
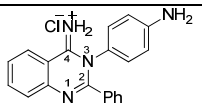
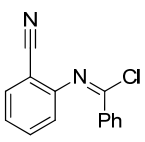
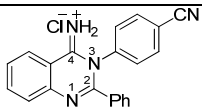
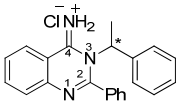
In this method of synthesis, neutralization of the salt with an ammonia solution (25% aqueous NH_3) allows isolation of the 3-(4-methoxyphenyl)-2-phenylquinazolin-4(3*H*)-imine **4**, Scheme 2 (II). The ^{1}H and ^{13}C NMR spectra in CD_2Cl_2 are consistent with the formation of a single isomer of **4**. The ^{1}H NMR spectrum features the imine-H signal (–C_4N-H) as a broad singlet at δ 6.66 (^{13}C: 155.37 ppm) and a singlet resonance of MeO at δ 3.76 (^{13}C: 56.0 ppm). For further details see Table S6 and additional data in Supporting Information. The IR (ν C=NH) band of compound **4** was found at 3311 cm^{-1} and the HRMS analysis supports these results ($C_{21}H_{18}N_3O$ $[M+H]^+$: m/z calcd: 328.144, found: 328.144).

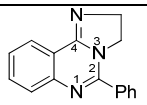
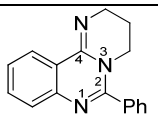
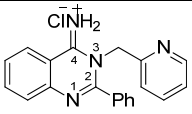
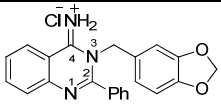
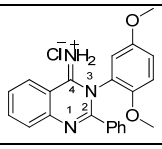
Single crystals of **4** suitable for solid-state characterization were obtained by slow evaporation from ethyl acetate. Similarly to what was seen in compounds **1** and **2** (Figures 2), the imine presents a planar environment, while the N3 substituent is orthogonal to the fused heterocyclic

ring. The bond lengths and angles around N3 follow the same trends seen for **1** and **2**. (For further details see Figure S3 and Table S1, Supporting Information).

The potential of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride as a starting material in the synthesis of quinazoliminium chlorides, with alternatives at N3, was studied by direct reaction at position 3 with monosubstituted and disubstituted aromatic amines, chiral amines, and aliphatic diamines as outlined in Scheme 2 and Table 2.

Table 2. Synthesis of 4(3H)Quinazolinimines (**1**-**13**) by Reaction of Imidoyl chloride with various Amines.

Imidoyl chloride	Amine	Compound	Yield (%)
	2-aminobenzonitrile	 **1**	66
	2-aminobenzonitrile	 **2**	68
	p-anisidine	 **3**	80
	p-anisidine	 **4***	75
	aniline	 **5**	70
	p-phenylenediamine	 **6**	69
	4-aminobenzonitrile	 **7**	65
	(*R*)-(+)-α-methyl benzilamine	 **8**	75

	ethylenediamine	 **9**	75
	1,3-diaminopropane	 **10**	60
	2-picolinamina	 **11**	45
	piperonylamine	 **12**	55
	2,5-dimethoxyaniline	 **13**	65

*Neutralization of the corresponding salt (**3**).

The reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride with one molar equivalent of aniline, *p*-phenylendiamine and 4-aminobenzonitrile (toluene, reflux) gave the quinazoliniminium products 2,3-diphenylquinazolin-4(3*H*)-iminium chloride **5**; 3-(4-aminophenyl)-2-phenylquinazolin-4(3*H*)-iminium chloride **6;** and 3-(4-cyanophenyl)-2-phenylquinazolin-4(3*H*)-iminium chloride **7**, isolated as light yellow to light brown solids in 70, 69 and 65% yields, respectively, Scheme 2 (I) and Table 2. The ^{1}H and ^{13}C NMR spectra feature the C_5-H signals as doublets at δ 9.17, 8.77 and 8.43 (^{13}C: 127.66, 126.67 and 125.90 ppm) for **5**, **6** and **7**, respectively. The resonances from the "exocyclic" and cyclic imine carbon (C4 and C2) at δ 157.37 and 152.13 ppm for **5**, 159.06 and 154.03 ppm for **6,** and 158.87 and 153.78 ppm for **7,** support the formation of the compounds. For further details see the Supporting Information. The IR bands for (ν, C=NH_2Cl) of **5**, (NH_2, -C=NH_2Cl) of **6**, and (-C=NH_2Cl, CN) of **7** were found at 3378 cm^{-1}, [3411, 3328] cm^{-1} and [3396, 2237] cm^{-1}, respectively, and the HRMS analysis of compound **7** supports the formation of the salts ($C_{21}H_{15}N_4^+$: m/z; calcd: 323.129, found: 323.129).

Single crystals of **5** suitable for X-ray crystal structure analysis were grown by slow evaporation of the solvent mixture (chloroform/methanol). As expected, the molecular structure corroborates the proposed structure of the salt (see Figure S4, Supporting Information).

The use of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride as starting material in the synthesis of quinazolinimine or its salts may extend to heterocycles with alternatives on aliphatic N3. Scheme 2 (III-V) and Table 2 (Compounds **8**-**12**) shows five examples with this type of amines that illustrate the versatility and synthetic power of the suggested route. The reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride with one molar equivalent of (*R*)-(+)-*α*-methyl benzylamine in toluene at room temperature gave the quinazoliniminium product 2-phenyl-3-(1-phenyl-ethyl)-(3*H*)-quinazolin-4-ylidene-iminium chloride, **8**. This compound was isolated and purified by silica gel column chromatography using ethyl acetate/chloroform as eluent. Compound **8** was recovered as a light yellow oil in 75% yield, Scheme 2 (III) and Table 2.

The ^{1}H, ^{13}C and 2D NMR spectroscopic characterization of compound **8** supports the formation of a single isomer. The resonances at *δ,* 7.80 ppm, (d, *J* = 8.0 Hz, 1H, H_5), 5.57 (q, *J* = 6.8 Hz, 1H, H_{15}), and 1.82 (d, *J* = 7.2 Hz, 3H, H_{16}) are consistent with the proposed structure and purity of compound **8**. Because the resonances of the NH_2 and the -NH_2Cl functionalities are not seen by ^{1}H NMR, and although the full analysis by 2D NMR supports the proposed structure, efforts to detect their presence in the compound were focused on getting high quality monocrystals to resolve the structure, but they were not successful; however, the MS analysis supports the formation of the salt, compound **8**.

