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# The Conversion of 4-Anilinoquinazoline- and 3-Aryl-4-imino-3,4-dihydro-quinazoline-2-carbonitriles into Benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitriles via Oxidative and Nonoxidative C−N Couplings

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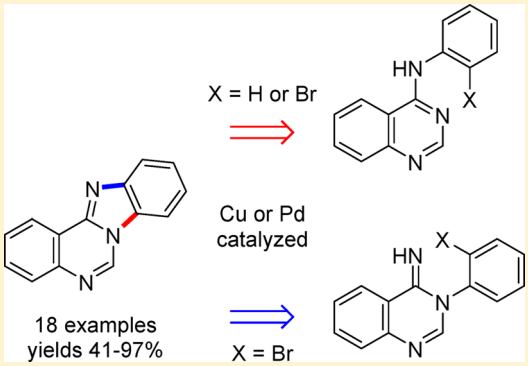
Supporting Information

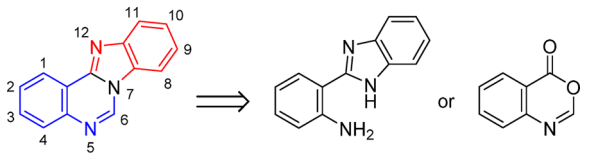
**ABSTRACT:** Benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitriles are prepared in high yields via three new routes: (1) a $Cu(OTf)_2$ (0−5 mol %) catalyzed hypervalent iodine [$PhI(OTf)_2$] mediated oxidative coupling of 4-anilinoquinazoline-2-carbonitriles in neat trifluoroacetic acid (TFA); (2) a $Pd(OAc)_2$ (10 mol %) or CuI (10 mol %) mediated nonoxidative coupling of 4-(2-bromoanilino)quinazoline-2-carbonitrile; and (3) a nonoxidative $Pd(Ar_3P)_3$ [Ar = 3,5-$(F_3C)_2C_6H_3$] [aka Superstable Pd(0) Catalyst] (10 mol %) mediated intramolecular C−N cyclization of 3-(2-bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitriles. All new compounds are fully characterized.




## 1. INTRODUCTION

Benzo[4,5]imidazo[1,2-*c*]quinazoline (**1**) is a planar trinitrogen heteroacene that hosts both benzimidazole and quinazoline structures fused together via a shared bond (Scheme 1).[1] Not surprisingly, benzo[4,5]imidazo[1,2-*c*]quinazolines display a wide array of biological activities. Some act as DNA interchelators and show antitumor,[2] anticancer,[3] antiviral,[4] and antimicrobial[5] activities, while others act as anticonvulsant agents[6] or as bronchodilators.[7] Metal chelates with ruthenium(II),[8] tin,[9] and lead[9] have also been studied. Benzo[4,5]imidazo[1,2-*c*]quinazolines also have hole transporting properties.[10]

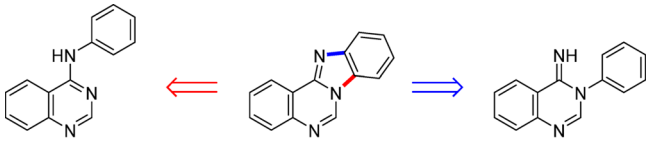
**Scheme 1. Structure and Numbering Scheme for Benzo[4,5]imidazo[1,2-*c*]quinazoline (1) and Two Common Precursors 2-(2-Aminophenyl)benzimidazole (2) and 4*H*-Benzo[*d*][1,3]oxazin-4-ones (3)**




Most syntheses of benzo[4,5]imidazo[1,2-*c*]quinazolines focus on building the pyrimidine ring starting from 2-(2-aminophenyl)benzimidazoles **2**[1,3b,4b,6,11] or via structurally related precursors, e.g., 2-(2-nitrophenyl)benzimidazoles,[12] *N*-[2-(benzimidazol-2-yl)phenyl]phosphanimines,[13] 2-(2-azidophenyl)benzimidazoles,[14] *N*-[2-(benzimidazol-2-yl)-phenyl]methanimines,[5c,d,15] and 2-(2-halophenyl)benzimidazoles.[16] A second major synthetic route of benzo[4,5]imidazo[1,2-*c*]quinazolines is via construction of the imidazole ring which has been limited to treatment of 4*H*-benzo[*d*][1,3]-oxazin-4-ones **3** with 1,2-benzenediamines either directly[5a,b,e,7b,11i,17] or via the isolable intermediate 3-(2-aminophenyl)-3*H*-quinazolin-4-ones[7b,18] or structurally related benzo[1,3]thiazin-4-ones.[19]

A structural analysis of both 4-anilinoquinazoline (**4**) and 3-phenylquinazolin-4(3*H*)-imine (**5**) reveals that their structures are just one C−N bond short of the benzo[4,5]imidazo[1,2-*c*]quinazoline skeleton (Scheme 2). Our ongoing studies on the synthesis and chemistry of 2-amino-*N*′-arylbenzamidines[20]

**Scheme 2. Retrosynthetic Analysis of Benzo[4,5]imidazo[1,2-*c*]quinazoline Skeleton to Give Either 4-Anilinoquinazoline (4) or 3-Phenylquinazolin-4(3*H*)-imine (5)**

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provided us with a small library of 4-anilinoquinazoline- and 3-aryl-4-imino-3,4-dihydroquinazoline-2-carbonitriles.[21] In light of the limited number of routes to the benzo[4,5]imidazo-[1,2-*c*]quinazoline skeleton via construction of the imidazole ring, we investigated both oxidative and nonoxidative methods for converting these readily available quinazoline-2-carbonitriles into benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitriles. The development of synthetic routes that hosted nitriles in the final products is worthwhile since these can readily be converted into a wide range of other functionalities.[22] Furthermore, the presence of a cyano group in this tetracycle improved the cytotoxicity in comparison to the parent compound.[3b]

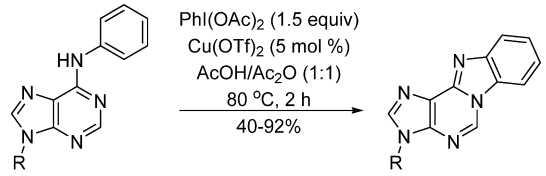
## 2. RESULTS AND DISCUSSION

**2.1. Oxidative and Nonoxidative Cyclization Chemistry of 4-Anilinoquinazoline-2-carbonitriles 4.** The 4-anilinoquinazolines **4** host a *N*,*N*′-disubstituted benzamidine motif within their structures, cyclization of which affords the desired benzo[4,5]imidazo[1,2-*c*]quinazolines. The literature on the preparation of benzo- or hetareno-fused imidazoles from amidines via oxidative C−N coupling highlighted the use of electro-oxidation[23] and the use of a variety of oxidants including $H_2O_2$,[24] cerium ammonium nitrate (CAN),[23a] NaOCl,[25] NCS,[26] $MnO_2$,[27] $Pb(OAc)_4$,[23a,28] and hypervalent iodine(III) reagents.[29] In our hands, cyclization efforts using either $H_2O_2$, CAN, NCS, $MnO_2$, or $Pb(OAc)_4$ failed but succeeded with hypervalent iodine(III) reagents.

$PhI(OAc)_2$ (PIDA or DAIB) and $PhI(OTf)_2$ (PIFA or BFIB) either alone in equimolar or greater quantities,[28c,30] or catalytically in the presence of co-oxidants,[31] are typically used for such cyclizations. Variations where the hypervalent iodine(III) reagent is generated *in situ* have also been reported.[32]

The closest reported reaction to our targeted cyclization was the oxidative ring closure of the structurally related 6-anilinopurines **6** to give the benzo[4,5]imidazo[2,1-*i*]purines **7**, using PIDA (1.5 equiv) and $Cu(OTf)_2$ (5 mol %) in a solvent mixture of $AcOH/Ac_2O$ (1:1) heated at reflux (Scheme 3).[31b]

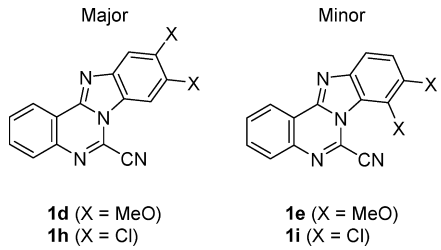
**Scheme 3. Copper(II)-Mediated Oxidative Ring Closure of 6-Anilinopurines 6 To Give Benzo[4,5]imidazo[2,1-*i*]purines 7**[31b]




In our hands these conditions worked well for converting 4-anilinoquinazoline-2-carbonitrile (**4a**) into benzo[4,5]imidazo-[1,2-*c*]quinazoline-6-carbonitrile (**1a**) which was isolated in 81% yield together with a small quantity of an unidentified side product (see Supporting Information, Section S1, Table S1, entry 1). Side products have also been observed by Chu et al.,[30b] who noted that their formation could be avoided by using PIFA in place of PIDA. With this in mind the reaction was reoptimized (see Supporting Information, Section S1) and found to work better when only PIFA (1.1 equiv) was used in neat trifluoroacetic acid (TFA) at ca. 20 °C to give the desired benzo[4,5]imidazo[1,2-*c*]quinazoline **1a** in 92% yield after only 30 min (Table 1, entry 1 and Supporting Information, Table S1, entry 7).

Having partially optimized this oxidative ring closure, the mildest conditions, PIFA (1.1 equiv) in neat TFA at room temperature, were then applied to a range of 4-anilinoquinazoline-2-carbonitriles **4a**−**j** (Table 1). These metal free conditions worked well for the parent, the 4-Me and the 4-MeO substituted analogues (Table 1, entries 1−3), however, the reactions with 4-anilinoquinazolines that hosted inductively electron-withdrawing halogen substituents on the aniline moiety (Table 1, entries 6−17) required prolonged reaction times. As such, we reoptimized the reaction conditions for 4-(4-fluoroanilino)quinazoline-2-carbonitrile (**4e**) (Table 1, entries 6−9): Increasing the equivalents of PIFA (from 1.1 to 2 equiv) or raising the reaction temperatures (from 20 to 80 °C) did not significantly improve the reaction (data not shown). Fortunately, a shorter reaction time (1.5 h) was achieved by reintroducing $Cu(OTf)_2$ (5 mol %), increasing the amount of PIFA (1.5 equiv) and raising the reaction temperature to 80 °C (Table 1, entry 9). Worthy of note was that with the reagents in this stoichiometry, the reaction worked well even at 20 °C to give the product **1f** in 85% yield, although the reaction required more time (6 h) to consume the starting material (Table 1, entry 8). These Cu-catalyzed conditions worked equally well for the remaining halogen bearing analogues (Table 1, entries 11, 13, 15, and 17). Tentatively, we assume that the Lewis acidity of the Cu species assists to activate the hypervalent iodine oxidant (for a brief mechanistic discussion see Supporting Information, Section S1.1).

Not surprisingly, the reactions of 4-anilinoquinazolines that hosted unsymmetrically substituted anilines **4d** [$R^2$ = 3,4-$(MeO)_2$] and **4g** [$R^2$ = 3,4-$(Cl)_2$] gave mixtures of two cyclization products a major and minor the ratio of ca. 2.6:1, which tentatively reflected steric phenomena.




With 4-(2-bromoanilino)quinazoline-2-carbonitrile (**4h**) in hand, we considered a regio-controlled transition-metal-catalyzed nonoxidative coupling. A number of nonoxidative cyclization protocols are known for the transformation of *N*-alkyl or aryl-substituted *N*′-(2-halophenyl)benzamidines to give 1-alkyl- or 1-aryl-substituted 2-aryl-1*H*-benzimidazoles; some involve transition-metal catalysis (e.g., Pd,[33] Cu,[33d,34] or Co[35]), while others invoke base-mediated aryne intermediates[34b,36] or simply intramolecular nucleophilic aromatic substitution.[34b,37]

After screening several Pd catalysts [$Pd(OAc)_2$, $Pd(dppf)Cl_2 \cdot CH_2Cl_2$, $Pd(MeCN)_2$, $Pd(PhCN)_2$, $PdCl_2(Ph_3P)_2$, and $Pd(Ar_3P)_3$, where Ar = 3,5-$(F_3C)_2C_6H_3$ (aka Superstable Pd(0) Catalyst)], ligands [2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP), 1,10-phenanthroline (1,10-Phen), 1,1′-bis(diphenylphosphino)ferrocene (DPPF), and *N*,*N*′-dimethylethylenediamine (DMEDA)], bases [$KHCO_3$, $K_3PO_4$, $M_2CO_3$ (M = Na, K, Cs), KOH and DBU], and solvents (PhMe, MeCN, 1,4-dioxane, THF, DMSO, DMF, DMA and EtOH),


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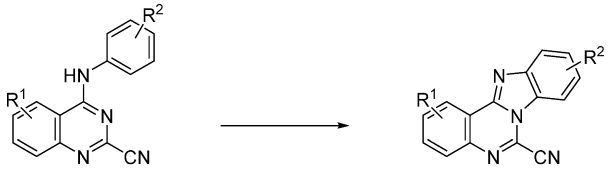
**Table 1. Reactions of 4-Anilinoquinazoline-2-carbonitriles 4a–j (0.20 mmol) with PIFA (1.1–1.5 equiv) and $Cu(OTf)_2$ (0-5 mol %) in Neat TFA To Give Benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitriles 1a–r**



