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Suzuki–Miyaura cross-coupling reaction as the key step for the synthesis of some new 4′-aryl and alkyl substituted analogues of amodiaquine and amopyroquine

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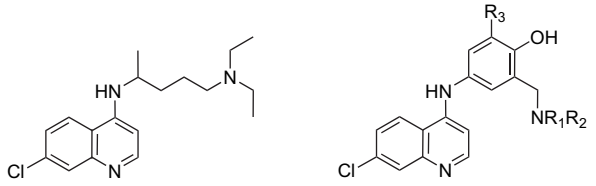
Abstract—A versatile methodology for the synthesis of some new 4-aminoquinoquinoline antimalarial drugs, using Csp^2–Csp^2 and Csp^2–Csp^3 Suzuki–Miyaura cross-coupling reactions as a key step, is presented. The proposed strategy allowed the synthesis of 26 new amodiaquine (AQ) and amopyroquine (ApQ) derivatives. These new compounds constitute the base of the development of a new library, designed in order to obtain derivatives that present not only improved antimalarial activity, but also a better stability towards bioactivation in potentially toxic metabolites.

1. Introduction

Malaria is considered as one of the most widespread diseases in the world with almost one-half of the world's population exposed to risk of infection and two million deaths each year.[1] Chloroquine (CQ, Fig. 1), a 4-aminoquinoline compound, has been the mainstream drug in the fight against *Plasmodium falciparum* since 1950s, but its efficacy was eroded by the emergence of resistant parasites. The development of new drugs that overcome the parasite resistance mechanism is thus an important issue.

Amodiaquine (AQ, Fig. 1), another 4-aminoquinoline drug, maintains an important antimalarial activity against many CQ-resistant strains. Though resistance to AQ is also developing, last WHO's guidelines for treatment still recommend the use of this drug in combination with other antimalarial drugs.[1] However, its hepatotoxicity, explained by the presence of the 4-hydroxyanilino moiety, which is believed to undergo extensive metabolization to a quinonimine variant, has limited its use in prophylaxis (Fig. 2). Moreover, metabolic stability of AQ could be increased by the replacement of the diethylamino group in the side chain by a pyrrolidine moiety providing amopyroquine (ApQ) analogue, which is more active than AQ against CQ-resistant strains *P. falciparum*. With the aim of diminishing the toxicity, great effort has been made for the preparation of various AQ analogues.[2] Among them, compounds bearing alkyl or aryl substituent in



Chloroquine (CQ)

Amodiaquine (AQ): $NR_1R_2 = NEt_2$ - R_3 = H
Amopyroquine (ApQ): NR_1R_2 = pyrrolidine - R_3 = H
Tebuquine (TBQ): NR_1R_2 = NH-tBu - R_3 = p-chlorophenyl

Figure 1. Structure of chloroquine, amodiaquine, and analogues.

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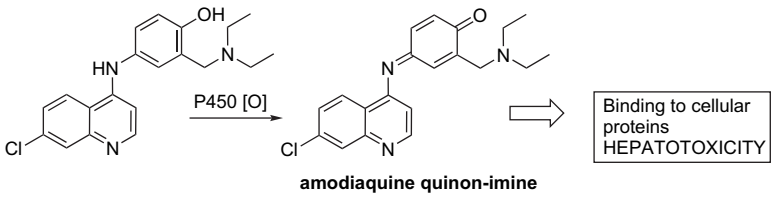


Figure 2. Metabolization of AQ through oxidative pathway.

5′-position, as tebuquine (TBQ), presented increased activity upon CQ-resistant strains. 4-Aminoquinoline antimalarials are believed to exert their activity by inhibiting hemozoin formation in the food vacuole, which is a crucial heme detoxification process of the parasite.[3]

We describe here the synthesis of some novel AQ and ApQ analogues in which the 4′-hydroxyl function was replaced with various aliphatic or aromatic groups (Fig. 3). We hypothesize that the introduction of these substituents may enhance interaction with heme via π–π stacking, thus inhibiting the formation of hemozoin. As low-cost preparation and easy accessibility were the main criteria for the design of new antimalarial compounds, we were interested in developing an efficient synthesis of aminoquinoline-biphenyl or aminoquinoline-phenyl-alkyl moiety.