An interesting result was obtained from the reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride with ethylenediamine. At room temperature, and after 48 h followed by chromatographic purification, a light yellow oil was isolated. The ^{1}H NMR analysis of the product shows C5-H hydrogen atoms as a doublet at *δ* 8.04, (1H), and the resonance associated with the aliphatic -CH_2-

of the ethylene fragment (multiplet) at 4.12-3.99 ppm (4H). The resonances associated with -NH_2 and –NH_2Cl were not seen in the spectra. The IR (NH_2 and –NH_2Cl) bands were not seen (NMR and IR details are available in the Supporting Information). The absence of the stretching bands of the primary amine as well as of the C=NH_2Cl group in the IR spectrum made us redouble our efforts to complete the structural resolution of the product. Fortunately, the effort to grow a crystal was successful; single crystals of **9** suitable for the X-ray crystal structure analysis were obtained by slow evaporation (ethyl acetate/chloroform). The X-ray crystal structure of the product (see Figure S5, Supporting Information) shows that the ethyl fragment is part of a second cycle in this compound. The product of this reaction corresponds to the previously reported compound 5-phenyl-2,3-dihydroimidazo[1,2-*c*] quinazoline **9**,[9–10e] in our case obtained as a product of the reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride with ethylenediamine, Scheme 2 (IV) and Table 2.

Confirming the versatility of this new synthetic method the compound **10**, Scheme 2 (IV) and Table 2, which had been previously synthesized from thiazines and corresponding diamine was prepared.[16] (For more details see supporting Information). Additionally following this new synthesis protocols, an equimolar amount of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride was reacted with 2-picolinamine and piperonylamine (toluene, reflux) generating the quinazoliniminium products 2-phenyl-3-(pyridin-2-ylmethyl)quinazolin-4(3H)-iminium chloride **11** and 3-(benzo[d][1,3]dioxol-5-ylmethyl)-2-phenylquinazolin-4(3H)-iminium chloride **12**, isolated as white and pale yellow solids in 45 and 55% yields, respectively, Scheme 2 (V) and Table 2. The ^{1}H and ^{13}C NMR spectra feature the C_5-H signals as doublets at δ 8.81 and 9.44 (^{13}C: 121.72 and 127.70 ppm) and the resonance of carbon (C4) at δ 160.07 and 157.16 ppm for **11** and **12**, respectively, support the formation of the compounds. Additionally, the resonance corresponding to the C_{15}-H of each compound appear as a singlet at δ 5.15 y 5.84 (^{13}C: 46.41 and 53.40 ppm)

respectively, confirming the presence of an aliphatic group on the fragment bonded to the N3 atoms of the quinazolinimine. For further details see the Supporting Information. The IR bands for (-C=NH_2Cl) of **11** and **12** were found at 3302 cm^{-1} and 3425 cm^{-1}, respectively. Efforts to obtain single crystals of these compounds suitable for X-ray analysis were unsuccessful, however the MS analysis supports the purity of the compounds; for compound **11** (for $C_{20}H_{17}N_4^+$: m/z calcd: 313.15, found: 313) and for compound **12** (for $C_{22}H_{18}N_3O_2^+$: m/z calcd: 356.14, found: 356).

Finally, to prove the efficiency of this method with larger size aniline, was reacted (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride with 2,5-dimethoxyaniline (toluene, reflux) yielding the desired product 3-(2,5-dimethoxyphenyl)-2-phenylquinazolin-4(3H)-iminium chloride **13** isolated as a gray solid in 65% yield, Scheme 2 (V) and Table 2. The ^1H and ^{13}C NMR spectra feature the C_5-H signals as doublets at δ 9.54 (^{13}C: 128.54 ppm). The resonances from the carbon (C4) at δ 157.03 ppm and two singlet signals corresponding to methoxy groups $C_{21,22}$-H at δ 3.74 and 3.72 ppm (^{13}C: 56.13 and 56.12 ppm) supporting the formation of the compound. For further details see the Supporting Information. The IR bands for (-C=NH_2Cl) of **13** was found at 3393 cm^{-1}. The MS analysis confirm the proposed structure and purity of the compound **13** [$C_{22}H_{20}N_3O_2^+$: m/z calcd: 358.16 , found: 359].

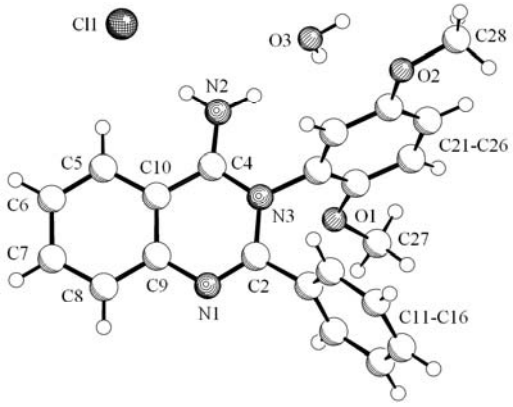


Figure 3. Molecular structure of compound **13**.

Single crystals of **13** suitable for X-ray crystal structure analysis were grown by slow diffusion of solvent (dichloromethane/pentane). As expected, the molecular structure corroborates the proposed structure of the salt (see Figure 3). The structural parameters were consistent with the other ones shown. (For further details see Supporting Information).

Cytotoxicity studies of these compounds and other derivatives are in progress.

CONCLUSIONS

In summary, we have presented results on a novel and efficient route for the synthesis of functionalized 4(*3H*)quinazolinimines and C2,N3-substituted quinazoliniminium chlorides, starting from phenylchloroimines and (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride, respectively. The synthetic method provides an easy new route and flexible access to iminoquinazolines with different substituents at the C2, N3 positions with good yields (45-80%).

EXPERIMENTAL SECTION

General

All manipulations were performed in air. Reagent-grade solvents were obtained from E. Merck. Toluene was distilled from benzophenone ketyl. The compounds 2-aminobenzonitrile, aniline, *p*-phenylendiamine, 4-aminobenzonitrile and *p*-anisidine were purchased from Aldrich and used as received. The imidoyl chlorides (*E*)-*N*-(2,6-diisopropylphenyl)acetimidoyl chloride[12] and (*E*)-*N*-(2,6-diisopropylphenyl)benzimidoyl chloride[13] were prepared according to published procedures. The compound (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride was prepared according to a modified literature procedure.[15a] The following instruments were used for the physical characterization of the compounds. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer. Chemical shifts and the coupling constants are reported in parts per million ($SiMe_4$ as standard) and Hertz, respectively. Most of the NMR assignments were supported by additional 2D experiments and the numbers of scans used for ^{13}C NMR were ranged from 0.5–8K depending on

the sample concentration. FT-IR spectra were recorded on a Bruker Vector-22 spectrophometer using KBr pellets and the infrared frequencies are reported in cm^{-1}. Mass spectra were acquired using a Micro Tof (Bruker) or a Clarus SQ 8T GC/MS (PerkinElmer). The structures and their labels assignments are described on the supporting informations.