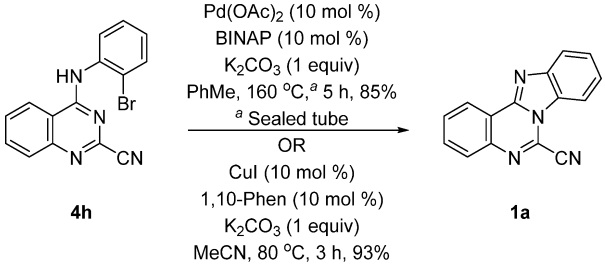

4 1

| entry[a] | $R^1$ | $R^2$ | PIFA (equiv) | $Cu(OTf)_2$ (mol %) | temp (°C) | time (h) | yield **1** (%) |
|---|---|---|---|---|---|---|---|
| 1 | H | H | 1.1 | – | 20 | 0.5 | **1a** (92) |
| 2 | H | 9-Me | 1.1 | – | 20 | 1 | **1b** (80) |
| 3 | H | 9-MeO | 1.1 | – | 20 | 1 | **1c** (82) |
| 4 | H | 9,10-$(MeO)_2$ | 1.1 | – | 20 | 26 | **1d/e** (85)[b] |
| 5 | H | 9,10-$(MeO)_2$ | 1.5 | 5 | 80 | 3 | **1d/e** (82)[b] |
| 6 | H | 9-F | 1.1 | – | 20 | 7 d | **1f** (81)[c] |
| 7 | H | 9-F | 1.1 | 5 | 80 | 25 | **1f** (86) |
| 8 | H | 9-F | 1.5 | 5 | 20 | 6 | **1f** (85) |
| 9 | H | 9-F | 1.5 | 5 | 80 | 1.50 | **1f** (89) |
| 10 | H | 9-Cl | 1.1 | – | 20 | 32 | **1g** (86) |
| 11 | H | 9-Cl | 1.5 | 5 | 80 | 4 | **1g** (88) |
| 12 | H | 9,10-$(Cl)_2$ | 1.1 | – | 20 | 4 d | **1h/i** (41)[d,e] |
| 13 | H | 9,10-$(Cl)_2$ | 1.5 | 5 | 80 | 2 | **1h/i** (77)[d] |
| 14 | H | 11-Br | 1.1 | – | 20 | 7 d | **1j** (77)[f] |
| 15 | H | 11-Br | 1.5 | 5 | 80 | 0.75 | **1j** (82) |
| 16 | H | 9-Br | 1.1 | – | 20 | 32 | **1k** (87) |
| 17 | H | 9-Br | 1.5 | 5 | 80 | 4 | **1k** (87) |
| 18 | 2,3-$(MeO)_2$ | H | 1.1 | – | 20 | 16 | **1l** (83) |
| 19 | 2,3-$(MeO)_2$ | H | 1.5 | 5 | 80 | 8 | **1l** (85) |

[a]Substituent numbering based on major product. [b]Two inseparable products **1d/1e** (2.6:1) by $^1H$ NMR of crude. [c]Incomplete reaction: 4% of starting material recovered (note at 24 h there was 53% of product). [d]Two inseparable products **1h/1i** (2.6:1) by $^1H$ NMR of crude. [e]Incomplete reaction: 35% of starting material recovered. [f]Incomplete reaction: 2% of starting material recovered (note at 24 h there was 45% of product).

we identified the following conditions: After 5 h $Pd(OAc)_2$ (10 mol %), BINAP (10 mol %), $K_2CO_3$ (1 equiv), PhMe at ca. 160 °C (sealed tube – Wood's metal bath temperature) completely consumed the starting material and gave the target **1a** in a 85% yield (Scheme 4).

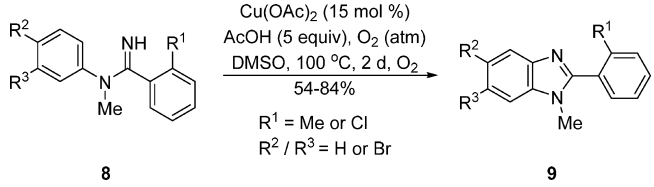
**Scheme 4. Nonoxidative C–N Couplings of 4-(2-Bromoanilino)quinazoline-2-carbonitrile (4h) To Give Benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitrile (1a)**




Worthy of note was the need for high reaction temperatures (160 °C): lower temperatures (ca. 110 °C) led to long reaction times (>2 d) and incomplete consumption of the starting material (up to 12% recovered). Attempts to lower the reaction temperatures or reduce the Pd catalyst loading were unsuccessful, however, the alternative use of CuI (10 mol %) with 1,10-Phen (10 mol %) as ligand using $K_2CO_3$ (1 equiv) as base in MeCN heated at reflux enabled the cyclization at significantly lower reaction temperature (ca. 80 °C) in 3 h to give the desired tetracycle **1a** in an improved 93% yield (Scheme 4). The use of less CuI (5 mol %) and alternative ligands (BINAP or DMEDA) failed to drive the reaction to completion, while the use of "ligand free" reaction conditions (CuI, DBU, and DMSO)[34e] led to no reaction. Interestingly, most reported reactions of this type invoked the need for 2 equiv of base, however, this led to a lower yield (80%).

**2.2. Oxidative and Nonoxidative Cyclization Chemistry of 3-Aryl-4-imino-3,4-dihydroquinazoline-2-carbonitriles 5.** Unlike the above *N,N′*-disubstituted benzamidines and to the best of our knowledge, there is only one report on the oxidative coupling of *N,N*-disubstituted benzamidines: The $O_2/Cu(OAc)_2$-mediated oxidative cyclization of three *N*-aryl-*N*-methylbenzamidines **8** to 1-methyl-2-arylbenzimidazoles **9** in 54–84% yields (Scheme 5),[38] and there are no reports of nonoxidative couplings.

**Scheme 5. Copper-Mediated Oxidative C–N Coupling of *N*-Aryl-*N*-methylbenzamidines 8 To Give 1-Methyl-2-arylbenzimidazoles 9[38]**



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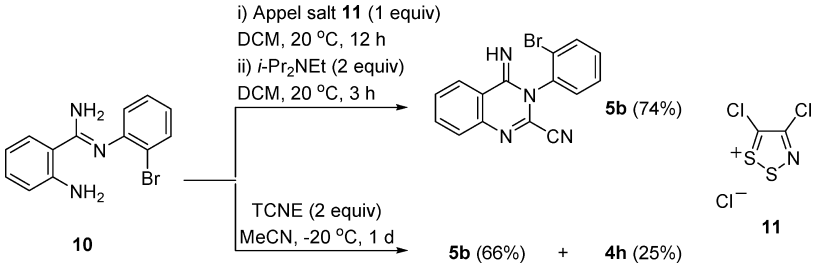
**Scheme 6. Preparation of 3-(2-Bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (5b) via Appel salt 11 (Conditions A)[21a] and TCNE (Conditions B)[21b]**

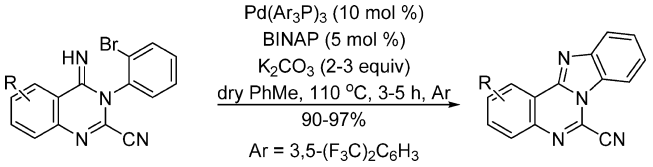



Attempted oxidative couplings of 4-imino-3-phenyl-3,4-dihydroquinazoline-2-carbonitrile (**5a**) using either Buchwald's conditions (Scheme 5), alternative oxidants such as $H_2O_2$, NCS, $MnO_2$, $Pb(OAc)_4$, DDQ, benzoquinone, and CAN, or the $Cu(OTf)_2$/PIFA conditions described above (Table 1) failed to give any reaction or led to complex reaction mixtures (by TLC).

As such, we then investigated the alternative nonoxidative coupling. The desired 3-(2-bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5b**) was prepared via two routes: First, by reaction of 2-amino-*N*′-(2-bromophenyl)benzamidine (**10**) with 4,5-dichloro-1,2,3-dithiazolium chloride (**11**) (aka Appel salt) (Conditions A)[21a] which gave the product **5b** in 74% yield, and the second by reaction of 2-amino-*N*′-(2-bromophenyl)benzamidine (**10**) with tetracyanoethene (TCNE) at −20 °C (Conditions B)[21b] which gave the product **5b** in 66% yield together with the isomeric 4-(2-bromoanilino)quinazoline **4h** in 25% yield (Scheme 6).

Initially, Cu-mediated nonoxidative C−N coupling reactions of 3-(2-bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5b**) were attempted, however, our best conditions for the 4-anilino analogue **4a**, i.e., CuI (10 mol %), 1,10-Phen (10 mol %), and $K_2CO_3$ (1 equiv) in MeCN heated at reflux failed to give the desired cyclization. In light of this we switched back to the Pd-catalyzed conditions and identified the following semioptimized conditions: $Pd(OAc)_2$ (10 mol %), BINAP (10 mol %), and $Cs_2CO_3$ (1 equiv) in dry PhMe heated at reflux for 17 h under an argon atmosphere which led to complete consumption of the starting material and gave the target tetracycle **1a** in 78% yield. By switching the Pd catalyst to Superstable Pd(0) Catalyst (10 mol %) and using $K_2CO_3$ (2 equiv) as base we were able to lower the quantity of BINAP (5 mol %) and shorten the reaction time to only 5 h improving the product yield to a satisfactory 93%. Interestingly, traces of moisture or air led to significantly reduced product yields (62−65%) and longer reaction times, while the reaction with Superstable Pd(0) Catalyst also worked in the absence of BINAP to give benzimidazo[1,2-*c*]quinazoline-2-carbonitrile (**1a**) in near quantitative yield (98%), but this reaction needed 3 days to come to completion. These conditions were also suitable for preparing the 2,3-dimethoxy-substituted benzimidazo[1,2-*c*]quinazoline **1l** (Table 2, entry 4) but were unsuitable for preparing the 2-Cl, 2-Br, 3-Cl, 1-Me, and 3-MeO analogues: After 24 h the reactions failed to come to completion (data not shown). Attempts to run these reactions at higher temperatures (140−160 °C) using either microwave irradiation or by immersing the sealed reactions mixtures into preheated Wood's metal baths led to complex reaction mixtures and low to moderate yields of the desired product (data not shown). Fortunately, in these cases, increasing the quantity of $K_2CO_3$ to 3 equiv led to total consumption of the starting material within 6 h (Table 2).

**Table 2. Nonoxidative Cyclization of 3-(2-Bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitriles 5b−h (0.2 mmol) To Give Benzimidazo[1,2-*c*]quinazoline-2-carbonitriles 1a,l,m−q**




| entry | R[a] | $K_2CO_3$ (equiv) | time (h) | yields **1** (%) |
|---|---|---|---|---|
| 1 | H | 2 | 5 | **1a** (93) |
| 2 | H | 3 | 5 | **1a** (95) |
| 3 | 1-Me | 3 | 3 | **1m** (97) |
| 4 | 3-MeO | 3 | 6 | **1n** (91) |
| 5 | 2,3-$(MeO)_2$ | 2 | 5 | **1l** (94) |
| 6 | 2,3-$(MeO)_2$ | 3 | 5 | **1l** (96) |
| 7 | 2-Cl | 3 | 6 | **1o** (92) |
| 8 | 3-Cl | 3 | 5 | **1p** (94) |
| 9 | 2-Br | 3 | 6 | **1q** (90) |

[a]Substituent numbering based on product.

Interestingly, the more sterically hindered 1-Me analogue **5c** reacted the fastest (3 h) (Table 2, entry 3), suggesting that steric compression at the reaction site may promote the reaction. Furthermore, repeating the reaction of the unsubstituted analogue **5b** with 3 equiv of $K_2CO_3$ did not shorten the reaction time and gave the cyclized product in an identical yield compared to the analogous reaction using 2 equiv of $K_2CO_3$ (data not shown). With these improved conditions we attempted to reoptimize the reactions by switching back to a stronger base $Cs_2CO_3$ (2 and 3 equiv) or to reduce the Pd catalyst to 5 mol %, however, in both cases the reactions failed to come to completion. Switching the Pd catalyst also led to a slower consumption of the starting materials. Tentatively, we believe that increasing the equivalents of $K_2CO_3$, which was heterogeneous in the reaction mixture, from 2 to 3 assists the reaction simply by increasing the surface area. We note that our inorganic bases are typically powdered and vacuum dried at 80−90 °C before use to improve the available surface area.[39] This may also explain the need for dry PhMe since traces of moisture in the solvent can affect the dispersion of the anhydrous base. Attempts to overcome this by using a biphasic reaction mixture or by using phase transfer catalysts (18-crown-6, $BnEt_3NCl$),[39] failed.



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## 3. CONCLUSIONS

A $Cu(OTf)_2$-catalyzed PIFA-mediated oxidative cyclization of 4-anilinoquinazoline-2-carbonitriles affords 13 substituted benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitriles hosting electron-releasing Me and MeO substituents or electron-withdrawing halogen substituents in good to excellent yields. Interestingly, in at least two cases (the unsubstituted and the dimethoxy-substituted analogues) the reactions work equally well in the absence of the copper catalyst. Where the anilino moiety is unsymmetrical, the oxidative cyclization suffers from regioselectivity, however, this can be overcome by switching to a nonoxidative strategy: $Pd(OAc)_2$- and CuI-catalyzed protocols were developed that successfully cyclized 4-(2-bromoanilino)quinazoline-2-carbonitrile (**4h**) to benzo[4,5]-imidazo[1,2-*c*]quinazoline-6-carbonitrile (**1a**) in high yields. An alternative Pd(0)-catalyzed nonoxidative C−N coupling was also developed that enabled the cyclization of seven 3-(2-bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitriles again in high yields (90−97%). These methods expand the synthetic routes of benzo[4,5]imidazo[1,2-*c*]quinazolines and potentially can find application in the synthesis of structurally related heterocycles.

## 4. EXPERIMENTAL SECTION

**4.1. General Procedures.** Anhydrous $Na_2SO_4$ was used for drying organic extracts, and all volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial glass-backed thin layer chromatography (TLC) plates (Kieselgel 60 $F_{254}$). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography[40] was used throughout for all non-TLC scale chromatographic separations using silica gel 60 (<0.063 mm). Melting points were determined using a hotstage microscope apparatus or a DSC with samples hermetically sealed in aluminum pans under an argon atmosphere, using heating rates of 5 °C/min. Solvents used for recrystallization are indicated after the melting point. UV spectra were obtained using a UV−vis spectrophotometer, and inflections are identified by the abbreviation "inf". IR spectra were recorded on a FTIR-NIR spectrometer with a Ge ATR accessory, and strong, medium, and weak peaks are represented by s, m and w, respectively. $^1H$ and $^{13}C$ NMR spectra were recorded at 300 and 75 MHz or at 500 and 125 MHz, respectively. Deuterated solvents were used for homonuclear lock, and the signals are referenced to the deuterated solvent peaks. DEPT or APT NMR studies identified quaternary, tertiary, secondary, and primary carbons, which are indicated by (s), (d), (t), and (q) notations, respectively. Low-resolution (EI) mass spectra were recorded on a GCMS with direct inlet probe. MALDI-TOF mass spectra were conducted on a time-of-flight (TOF) mass spectrometer. 4,5-Dichloro-1,2,3-dithiazolium chloride (**11**),[41] tetracyanoethene (TCNE),[42] 2-amino-*N*′-(3,4-dimethoxyphenyl)benzamidine,[21b] 2-amino-*N*′-(3,4-dichlorophenyl)benzamidine,[20] 4-(arylamino)-quinazoline-2-carbonitriles **4a−c,e,f,i,j**,[21b] and 4-imino-3-phenyl-3,4-dihydroquinazoline-2-carbonitrile (**5a**)[21a] were prepared according to literature procedures.