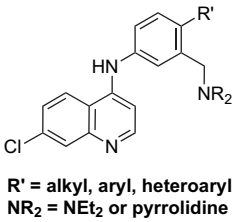


Figure 3. Structure of target compounds.

Palladium-catalyzed cross-coupling of aryl halides with organoboronic acids, namely Suzuki–Miyaura cross-coupling reaction, is a useful reaction for the formation of carbon–carbon bonds, in particular for the synthesis of biaryls.[4] Aryl–aryl bond in tebuquine was built using this cross-coupling reaction.[5] Usually, aromatic iodides or bromides are involved in the coupling. Recently, efforts have been focused on the development of efficient and selective catalytic systems for Suzuki–Miyaura reaction allowing the use of aryl chlorides.[6]

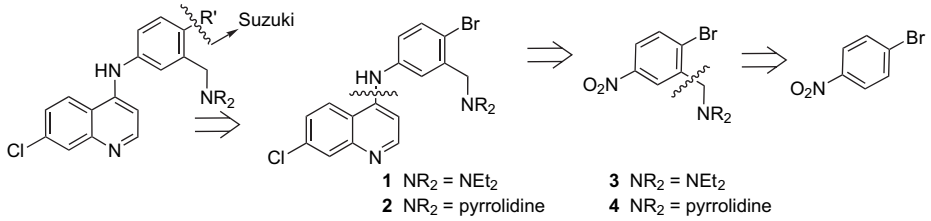
The synthetic application of Suzuki–Miyaura cross-coupling has been also extended to the formation of Csp^2–Csp^3 or Csp^3–Csp^3 bonds.[7]

Because of the lower reactivity of alkylboronic acids, trialkylboranes,[8] alkylboronates, or alkylboronic acid esters[9] are preferred as partners. The development and use of more active catalytic systems, such as oxime-derived palladacycles,[10] or of ligands, i.e., ferrocenyldialkylphosphines,[11] Tedicyp (*cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane)[12] or *i*-Pr (*N*,*N*-bis-(2,6-diisopropylphenyl)dihydroimidazolium chloride or tetrafluoroborate),[13] allowed the realization of the Csp^2–Csp^3 cross-coupling reactions using alkylboronic acids in good yields and even with low catalyst loading.[14]

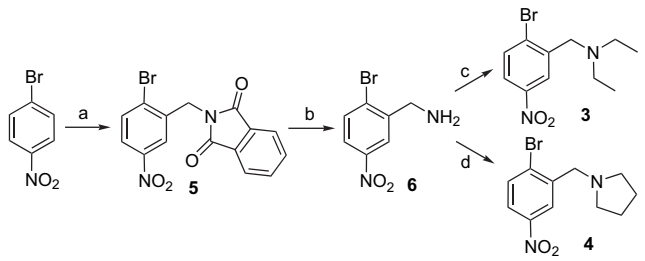
2. Results and discussion

Retrosynthetic analysis of the target compounds suggested that aryl and alkyl R′ substituents could be introduced by Suzuki–Miyaura cross-coupling reactions using bromides **1** and **2** as substrates (Scheme 1), allowing the convergent introduction of the structural diversity in the last step. These intermediates **1** and **2** were expected to be constructed from nitro compounds **3** and **4** after reduction of the nitro function and aromatic nucleophilic substitution with 4,7-dichloroquinoline. The aminomethylene side chain could be introduced on the commercially available bromonitrobenzene. As we anticipated that the reactivity of arylbromides **1** and **2** could not be sufficient to obtain good yields, the synthetic steps could be reversed and the target compounds could be also obtained by performing Suzuki cross-coupling reaction on bromo intermediates **3** and **4**, followed by nitro reduction and aromatic nucleophilic substitution.

Thus, the first step was the synthesis of the key intermediates **3** and **4** (Scheme 2). The amino side chain was introduced via a super-electrophilic Tscherniac amidomethylation of the commercially available 4-bromonitrobenzene with *N*-hydroxymethylphthalimide in trifluoromethanesulfonic acid. The synthesis was performed according to Olah et al.[15] As the substrate was deactivated by the presence of strong electron-withdrawing halogeno and nitro groups, the use of a super acid (trifluoromethanesulfonic acid) as catalyst and solvent was necessary. Bromo derivative of 2 equiv was used in order to avoid the disubstitution side reaction.