Preparation of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride: A mixture of *N*-(cyanophenyl)benzamide[15a] (1.20 g, 5.40 mmol) and an excess of thionyl chloride (2 mL, 27 mmol) was stirred for 8 hour under reflux. The remainder thionyl chloride was distilled off raising temperature to 120 °C. The residues were removed under vacuum to give yellow solid (1.17 g, 90%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K) δ/ppm = 8.21 (d, *J* = 7.8 Hz, 2H, H_3), 7.69 (d, *J* = 7.8 Hz, 1H, H_8), 7.66 – 7.55 (m, 2H, $H_{10,5}$), 7.49 (t, *J* = 7.8 Hz, 2H, H_4), 7.27 (t, *J* = 7.7 Hz, 1H, H_9), 7.11 (d, *J* = 8.1 Hz, 1H, H_{11}). **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K) δ/ppm = 150.6 (C_6), 147.6 (C_1), 134.6 (C_2), 133.5 (C_{10}), 133.0 (C_5), 133.0 (C_8), 129.9 (C_3), 128.7 (C_4), 125.2 (C_9), 120.9 (C_{11}), 116.7 (C_{12}), 104.9 (C_7). **FT-IR (KBr)**: ν / cm^{-1} = 3055, 3052, 2230 (CN), 1681, 1666, 1590, 1579, 1567, 1547, 1518, 1488, 1478, 1446, 1336, 1315, 1301, 1281, 1254, 1211, 1191, 1172, 1095, 1076, 1041, 1028, 1000, 979, 956, 925, 890, 869, 838, 764, 749, 734, 703, 682, 653, 633, 617, 604, 588, 561, 540, 504. **MS (ESI)** for $C_{14}H_9ClN_2$ $[M]^+$: m/z calcd: 240, found: 240.

Synthesis of 3-(2,6)-diisopropylphenyl)-2-methylquinazolin-4(3*H*)-imine (1): (*E*)-*N*-(2,6-diisopropylphenyl)acetimidoyl chloride (0.48 g, 2.03 mmol) was added to a solution of 2-aminobenzonitrile (0.24 g, 2.03 mmol) and trietylamine (0.31 mL, 2.23 mmol) in 30 mL of toluene and the reaction mixture was stirred for 6 hours under reflux. All volatiles were removed under vacuum. The solid residue was dissolved in 30 mL of CH_2Cl_2 and washed twice with 15 mL of water. The solution was evaporated to dryness and the crude product was crystallized from methanol to give colorless crystals (0.43 g, 66%). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K) δ/ppm = 8.30 (br. s, 1H, H_5), 7.58 (t, *J* = 7.6 Hz, 1H, H_7), 7.48 (m, 2H, $H_{8,15}$), 7.32 (m, 3H, $H_{6,14}$), 6.10 (br. s, 1H, NH), 2.69 (hept, *J* = 6.8 Hz, 2H, H_{16}), 1.99 (s, 3H, H_{11}), 1.17 (d, *J* = 6.9 Hz, 6H, H_{17}), 1.11 (d, *J* = 6.9 Hz, 6H, H_{18}). **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K) δ/ppm = 154.4 (C_4), 153.6 (C_2), 146.6 (C_{13}), 144.6 (C_9), 132.8 (C_7), 131.4 (C_{12}), 130.6 (C_{15}), 126.4 (C_8), 126.4 (C_5 Not Clear), 126.2 (C_6), 125.4 (C_{14}), 120.6 (C_{10}), 28.4 (C_{16}), 25.0(C_{18}), 24.0 (C_{11}), 23.5 (C_{17}). **FT-IR (KBr)**: ν / cm^{-1} = 3442, 3288, 3078, 3061, 3034, 3009, 2963, 2929, 2870, 1630, 1594, 1582, 1466, 1379, 1364, 1352, 1306, 1276, 1249, 1230, 1207, 1178, 1144,

1058, 1030, 870, 838, 8.15, 766, 662, 643, 627, 615, 560, 544. **HRMS (ESI)** for $C_{21}H_{26}N_3$ $[M+H]^+$: m/z calcd: 320.212, found: 320.212.

Synthesis of 3-(2,6-diisopropylphenyl)-2-phenylquinazolin-4(3*H*)-imine (2): (*E*)-*N*-(2,6-diisopropylphenyl)benzimidoyl chloride (0.84 g, 2.80 mmol) was added to a solution of 2-aminobenzonitrile (0.33 g, 2.80 mmol) and trietylamine (0.43 mL, 3.08 mmol) in 30 mL of toluene and the reaction mixture was stirred for 36 hours under reflux. All volatiles were removed under vacuum and the residue was dissolved in 30 mL CH_2Cl_2 and washed twice with 15 mL of water. After removal of solvent and drying, the crude product was crystallized from ethyl acetate to give colorless crystals (0.73 g, 68 %). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K) δ/ppm = 8.36 (br. s, 1H, H_5), 7.67 (m, 2H, $H_{7,8}$), 7.44 (m, 2H, $H_{6,18}$), 7.34 - 7.12 (m, 7H, $H_{17,12,13,14}$), 6.33 (br. s, 1H, NH), 2.86 (hept, *J* = 6.7 Hz, 2H, H_{19}), 1.14 (d, *J* = 6.7 Hz, 6H, H_{20}), 1.00 (d, *J* = 6.8 Hz, 6H, H_{21}). **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K) δ/ppm = 155.0 (C_4, Not Clear), 154.9 (C_2), 147.7 (C_{16}), 145.5 (C_9), 136.2 (C_{11}), 133.2 (C_7), 132.4 (C_{15}), 131.0 (C_{18}), 129.78 (C_{14}), 129.7 (C_{13}), 127.9 (C_{12}), 127.9 (C_8), 127.2 (C_6), 126.5 (C_5), 125.6 (C_{17}), 121.8 (C_{10}), 29.2 (C_{19}), 25.8 (C_{20}), 23.1 (C_{21}). **FT-IR (KBr)**: ν / cm^{-1} = 3448, 3301, 3258, 3064, 2960, 2927, 2865, 1744, 1625, 1608, 1557, 1494, 1474, 1444, 1384, 1360, 1322, 1297, 1248, 1235, 1205, 1177, 1154, 1142, 1050, 1031, 1020, 900, 873, 819, 800, 768, 757, 730, 704, 696, 671, 637. **HRMS (ESI)** for $C_{26}H_{28}N_3$ $[M+H]^+$: m/z calcd: 382.228, found: 382,228.