**4.2. Preparation of *N*-Arylbenzamidines.** *4.2.1. 2-Amino-N′-(2-bromophenyl)benzamidine (**10**) (Typical Procedure).* To stirred anthranilonitrile (343 mg, 2.91 mmol) at ca. 20 °C was added powdered anhydrous $AlCl_3$ (387 mg, 2.91 mmol). The reaction mixture was then heated (ca. 100 °C) until a homogeneous melt formed. To this was added 2-bromoaniline (500 mg, 2.91 mmol), and the mixture was heated for 6 h and then allowed to cool to ca. 20 °C. The resultant solid mass was then crushed and slurried in 12.5% NaOH (40 mL). The resulting mixture was extracted (DCM, 3 × 50 mL), washed ($H_2O$, 1 × 50 mL), and dried ($Na_2SO_4$). The organic phase adsorbed onto silica and chromatographed (*t*-BuOMe) to give the title compound **10** (306 mg, 36%) as colorless needles, mp (hotstage) 125.5−126.5 °C (lit.,[43] 127−129 °C) (from *c*-hexane/EtOH, 90:10); $R_f$ 0.74 (*t*-BuOMe); $\lambda_{max}$(DCM)/nm 250 (log $\varepsilon$ 4.45), 304 (3.78), 352 (3.76); $\nu_{max}/cm^{-1}$ 3478w, 3451w and 3370w (N−H), 3169w and 3046w (aryl C−H), 1630s, 1614s, 1580m, 1562m, 1545m, 1493w, 1464m, 1433w, 1387m, 1319w, 1310w, 1271w, 1258w, 1233w, 1161w, 1121w, 1040w, 1024m, 835m, 748m; $\delta_H$(500 MHz; $CDCl_3$) 7.64 (1H, d, *J* 8.0), 7.43 (1H, d, *J* 8.0), 7.30 (1H, dd, *J* 7.5, 7.5), 7.20 (1H, dd, *J* 7.8, 7.8), 7.04 (1H, d, *J* 7.5), 6.95 (1H, dd, *J* 7.8, 7.8), 6.74 (1H, d, *J* 8.0), 6.69 (1H, dd, *J* 7.5, 7.5), 5.96 (2H, br s), 4.77 (2H, br s); $\delta_C$(125 MHz; $CDCl_3$) 156.1 (s), 147.9 (s), 147.4 (s), 133.3 (d), 131.4 (d), 128.5 (d), 127.5 (d), 124.5 (d), 123.2 (d), 117.2 (d), 116.6 (s), 116.5 (d), 116.4 (s); *m*/*z* (EI) 291 ($M^+$ + 2, 38%), 289 ($M^+$, 39), 274 (13), 272 (14), 210 (100), 193 (23), 173 (69), 171 (71), 119 (92), 105 (34), 92 (63), 76 (16), 65 (57).

*4.2.2. 2-Amino-N′-(2-bromophenyl)-6-methylbenzamidine (**12**).* Similar treatment of 6-methylanthranilonitrile (384 mg, 2.91 mmol) with anhydrous $AlCl_3$ (387 mg, 2.91 mmol) and 2-bromoaniline (500 mg, 2.91 mmol) gave the title compound **12** (1.33 g, 43%) as colorless plates, mp (hotstage) 153.3−154.3 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.76 (*t*-BuOMe); (found: C, 55.40; H, 4.57; N, 13.62. $C_{14}H_{14}BrN_3$ requires C, 55.28; H, 4.64; N, 13.81%); $\lambda_{max}$(DCM)/nm 287 (log $\varepsilon$ 3.71); $\nu_{max}/cm^{-1}$ 3429w, 3350w and 3269w (N−H), 3123w (aryl C−H), 1626s, 1599s, 1578s, 1466m, 1433w, 1379w, 1302w, 1285w, 1169w, 1101w, 1070w, 1041w, 1026m, 783m, 754s; $\delta_H$(500 MHz; $CD_3CN$) 7.63 (1H, d, *J* 8.0), 7.34 (1H, dd, *J* 7.0, 7.0), 7.02 (2H, dd, *J* 9.0, 9.0), 6.97 (1H, dd, *J* 7.0, 7.0), 6.57 (2H, dd, *J* 7.8, 7.8), 5.35 (2H, br s), 4.64 (2H, br s), 2.40 (3H, s); $\delta_C$(125 MHz; DMSO-$d_6$) 155.7 (s), 148.6 (s), 145.9 (s), 135.6 (s), 132.9 (d), 128.8 (d), 128.6 (d), 123.7 (d), 123.0 (s), 122.5 (d), 118.0 (d), 116.5 (s), 112.8 (d), 19.9 (q); *m*/*z* (MALDI-TOF) 306 ($MH^+$ + 2, 100%), 304 ($MH^+$, 88), 289 (34), 287 (35), 224 (27), 209 (13), 173 (8), 133 (26).

*4.2.3. 2-Amino-N′-(2-bromophenyl)-4-methoxybenzamidine (**13**).* Similar treatment of 4-methoxyanthranilonitrile (431 mg, 2.91 mmol) with anhydrous $AlCl_3$ (387 mg, 2.91 mmol) and 2-bromoaniline (500 mg, 2.91 mmol) gave the title compound **13** (1.62 g, 51%) as colorless plates, mp (hotstage) 121.5−122.5 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.58 (*t*-BuOMe); (found: C, 52.43; H, 4.35; N, 13.02. $C_{14}H_{14}BrN_3O$ requires C, 52.52; H, 4.41; N, 13.12%); $\lambda_{max}$(DCM)/nm 266 (log $\varepsilon$ 4.15), 286 inf (3.89), 321 (3.94); $\nu_{max}/cm^{-1}$ 3466w and 3350w (N−H), 2999w (aryl C−H), 2965w and 2895w (alkyl C−H), 1618s, 1614s, 1593m, 1572m, 1553m, 1508m, 1466w, 1441w, 1427w, 1377s, 1306w, 1256m, 1231m, 1215s, 1164m, 1157w, 1092w, 1067w, 1034w, 1024m, 833s, 795m, 758s; $\delta_H$(500 MHz; $CDCl_3$) 7.63 (1H, d, *J* 8.0), 7.35 (1H, d, *J* 8.5), 7.28 (1H, dd, *J* 7.5, 7.5), 7.03 (1H, d, *J* 7.5), 6.94 (1H, dd, *J* 8.0, 8.0), 6.27 (1H, dd, *J* 6.0, 2.5), 6.22 (1H, d, *J* 2.5), 6.15 (2H, br s), 4.70 (2H, br s), 3.79 (3H, s); $\delta_C$(125 MHz; $CDCl_3$) 162.2 (s), 156.0 (s), 149.9 (s), 147.4 (s), 133.3 (d), 129.0 (d), 128.4 (d), 124.4 (d), 123.4 (d), 116.9 (s), 109.4 (s), 103.7 (d), 100.8 (d), 55.1 (q); *m*/*z* (MALDI-TOF) 322 ($M^+$ + 2, 100%), 320 ($MH^+$, 100), 305 (21), 303 (22), 242 (1), 149 (4).

*4.2.4. 2-Amino-N′-(2-bromophenyl)-4,5-dimethoxybenzamidine (**14**).* Similar treatment of 4,5-dimethoxyanthranilonitrile (518 mg, 2.91 mmol) with anhydrous $AlCl_3$ (387 mg, 2.91 mmol) and 2-bromoaniline (500 mg, 2.91 mmol) gave the title compound **14** (0.71 g, 20%) as colorless needles, mp (hotstage) 151−152 °C (from *c*-hexane/DCM, 80:20); $R_f$ 0.44 (*t*-BuOMe); (found: C, 51.35; H, 4.54; N, 12.17. $C_{15}H_{16}BrN_3O_2$ requires C, 51.44; H, 4.61; N, 12.00%); $\lambda_{max}$(DCM)/nm 275 inf (log $\varepsilon$ 4.05), 337 (3.94); $\nu_{max}/cm^{-1}$ 3468w, 3370w and 3291w (N−H), 3138w and 3065w (aryl C−H), 2934w and 2833w (alkyl C−H), 1626s, 1558w, 1522m, 1468w, 1440w, 1387m, 1350w, 1277w, 1246m, 1229s, 1213s, 1192w, 1179w, 1159w, 1031w, 1022w, 854m, 768m, 743s; $\delta_H$(500 MHz; $CDCl_3$) 7.63 (1H, d, *J* 8.0), 7.29 (1H, dd, *J* 7.3, 7.3), 7.04 (1H, d, *J* 8.0), 6.96 (1H, br s), 6.94 (1H, dd, *J* 8.0, 8.0), 6.27 (1H, s), 5.82 (2H, br s), 4.68 (2H, br s), 3.87 (3H, s), 3.83 (3H, s); $\delta_C$(125 MHz; $CDCl_3$) 155.9 (s), 152.5 (s), 147.4 (s), 143.9 (s), 140.8 (s), 133.3 (d), 128.4 (d), 124.4 (d), 123.3 (d), 116.8 (s), 111.8 (d), 107.6 (s), 100.9 (d), 57.1 (q), 55.8 (q); *m*/*z* (MALDI-TOF) 352 ($MH^+$ + 2, 97%), 350 ($MH^+$, 100), 349 ($M^+$, 12), 339 (6), 337 (6), 335 (4), 333 (3), 272 (3).

*4.2.5. 2-Amino-N′-(2-bromophenyl)-5-chlorobenzamidine (**15**).* Similar treatment of 5-chloroanthranilonitrile (442 mg, 2.91 mmol)



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with anhydrous $AlCl_3$ (387 mg, 2.91 mmol) and 2-bromoaniline (500 mg, 2.91 mmol) gave the title compound **15** (1.70 g, 52%) as colorless needles, mp (hotstage) 147−147.5 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.65 (*t*-BuOMe); (found: C, 48.03; H, 3.36; N, 12.87. $C_{13}H_{11}BrClN_3$ requires C, 48.10; H, 3.42; N, 12.95%); $\lambda_{max}$(DCM)/nm 243 inf (log $\varepsilon$ 4.56), 286 inf (3.94), 343 (3.92); $\nu_{max}/cm^{-1}$ 3428w, 3397w, 3312w and 3198w (N−H), 3065w (aryl C−H), 1630m, 1614m, 1585m, 1572w, 1541w, 1487w, 1464m, 1435w, 1375m, 1301w, 1254w, 1236w, 1161w, 1115w, 1083w, 1038w, 1024w, 819s, 747s; $\delta_H$(500 MHz; $CDCl_3$) 7.64 (1H, d, *J* 8.0), 7.41 (1H, br s), 7.30 (1H, dd, *J* 7.5, 7.5), 7.15 (1H, dd, *J* 9.0, 2.5), 7.02 (1H, d, *J* 8.0), 6.97 (1H, ddd, *J* 7.8, 7.8, 1.5), 6.67 (1H, d, *J* 9.0), 5.96 (2H, br s), 4.78 (2H, br s); $\delta_C$(125 MHz; $CDCl_3$) 155.2 (s), 146.9 (s), 146.5 (s), 133.4 (d), 131.3 (d), 128.5 (d), 127.2 (d), 124.8 (d), 123.0 (d), 120.9 (s), 118.4 (d), 117.3 (s), 116.5 (s); *m*/*z* (MALDI-TOF) 328 ($MH^+$ + 4, 24%), 326 ($MH^+$ + 2, 100), 324 ($MH^+$, 76), 312 (5), 310 (4).

*4.2.6. 2-Amino-N′-(2-bromophenyl)-4-chlorobenzamidine (**16**).* Similar treatment of 4-chloroanthranilonitrile (442 mg, 2.91 mmol) with anhydrous $AlCl_3$ (387 mg, 2.91 mmol) and 2-bromoaniline (500 mg, 2.91 mmol) gave the title compound **16** (1.84 g, 57%) as colorless needles, mp (hotstage) 130−131 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.62 (*t*-BuOMe); (found: C, 47.97; H, 3.40; N, 12.83. $C_{13}H_{11}BrClN_3$ requires C, 48.10; H, 3.42; N, 12.95%); $\lambda_{max}$(DCM)/nm 261 inf (log $\varepsilon$ 4.09), 286 inf (3.82), 330 (3.81); $\nu_{max}/cm^{-1}$ 3476w, 3375w and 3283w (N−H), 3188w and 3067w (aryl C−H), 1624s, 1578m, 1549m, 1491m, 1470m, 1435w, 1420w, 1375m, 1321w, 1258w, 1234w, 1113w, 1053w, 1024m, 914s, 854m, 835m, 748s; $\delta_H$(500 MHz; $CDCl_3$) 7.64 (1H, dd, *J* 8.0, 1.0), 7.35 (1H, d, *J* 8.5), 7.30 (1H, dd, *J* 7.5, 7.5), 7.22 (1H, d, *J* 7.5), 6.96 (1H, ddd, *J* 8.0, 8.0, 1.0), 6.72 (1H, d, *J* 2.0), 6.64 (1H, d, *J* 9.0, 2.0), 6.12 (2H, br s), 4.75 (2H, br s); $\delta_C$(125 MHz; $CDCl_3$) 155.5 (s), 149.0 (s), 146.9 (s), 137.1 (s), 133.4 (d), 128.8 (d), 128.5 (d), 124.7 (d), 123.1 (d), 116.6 (s), 116.5 (d), 116.4 (d), 114.6 (s); *m*/*z* (MALDI-TOF) 328 ($MH^+$ + 4, 26%), 326 ($MH^+$ + 2, 100), 324 ($MH^+$, 76), 312 (12), 310 (9), 309 (12), 307 (7).