Scheme 1. Retrosynthetic scheme proposed for the obtainment of the 4′-alkyl, aryl, and heteroaryl AQ and ApQ analogues.



Scheme 2. Synthesis of key intermediates **3** and **4**. Reagents: (a) *N*-hydroxymethylphthalimide, CF_3SO_3H, rt, 24 h; (b) hydrazine hydrate, CH_3CN, reflux, 24 h; (c) ethylbromide, NaOH, CH_3CN, 40 °C, 48 h; (d) 1,4-dibromobutane, K_2CO_3, CH_3CN, reflux, 48 h.

Hydrazinolysis of compound **5** with hydrazine hydrate provided benzylamine **6**, which was further reacted with the appropriate bromide derivatives via nucleophilic substitution reactions to yield compound **3** or **4**.

Reduction of the bromo intermediates **3** and **4** with tin chloride in acidic media and regioselective nucleophilic aromatic substitution of the chlorine atom in position 4 of the 4,7-dichloroquinoline by the aniline compounds **7** and **8** (Scheme 3) allowed the synthesis of derivatives **1** and **2** in good yields. The yield of the last step was considerably enhanced by the use of 1 equiv of HCl. By protonating quinoline nitrogen, the electrophilicity of carbon atom in position 4 of the quinoline nucleus was increased.

The ability of derivative **2** to act as a substrate in Suzuki–Miyaura cross-coupling reactions was further explored. First a preliminary study was realized using derivative **2** and phenylboronic acid in order to optimize the reaction conditions (Table 1). Several catalytic systems were studied. No evolution was observed when *N*,*N*-bis-(2,6-diisopropylphenyl)dihydroimidazolium tetrafluoroborate (*i*-Pr·HBF_4) was used. The role of the solvent was also evaluated together with the importance of additional compounds.

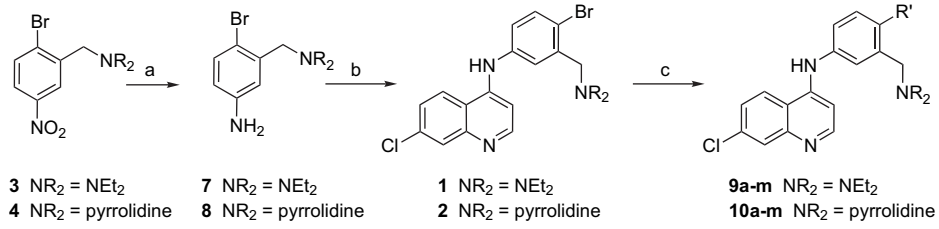
Conditions of assay 9 provided the best results and were further applied for the synthesis of the other target aryl compounds using derivatives **1** and **2** as substrates and various arylboronic acids. Results are presented in Table 2.

Unfortunately, only moderate yields were obtained. Parallel experiments conducted on the bromo derivative **1** (possessing a diethylaminomethyl side chain) provided even lower yields of the coupled products. The substrates presented incomplete conversion, and the unreacted bromo derivatives raised important problems in the purification of the coupled products. Some degradation of the reaction media was observed in the case of the reactions conducted with substrate **2** with *para*-acetylbenzene, 2-thiophene, and 2-furaneboronic acids. Moreover, the conditions were completely unsuccessful with alkylboronic acids. We could isolate the expected 4′-ethyl derivatives with low yields but with different conditions of solvent, base, temperature, and quantities of catalytic system (entry 12, Table 2). 4′-Methyl derivatives could not be obtained in those conditions.

Low yields and difficulties encountered in the purification of the coupling product (observed in the preliminary optimization study) lead us to reconsider and develop alternative synthetic pathway in which Suzuki–Miyaura cross-coupling reaction was performed on the more reactive bromo substrates **3** and **4**, activated by the presence of an electron-withdrawing nitro group in *para* position (Scheme 4).

A rapid optimization process run with compound **4** showed that the experimental conditions used with compound **2** could be also successfully applied in this case. Results of the obtained coupled intermediates **11a–m** and **12a–m** are presented in Table 3.