Synthesis of 3-(4-methoxyphenyl)-2-phenylquinazolin-4(3*H*)-iminium chloride (3): (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.12 g, 0.49 mmol) was added to a solution of *p*-anisidine (0.06 g, 0.49 mmol) in 30 mL of toluene and the reaction mixture was stirred for 36 hours under reflux. All volatiles were removed under vacuum and the crude product was washed with acetone and dried to give yellow solid (0.14 g, 80 %). **^{1}H NMR** (400 MHz, $CDCl_3$/CD_3OD (97:3), 298 K) δ/ppm = 8.65 (d, *J* = 7.8 Hz, 1H, H_5), 8.36 (d, *J* = 7.6 Hz, 2H, H_{12}), 8.29 (d, *J* = 8.0 Hz, 1H, H_8), 7.77 (d, *J* = 8.4 Hz, 2H, H_{16}), 7.58 (t, *J* = 7.2 Hz, 1H, H_{14}), 7.54 – 7.45 (m, 3H, $H_{13,7}$), 7.32 (t, *J* = 7.3 Hz, 1H, H_6), 6.93 (d, *J* = 8.5 Hz, 2H, H_{17}), 3.83 (s, 3H, H_{19}). **^{13}C NMR** (100 MHz, $CDCl_3$/CD_3OD (97:3), 298 K) δ/ppm = 158.3 (C_{18}), 158.2 (C_4), 157.2 (C_2), 138.8 (C_9), 135.4 (C_7), 134.0 (C_{13}), 130.2 (C_{11}), 129.5 (C_{12}), 129.4 (C_{14}), 129.3 (C_{15}), 128.2 (C_6), 125.7 (C_{16}), 124.6 (C_5), 119.8 (C_8), 114.0 (C_{17}), 112.0 (C_{10}), 55.6 (C_{19}). **FT-IR (KBr)**: ν / cm^{-1} = 3288, 3066, 3048, 3004, 2955, 2934, 2910, 2836, 1734, 1634, 1600, 1561, 1508, 1458, 1431, 1416, 1380, 1366, 1331, 1296, 1252, 1236, 1175, 1156, 1109, 1081, 1032, 1002,

933, 827, 801, 768, 704, 675, 581, 529, 513. **HRMS (ESI)** for $C_{21}H_{18}N_3O^+$: m/z calcd: 328.144, found: 328.144.

Synthesis of 3-(4-methoxyphenyl)-2-phenylquinazolin-4(3*H*)-imine (4): (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.12 g, 0.49 mmol) was added to a solution of *p*-anisidine (0.06 g, 0.49 mmol) in 30 mL of toluene and the reaction mixture was stirred for 36 hours under reflux. All volatiles were removed under vacuum and the residue was dissolved in 30 mL CH_2Cl_2 and washed twice with 15 mL of 25% aqueous NH_3 solution. After removal of solvent and drying, the crude product was crystallized from ethyl acetate to give colorless crystals (0.12 g, 75 %). **^{1}H NMR** (400 MHz, CD_2Cl_2, 298 K) δ/ppm = 8.30 (br. s, 1H, H_5), 7.64 (t, *J* = 7.4 Hz, 1H, H_7), 7.57 (d, *J* = 7.9 Hz, 1H, H_8), 7.41 (t, *J* = 7.5 Hz, 1H, H_6), 7.32 – 7.18 (m, 5H, $H_{12,13,14}$), 7.07 (d, *J* = 8.8 Hz, 2H, H_{16}), 6.87 (d, *J* = 8.7 Hz, 2H, H_{17}), 6.66 (br. s, 1H, NH), 3.76 (s, 3H, H_{19}). **^{13}C NMR** (100 MHz, CD_2Cl_2, 298 K) δ/ppm = 160.2 (C_{18}), 155.4 (C_4 Not Clear), 155.4 (C_2), 145.2 (C_9), 137.1 (C_{11}), 133.2 (C_7), 131.6 (C_{16}), 130.8 (C_{15}), 129.2 (C_{14}), 129.2 (C_{13}), 128.3 (C_{12}), 127.8 (C_8), 127.2 (C_6), 126.1 (C_5), 122.0 (C_{10}), 115.5 (C_{17}), 56.0 (C_{19}). **FT-IR (KBr)**: ν / cm^{-1} = 3311, 3297, 3060, 3033, 3002, 2859, 2936, 2909, 2835, 1678, 1632, 1606, 1584, 1565, 1508, 1473, 1463, 1442, 1362, 1317, 1298, 1251, 1176, 1152, 1136, 1108, 1075, 1053, 1029, 949, 916, 887, 875, 839, 821, 806, 766, 725, 698, 673, 656, 631, 583, 543, 481. **HRMS (ESI)** for $C_{21}H_{18}N_3O$ $[M+H]^+$: m/z calcd: 328.144, found: 328.144.

Synthesis of 2,3-Diphenylquinazolin-4(3*H*)-iminium chloride (5): (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.21 g, 0.86 mmol) was added to a solution of aniline (0.08 g, 0.86 mmol) in 30 mL of toluene and the reaction mixture was stirred for 36 hours under reflux. All volatiles were removed under vacuum and the light yellow solid was washed with acetone and crystallized from chloroform/methanol to give light yellow crystals (0.20 g, 70 %). **^{1}H NMR** (400 MHz, $CDCl_3$/MeOH*, 298 K) δ/ppm = 9.17 (d, *J* = 8.2 Hz, 1H, H_5), 7.98 (t, *J* = 7.6 Hz, 1H, H_7), 7.89 (d, *J* = 8.0 Hz, 1H, H_8), 7.76 (t, *J* = 7.5 Hz, 1H, H_6), 7.48 (m, 3H, $H_{17,18}$), 7.34 – 7.19 (m,7H, $H_{16,12,13,14}$). **^{13}C NMR** (100 MHz, $CDCl_3$/MeOH*, 298 K) δ/ppm = 157.4 (C_4), 152.1 (C_2), 145.7 (C_9), 137.6 (C_7), 134.4 (C_{15}), 133.2 (C_{11}), 131.4 (C_{18}), 131.2 (C_{17}), 130.2 (C_{14}), 120.0 (C_6), 129.0 (C_{16}), 128.6 (C_8), 128.5 (C_{13}), 128.2 (C_{12}), 127.7 (C_5), 113.2 (C_{10}). ***Note**: A drop of methanol HPLC (MeOH*) was added to the RMN sample ($CDCl_3$) to increase the solubility of the product.* **FT-IR (KBr)**: ν / cm^{-1} = 3378, 3201, 3052, 3027, 2940, 2780, 1654, 1606, 1595, 1570, 1536, 1489, 1472, 1458, 1444, 1338, 1308, 1291, 1280,

1222, 1156, 1076, 1037, 1017, 999, 972, 953, 923, 891, 873, 850, 773, 698, 677, 630, 614, 581, 560, 537, 522, 487. **HRMS (ESI)** for $C_{20}H_{16}N_3^+$: m/z calcd: 298.134, found: 298.134.