*4.2.7. 2-Amino-5-bromo-N′-(2-bromophenyl)benzamidine (**17**).* Similar treatment of 5-bromoanthranilonitrile (571 mg, 2.91 mmol) with anhydrous $AlCl_3$ (387 mg, 2.91 mmol) and 2-bromoaniline (500 mg, 2.91 mmol) gave the title compound **17** (2.15 g, 58%) as colorless plates, mp (hotstage) 136.5−137.8 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.60 (*t*-BuOMe); (found: C, 42.19; H, 2.92; N, 11.26. $C_{13}H_{11}Br_2N_3$ requires C, 42.31; H, 3.00; N, 11.39%); $\lambda_{max}$(DCM)/nm 244 inf (log $\varepsilon$ 4.38), 265 inf (4.21), 343 (3.70); $\nu_{max}/cm^{-1}$ 3428w, 3393w, 3318w and 3196w (N−H), 3067w (aryl C−H), 1632s, 1611s, 1582m, 1568m, 1537m, 1485m, 1462s, 1435w, 1375s, 1304w, 1254m, 1234w, 1163m, 1119w, 1115w, 1051w, 1022w, 839m, 818s, 745s; $\delta_H$(500 MHz; $CDCl_3$) 7.64 (1H, d, *J* 8.0), 7.55 (1H, br s), 7.31 (1H, dd, *J* 7.5, 7.5), 7.27 (1H, dd, *J* 7.5, 2.0), 7.02 (1H, d, *J* 8.0), 6.97 (1H, dd, *J* 7.5, 7.5), 6.63 (1H, d, *J* 9.0), 5.99 (2H, br s), 4.76 (2H, br s); $\delta_C$(125 MHz; $CDCl_3$) one C (s) resonance missing, 155.1 (s), 146.9 (s), 134.0 (d), 133.4 (d), 130.1 (d), 128.5 (d), 124.8 (d), 123.0 (d), 118.7 (d), 117.9 (s), 116.5 (s), 107.6 (s); *m*/*z* (MALDI-TOF) 372 ($MH^+$ + 4, 76%), 370 ($MH^+$ + 2, 100), 368 ($MH^+$, 74), 358 (18), 356 (36), 351 (25), 306 (7), 304 (8), 290 (7), 174 (5), 172 (5).

**4.3. Preparation of 4-(Arylamino)quinazoline-2-carbonitriles 4d,g,h.** *4.3.1. 6,7-Dimethoxy-4-(phenylamino)quinazoline-2-carbonitrile (**4d**) (Typical Procedure).* To a stirred solution of 2-amino-*N*′-(3,4-dimethoxyphenyl)benzamidine[21b] (271 mg, 1.00 mmol) in MeCN (10 mL) at ca. 20 °C was added glacial AcOH (57.0 $\mu$L, 1.00 mmol). To that mixture, at ca. 20 °C was added dropwise a solution of TCNE (128 mg, 1.00 mmol) in MeCN (10 mL) and left to stir for 7 h. The reaction mixture was then adsorbed onto silica and chromatographed (DCM/*t*-BuOMe, 95:05) to give the title compound **4d** (104.8 mg, 34%) as yellow needles, mp (hotstage) 285.9−287 °C (*c*-hexane/THF, 80:20), mp (DSC) onset 286.6 °C, peak max. 287.1 °C; $R_f$ 0.55 (DCM/*t*-BuOMe, 95:05); (found: C, 66.60; H, 4.47; N, 18.13. $C_{17}H_{14}N_4O_2$ requires C, 66.66; H, 4.61; N, 18.29%); $\lambda_{max}$(DCM)/nm 258 inf (log $\varepsilon$ 4.16), 268 inf (4.14), 281 inf (4.09), 332 (4.29); $\nu_{max}/cm^{-1}$ 3401w (N−H), 3015w (aryl C−H), 2928w and 2855w (alkyl C−H), 2239w (C≡N), 1611m, 1578m, 1514s, 1460s, 1425m, 1396w, 1360w, 1294w, 1273m, 1242m, 1205m, 1161m, 1074w, 1036w, 1001m, 841m, 737s; $\delta_H$(500 MHz; DMSO-$d_6$) 9.93 (1H, br s), 7.91 (1H, s), 7.69 (2H, d, *J* 7.5), 7.45 (2H, dd, *J* 7.8, 7.8), 7.30 (1H, s), 7.21 (1H, dd, *J* 7.5, 7.5), 3.98 (3H, s), 3.95 (3H, s); $\delta_C$(125 MHz; DMSO-$d_6$) 156.9 (s), 155.1 (s), 151.0 (s), 146.1 (s), 138.4 (s), 138.1 (s), 128.8 (d), 124.8 (d), 123.3 (d), 117.3 (s), 109.7 (s), 107.6 (d), 102.2 (d), 56.6 (q), 56.3 (q); *m*/*z* (MALDI-TOF) 308 ($MH^+$ + 1, 12%), 307 ($MH^+$, 100), 100 (5). Further elution (DCM/*t*-BuOMe, 60:40) gave 4-imino-6,7-dimethoxy-3-phenyl-3,4-dihydroquinazoline-2-carbonitrile (**18**) (2.1 mg, 1%) as colorless needles, mp (hotstage) 230 °C (sub.) [lit.,[21a] 230 °C (sub.)] (from acetone); $R_f$ 0.59 (*t*-BuOMe/EtOH, 60:40); $\delta_H$(300 MHz; $CDCl_3$) 7.72−7.66 (4H, m), 7.44−7.41 (2H, m), 7.08 (1H, s), 6.34 (1H, br s), 4.01 (3H, s), 4.00 (3H, s); $\delta_C$(75 MHz; $CDCl_3$) 153.6 (s), 152.7 (s), 151.1 (s), 138.7 (s), 134.9 (s), 131.3 (d), 131.1 (d), 129.5 (s), 129.1 (d), 116.2 (s), 111.5 (s), 109.0 (d), 105.6 (d), 56.5 (q), 56.3 (q); identical to an authentic sample.

*4.3.2. 4-[(3,4-Dichlorophenyl)amino]quinazoline-2-carbonitrile (**4g**).* Similar treatment of 2-amino-*N*′-(3,4-dichlorophenyl)-benzamidine[20] with TCNE gave the title compound **4g** (138 mg, 44%) as colorless needles, mp (hotstage) 257.7−258.7 °C (*c*-hexane/THF, 80:20), mp (DSC) onset 258.6 °C, peak max. 259.2 °C; $R_f$ 0.62 (DCM/*t*-BuOMe, 95:05); (found: C, 57.02; H, 2.53; N, 17.66. $C_{15}H_8Cl_2N_4$ requires C, 57.17; H, 2.56; N, 17.78%); $\lambda_{max}$(DCM)/nm 248 inf (log $\varepsilon$ 4.23), 268 (4.07), 282 inf (3.99), 336 (4.23), 396 (3.11), 424 (3.02); $\nu_{max}/cm^{-1}$ 3366w (N−H), 3129w and 3032w (aryl C−H), 2251w (C≡N), 1618w, 1602w, 1570m, 1555w, 1522s, 1499w, 1474m, 1425m, 1366m, 1314w, 1219w, 1132w, 1092w, 1030w, 806m, 793m, 760s; $\delta_H$(500 MHz; DMSO-$d_6$) 10.39 (1H, br s), 8.59 (1H, d, *J* 8.0), 8.14 (1H, d, *J* 2.5), 8.01 (1H, dd, *J* 7.8, 7.8), 7.91 (1H, d, *J* 8.0), 7.85−7.82 (2H, m), 7.70 (1H, d, *J* 8.5); $\delta_C$(125 MHz; DMSO-$d_6$) 158.2 (s), 149.0 (s), 139.6 (s), 138.5 (s), 134.8 (d), 130.9 (s), 130.6 (d), 129.4 (d), 128.3 (d), 126.4 (s), 124.2 (d), 123.5 (d), 122.9 (d), 116.8 (s), 115.6 (s); *m*/*z* (MALDI-TOF) 317 ($MH^+$ + 2, 9%), 315 ($MH^+$, 22), 266 (14), 215 (39), 153 (100), 130 (5). Further elution (DCM/*t*-BuOMe, 90:20) gave 3-(3,4-dichlorophenyl)-4-imino-3,4-dihydroquinazol-ine-2-carbonitrile (**19**) (5.4 mg, 2%) as beige plates, mp (hotstage) 175−176 °C (lit.,[21a] 175−176 °C) (from *n*-pentane/DCM); $R_f$ 0.77 (DCM/*t*-BuOMe, 90:10); $\delta_H$(300 MHz; $CDCl_3$) 8.12 (1H, d, *J* 7.2), 7.73 (1H, d, *J* 8.7), 7.70−7.65 (2H, m), 7.60−7.54 (2H, m), 7.30 (1H, dd, *J* 8.4, 2.4); $\delta_C$(125 MHz; $CDCl_3$) 154.1 (s), 142.8 (s), 135.9 (s), 133.9 (s), 134.8 (s) 133.7 (d), 132.5 (s), 131.1 (d), 130.5 (s), 130.2 (d), 128.8 (d), 128. (d), 125.1 (d), 121.7 (s), 111.1 (s); identical to an authentic sample.

*4.3.3. 4-[(2-Bromophenyl)amino]quinazoline-2-carbonitrile (**4h**).* Similar treatment of 2-amino-*N*′-(2-bromophenyl)benzamidine (**10**) with TCNE gave the title compound **4h** (290 mg, 89%) as colorless plates, mp (hotstage) 181−182 °C (*c*-hexane/THF, 90:10), mp (DSC) onset 181.8 °C, peak max. 182.6 °C; $R_f$ 0.76 (DCM/*t*-BuOMe, 95:05); (found: C, 55.33; H, 2.70; N, 17.00. $C_{15}H_9BrN_4$ requires C, 55.41; H, 2.79; N, 17.23%); $\lambda_{max}$(DCM)/nm 258 inf (log $\varepsilon$ 3.97), 270 inf (3.93), 283 inf (3.85), 297 inf (3.79), 337 (4.14); $\nu_{max}/cm^{-1}$ 3395w (N−H), 3062w (aryl C−H), 2245w (C≡N), 1614m, 1595m, 1584m, 1570m, 1558m, 1530s, 1495m, 1460m, 1441m, 1420m, 1369w, 1356m, 1319m, 1236w, 1217w, 1171w, 1130w, 1092w, 1022m, 1018m, 991m, 760s, 752s, 746s; $\delta_H$(500 MHz; $CDCl_3$) 8.78 (1H, d, *J* 8.5), 8.35 (1H, br s), 8.02 (2H, dd, *J* 9.3, 9.3), 7.95 (1H, dd, *J* 7.8, 7.8), 7.78 (1H, dd, *J* 7.5, 7.5), 7.66 (1H, d, *J* 8.0), 7.45 (1H, dd, *J* 7.5, 7.5), 7.10 (1H, dd, *J* 7.8, 7.8); $\delta_C$(125 MHz; $CDCl_3$) 157.1 (s), 149.6 (s), 140.4 (s), 135.1 (s), 134.3 (d), 132.4 (d), 129.8 (d), 129.7 (d), 128.8 (d), 125.8 (d), 122.9 (d), 120.4 (d), 116.5 (s), 115.6 (s), 114.8 (s); *m*/*z* (MALDI-TOF) 327 ($MH^+$ + 2, 100%), 325 ($MH^+$, 64), 245 (19). Further elution (DCM/*t*-BuOMe, 90:10) gave 3-(2-bromophenyl)-4-imino-3,4-dihydro-quinazoline-2-carbonitrile (**5b**) (3.3 mg, 1%) as colorless needles, mp (hotstage) 183.6−185.7 °C (from *c*-hexane/DCM, 90:10), mp (DSC) onset 183.7 °C, peak max. 186.2 °C; $R_f$ 0.54 (DCM/*t*-BuOMe, 90:10); (found: C, 55.56; H, 2.64; N, 17.26. $C_{15}H_9BrN_4$ requires C, 55.41; H, 2.79; N, 17.23%); $\lambda_{max}$(DCM)/nm 274 (log $\varepsilon$ 4.16), 283 (4.22), 293 (4.15), 318 inf (3.81), 330 (3.94), 343 (3.97), 360 inf (3.80); $\nu_{max}/cm^{-1}$ 3323w (N−H), 3013w (aryl C−H), 2239 (C≡N), 1641s, 1605w, 1589m, 1564m, 1472m, 1462m,



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1354s, 1337w, 1321w, 1302w, 1231w, 1182w, 1161w, 1121m, 1065m, 1024w, 1003m, 880m, 816s, 779s, 762s; $\delta_H$(500 MHz; $CDCl_3$) 8.21 (1H, br s), 7.89 (1H, d, *J* 8.0), 7.73−7.68 (2H, m), 7.61 (1H, dd, *J* 7.8, 7.8), 7.58−7.50 (3H, m), 6.72 (1H, br s); $\delta_C$(125 MHz; $CDCl_3$) one C (d) resonance missing, 152.6 (s), 143.1 (s), 134.8 (d), 134.6 (s), 133.5 (d), 132.7 (d), 131.0 (d), 130.0 (d), 129.8 (d), 128.7 (d), 125.5 (s), 123.9 (s), 122.5 (s), 111.1 (s); *m*/*z* (MALDI-TOF) 326 ($MH^+$ + 1, 6%), 325 ($MH^+$, 68), 324 ($M^+$, 24), 323 (100).

**4.4. Preparation of 3-(2-Bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitriles 5b−h.** *4.4.1. 3-(2-Bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5b**). 4.4.1.1. Method A via TCNE (Typical Procedure).* To a stirred solution of TCNE (256 mg, 2.00 mmol) in dry MeCN (10 mL) at ca. −20 °C was added a solution of 2-amino-*N*′-(2-bromophenyl)benzamidine (**10**) (289 mg, 1.00 mmol) in dry MeCN (10 mL). The reaction mixture was then left to stir at ca. −20 °C for 1 d, after which time it was adsorbed onto silica and chromatographed (DCM/*t*-BuOMe, 95:05) to give the title compound **5b** (215 mg, 66%) as colorless plates, mp (hotstage) 183.6−185.7°C (from *c*-hexane); $R_f$ 0.54 (DCM/*t*-BuOMe, 90:10); identical to that described above.

*4.4.1.2. Method B via Appel salt **11** (Typical Procedure).* To a stirred solution of 4,5-dichloro-1,2,3-dithiazolium chloride (**11**) (826 mg, 3.97 mmol) in DCM (40 mL) at ca. 20 °C was added 2-amino-*N*′-(2-bromophenyl)benzamidine (**10**) (1.15 g, 3.97 mmol), and the mixture was then left to stir at ca. 20 °C for 12 h. Then, to the reaction mixture was added Hünig's base (1.36 μL, 7.92 mmol) and left to stir at ca. 20 °C for an additional 3 h. The reaction mixture was then adsorbed onto silica and chromatographed (*n*-hexane) to give traces of $S_8$, followed by (*n*-hexane/DCM, 80:20) 4-chloro-5*H*-1,2,3-dithiazol-5-one (65 mg, 11%). Further elution (DCM/*t*-BuOMe, 90:10) gave the title compound **5b** (856 mg, 74%) as colorless plates, mp (hotstage) 183.6−185.7 °C (from *c*-hexane); $R_f$ 0.54 (DCM/*t*-BuOMe, 90:10); identical to that described above.