In this case, analogues of both the series (with a diethylamino group and a pyrrolidine cycle) were obtained in moderate to good yields by the cross-coupling reaction of intermediates **3**



Scheme 3. Synthesis of target compounds via Suzuki cross-coupling reaction of intermediates **1** and **2**. Reagents: (a) $SnCl_2$, 1 M HCl, THF, reflux; (b) 4,7-dichloroquinoline, HCl, CH_3CN, reflux; (c) R′–$B(OH)_2$, $Pd(OAc)_2$, P(*o*-tol)$_3$, TBAB, Na_2CO_3, toluene, EtOH, 60 °C.

Table 1. Optimization of cross-coupling reaction of bromo derivative **2** with phenylboronic acid

Assay	Catalytic system (equiv)	Base (equiv)	Additive (equiv)	Solvent	Temp (°C)	Reaction time (h)	Yield (%)
1	$Pd(PPh_3)_4$ (0.075)	Na_2CO_3 (1)	—	Toluene/EtOH/H_2O, 3/2/1	78	24	34
2	$Pd(PPh_3)_4$ (0.1)	Na_2CO_3 (1)		Toluene/EtOH/H_2O, 3/2/1	60	52	29
3	$Pd(PPh_3)_4$ (0.075)	Na_2CO_3 (2)		1,4-Dioxane/EtOH/H_2O, 3/2/1	78	36	30
4	$Pd(PPh_3)_4$ (0.075)	Cs_2CO_3 (2)		Toluene/EtOH/H_2O, 3/2/1	78	30	31
5	PPh_3 (0.1), $Pd(OAc)_2$ (0.05)	Na_2CO_3 (2)	—	Toluene/EtOH/H_2O, 3/2/1	65	2	31
6	P(*o*-tol)$_3$ (0.1), $Pd(OAc)_2$ (0.05)	Na_2CO_3 (2)	—	Toluene/EtOH/H_2O, 3/2/1	65	18	17
7	P(*o*-tol)$_3$ (0.15), $Pd(OAc)_2$ (0.075)	Na_2CO_3 (2)	—	Toluene/EtOH/H_2O, 3/2/1	60	26	35
8	P(*o*-tol)$_3$ (0.15), $Pd(OAc)_2$ (0.075)	Na_2CO_3 (2)	—	Toluene/EtOH/H_2O, 3/2/1	50	46	40
9	P(*o*-tol)$_3$ (0.15), $Pd(OAc)_2$ (0.075)	Na_2CO_3 (2)	TBAB (0.2)	Toluene/EtOH/H_2O, 3/2/1	60	42	42
10	*i*-Pr·HBF_4 (0.05), $Pd(OAc)_2$ (0.05)	Cs_2CO_3 (2)	—	1,4-Dioxane	80	24	—
11	*i*-Pr·HBF_4 (0.05), $Pd(OAc)_2$ (0.05)	Cs_2CO_3 (2)	—	1,4-Dioxane	65	48	—

Table 2. Suzuki cross-coupling reaction of intermediate **2**[a]

Assay	Compd	R′	Reaction time (h)	Yield (%)	HPLC purity (%)
1	**10a**	C_6H_5–	42	40	95
2	**10b**	*p*-CH_3–C_6H_4–	72	36	92
3	**10c**	*p*-(*t*-Bu)–C_6H_4–	40	22	88
4	**10d**	*p*-CF_3–C_6H_4–	72	43	90
5	**10e**	*p*-CH_3O–C_6H_4–	40	65	97
6	**10f**	*p*-CH_3CO–C_6H_4–	24	9	72
7	**10g**	*p*-F–C_6H_4–	48	11	99
8	**10h**	2-Thienyl–	140	12	96
9	**10i**	2-Furyl–	140	8	97
10	**10l**	Me	168	—	—
11	**10m**	Et	144	—	—
12	**10m**	Et	144	16[b]	95

[a] R′–$B(OH)_2$, $Pd(OAc)_2$ 7.5 mol %, P(*o*-tol)$_3$ 15 mol %, TBAB 20 mol %, Na_2CO_3 2 equiv, toluene, EtOH, 60 °C.
[b] $Pd(OAc)_2$ 15 mol %, P(*o*-tol)$_3$ 30 mol %, K_2CO_3 2 equiv, THF, H_2O, 70 °C.

and **4** with a series of aryl and heteroarylboronic acids. An improvement of yields was observed in the case of reactions run with benzeneboronic acids substituted in *para* position with hydrophobic groups. Also, in most cases, better results were obtained when cross-coupling reactions were conducted on substrate **4**, with a pyrrolydinylmethyl side chain. The presence of carbonyl (entry f, Table 3) and ether groups (entry e, Table 3) in *para* position of the arylboronic acid was well tolerated.