Synthesis of 3-(4-aminophenyl)-2-phenylquinazolin-4(3*H*)-iminium chloride (6): (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.11g, 0.46 mmol) was added to a solution of *p*-phenylenediamine (0.05 g, 0.46 mmol) in 30 mL of toluene and the reaction mixture was stirred for 18 hours under reflux. Light brown solid was formed, which were filtered and dried under vacuum (0.11 g, 69 %). **^{1}H NMR** (400 MHz, CD_2Cl_2/CD_3OD (97:3), 298 K) δ/ppm = 8.77 (d, *J* = 8.2 Hz, 1H, H_5), 8.08 (t, *J* = 7.6 Hz, 1H, H_7), 7.96 (d, *J* = 8.3 Hz, 1H, H_8), 7.83 (t, *J* = 7.6 Hz, 1H, H_6), 7.37 – 7.25 (m, 5H, $H_{12,13,14}$), 6.96 (d, *J* = 8.0 Hz, 2H, H_{17}), 6.70 (d, *J* = 8.0 Hz, 2H, H_{16}), 3.74 (br. s, 2H, H_{19}, Not clear). **^{13}C NMR** (100 MHz, CD_2Cl_2/CD_3OD (97:3), 298 K) δ/ppm = 159.1 (C_4), 154.0 (C_2), 150.8 (C_{15}), 146.6 (C_9), 138.4 (C_7), 134.2 (C_{11}), 130.6 (C_{14}), 130.5 (C_6), 129.7 (C_{13}), 129.5 (C_{17}), 129.5 (C_8), 128.7 (C_{12}), 126.7 (C_5), 123.5 (C_{18}) , 116.5 (C_{16}), 113.5 (C_{10}). **FT-IR (KBr)**: ν / cm^{-1} = 3411, 3328, 3224, 3181, 3026, 2950, 2881, 2675, 2603, 2563, 1649, 1628, 1613, 1577, 1506, 1445, 1338, 1311, 1292, 1198, 1178,1159, 1113, 1031, 954, 825, 769, 708, 696, 677, 623, 593, 584, 540, 511. **HRMS (ESI)** for $C_{20}H_{17}N_4^+$: m/z calcd: 313.145, found: 313.145.

Synthesis of 3-(4-cyanophenyl)-2-phenylquinazolin-4-(3*H*)-iminium chloride (7): (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.12g, 0.51mmol) was added to a solution of 4-aminobenzonitrile (0.06g, 0.51mmol) in 30 mL of toluene and the reaction mixture was stirred for 96 hours under reflux. All volatiles were removed under vacuum and the crude product was washed with acetone and dried to give light yellow solid (0.12 g, 65 %). **^{1}H NMR** (400 MHz, D_2O/CD_3OD (97:3), 298 K) δ/ppm = 8.43 (d, *J* = 8.4 Hz, 1H, H_5), 8.19 (t, *J* = 7.7 Hz, 1H, H_7), 7.96 (d, *J* = 8.3 Hz, 1H, H_8), 7.90 (m, 3H, $H_{6,17}$), 7.68 (d, *J* = 8.4 Hz, 2H, H_{16}), 7.43 – 7.28 (m, 5H, $H_{12,13,14}$). **^{13}C NMR** (100 MHz, D_2O/CD_3OD (97:3), 298 K) δ/ppm = 158.9 (C_4), 153.8 (C_2), 145.9 (C_9), 139.4 (C_{15}), 139.3 (C_7), 136.1 (C_{17}), 133.0 (C_{11}), 131.5 (C_{14}), 131.1 (C_6), 130.8 (C_{16}), 129.9 (C_{13}), 129.4 (C_{12}), 128.9 (C_8), 125.9 (C_5), 118.7 (C_{19}), 115.5 (C_{18}), 113.8 (C_{10}). **FT-IR (KBr)**: ν / cm^{-1} = 3396, 3213, 3091, 3031, 2963, 2237 (CN), 1632, 1604, 1578, 1549, 1506, 1480, 1459, 1444, 1432, 1411, 1383, 1338, 1318, 1292, 1261, 1160, 1097, 1021, 956, 928, 864, 800, 734, 699, 673, 627, 583, 564, 546, 521. **HRMS (ESI)** for $C_{21}H_{15}N_4^+$: m/z calcd: 323.129, found: 323.129.

Synthesis of 2-Phenyl-3-(1-phenyl-ethyl)-(3*H*)-quinazolin-4-ylidene-iminium chloride (8): Compound **8** was prepared by reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.15 g, 0.59

mmol) with (*R*)-(+)-α-methyl benzilamine (0.08 mL, 0.59 mmol) in 20 mL of toluene. Then was added at 0°C and stirred at this temperature for 2 hours. Then the reaction mixture was stirred for 48 hours at room temperature. The precipitate was filtrated and discarded. All volatiles were removed under vacuum from the solution; the product was separated by a short column of silica gel, using ethyl acetate and then chloroform. The chloroform was removed under vacuum and the light yellow oil was obtained. Crystals of this compound were acquired from solution chloroform/ethyl acetate to give light yellow crystals (0.16 g, 70 %). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K) δ/ppm = 7.80 (d, *J* = 8.0 Hz, 1H, H_5), 7.51 – 7.47 (m, 2H, $H_{7, 14}$), 7.41 – 7.39 (m, 2H, H_{12}), 7.32 – 7.31 (m, 3H, $H_{13,8}$), 7.26 – 7.22 (m, 1H, H_6), 7.20 – 7.19 (m, 2H, H_{19}), 7.16 – 7.10 (m, 3H, $H_{18, 20}$), 5.57 (q, *J* = 6.8 Hz, 1H, H_{15}), 1.82 (d, *J* = 7.2 Hz, 3H, H_{16}). **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K) δ/ppm = 156.8 (C_2), 154.9 (C_4), 143.7 (C_{10}), 139.8 (C_{17}), 136.8 (C_9), 132.3 (C_7), 129.4 (C_8), 128.7 (C_{13}), 128.5 (C_{19}), 127.4 (C_{14}), 127.2 (C_{12}), 126.8 (C_{20}), 126.5 (C_6), 125.6 (C_{18}), 124.0 (C_5), 121.2 (C_{11}), 57.4 (C_{15}), 16.2 (C_{16}). **FTIR (KBr):** ν / cm^{-1} = 3059, 3028, 2964, 2906, 2362, 2027, 1919, 1622, 1604, 1566, 1523, 1494, 1476, 1460, 1446, 1414, 1391, 1357, 1319, 1262, 1209, 1096, 1025, 875, 800, 698, 670, 642, 594, 539, 520, 394, 297. **HRMS (ESI)** for $C_{20}H_{20}N_3^+$: m/z calcd: 326.165, found: 326.165**.**