*4.4.2. 3-(2-Bromophenyl)-4-imino-5-methyl-3,4-dihydroquinazoline-2-carbonitrile (**5c**) via Method B.* Similar treatment of 4,5-dichloro-1,2,3-dithiazolium chloride (**11**) (826 mg, 3.97 mmol) with 2-amino-*N*′-(2-bromophenyl)-6-methylbenzamidine (**12**) (1.207 g, 3.97 mmol) gave the title compound **5c** (338.1 mg, 74%) as colorless plates, mp (hotstage) 122.9−124.5 °C (from *c*-hexane/DCM, 90:10); mp (DSC) onset 123.2 °C, peak max. 129.0 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.73 (DCM/*t*-BuOMe, 90:10); (found: C, 56.19; H, 3.36; N, 16.51. $C_{16}H_{11}BrN_4$ requires C, 56.66; H, 3.27; N, 16.52%); $\lambda_{max}$(DCM)/nm 245 inf (log ε 4.09), 260 inf (3.91), 269 (3.93), 279 (3.85), 315 inf (3.78), 328 (3.84), 342 (3.80), 360 inf (3.59); $\nu_{max}$/$cm^{-1}$ 3408w (N−H), 3055w (aryl C−H), 2237 (C≡N), 1626s, 1591m, 1560m, 1516w, 1470m, 1435w, 1360s, 1325w, 1305w, 1290w, 1217w, 1173w, 1156w, 1086w, 1065w, 1047w, 1024w, 1005s, 802s, 760s, 725m; $\delta_H$(500 MHz; $CDCl_3$) N*H* deuterium exchanged, 7.88 (1H, dd, *J* 7.8, 1.0), 7.61 (1H, ddd, *J* 7.8, 7.8, 1.3), 7.55−7.48 (4H, m), 7.33 (1H, dd, *J* 7.0, 1.3), 2.83 (3H, s); $\delta_C$(75 MHz; $CDCl_3$) two C (s) resonances missing, 145.0 (s), 139.7 (s), 134.9 (d), 133.3 (d), 132.6 (d), 132.3 (d), 131.4 (d), 129.8 (d), 128.6 (s), 126.9 (d), 124.4 (s), 121.3 (s), 111.2 (s), 31.0 (q); *m*/*z* (MALDI-TOF) 341 ($MH^+$ + 2, 97%), 339 ($MH^+$, 100).

*4.4.3. 3-(2-Bromophenyl)-4-imino-7-methoxy-3,4-dihydroquinazoline-2-carbonitrile (**5d**) via Method B.* Similar treatment of 4,5-dichloro-1,2,3-dithiazolium chloride (**11**) (826 mg, 3.97 mmol) with 2-amino-*N*′-(2-bromophenyl)-4-methoxybenzamidine (**13**) (1.270 g, 3.97 mmol) gave the title compound **5d** (275.4 mg, 77%) as colorless plates, mp (hotstage) 158.9−161.2 °C (from *c*-hexane/DCM, 90:10), mp (DSC) onset 160.3 °C, peak max. 162.6 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.47 (DCM/*t*-BuOMe, 90:10); (found: C, 54.28; H, 2.98; N, 15.70. $C_{16}H_{11}BrN_4O$ requires C, 54.10; H, 3.12; N, 15.77%); $\lambda_{max}$(DCM)/nm 247 inf (log ε 4.29), 256 (4.36), 265 (4.39), 275 (4.30), 300 inf (3.61), 313 (3.70), 327 (3.68), 354 inf (3.49); $\nu_{max}$/$cm^{-1}$ 3298w (N−H), 3009w (aryl C−H), 2967w, 2940w and 2839w (alkyl C−H), 2237 (C≡N), 1634s, 1613s, 1592s, 1574w, 1562w, 1491s, 1472m, 1437w, 1352m, 1308s, 1283m, 1224w, 1200w, 1167s, 1130w, 1069w, 1026s, 1001w, 839m, 797m, 764s, 754s, 727m; $\delta_H$(500 MHz; $CDCl_3$) N*H* deuterium exchanged, 8.10 (1H, br s), 7.88 (1H, d, *J* 8.3), 7.61 (1H, ddd, *J* 7.5, 7.5, 1.5), 7.53−7.49 (2H, m), 7.13−7.11 (2H, m), 3.93 (3H, s); $\delta_C$(125 MHz; $CDCl_3$) one C (s) resonance missing, 163.8 (s), 144.9 (s), 134.8 (d), 132.6 (d), 131.5 (s), 131.0 (d), 129.7 (d), 127.0 (d), 124.0 (s), 118.8 (d), 115.4 (s), 111.1 (s), 110.3 (d), 55.8 (q); *m*/*z* (MALDI-TOF) 357 ($MH^+$ + 2, 100%), 355 ($MH^+$, 89).

*4.4.4. 3-(2-Bromophenyl)-4-imino-6,7-dimethoxy-3,4-dihydroquinazoline-2-carbonitrile (**5e**) via Method B.* Similar treatment of 4,5-dichloro-1,2,3-dithiazolium chloride (**11**) (826 mg, 3.97 mmol) with 2-amino-*N*′-(2-bromophenyl)-4,5-dimethoxybenzamidine (**14**) (1.390 g, 3.97 mmol) gave the title compound **5e** (256.3 mg, 66%) as colorless plates, mp (hotstage) 225.9−226.6 °C (from *c*-hexane/DCM, 90:10); mp (DSC) onset 226.7 °C, peak max. 227.4 °C, decomp. onset 232.6 °C, peak max 239.5 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.32 (DCM/*t*-BuOMe, 90:10); (found: C, 53.10; H, 3.27; N, 14.63. $C_{17}H_{13}BrN_4O_2$ requires C, 53.01; H, 3.40; N, 14.54%); $\lambda_{max}$(DCM)/nm 258 inf (log ε 4.33), 268 (4.39), 277 inf (4.33), 304 inf (3.60), 316 (3.78), 330 (3.88), 355 (3.87), 374 inf (3.77), 396 inf (3.40); $\nu_{max}$/$cm^{-1}$ 3291w (N−H), 3092w, 3067w and 3009w (aryl C−H), 2965w, 2938w and 2837w (alkyl C−H), 2237w (C≡N), 1636s, 1609s, 1504s, 1472m, 1452m, 1442m, 1423w, 1379m, 1346w, 1304s, 1283m, 1265m, 1250m, 1207m, 1182w, 1126s, 1119s, 1076w, 1049w, 1024m, 997m, 885m, 864s, 851m, 831m, 775m, 760s; $\delta_H$(500 MHz; $CDCl_3$) 7.90 (1H, d, *J* 8.0), 7.67 (1H, br s), 7.63 (1H, dd, *J* 8.0, 8.0), 7.54 (1H, dd, *J* 8.0, 8.0), 7.51 (1H, dd, *J* 7.8, 1.8), 7.11 (1H, s), 6.28 (1H, br s), 4.02 (3H, s), 4.00 (3H, s); $\delta_C$(75 MHz; $CDCl_3$) 153.8 (s), 151.2 (s), 138.6 (s), 134.9 (d), 134.4 (s), 132.8 (d), 131.1 (d), 129.9 (d), 129.2 (s), 124.2 (s), 116.1 (s), 111.3 (s), 109.3 (d), 105.7 (d), 56.5 (q), 56.4 (q); *m*/*z* (MALDI-TOF) 387 ($MH^+$ + 2, 83%), 385 ($MH^+$, 100), 305 (10).

*4.4.5. 3-(2-Bromophenyl)-6-chloro-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5f**) via Method B.* Similar treatment of 4,5-dichloro-1,2,3-dithiazolium chloride (**11**) (826 mg, 3.97 mmol) with 2-amino-*N*′-(2-bromophenyl)-5-chlorobenzamidine (**15**) (1.290 g, 3.97 mmol) gave the title compound **5f** (290.1 mg, 81%) as colorless plates, mp (hotstage) 226.5−227.8 °C (from *c*-hexane/DCM, 90:10); mp (DSC) onset 227.0 °C, peak max. 228.7 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.70 (DCM/*t*-BuOMe, 90:10); (found: C, 49.96; H, 2.18; N, 15.47. $C_{15}H_8BrClN_4$ requires C, 50.10; H, 2.24; N, 15.58%); $\lambda_{max}$(DCM)/nm 242 inf (log ε 4.05), 250 (4.04), 256 inf (4.02), 266 (4.05), 276 (3.95), 304 inf (3.74), 316 (3.91), 329 (3.96), 343 inf (3.85), 359 inf (3.68), 379 inf (3.20); $\nu_{max}$/$cm^{-1}$ 3298w (N−H), 3055w (aryl C−H), 2243w (C≡N), 1643m, 1630m, 1601w, 1587w, 1570w, 1557w, 1464w, 1424m, 1344m, 1312s, 1296m, 1165m, 1121w, 1080w, 1047w, 1030w, 1003w, 837s, 771s, 729m, 721m; $\delta_H$(500 MHz; $CDCl_3$) 8.28 (1H, br s), 7.90 (1H, d, *J* 8.0), 7.66 (2H, dd, *J* 8.5, 2.0), 7.62 (2H, dd, *J* 6.5, 6.5), 7.54 (1H, dd, *J* 7.5, 7.5), 7.49 (1H, dd, *J* 8.0, 1.5), 6.67 (1H, br s); $\delta_C$(75 MHz; $CDCl_3$) 3 C (s) and 1 C (d) resonances missing, 141.6 (s), 136.1 (s), 135.0 (d), 133.9 (d), 133.0 (d), 131.0 (d), 130.0 (d), 125.5 (d), 124.0 (s), 111.0 (s); *m*/*z* (MALDI-TOF) 363 ($MH^+$ + 4, 13%), 361 ($MH^+$ + 2, 100), 359 ($MH^+$, 55), 130 (2).

*4.4.6. 3-(2-Bromophenyl)-7-chloro-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5g**) via Method B.* Similar treatment of 4,5-dichloro-1,2,3-dithiazolium chloride (**11**) (826 mg, 3.97 mmol) with 2-amino-*N*′-(2-bromophenyl)-4-chlorobenzamidine (**16**) (1.290 g, 3.97 mmol) gave the title compound **5g** (284.5 mg, 79%) as colorless plates, mp (hotstage) 145.7−147.8 °C (from *c*-hexane/DCM, 90:10); mp (DSC) onset 146.1 °C, peak max. 150.7 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.67 (DCM/*t*-BuOMe, 90:10) ; (found: C, 49.99; H, 2.17; N, 15.46. $C_{15}H_8BrClN_4$ requires C, 50.10; H, 2.24; N, 15.58%); $\lambda_{max}$(DCM)/nm 245 (log ε 4.23), 254 (4.23), 264 (4.25), 274 (4.14), 302 inf (3.63), 313 (3.76), 326 (3.80), 344 inf (3.63), 362 inf (3.41), 383 inf (2.89); $\nu_{max}$/$cm^{-1}$ 3298w and 3273w (N−H), 3069w (aryl C−H), 2241w (C≡N), 1640s, 1585m, 1571m, 1557w, 1472w, 1462m, 1416m, 1346m, 1298s, 1155s, 1115w, 1080m, 1028w, 1003w, 920m, 835m, 824m, 760m, 727m, 718m; $\delta_H$(500 MHz; $CDCl_3$) N*H* deuterium exchanged, 8.29 (1H, br s), 7.91 (1H, d, *J* 8.0), 7.67 (1H, d, *J* 1.5), 7.63 (1H, dd, *J* 7.5, 7.5), 7.55−7.49 (3H, m); $\delta_C$(125 MHz; $CDCl_3$) 4 C (s) and 1 C (d) resonances missing, 144.1 (s), 139.7 (s), 135.0 (d), 133.0 (d), 131.0 (d), 130.2 (d), 130.0 (d), 128.1



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(d), 124.0 (s), 110.9 (s); *m*/*z* (MALDI-TOF) 363 ($MH^+$ + 4, 17%), 361 ($MH^+$ + 2, 100), 359 ($MH^+$, 96), 340 (7), 338 (45), 336 (35).

*4.4.7. 6-Bromo-3-(2-bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5h**) via Method B.* Similar treatment of 4,5-dichloro-1,2,3-dithiazolium chloride (**11**) (826 mg, 3.97 mmol) with 2-amino-5-bromo-*N*′-(2-bromophenyl)benzamidine (**17**) (1.465 g, 3.97 mmol) gave the title compound **5h** (306.6 mg, 76%) as colorless plates, mp (hotstage) 239.9−245.0 °C (from *c*-hexane/DCM, 90:10); mp (DSC) onset 244.4 °C, peak max. 246.9 °C (from *c*-hexane/DCM, 90:10); $R_f$ 0.63 (DCM/*t*-BuOMe, 90:10); (found: C, 44.42; H, 1.99; N, 13.83. $C_{15}H_8Br_2N_4$ requires C, 44.59; H, 2.00; N, 13.87%); $\lambda_{max}$(DCM)/nm 243 (log $\varepsilon$ 4.06), 251 (4.04), 267 (4.05), 277 (3.95), 304 inf (3.74), 317 inf (3.91), 329 (3.98), 343 inf (3.88), 360 inf (3.70), 379 inf (3.23); $\nu_{max}$/$cm^{-1}$ 3294w (N−H), 3053w and 3030w (aryl C−H), 2243w (C≡N), 1643m, 1630m, 1585m, 1570m, 1462m, 1418w, 1346m, 1310s, 1296m, 1277w, 1163m, 1067w, 1047w, 1030w, 1001w, 835s, 813s, 770s, 727m, 714m; $\delta_H$(500 MHz; $CDCl_3$) 8.48 (1H, br s), 7.90 (1H, d, *J* 8.0), 7.80 (1H, dd, *J* 8.8, 2.3), 7.63 (1H, dd, *J* 7.5, 7.5), 7.55 (2H, dd, *J* 7.5, 7.5), 7.49 (1H, dd, *J* 9.0, 1.5), 6.66 (1H, br s); $\delta_C$(75 MHz; $CDCl_3$) 4 C (s) resonances missing, 142.0 (s), 136.8 (d), 135.0 (d), 133.0 (d), 131.0 (d), 130.1 (d), 130.0 (d), 128.6 (d), 124.1 (s), 124.0 (s), 111.0 (s); *m*/*z* (MALDI-TOF) 407 ($MH^+$ + 4, 20%), 405 ($MH^+$ + 2, 29), 403 ($MH^+$, 15), 130 (100), 128 (51).