The system seemed to be more sensitive to the presence of *ortho* groups on the boronic acid. This effect may be due to the fact that the bromo partner is also substituted in *ortho* position and thus steric hindrance at the reaction center is favored. Thus, in the case of the cross-coupling reaction realized on substrate **3** the coupled product was isolated with a very low yield, whereas in the case of the reaction realized on substrate **4** the coupled product was not obtained (entry l, Table 3).

The important side reaction observed in some cases is the debromination of starting material as shown by the isolation of 5–10% yields of (5-nitro-benzyl)-diethylamine or 1-(5-nitro-benzyl)-pyrrolidine, reducing thus the conversion of substrates **3** and **4** into the desired coupled product. In the cross-coupling reactions with the heteroaromatic boronic acids the conversion of the brominated substrates in the coupled products was lower, probably because of the lower reactivity and thermal stability of these boronic acids.

In the case of some analogues with a pyrrolidine in the amino side chain, a side reaction of dehydrogenation of the pyrrolidine cycle to pyrrole was also observed. As a possible explanation, we suspect that in the reaction conditions used (oxidant character of the medium) the pyrrolidine cycle

Table 3. Suzuki cross-coupling reaction[a] of intermediates **3** and **4**

Compd	R′	NR_2	Reaction time (h)	Yield (%)	HPLC purity (%)
11a	C_6H_5–	NEt_2	40	43	95
12a		Pyrrolidine	40	75	95
11b	*p*-CH_3–C_6H_4–	NEt_2	16	78	99
12b		Pyrrolidine	16	71	97
11c	*p*-(*t*-Bu)–C_6H_4–	NEt_2	40	54	99
12c		Pyrrolidine	16	84	98
11d	*p*-CF_3–C_6H_4–	NEt_2	40	60	98
12d		Pyrrolidine	16	66	98
11e	*p*-CH_3O–C_6H_4–	NEt_2	120	45	99
12e		Pyrrolidine	120	59	98
11f	*p*-CH_3CO–C_6H_4–	NEt_2	40	39	98
12f		Pyrrolidine	40	70	97
11g	*p*-F–C_6H_4–	NEt_2	48	34	97
12g		Pyrrolidine	48	38	99
11h	2-Thienyl–	NEt_2	120	15	96
12h		Pyrrolidine	140	43	97
11i	2-Furyl–	NEt_2	120	16	98
12i		Pyrrolidine	140	40	97
11j	*o*-F–C_6H_4–	NEt_2	54	16	99
12j		Pyrrolidine	310	0	—
11k	*p*-Cl–C_6H_4–	NEt_2	16	64	98
12k		Pyrrolidine	16	58	98
11l	Me[b]	NEt_2	310	68	98
12l		Pyrrolidine	170	73	>99
11m	Et[b]	NEt_2	310	68	93
12m		Pyrrolidine	240	48	94

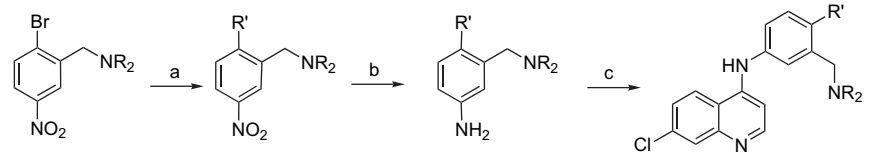
[a] R′–$B(OH)_2$, $Pd(OAc)_2$ 7.5 mol %, P(*o*-tol)$_3$ 15 mol %, TBAB 20 mol %, Na_2CO_3 2 equiv, toluene, H_2O, EtOH, 60 °C.
[b] Experimental conditions for alkylboronic acids: THF/H_2O, 10/1 as solvent; K_2CO_3 as base; 75 °C.

may act as a hydrogen donor, and the formation of a heteroaromatic cycle may favor this side reaction.[16–19]

This reaction proved to be time dependant as the pyrrole coupled derivative become predominant if the reaction is continued for further 24 h (Table 4).