Synthesis of 5-phenyl-2,3-dihydroimidazo[1,2-*c*] quinazoline (9): Compound **9** was prepared by reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.15 g, 0.59 mmol) with ethylenediamine (0.04 mL, 0.59 mmol) in 20 mL of toluene. The ethylendiamine was added at 0°C and stirred at this temperature for 2 hours. Then the reaction mixture was stirred for 48 hours at room temperature. The precipitate was filtrated and discarded. All volatiles were removed under vacuum from the solution; the product was separated by a short column of silica gel, using ethyl acetate and then chloroform. The chloroform was removed under vacuum and the light yellow oil was obtained. Crystals of this compound were acquired from a solution chloroform/ethyl acetate to give light yellow crystals (0.09 g, 57 %). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K) δ/ppm = 8.04 (d, *J* = 7.6 Hz, 1H, H_5), 7.64 – 7.61 (m, 2H, H_{13}), 7.58 (d, *J* = 1.2 Hz, 1H, H_8), 7.56 (br. s, 1H, H_7), 7.50 (d, *J* = 2.4 Hz, 2H, H_{12}), 7.48 (d, *J* = 1.2 Hz, 1H, H_{14}), 7.33 – 7.31 (m, 1H, H_6), 4.12 – 3.99 (m, 1H, $H_{15, 16}$). **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K) δ/ppm = 155.5 (C_4), 153.8 (C_{11}), 146.7 (C_9), 135.1 (C_2), 133.1 (C_7), 130.2 (C_{14}), 128.7 (C_{12}), 127.7 (C_{13}), 127.2 (C_8), 126.5 (C_6), 125.2 (C_5), 117.9 (C_{10}), 53.4 (C_{15}), 48.9 (C_{16}). **FTIR (KBr):** ν / cm^{-1} = 3423, 3332, 3233, 3065, 2952, 2873, 1647, 1614, 1601, 1582, 1550, 1498, 1478, 1467, 1447, 1405, 1352, 1297, 1277, 1242, 1179, 1154, 1076, 1044, 1028, 1001, 979, 919, 856, 841, 779, 712,

701, 683, 670, 640, 586, 542, 435, 347, 297. **HRMS (ESI)** for $C_{16}H_{14}N_3$ $[M+H]^+$: m/z calcd: 248.118 , found: 248.118.

Synthesis of 6-phenyl-3,4-dihydro-2*H*-pyrimido[1,2-*c*] quinazoline (10): Compound **10** was prepared by reaction of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.15 g, 0.59 mmol) with 1,3-diaminopropane (0.05 mL, 0.59 mmol) in 20 mL of toluene. The reaction mixture was stirred for 48 hours under reflux. The precipitate was filtrated and discarded. All volatiles were removed under vacuum from the solution and the crude product was crystallized from diethyl ether to give light yellow crystals (0.09 g, 60 %). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K) δ/ppm = 8.17 (d, *J* = 7.6 Hz, 1H, H_5), 7.51 – 7.45 (m, 7H, $H_{7,8,12,13,14}$), 7.32 (t, *J* = 7.2 Hz, 1H, H_6), 3.69 – 3.64 (m, 4H, $H_{15,17}$), 1.92 – 1.86 (m, 2H, H_{16}). **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K) δ/ppm = 155.5, 146.6, 144.0, 135.6, 122,66 ($C_{2,4,9,10,11}$), 132.0, 129.8, 129.00, 127.9, 127.0 ($C_{7,8,12,13,14}$), 126.8 (C_6), 124.6 (C_5), 47.7, 44.6 ($C_{15,17}$), 20.8 (C_{16}). **FTIR (KBr):** ν / cm^{-1} = 3424, 3332, 3223, 3073, 2932, 2857, 1635, 1600, 1585, 1564, 1493, 1479, 1461, 1443, 1378, 1352, 1287, 1242, 1174, 1146, 1075, 1036, 1007, 956, 772, 718, 706, 672, 594, 542, 408, 348, 297.

Synthesis of 2-phenyl-3-(pyridin-2-ylmethyl)quinazolin-4(3H)-iminium chloride (11): 2-picolinamina (0.22 g, 2.08 mmol) was added to a solution of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.50g, 2.08 mmol) in 20 mL of toluene and the reaction mixture was stirred for 26 hours under reflux. The precipitate was filtrated and discarded and from the solution a white solid was precipited from, which were filtered and dried under vacuum (0.32 g, 45 %). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K) δ/ppm = 10.21 (br. s. 1H, NH), 8.81 (d, *J* = 8.4, 1H, H_5), 8.60 – 8.51 (m, 4H, $H_{6,\ 7,\ 8,\ 18}$), 7.72 – 7.69 (m, 2H, $H_{19,\ 20}$), 7.53 – 7.44 (m, 5H, $H_{12,\ 13,\ 14}$), 7.24 – 7.23 (m, 1H, H_{21}), 5.15 (s, 2H, H_{15}). **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K) δ/ppm = 160.07 (C_4), 157.86, 155.36, 130.85, 120.30 ($C_{2,\ 9,\ 11,\ 16}$), 148.67, 129.90, 123.69 ($C_{6,\ 7,\ 8}$), 137.72, 135.49 ($C_{19,\ 20}$), 133.65, 129.06, 122.42 ($C_{12,\ 13,\ 14}$), 128.21 (C_{18}), 123.09 (C_{21}), 121.72 (C_5), 46.41 (C_{15}). **FT-IR (KBr)**: ν / cm^{-1} = 3302, 3062, 2851, 1632, 1616, 1563, 1519, 1504, 1477, 1458, 1431, 1404, 1383, 1330, 1288, 1274, 1213, 1189, 1153, 1117, 1030, 1018, 995, 966, 930, 881, 821, 767, 702, 678, 628, 581. **HRMS (ESI)** for $C_{20}H_{17}N_4^+$: m/z calcd: 313.15 , found: 313.