**4.4. Preparation of Benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitriles 1a−q.** *4.4.1. Benzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1a**). 4.4.1.1. Method A: via the PIFA Only Mediated Oxidative Cyclization of 4-(Phenylamino)quinazoline-2-carbonitrile (**4a**) (Typical Procedure).* To a stirred solution of 4-(phenylamino)-quinazoline-2-carbonitrile (**4a**) (49.2 mg, 0.20 mmol) in trifluoroacetic acid (TFA) (1 mL) was added phenyliodine bis(trifluoroacetate) (PIFA) (94.6 mg, 0.22 mmol) at ca. 20 °C and left to stir for 30 min. The reaction mixture was then diluted (water, 5 mL), extracted (DCM, 3 × 5 mL), and dried ($Na_2SO_4$). The organic phase was then adsorbed onto silica and chromatographed (DCM) to give benzo-[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitrile (**1a**) (45.1 mg, 92%) as pale yellow fibers, mp (hotstage) 258.1−259.0 °C (lit.,[3b] 252−254 °C) (*n*-pentane/THF, 80:20), mp (DSC) onset 259.0 °C, peak max. 259.5 °C; $R_f$ 0.65 (DCM); (found: C, 73.61; H, 3.42; N, 22.79. $C_{15}H_8N_4$ requires C, 73.76; H, 3.30; N, 22.94%); $\lambda_{max}$(DCM)/nm 236 (log $\varepsilon$ 4.32), 276 inf (4.46), 286 (4.60), 296 (4.59), 317 (3.87), 331 (3.82), 346 (3.59), 390 (3.03); $\nu_{max}$/$cm^{-1}$ 3048w (aryl C−H), 2243w (C≡N), 1620w, 1587w, 1526w, 1468w, 1449m, 1383m, 1327w, 1312w, 1261w, 1252w, 1223w, 1204w, 1159w, 1119w, 1013w, 793m, 775w, 758m, 746s; $\delta_H$(500 MHz; $CDCl_3$) 8.73 (1H, dd, *J* 7.5, 1.5), 8.58 (1H, d, *J* 8.5), 8.06 (2H, dd, *J* 7.0, 7.0), 7.88 (1H, ddd, *J* 7.5, 7.5, 1.5), 7.84 (1H, ddd, *J* 7.5, 7.5, 1.0), 7.67 (1H, ddd, *J* 7.5, 7.5, 1.0), 7.60 (1H, ddd, *J* 7.8, 7.8, 1.0); $\delta_C$(125 MHz; DMSO-$d_6$) 146.0 (s), 144.1 (s), 141.2 (s), 132.4 (d), 131.3 (d), 129.3 (d), 127.4 (s), 127.1 (d), 124.44 (d), 124.38 (d), 122.2 (s), 120.6 (d), 120.0 (s), 112.4 (d), 112.2 (s); *m*/*z* (MALDI-TOF) 246 ($MH^+$ + 1, 23%), 245 ($MH^+$, 100), 244 ($M^+$, 29).

*4.4.1.2. Method B: via the PIFA and Cu(OTf)$_2$-Mediated Oxidative Cyclization of 4-(Phenylamino)quinazoline-2-carbonitrile (**4a**) (Typical Procedure).* To a stirred solution of 4-(phenylamino)-quinazoline-2-carbonitrile (**4a**) (49.2 mg, 0.20 mmol) in trifluoroacetic acid (1 mL) was added phenyliodine bis(trifluoroacetate) (PIFA) (129.0 mg, 0.30 mmol) and $Cu(OTf)_2$ (3.6 mg, 5 mol %) at ca. 20 °C. The reaction mixture was then immersed in a preheated oil bath at ca. 80 °C and left to stir for 30 min. The reaction mixture was then diluted (water, 5 mL), extracted (DCM, 3 × 5 mL), and dried ($Na_2SO_4$). The organic phase was then adsorbed onto silica and chromatographed (DCM) to give benzo[4,5]imidazo[1,2-*c*]-quinazoline-6-carbonitrile (**1a**) (44.1 mg, 90%) as pale yellow fibers, mp (hotstage) 258.1−259.0 °C (lit.,[3b] 252−254 °C) (*n*-pentane/THF, 80:20); $R_f$ 0.65 (DCM); identical to that described above.

*4.4.1.3. Method C: via the Pd(OAc)$_2$-Mediated Nonoxidative Cyclization of 4-[(2-Bromophenyl)amino]quinazoline-2-carbonitrile (**4h**) (Typical Procedure).* A mixture of 4-[(2-bromophenyl)amino]-quinazoline-2-carbonitrile (**4h**) (32.5 mg, 0.10 mmol), $Pd(OAc)_2$ (2.2 mg, 10 mol %), BINAP (6.2 mg, 10 mol %), and powdered dry $K_2CO_3$ (13.8 mg, 0.10 mmol) was placed in a sealed tube, deaerated with argon, and dissolved in dry PhMe (1 mL) at ca. 20 °C. The reaction mixture was then immersed into a preheated Wood's metal bath at ca. 160 °C and left to stir for 5 h. The reaction mixture was then cooled to ca. 20 °C and adsorbed onto silica and chromatographed (DCM) to give benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitrile (**1a**) (20.8 mg, 85%) as pale yellow fibers, mp (hotstage) 258.1−259.0 °C (lit.,[3b] 252−254 °C) (*n*-pentane/THF, 80:20); $R_f$ 0.65 (DCM); identical to that described above.

*4.4.1.4. Method D: via the CuI-Mediated Nonoxidative Cyclization of 4-[(2-Bromophenyl)amino]quinazoline-2-carbonitrile (**4h**) (Typical Procedure).* A mixture of 4-[(2-bromophenyl)amino]-quinazoline-2-carbonitrile (**4h**) (32.5 mg, 0.10 mmol), CuI (1.9 mg, 10 mol %), 1,10-phenanthroline (2.0 mg, 10 mol %), and powdered dry $K_2CO_3$ (13.8 mg, 0.10 mmol) dissolved in dry MeCN (1 mL) at ca. 20 °C, and the stirred reaction mixture was heated at reflux (ca. 80 °C) for 3 h, then cooled to ca. 20 °C, adsorbed onto silica, and chromatographed (DCM) to give benzo[4,5]imidazo[1,2-*c*]-quinazoline-6-carbonitrile (**1a**) (22.6 mg, 93%) as pale yellow fibers, mp (hotstage) 258.1−259.0 °C (lit.,[3b] 252−254 °C) (*n*-pentane/THF, 80:20); $R_f$ 0.65 (DCM); identical to that described above.

*4.4.1.5. Method E: via the Pd(OAc)$_2$-Mediated Nonoxidative Cyclization of 3-(2-Bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5b**) (Typical Procedure).* A mixture of 3-(2-bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5b**) (32.5 mg, 0.10 mmol), $Pd(OAc)_2$ (2.2 mg, 10 mol %), BINAP (6.2 mg, 10 mol %), and $Cs_2CO_3$ (32.6 mg, 0.10 mmol) was deaerated with argon and dissolved in dry PhMe (1 mL) at ca. 20 °C. The stirred reaction mixture was then heated at reflux (ca. 110 °C) for 17 h, then cooled to ca. 20 °C, adsorbed onto silica, and chromatographed (DCM) to give benzo[4,5]imidazo[1,2-*c*]quinazoline-6-carbonitrile (**1a**) (19.0 mg, 78%) as pale yellow fibers, mp (hotstage) 258.1−259.0 °C (lit.,[3b] 252−254 °C) (*n*-pentane/THF, 80:20); $R_f$ 0.65 (DCM); identical to that described above.

*4.4.1.6. Method F: via the Pd[3,5-(F$_3$C)$_2$C$_6$H$_3$]$_3$-Mediated Nonoxidative Cyclization of 3-(2-Bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5b**) (Typical Procedure).* A mixture of 3-(2-bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5b**) (65.0 mg, 0.20 mmol), $Pd[3,5\text{-}(F_3C)_2C_6H_3]_3$ (42.4 mg, 10 mol %), BINAP (6.2 mg, 5 mol %) and powdered dry $K_2CO_3$ (82.8 mg, 0.60 mmol) was deaerated with argon and dissolved in dry PhMe (2 mL) at ca. 20 °C. The stirred reaction mixture was then heated at reflux (ca. 110 °C) for 5 h, then cooled to ca. 20 °C, adsorbed onto silica, and chromatographed (DCM) to give benzo[4,5]imidazo[1,2-*c*]-quinazoline-6-carbonitrile (**1a**) (46.6 mg, 95%) as pale yellow fibers, mp (hotstage) 258.1−259.0 °C (lit.,[3b] 252−254 °C) (*n*-pentane/THF, 80:20); $R_f$ 0.65 (DCM); identical to that described above.

*4.4.2. 9-Methylbenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1b**) (Method A).* Similar treatment of 4-(*p*-tolylamino)-quinazoline-2-carbonitrile (**4b**) (52.0 mg, 0.20 mmol) with PIFA (94.6 mg, 0.22 mmol) in TFA gave the title compound **1b** (41.1 mg, 80%) as pale yellow fibers, mp (hotstage) 252.9−253.5 °C (*n*-pentane/THF, 80:20), mp (DSC) onset 253.2 °C, peak max. 253.4 °C; $R_f$ 0.63 (DCM); (found: C, 74.32; H, 3.87; N, 21.57. $C_{16}H_{10}N_4$ requires C, 74.40; H, 3.90; N, 21.69%); $\lambda_{max}$(DCM)/nm 237 (log $\varepsilon$ 4.56), 279 inf (4.62), 291 (4.78), 303 (4.77), 320 (4.16), 335 (4.06), 352 inf (3.67), 396 (3.22); $\nu_{max}$/$cm^{-1}$ 3028w (aryl C−H), 2922w (alkyl C−H), 2243w (C≡N), 1622w, 1589w, 1582w, 1526w, 1487w, 1466m, 1433w, 1387m, 1334w, 1294w, 1263w, 1254w, 1223w, 1217m, 1171m, 808s, 772s; $\delta_H$(500 MHz; $CDCl_3$) 8.69 (1H, dd, *J* 7.8, 1.8), 8.32 (1H, br s), 8.04 (1H, d, *J* 8.0), 7.90 (1H, d, *J* 8.0), 7.84 (1H, ddd, *J* 7.6, 7.6, 1.8), 7.81 (1H, ddd, *J* 7.5, 7.5, 1.5), 7.47 (1H, d, *J* 8.5), 2.64 (3H, s); $\delta_C$(125 MHz; DMSO-$d_6$) 145.5 (s), 142.1 (s), 141.0 (s), 134.9 (s), 132.1 (d), 131.2 (d), 129.2 (d), 128.8 (d), 127.6 (s), 124.3 (d), 122.2 (s), 120.05 (s), 120.01 (d), 112.2 (s), 112.1 (d), 22.1 (q); *m*/*z* (MALDI-TOF) 260 ($MH^+$ + 1, 53%), 259 ($MH^+$, 100), 258 ($M^+$, 11).

*4.4.3. 9-Methoxybenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1c**) (Method A).* Similar treatment of 4-[(4-methoxyphenyl)-amino]quinazoline-2-carbonitrile (**4c**) (55.3 mg, 0.20 mmol) with PIFA (94.6 mg, 0.22 mmol) in TFA gave the title compound **1c** (44.6 mg, 82%) as pale yellow plates, mp (hotstage) 210.5−211.6 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 211.1 °C, peak max. 211.8


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°C; $R_f$ 0.43 (DCM); (found: C, 69.95; H, 3.62; N, 20.31. $C_{16}H_{10}N_4O$ requires C, 70.06; H, 3.68; N, 20.43%); $\lambda_{max}$(DCM)/nm 235 inf (log $\varepsilon$ 4.44), 254 inf (4.19), 284 inf (4.41), 295 (4.61), 306 (4.69), 324 inf (4.17), 340 (4.02), 402 (2.14); $\nu_{max}$/cm$^{-1}$ 3046w (aryl C−H), 2995w and 2839w (alkyl C−H), 2237w (C≡N), 1624m, 1595w, 1556w, 1526w, 1491m, 1466m, 1433m, 1387m, 1337w, 1290m, 1273w, 1254w, 1221s, 1205m, 1178w, 1125w, 1032m, 831m, 818m, 768s; $\delta_H$(500 MHz; $CDCl_3$) 8.64 (1H, dd, *J* 6.8, 1.5), 8.03−8.01 (2H, m), 7.91 (1H, d, *J* 9.0), 7.84−7.79 (2H, m), 7.27 (1H, dd, 9.0, 2.5), 3.98 (3H, s); $\delta_C$(125 MHz; $CDCl_3$) 157.4 (s), 145.0 (s), 140.7 (s), 138.3 (s), 131.8 (d), 131.2 (d), 129.2 (d), 127.8 (s), 124.0 (d), 122.0 (s), 121.1 (d), 120.2 (s), 117.0 (d), 112.2 (s), 95.3 (d), 56.0 (q); *m*/*z* (MALDI-TOF) 275 ($MH^+$, 15%), 274 ($M^+$, 100), 153 (2).

*4.4.4. Mixture of 9,10-Dimethoxybenzo[4,5]imidazo[1,2-c]-quinazoline-6-carbonitrile (**1d**) and 8,9-Dimethoxybenzo[4,5]-imidazo[1,2-c]quinazoline-6-carbonitrile (**1e**) (Method B).* Similar treatment of 4-[(3,4-dimethoxyphenyl)amino]quinazoline-2-carbonitrile (**4d**) (61.2 mg, 0.20 mmol) with PIFA (129.0 mg, 0.30 mmol) and $Cu(OTf)_2$ (3.6 mg, 5 mol %) in TFA gave a mixture of the title compounds **1d** and **1e** (50.2 mg, 82%) as pale yellow plates, mp (hotstage) 234.1−235.9 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 235.5 °C, peak max. 235.7 °C, onset 235.5 °C, peak max. 236.2 °C; $R_f$ 0.52;0.50 (DCM); (found: C, 66.93; H, 3.90; N, 18.36. $C_{17}H_{12}N_4O_2$ requires C, 67.10; H, 3.97; N, 18.41%); $\lambda_{max}$(DCM)/nm 250 (log $\varepsilon$ 4.23), 285 inf (4.41), 306 (4.54), 315 inf (4.54), 348 inf (3.98), 428 inf (3.17); $\nu_{max}$/cm$^{-1}$ 3092w and 3032w (aryl C−H), 2997w, 2936w and 2839w (alkyl C−H), 2236w (C≡N), 1593w, 1524w, 1489s, 1468w, 1460w, 1439m, 1391w, 1348w, 1333w, 1300m, 1271w, 1248m, 1224m, 1204s, 1163w, 1148s, 1028w, 1018w, 826s, 814m, 762s; $\delta_H$(500 MHz; $CDCl_3$) ratio based on ($^1$H NMR is **1d**/**1e** 2.6:1) 8.65−8.63 (3.6H, m), 8.05−8.03 (4.6H, m), 7.85−7.78 (7.4H, m), 7.48 (1H, s), 7.08 (2.6H, s), 4.08 (3H, s), 4.04 (3H, s), 4.010 and 4.006 (15.3H, 2 × s); $\delta_C$(125 MHz; DMSO-$d_6$) one C (d) resonance missing, 153.4 (s), 149.6 (s), 147.2 (s), 146.4 (s), 144.4 (s), 140.7 (s), 140.3 (s), 139.2 (s), 137.9 (s), 133.9 (s), 131.9 (d), 131.7 (d), 131.0 (d), 130.7 (d), 128.7 (d), 128.2 (d), 124.0 (d), 123.6 (d), 123.3 (d), 122.8 (s), 120.7 (s), 119.6 (s), 119.59 (s), 119.2 (s), 113.6 (s), 112.9 (s), 112.6 (s), 101.6 (d), 94.9 (d), 92.5 (d), 61.0 (q), 56.5 (q), 56.0 (q), 56.0 (q); *m*/*z* (MALDI-TOF) 305 ($MH^+$, 100%), 304 ($M^+$, 62).