This strategy could be also applied for Csp^2–Csp^3 cross-coupling of substrates **3** and **4** with methyl and ethylboronic acids, which lead to the expected coupled compounds with good yields around 70%. Nevertheless different experimental conditions appeared necessary in that case.

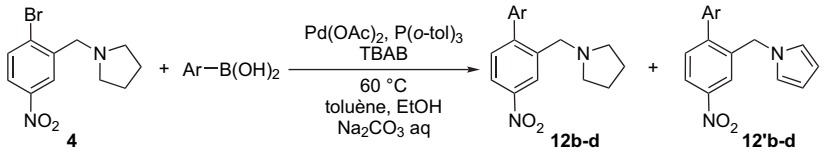
Intermediates **11a–m** and **12a–m** were subjected to a two-step reaction sequence (Scheme 4), consisting in the reduction of the nitro group and the substitution of the chlorine atom in the 4-position of the 4,7-dichloroquinoline with aniline



3 NR_2 = NEt_2 **4** NR_2 = pyrrolidine
11a-m NR_2 = NEt_2 **12a-m** NR_2 = pyrrolidine
13a-m NR_2 = NEt_2 **14a-m** NR_2 = pyrrolidine
9a-m NR_2 = NEt_2 **10a-m** NR_2 = pyrrolidine

Scheme 4. Synthesis of target compounds via Suzuki cross-coupling reaction of aromatic bromides **3** and **4**. Reagents: (a) R′–$B(OH)_2$, $Pd(OAc)_2$, P(*o*-tol)$_3$, TBAB, Na_2CO_3, toluene, EtOH, 60 °C; (b) $SnCl_2$, HCl, THF, reflux; (c) 4,7-dichloroquinoline, HCl, acetonitrile, reflux.

Table 4. Dehydrogenation of pyrrolidine amino side chain during Suzuki cross-coupling reaction of intermediates **4**



Ar	Reaction time (h)	Yield of **12** (%)	Yield of **12′** (%)
p-CH_3–C_6H_4–	16	**12b** (78)	**12′b** (—)
	40	**12b** (22)	**12′b** (12)
p-(*t*-Bu)–C_6H_4–	16	**12c** (84)	**12′c** (—)
	40	**12c** (22)	**12′c** (29)
	140	**12c** (—)	**12′c** (63)
p-CF_3–C_6H_4–	16	**12d** (66)	**12′d** (2)
	48	**12d** (6)	**12′d** (53)

derivatives **13a–m** and **14a–m**, thus providing, respectively, AQ (**9a–m**) and ApQ (**10a–m**) analogues with good yields.

Figure 4 compares the global yields by the two synthetic pathways according to Scheme 3 or 4. In most of the cases, global yields of the desired products are better if the cross-coupling reaction is conducted on the bromo *para*-nitro substituted intermediate **4** (Scheme 4), instead of the quinoline bromo derivative **2** (Scheme 3).

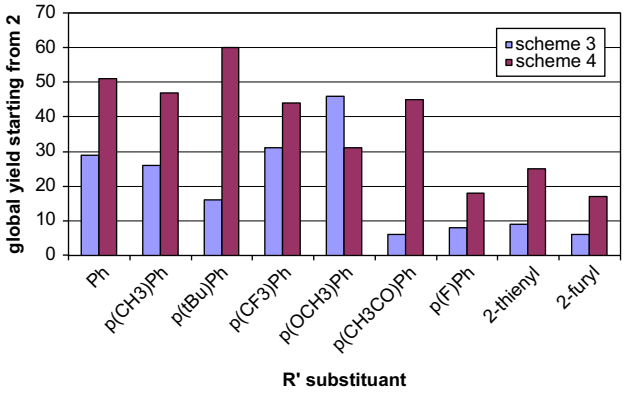


Figure 4. Global yields for the synthesis of target compounds starting from bromonitro derivative **4**.

3. Conclusion

This study presents the synthesis of some new 4′-substituted aryl and alkyl AQ and ApQ analogues following a general protocol, which allowed the introduction of the convenient diversity using Suzuki–Miyaura cross-coupling reactions between bromine activated intermediates and commercially available boronic acids. These compounds will be further evaluated for their antimalarial properties, cytotoxicity, and ability to inhibit β-hematine formation.