Synthesis of 3-(benzo[d][1,3]dioxol-5-ylmethyl)-2-phenylquinazolin-4(3H)-iminium chloride (12): piperonylamine (0.31 g, 2.08 mmol) was added to a solution of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.50g, 2.08 mmol) in 20 mL of toluene and the reaction mixture was stirred for 24 hours

under reflux. Pale yellow solid was formed, which were filtered and dried under vacuum (0.44 g, 55 %). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K) δ/ppm = 11.49 (br. s. 1H, HCl), 10.55 (br. s. 1H, NH), 9.44 (d, *J* = 8.2 Hz, 1H, H_5), 8.00 – 7.85 (m, 2H, $H_{7, 8}$), 7.77 (t, *J* = 7.5 Hz, 1H, H_6), 7.61 – 7.51 (m, 5H, $H_{12, 13, 14}$), 6.64 – 6.61 (m, 3H, $H_{17, 20, 21}$), 5.98 (s, 2H, H_{15}), 5.84 (s, 2H, H_{22}). **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K) δ/ppm = 157.16 (C_4), 154.08 (C_2), 148.30 (C_{19}), 147.88 (C_{18}), 145.55 (C_9), 137.14, 128.53 ($C_{7, 8}$), 133.72 (C_{15}), 131.20 (C_{14}), 129.81 (C_6), 129.31, 128.74 ($C_{12, 13}$), 127.70 (C_5), 126.55 (C_{11}), 120.93, 108.76, 107.42 ($C_{17, 20, 21}$), 114.30 (C_{10}), 101.30 (C_{22}), 53.40 (C_{15}). **FT-IR (KBr)**: ν / cm^{-1} = 3425, 2995, 2875, 2782, 2560, 2057, 1854, 1695, 1613, 1599, 1585, 1500, 1486, 1467, 1445, 1388, 1358, 1322, 1275, 1249, 1206, 1189, 1154, 1132, 1118, 1105, 1089, 1043, 970, 939, 915, 892, 812, 772, 727, 711, 700, 675, 631, 614, 600, 585, 517, 498, 448, 425, 388, 318. **HRMS (ESI)** for $C_{22}H_{18}N_3O_2^+$: m/z calcd: 356.14 , found: 356.

Synthesis of 3-(2,5-dimethoxyphenyl)-2-phenylquinazolin-4(3H)-iminium chloride (13): 2,5-dimethoxyaniline (0.32 g, 2.08 mmol) was added to a solution of (*E*)-*N*-(2-cyanophenyl)benzimidoyl chloride (0.50g, 2.08 mmol) in 20 mL of toluene and the reaction mixture was stirred for 24 hours under reflux. Gray solid was formed, which were filtered and dried under vacuum (0.53 g, 65 %). **^{1}H NMR** (400 MHz, $CDCl_3$, 298 K) δ/ppm = 13.01 (s, 1H, NH), 9.54 (d, *J* = 8.1 Hz, 1H, H_5), 8.09 – 7.82 (m, 3H, $H_{6, 7, 8}$), 7.39 – 7.28 (m, *5*H, $H_{12, 13, 14}$), 7.04 – 6.89 (m, 2H, $H_{17, 18}$), 6.79 (br. s, 1H, H_{20}), 3.74 (s, 3H, $H_{21,22}$), 3.72 (s, 3H, $H_{21, 22}$). **^{13}C NMR** (100 MHz, $CDCl_3$, 298 K) δ/ppm = 157.03 (C_4), 154.35, 152.32, 132.94, 121.98 ($C_{2, 11, 15, 19}$) 147,62 (C_{16}), 145.86 (C_9), 137.78 (C_7), 130.42 (C_{14}), 130.06 (C_6), 128.54 (C_5), 128.50 (C_8), 128.27, 128.05 ($C_{12, 13}$) , 118.75, 114.10 ($C_{17, 18}$), 114.45 (C_{20}) , 112.78 (C_{10}), 56.13 , 56.12 ($C_{21, 22}$). **FT-IR (KBr)**: ν / cm^{-1} = 3393, 3029, 3000, 2938, 2834, 2745, 2663, 2012, 1830, 1658, 1625, 1599, 1573, 1530, 1506, 1479, 1465, 1446, 1340, 1314, 1298, 1275, 1234, 1204, 1160, 1144, 1117, 1078, 1041, 1016, 964, 935, 904, 887, 858, 808, 796, 779, 737, 726, 706, 678, 642, 586, 519, 492, 397, 355. **HRMS (ESI)** for $C_{22}H_{20}N_3O_2^+$: m/z calcd: 358.16 , found: 359.

X-ray crystal structure analyses: For compounds **1**, **2**, **4**, **9** and **13** data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection, COLLECT (Nonius B.V., 1998); data reduction Denzo-SMN (Z. Otwinowski, W. Minor, *Methods Enzymol.* **1997**, *276*, 307-326); absorption correction, Denzo (Z. Otwinowski, D. Borek, W. Majewski, W. Minor, *Acta Crystallogr*. **2003**, *A59*, 228-234); structure solution SHELXS-97 (G. M. Sheldrick, *Acta Crystallogr*. **1990**, *A46*, 467-473); structure refinement SHELXL-97 (G. M. Sheldrick, *Acta Crystallogr*. **2008**, *A64*, 112-122)

and graphics, XP (BrukerAXS, 2000). Thermals ellipsoids are shown with 30% probability, *R*-values are given for observed reflections, and wR^2 values are given for all reflections.

Exceptions and special features: For compound **2** a half badly disordered dichloromethane molecule was found in the asymmetrical unit and could not be satisfactorily refined. Compound **5** crystallized with one badly disordered over tree positions methanol molecule. The program SQUEEZE (A. L. Spek J. Appl. Cryst., 2003, 36, 7-13) was therefore used to remove mathematically the effect of the solvents. The quoted formula and derived parameters are not included the squeezed solvent molecules.

Crystallographic data for **1**, **2**, **4**, **5**, **9** and **13** have been deposited with Cambridge Crystallographic Data Centre, CCDC numbers 1008256, 1008257, 1008258, 1008259, 1008260 and 1057208. These data can be obtained free at www.ccdc.cam.ac.uk/conts/rtrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk].