*4.4.5. 9-Fluorobenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1f**) (Method B).* Similar treatment of 4-[(4-fluorophenyl)amino]-quinazoline-2-carbonitrile (**4e**) (52.8 mg, 0.20 mmol) with PIFA (129.0 mg, 0.30 mmol) and $Cu(OTf)_2$ (3.6 mg, 5 mol %) in TFA gave the title compound **1f** (46.8 mg, 89%) as pale yellow fibers, mp (hotstage) 240.0−241.9 °C (*n*-pentane/THF, 80:20), mp (DSC) onset 241.6 °C, peak max. 242.3 °C; $R_f$ 0.71 (DCM); (found: C, 68.72; H, 2.67; N, 21.22. $C_{15}H_7FN_4$ requires C, 68.70; H, 2.69; N, 21.36%); $\lambda_{max}$(DCM)/nm 247 inf (log $\varepsilon$ 4.18), 275 inf (4.58), 286 (4.76), 296 (4.81), 315 (4.12), 330 (4.06), 342 (3.82), 395 inf (3.25); $\nu_{max}$/cm$^{-1}$ 3026w (aryl C−H), 2243w (C≡N), 1626m, 1593m, 1485s, 1468m, 1439m, 1379m, 1342w, 1283m, 1252w, 1203m, 1184m, 1179m, 1161m, 1121w, 843s, 812s, 771s; $\delta_H$(500 MHz; $CDCl_3$) 8.68 (1H, dd, *J* 7.8, 1.8), 8.27 (1H, dd, *J* 8.5, 2.5), 8.05 (1H, dd, *J* 8.0, 1.0), 7.99 (1H, dd, *J* 9.0, 4.5), 7.88 (1H, ddd, *J* 7.5, 7.5, 1.5), 7.84 (1H, ddd, *J* 7.5, 7.5, 1.5), 7.43 (1H, ddd, *J* 9.0, 9.0, 2.0); $\delta_C$(125 MHz; $CDCl_3$) 159.7 (d, $^1J_{CF}$ 243.8), 146.5 (d, $^4J_{CF}$ 2.5), 141.0 (s), 140.4 (s), 132.5 (d), 131.5 (d), 129.4 (d), 127.3 (d, $^3J_{CF}$ 12.9), 124.3 (d), 121.8 (s), 121.5 (d, $^3J_{CF}$ 9.8), 119.9 (s), 115.8 (d, $^2J_{CF}$ 25.1), 111.2 (s), 99.7 (d, $^2J_{CF}$ 30.0); *m*/*z* (MALDI-TOF) 264 ($MH^+$ + 1, 11%), 263 ($MH^+$, 83), 262 ($M^+$, 100).

*4.4.6. 9-Chlorobenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1g**) (Method B).* Similar treatment of 4-[(4-chlorophenyl)-amino]quinazoline-2-carbonitrile (**4f**) (56.0 mg, 0.20 mmol) with PIFA (129.0 mg, 0.30 mmol) and $Cu(OTf)_2$ (3.6 mg, 5 mol %) in TFA gave the title compound **1g** (48.7 mg, 88%) as pale yellow fibers, mp (hotstage) 217.5−218.9 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 218.5 °C, peak max. 219.1 °C; $R_f$ 0.78 (DCM); (found: C, 64.57; H, 2.51; N, 20.21. $C_{15}H_7ClN_4$ requires C, 64.65; H, 2.53; N, 20.10%); $\lambda_{max}$(DCM)/nm 236 (log $\varepsilon$ 4.49), 247 inf (4.16), 278 inf (4.55), 288 (4.72), 298 (4.79), 317 (4.12), 333 (4.02), 344 inf (3.68), 385 (3.17); $\nu_{max}$/cm$^{-1}$ 3076w (aryl C−H), 2241w (C≡N), 1620m, 1589w, 1571w, 1460m, 1377m, 1329w, 1281m, 1261w, 1246w, 1221w, 1200m, 1117w, 1078w, 827m, 767s; $\delta_H$(500 MHz; $CDCl_3$) 8.69 (1H, dd, *J* 8.0, 1.5), 8.54 (1H, d, *J* 1.5), 8.07 (1H, d, *J* 7.5), 7.95 (1H, d, *J* 8.5), 7.89 (1H, ddd, *J* 7.8, 7.8, 1.3), 7.84 (1H, ddd, *J* 8.0, 8.0, 1.0), 7.62 (1H, dd, *J* 7.0, 2.0); $\delta_C$(125 MHz; $CDCl_3$) 146.5 (s), 142.6 (s), 141.1 (s), 132.7 (d), 131.6 (d), 130.2 (s), 129.4 (d), 128.0 (d), 127.8 (s), 124.5 (d), 121.8 (s), 121.4 (d), 119.8 (s), 112.6 (d), 111.9 (s); *m*/*z* (MALDI-TOF) 280 ($M^+$ + 2, 41%), 278 ($M^+$, 100).

*4.4.7. Mixture of 9,10-Dichlorobenzo[4,5]imidazo[1,2-c]-quinazoline-6-carbonitrile (**1h**) and 8,9-Dichlorobenzo[4,5]-imidazo[1,2-c]quinazoline-6-carbonitrile (**1i**) (Method B).* Similar treatment of 4-[(3,4-dichlorophenyl)amino]quinazoline-2-carbonitrile (**4g**) (63.0 mg, 0.20 mmol) with PIFA (129.0 mg, 0.30 mmol) and $Cu(OTf)_2$ (3.6 mg, 5 mol %) in TFA gave a mixture of the title compounds **1h** and **1i** (48.3 mg, 77%) as pale yellow plates, mp (hotstage) 205.1−208.4 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 206.5 °C, peak max. 210.0 °C; $R_f$ 0.75;0.73 (DCM/*t*-BuOMe, 95:05); (found: C, 57.28; H, 1.82; N, 17.69. $C_{15}H_6Cl_2N_4$ requires C, 57.53; H, 1.93; N, 17.89%); $\lambda_{max}$(DCM)/nm 265 inf (log $\varepsilon$ 4.27), 276 inf (4.52), 287 inf (4.67), 292 (4.70), 302 (4.73), 320 inf (4.13), 334 (4.02), 348 inf (3.70), 389 (3.16); $\nu_{max}$/cm$^{-1}$ 3092w and 3057w (aryl C−H), 2241w (C≡N), 1622w, 1585w, 1557w, 1468w, 1450w, 1438s, 1404m, 1377m, 1354w, 1327w, 1290w, 1233w, 1254w, 1225w, 1196m, 1171w, 1163w, 1128w, 1107m, 1099m, 1028w, 1018w, 870m, 789m, 773s; $\delta_H$(500 MHz; $CDCl_3$) ratio based on ($^1$H NMR is **1h**/**1i** 2.6:1) 8.69 (3.8H, m), 8.14 (1H, s), 8.09 (2.6H, dd, *J* 7.8, 7.8), 7.94−7.85 (7H, m), 7.76 (1H, d, *J* 8.5); $\delta_C$(125 MHz; $CDCl_3$) 3 C (s) resonances missing, 148.4 (s), 147.5 (s), 144.3 (s), 143.3 (s), 141.3 (s), 140.7 (s), 133.1 (d), 131.8 (d), 131.75 (s), 131.6 (d), 130.9 (d), 130.1 (s), 129.5 (d), 129.0 (d), 128.9 (d), 128.8 (d), 128.7 (s), 126.4 (s), 124.7 (d), 124.65 (d), 121.5 (s), 119.5 (s), 119.4 (s), 119.2 (d), 113.8 (d), 113.3 (s), 111.7 (s); *m*/*z* (MALDI-TOF) 317 ($MH^+$ + 4, 1%), 315 ($MH^+$ + 2, 32), 313 ($MH^+$, 100), 242 (15).

*4.4.8. 11-Bromobenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1j**) (Method B).* Similar treatment of 4-[(2-bromophenyl)-amino]quinazoline-2-carbonitrile (**4h**) (65.0 mg, 0.20 mmol) with PIFA (129.0 mg, 0.30 mmol) and $Cu(OTf)_2$ (3.6 mg, 5 mol %) in TFA gave the title compound **1j** (53.2 mg, 82%) as pale yellow plates, mp (hotstage) 258.1−259.1 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 258.9 °C, peak max. 259.3 °C; $R_f$ 0.86 (DCM); (found: C, 55.63; H, 2.09; N, 17.26. $C_{15}H_7BrN_4$ requires C, 55.75; H, 2.18; N, 17.34%); $\lambda_{max}$(DCM)/nm 238 (log $\varepsilon$ 4.41), 242 (4.44), 280 inf (4.48), 289 (4.60), 299 (4.55), 319 (3.93), 334 (3.84), 346 inf (3.60), 389 (3.11); $\nu_{max}$/cm$^{-1}$ 3086w and 3030w (aryl C−H), 2239w (C≡N), 1622w, 1607w, 1585m, 1466m, 1420s, 1377m, 1340w, 1327w, 1283m, 1261m, 1219w, 1182m, 1150w, 1128w, 1055w, 930m, 773s, 743s; $\delta_H$(500 MHz; $CDCl_3$) 8.88 (1H, dd, *J* 8.0, 1.5), 8.56 (1H, d, *J* 8.0), 8.08 (1H, d, *J* 8.0), 7.91 (1H, ddd, *J* 8.0, 8.0, 2.0), 7.89−7.85 (2H, m), 7.46 (2H, dd, *J* 8.0, 8.0); $\delta_C$(125 MHz; $CDCl_3$) 146.4 (s), 142.9 (s), 141.3 (s), 132.9 (d), 131.5 (d), 130.1 (d), 129.3 (d), 128.0 (s), 125.1 (d), 125.0 (d), 122.0 (s), 119.7 (s), 114.2 (s), 112.0 (s), 111.6 (d); *m*/*z* (MALDI-TOF) 325 ($MH^+$ + 2, 69%), 323 ($MH^+$, 100), 322 ($M^+$, 37), 244 (4).

*4.4.9. 9-Bromobenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1k**) (Method B).* Similar treatment of 4-[(4-bromophenyl)-amino]quinazoline-2-carbonitrile (**4i**) (65.0 mg, 0.20 mmol) with PIFA (129.0 mg, 0.30 mmol) and $Cu(OTf)_2$ (3.6 mg, 5 mol %) in TFA gave the title compound **1k** (56.1 mg, 87%) as pale yellow plates, mp (hotstage) 237.3−238.0 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 238.4 °C, peak max. 238.8 °C; $R_f$ 0.82 (DCM); (found: C, 55.75; H, 2.15; N, 17.21. $C_{15}H_7BrN_4$ requires C, 55.75; H, 2.18; N, 17.34%); $\lambda_{max}$(DCM)/nm 237 (log $\varepsilon$ 4.31), 248 inf (3.99), 278 inf (4.37), 288 (4.55), 300 (4.64), 318 (3.97), 333 (3.86), 345 inf (3.49), 387 inf (2.98); $\nu_{max}$/cm$^{-1}$ 3071w (aryl C−H), 2245w (C≡N), 1620w, 1585m, 1452s, 1423w, 1379s, 1329w, 1281m, 1260w, 1246w, 1219m, 1202m, 1136w, 1115w, 1061w, 1013w, 833m, 819s, 768s, 735m; $\delta_H$(500 MHz; $CDCl_3$) 8.70−8.68 (2H, m), 8.07 (1H, dd, *J* 8.3, 0.8), 7.91−7.88 (1H, m), 7.85 (1H, ddd, *J* 7.5, 7.5, 1.0), 7.76 (1H, dd, *J* 8.8, 1.3); $\delta_C$(125 MHz; $CDCl_3$) 146.4 (s), 143.0 (s), 141.1 (s), 132.7 (d),


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131.6 (d), 130.7 (d), 129.4 (d), 128.3 (s), 124.5 (d), 121.8 (s), 121.7 (d), 119.7 (s), 117.5 (s), 115.5 (d), 111.9 (s); *m*/*z* (MALDI-TOF) 325 ($MH^+$ + 2, 64%), 323 ($MH^+$, 100), 283 (3), 244 (2).