X-ray crystal structure analysis of 1: formula $C_{21}H_{25}N_3$, *M* = 319.44 colourless crystal, 0.38 x 0.35 x 0.15 mm, *a* = 11.8867(3), *b* = 12.5284(6), *c* = 13.0514(4) Å, α = 79.096(4), *β* = 89.444(2), γ = 77.230(5)°, *V* = 1860.3(1) $Å^3$, ρ_{calc} = 1.141 gcm^{-3}, μ = 0.521 mm^{-1}, empirical absorption correction (0.826 ≤ T ≤ 0.925), *Z* = 4, triclinic, space group $P\bar{1}$ (No. 2), λ = 1.54178 Å, *T* = 223(2) K, ω and ϕ scans, 21856 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.60 $Å^{-1}$, 6335 independent (R_{int} = 0.037) and 5970 observed reflections [*I*>2σ(*I*)], 441 refined parameters, *R* = 0.045, wR^2 = 0.118, max. (min.) residual electron density 0.15 (-0.16) e.$Å^{-3}$, the hydrogen atoms at N4A and N4B were refined freely, but with N-H distance restraints (SADI); others were calculated and refined as riding atoms.

X-ray crystal structure analysis of 2: formula $C_{26}H_{27}N_3$, *M* = 381.51 colourless crystal, 0.23 x 0.15 x 0.03 mm, *a* = 16.4490(8), *b* = 16.4490(8), *c* = 8.4714(4) Å, *V* = 2292.1(2) $Å^3$, ρ_{calc} = 1.106 gcm^{-3}, μ = 0.502 mm^{-1}, empirical absorption correction (0.893 ≤ T ≤ 0.985), *Z* = 4, tetragonal, space group *P*-4 (No. 81), λ = 1.54178 Å, *T* = 223(2) K, ω and ϕ scans, 8679 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.60 $Å^{-1}$, 3410 independent (R_{int} = 0.058) and 2945 observed reflections [*I*>2σ(*I*)], 269 refined parameters, *R* = 0.059, wR^2 = 0.162, max. (min.) residual electron density 0.19 (-0.23) e.$Å^{-3}$, the hydrogen at N3 atom was refined freely, but with N-H distance restraints (DFIX and U-fixed value); others were calculated and refined as riding atoms.

X-ray crystal structure analysis of 4: formula $C_{21}H_{17}N_3O$, *M* = 327.38 colourless crystal, 0.40 x 0.15 x 0.04 mm, *a* = 12.9137(5), *b* = 14.1902(4), *c* = 14.6060(6) Å, α = 107.781(2), *β* = 90.352(2), γ = 98.594(2)°, *V* = 2516.2(2) Å^3, ρ_{calc} = 1.296 gcm^{-3}, μ = 0.649 mm^{-1}, empirical absorption correction (0.781 ≤ T ≤ 0.974), *Z* = 6, triclinic, space group $P\bar{1}$ (No. 2), λ = 1.54178 Å, *T* = 223(2) K, ω and ϕ scans, 34337 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.60 Å^{-1}, 8764 independent (R_{int} = 0.040) and 7650 observed reflections [*I*>2σ(*I*)], 691 refined parameters, *R* = 0.038, wR^2 = 0.104, max. (min.) residual electron density 0.04 (-0.10) e.Å^{-3}, the hydrogen atoms at N4A, N4B and N4C were refined freely; others were calculated and refined as riding atoms.

X-ray crystal structure analysis of 5: formula $C_{20}H_{16}N_3Cl$, *M* = 333.81 pale yellow crystal, 0.38 x 0.28 x 0.18 mm, *a* = 14.6582(9), *b* = 17.3558(12), *c* = 7.0639(7) Å, *β* = 98.146(3) °, *V* = 1779.0(2) Å^3, ρ_{calc} = 1.246 gcm^{-3}, μ = 0.220 mm^{-1}, *Z* = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 0.71703 Å, *T* = 297(2) K, ω and ϕ scans, 14711 reflections collected (±*h*, ±*k*, ±*l*), 3634 independent (R_{int} = 0.053) and 2634 observed reflections [*I*>2σ(*I*)], 225 refined parameters, *R* = 0.041, wR^2 = 0.112, max. (min.) residual electron density 0.36 (-0.16) e.Å^{-3}, the hydrogen atoms at N4 were refined freely, but with N-H distance restraints (SADI); others were calculated and refined as riding atoms.

X-ray crystal structure analysis of 9: formula $C_{16}H_{13}N_3 \cdot H_2O$, *M* = 265.31 colourless crystal, 0.30 x 0.20 x 0.18 mm, *a* = 8.9276(2), *b* = 9.0785(2), *c* = 16.8687(3) Å, *β* = 96.058(2) °, *V* = 1359.6(1) Å^3, ρ_{calc} = 1.296 gcm^{-3}, μ = 0.084 mm^{-1}, empirical absorption correction (0.975 ≤ T ≤ 0.985), *Z* = 4, monoclinic, space group $P2_1/n$ (No. 14), λ = 0.71073 Å, *T* = 223(2) K, ω and ϕ scans, 8031 reflections collected (±*h*, ±*k*, ±*l*), [(sinθ)/λ] = 0.62 Å^{-1}, 2695 independent (R_{int} = 0.033) and 2386 observed reflections [*I*>2σ(*I*)], 189 refined parameters, *R* = 0.044, wR^2 = 0.110, max. (min.) residual electron density 0.18 (-0.15) e.Å^{-3}, the hydrogen atoms at O1 were refined freely; others were calculated and refined as riding atoms.

X-ray crystal structure analysis of 13: formula $C_{22}H_{20}N_3Cl \cdot H_2O$, M= 411.87 pale yellow needle-like crystals, 0.020 mm x 0.080 mm x 0.200 mm, *a* = 7.7886(2), *b* = 9.9350(3), *c* = 13.6151(4) Å, α = 83.463(2)°, β = 84.947(2)°, γ = 73.188(2)°, volume = 1000.26(5) Å^3, ρ_{calc} = 1.368 gcm^{-3}, μ = 1.932 mm^{-1}, *Z* = 2, triclinic, space group P -1, 16418 reflections collected (±*h*, ±*k*, ±*l*), 3365 independent (R_{int} = 0.0514) and 2859 observed reflections [*I*>2σ(*I*)], 285 refined parameters, *R* = 0.0443, wR^2 = 0.0910, max. (min.) residual electron density 0.241 (-0.223) e.Å^{-3}.

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