*4.4.10. 2,3-Dimethoxybenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1l**) (Method B).* Similar treatment of 6,7-dimethoxy-4-(phenylamino)quinazoline-2-carbonitrile (**4j**) (61.2 mg, 0.20 mmol) with PIFA (129.0 mg, 0.30 mmol) and $Cu(OTf)_2$ (3.6 mg, 5 mol %) in TFA gave the title compound **1l** (51.8 mg, 85%) as yellow fibers, mp (hotstage) 284.1−284.9 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 284.4 °C, peak max. 285.8 °C, decomp. onset 328.0 °C, peak max. 343.9 °C; $R_f$ 0.20 (DCM); (found: C, 66.97; H, 3.85; N, 18.41. $C_{17}H_{12}N_4O_2$ requires C, 67.10; H, 3.97; N, 18.41%); $\lambda_{max}$(DCM)/nm 246 (log $\varepsilon$ 4.30), 280 inf (3.54), 292 (4.66), 304 (4.74), 323 (4.07), 338 (4.04), 351 (3.76), 391 (3.57); $\nu_{max}/cm^{-1}$ 3024w (aryl C−H), 2978w and 2835w (alkyl C−H), 2239w (C≡N), 1628w, 1609w, 1587w, 1494s, 1470m, 1452m, 1437m, 1389m, 1315w, 1283w, 1256w, 1233s, 1209w, 1157w, 1123w, 1092m, 1026w, 1016w, 995m, 862m, 851m, 762s, 750s; $\delta_H$(500 MHz; $CDCl_3$) 8.55 (1H, d, *J* 8.5), 8.01 (1H, d, *J* 8.5), 7.99 (1H, s), 7.65 (1H, ddd, *J* 7.8, 7.8, 1.0), 7.54 (1H, ddd, *J* 7.8, 7.8, 1.0), 7.42 (1H, s), 4.14 (3H, s), 4.06 (3H, s); $\delta_C$(125 MHz; $CDCl_3$) 153.4 (s), 152.6 (s), 145.9 (s), 144.2 (s), 137.1 (s), 127.4 (s), 127.1 (d), 123.7 (d), 120.3 (s), 120.1 (d), 114.2 (s), 112.5 (s), 112.4 (d), 109.5 (d), 103.6 (d), 56.8 (q), 56.5 (q); *m*/*z* (MALDI-TOF) 306 ($MH^+$ + 1, 7%), 305 ($MH^+$, 100), 304 ($M^+$, 99).

*4.4.11. 2,3-Dimethoxybenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1l**) (Method F).* Similar treatment of 3-(2-bromophenyl)-4-imino-6,7-dimethoxy-3,4-dihydroquinazoline-2-carbonitrile (**5e**) (76.8 mg, 0.20 mmol) with $Pd[3,5\text{-}(F_3C)_2C_6H_3]_3$ (42.4 mg, 10 mol %), BINAP (6.2 mg, 5 mol %), and $K_2CO_3$ (82.8 mg, 0.60 mmol) in dry PhMe gave the title compound **1l** (58.6 mg, 96%) as yellow fibers, mp (hotstage) 284.1−284.9 °C (*n*-pentane/DCM, 80:20), $R_f$ 0.20 (DCM); identical to that described above.

*4.4.12. 1-Methylbenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1m**) (Method F).* Similar treatment of 3-(2-bromophenyl)-4-imino-5-methyl-3,4-dihydroquinazoline-2-carbonitrile (**5c**) (67.8 mg, 0.20 mmol) with $Pd[3,5\text{-}(F_3C)_2C_6H_3]_3$ (42.4 mg, 10 mol %), BINAP (6.2 mg, 5 mol %), and $K_2CO_3$ (82.8 mg, 0.60 mmol) in dry PhMe gave the title compound **1m** (50 mg, 97%) as yellow plates, mp (hotstage) 250.6−251.5 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 251.5 °C, peak max. 252.5 °C; $R_f$ 0.79 (DCM); (found: C, 74.41; H, 3.84; N, 21.55. $C_{16}H_{10}N_4$ requires C, 74.40; H, 3.90; N, 21.69%); $\lambda_{max}$(DCM)/nm 246 inf (log $\varepsilon$ 3.75), 276 inf (4.19), 286 (4.38), 297 (4.39), 322 inf (3.55), 335 (3.55), 353 (3.49), 399 (2.82); $\nu_{max}/cm^{-1}$ 3073w (aryl C−H), 2920w and 2851w (alkyl C−H), 2241w (C≡N), 1616w, 1591w, 1516w, 1446w, 1451m, 1389w, 1383w, 1358w, 1314w, 1278m, 1231w, 1211m, 1188w, 1132m, 1038w, 1018w, 812s, 737s; $\delta_H$(500 MHz; $CDCl_3$) 8.59 (1H, d, *J* 8.0), 8.08 (1H, d, *J* 8.0), 7.90 (1H, d, *J* 8.0), 7.72 (1H, dd, *J* 7.8, 7.8), 7.67−7.62 (2H, m), 7.58 (1H, ddd, *J* 7.8, 7.8, 1.0), 3.23 (3H, s); $\delta_C$(125 MHz; $CDCl_3$) 146.4 (s), 144.2 (s), 142.3 (s), 138.8 (s), 133.3 (d), 131.3 (d), 127.1 (d), 126.7 (d), 126.5 (s), 124.3 (d), 122.2 (s), 120.8 (d), 118.9 (s), 112.3 (s), 112.2 (d), 23.5 (q); *m*/*z* (MALDI-TOF) 260 ($MH^+$ + 1, 7%), 259 ($MH^+$, 100), 258 ($M^+$, 48).

*4.4.13. 3-Methoxybenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1n**) (Method F).* Similar treatment of 3-(2-bromophenyl)-4-imino-7-methoxy-3,4-dihydroquinazoline-2-carbonitrile (**5d**) (71.0 mg, 0.20 mmol) with $Pd[3,5\text{-}(F_3C)_2C_6H_3]_3$ (42.4 mg, 10 mol %), BINAP (6.2 mg, 5 mol %), and $K_2CO_3$ (82.8 mg, 0.60 mmol) in dry PhMe gave the title compound **1m** (49.8 mg, 91%) as yellow plates, mp (hotstage) 220.8−221.9 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 221.3 °C, peak max. 222.3 °C; $R_f$ 0.38 (DCM); (found: C, 69.93; H, 3.66; N, 20.37. $C_{16}H_{10}N_4O$ requires C, 70.06; H, 3.68; N, 20.43%); $\lambda_{max}$(DCM)/nm 242 (log $\varepsilon$ 4.42), 279 inf (4.66), 290 (4.77), 300 (4.77), 320 (4.04), 333 (3.93), 351 (3.58), 404 (3.28); $\nu_{max}/cm^{-1}$ 3057w (aryl C−H), 2241w (C≡N), 1628m, 1611m, 1587m, 1558w, 1521w, 1483s, 1452s, 1429w, 1385s, 1352w, 1318m, 1271m, 1227s, 1203w, 1163m, 1128w, 1098m, 1020m, 1011w, 955m, 843s, 837m, 829m, 764s, 746s; $\delta_H$(500 MHz; $CDCl_3$) 8.58 (1H, d, *J* 8.5), 8.52 (1H, d, *J* 8.5), 7.99 (1H, d, *J* 8.5), 7.63 (1H, dd, *J* 7.8, 7.8), 7.55 (1H, dd, *J* 7.8, 7.8), 7.43 (1H, d, *J* 2.0), 7.40 (1H, dd, *J* 7.0, 2.0), 3.99 (3H, s); $\delta_C$(125 MHz; $CDCl_3$) 162.9 (s), 146.2 (s), 144.2 (s), 143.1 (s), 127.3 (s), 127.1 (d), 125.7 (d), 123.8 (d), 122.6 (s), 121.3 (d), 120.2 (d), 113.3 (s), 112.3 (d), 112.1 (s), 110.1 (d), 55.9 (q); *m*/*z* (MALDI-TOF) 275 ($MH^+$, 22%), 274 ($M^+$, 100).

*4.4.14. 3-Chlorobenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1o**) (Method F).* Similar treatment of 3-(2-bromophenyl)-7-chloro-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5f**) (72.0 mg, 0.20 mmol) with $Pd[3,5\text{-}(F_3C)_2C_6H_3]_3$ (42.4 mg, 10 mol %), BINAP (6.2 mg, 5 mol %), and $K_2CO_3$ (82.8 mg, 0.60 mmol) in dry PhMe gave the title compound **1o** (51.0 mg, 92%) as yellow plates, mp (hotstage) 240.5−241.6 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 241.3 °C, peak max. 242.3 °C; $R_f$ 0.52 (DCM); (found: C, 64.57; H, 2.43; N, 19.99. $C_{15}H_7ClN_4$ requires C, 64.65; H, 2.53; N, 20.10%); $\lambda_{max}$(DCM)/nm 239 (log $\varepsilon$ 4.49), 249 inf (4.14), 279 inf (4.55), 289 (4.66), 300 (4.66), 320 (4.01), 335 (3.90), 352 inf (3.54), 395 (3.16); $\nu_{max}/cm^{-1}$ 3034w (aryl C−H), 2243w (C≡N), 1620w, 1585m, 1521w, 1449s, 1427m, 1389m, 1315m, 1278w, 1259w, 1238w, 1211m, 1205m, 1132m, 1124w, 1072m, 1018w, 1015w, 928m, 829m, 765s, 762s, 742s, 718m; $\delta_H$(500 MHz; $CDCl_3$) 8.64 (1H, d, *J* 8.5), 8.55 (1H, d, *J* 8.5), 8.05−8.04 (1H, m), 8.02 (1H, br s), 7.78 (1H, dd, *J* 8.5, 2.0), 7.68 (1H, ddd, *J* 7.8, 7.8, 1.0), 7.60 (1H, ddd, *J* 7.8, 7.8, 1.0); $\delta_C$(125 MHz; $CDCl_3$) 145.4 (s), 144.1 (s), 141.8 (s), 138.5 (s), 131.7 (d), 128.7 (d), 127.4 (d), 127.3 (s), 125.6 (d), 124.7 (d), 123.2 (s), 120.7 (d), 118.3 (s), 112.4 (d), 111.9 (s); *m*/*z* (MALDI-TOF) 280 ($MH^+$ + 1, 24%), 279 ($MH^+$, 100), 278 ($M^+$, 59), 130 (20).

*4.4.15. 2-Chlorobenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1p**) (Method F).* Similar treatment of 3-(2-bromophenyl)-6-chloro-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5g**) (72.0 mg, 0.20 mmol) with $Pd[3,5\text{-}(F_3C)_2C_6H_3]_3$ (42.4 mg, 10 mol %), BINAP (6.2 mg, 5 mol %), and $K_2CO_3$ (82.8 mg, 0.60 mmol) in dry PhMe gave the title compound **1p** (52.5 mg, 94%) as yellow plates, mp (hotstage) 246.1−248.2 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 246.6 °C, peak max. 251.0 °C; $R_f$ 0.62 (DCM); (found: C, 64.63; H, 2.46; N, 19.99. $C_{15}H_7ClN_4$ requires C, 64.65; H, 2.53; N, 20.10%); $\lambda_{max}$(DCM)/nm 240 inf (log $\varepsilon$ 4.42), 281 inf (4.57), 291 (4.68), 302 (4.68), 321 (4.03), 335 (4.00), 350 (3.82), 393 inf (3.33); $\nu_{max}/cm^{-1}$ 3063w (aryl C−H), 2237w (C≡N), 1622w, 1607w, 1585m, 1547w, 1466w, 1450m, 1427m, 1383m, 1323w, 1308w, 1277w, 1246m, 1225w, 1207w, 1136w, 1109m, 1076w, 1013w, 843m, 827m, 767m, 758m, 743s, 731s; $\delta_H$(500 MHz; $CDCl_3$) 8.71 (1H, d, *J* 2.0), 8.57 (1H, d, *J* 8.5), 8.06 (1H, d, *J* 8.0), 8.00 (1H, d, *J* 8.5), 7.80 (1H, dd, *J* 8.5, 2.3), 7.69 (1H, ddd, *J* 7.8, 7.8, 1.0), 7.62 (1H, ddd, *J* 7.8, 7.8, 1.0); $\delta_C$(125 MHz; $CDCl_3$) one C (s) resonance missing, 144.8 (s), 144.0 (s), 139.5 (s), 137.6 (s), 132.9 (d), 130.7 (d), 127.4 (d), 124.8 (d), 124.0 (d), 122.2 (s), 121.0 (s), 120.8 (d), 112.5 (d), 112.0 (s); *m*/*z* (MALDI-TOF) 281 ($MH^+$ + 2, 23%), 280 ($MH^+$ + 1, 47), 279 ($MH^+$, 100), 278 ($M^+$, 93).

*4.4.16. 2-Bromobenzo[4,5]imidazo[1,2-c]quinazoline-6-carbonitrile (**1q**) (Method F).* Similar treatment of 6-bromo-3-(2-bromophenyl)-4-imino-3,4-dihydroquinazoline-2-carbonitrile (**5h**) (80.8 mg, 0.20 mmol) with $Pd[3,5\text{-}(F_3C)_2C_6H_3]_3$ (42.4 mg, 10 mol %), BINAP (6.2 mg, 5 mol %), and $K_2CO_3$ (82.8 mg, 0.60 mmol) in dry PhMe gave the title compound **1q** (58.1 mg, 90%) as yellow plates, mp (hotstage) 262.4−263.6 °C (*n*-pentane/DCM, 80:20), mp (DSC) onset 263.1 °C, peak max. 264.6 °C; $R_f$ 0.66 (DCM); (found: C, 55.64; H, 2.11; N, 17.22. $C_{15}H_7BrN_4$ requires C, 55.75; H, 2.18; N, 17.34%); $\lambda_{max}$(DCM)/nm 241 inf (log $\varepsilon$ 4.22), 283 inf (4.36), 292 (4.48), 303 (4.47), 321 inf (3.85), 336 (3.80), 351 (3.63), 401 (3.00); $\nu_{max}/cm^{-1}$ 3084w (aryl C−H), 2245w (C≡N), 1622w, 1603w, 1582m, 1541w, 1481w, 1462w, 1445s, 1423m, 1331m, 1319w, 1304w, 1279w, 1244w, 1202m, 1134w, 1103w, 1067m, 1017w, 835s, 827m, 766s, 760s, 745s, 739s; $\delta_H$(500 MHz; $CDCl_3$) 8.89 (1H, d, *J* 2.0), 8.58 (1H, d, *J* 8.5), 8.06 (1H, d, *J* 8.5), 7.96 (1H, dd, *J* 8.8, 2.3), 7.92 (1H, d, *J* 8.5), 7.70 (1H, ddd, *J* 7.8, 7.8, 1.0), 7.62 (1H, ddd, *J* 7.8, 7.8, 1.0); $\delta_C$(125 MHz; $CDCl_3$) one C (s) resonance missing, 144.6 (s), 144.0 (s), 139.8 (s), 135.7 (d), 130.7 (d), 127.4 (d), 127.1 (d), 125.8 (s), 124.8 (d), 122.3 (s), 121.1 (s), 120.8 (d), 112.5 (d), 112.0 (s); *m*/*z* (MALDI-TOF) 325 ($MH^+$ + 2, 100%), 323 ($MH^+$, 100), 244 (4).



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## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01514.

Copies of $^{1}H$ and $^{13}C$ NMR spectra of all new compounds. Optimization and mechanistic rationale for the PIFA/$Cu(OTf)_2$ oxidative cyclization of 4-anilinoquinazoline-2-carbonitrile (**4a**) (PDF)

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### Notes

The authors declare no competing financial interest.

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