4. Experimental

4.1. General

All the reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254) using UV light as a visualizing agent and by HPLC. Thick-layer chromatography (TLC) was performed using silica gel from Merck, from which the compounds were extracted using the following solvent system: DCM/MeOH/NH_4OH, 8/2/0.2. All melting points were determined on a Büchi melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were obtained using a Bruker 300 MHz spectrometer and chemical shifts (δ) were expressed in parts per million relative to TMS used as an internal standard. Mass spectra were recorded on a MALDI-TOF Voyager-DE-STR spectrometer. The purity of final compounds was verified by two types of high-pressure liquid chromatographic (HPLC) columns: C18 Deltapak (C18N) and C4 Interchrom UP5WC4-25QS (C4). Analytical HPLC was performed on a Shimadzu system equipped with an UV detector set at 254 nm. Compounds were dissolved in CH_3CN/H_2O/TFA, 80/20/0.05 and injected through a 50 μL loop. The following eluent systems were used: A (H_2O/TFA, 100/0.05) and B (CH_3CN/H_2O/TFA, 80/20/0.05). HPLC retention times (HPLC t_R) were obtained, at flow rates of 1 mL/min, using the following conditions: for the 10 min method: a gradient run from 100% eluent A for 30 s, then to 100% eluent B over the next 8 min and for the 40 min method: a gradient run from 100% eluent A for 1 min, then to 100% eluent B over the next 30 min. Reagents were obtained from Acros, Aldrich, Lancaster, Novabiochem and Avocado.

The following abbreviations were used: EP (petroleum ether), AcOEt (ethyl acetate), Hex (*n*-hexane), Cyh (cyclohexane), DCM (dichloromethane), Quin (quinoline), Thio (2-thiophene), Fur (2-furane), and Phthal (phthaloyl).

4.2. 2-(2-Bromo-5-nitro-benzyl)-isoindole-1,3-dione 5

To a suspension of *N*-hydroxymethylphthalimide (2.0 g, 0.5 equiv) in trifluoromethanesulfonic acid (20 mL) at 0 °C was added 1-bromo-4-nitrobenzene (4.57 g, 22.6 mmol). After stirring the mixture at room temperature overnight, the reaction medium was added dropwise to cold water (150 mL). A white solid precipitated. The aqueous layer was extracted with DCM (3×100 mL). The organic layers were then combined, dried over $MgSO_4$, and the solvent was evaporated. The residue was purified from excess 1-bromo-4-nitrobenzene by flash chromatography (DCM) to yield compound **5** as a white solid (3.43 g, 84% yield); R_f 0.7

(DCM); mp=158–159 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 6.07 min; ^{1}H NMR ($CDCl_3$) δ 8.01 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.7 Hz), 7.98 (1H, d, Ar–H_6, $^4J_{6,4}$=2.7 Hz), 7.92–7.95 (2H, m, Phthal–H), 7.77–7.82 (3H, m, Ar–H_3, Phthal–H), 5.02 (2H, s, CH_2); ^{13}C NMR ($CDCl_3$) δ 134.5 (2C, Phthal), 133.9 (Ar–C_3), 123.8 (2C, Phthal), 123.6 (Ar–C_4), 122.9 (Ar–C_6), 41.5 (CH_2).

4.3. 2-Bromo-5-nitro-benzylamine 6

To a suspension of compound **5** (1.68 g, 4.65 mmol) in CH_3CN (150 mL) was added hydrazine hydrate (1.14 mL, 5 equiv) and the mixture was stirred at reflux for 22 h. A white solid precipitated. The reaction medium was cooled to 0 °C, filtered, and the filtrate was evaporated. The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **6** as a yellow solid (0.83 g, 78% yield); R_f 0.9 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=63–64 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 2.80 min; ^{1}H NMR ($CDCl_3$) δ 8.36 (1H, d, Ar–H_6, $^4J_{6,4}$=2.7 Hz), 7.98 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.7 Hz, $^4J_{4,6}$=2.7 Hz), 7.66 (1H, d, Ar–H_3, $^3J_{3,4}$=8.7 Hz), 4.02 (2H, s, CH_2), 1.58 (2H, s large, NH_2); ^{13}C NMR ($CDCl_3$) δ 133.6 (Ar–C_3), 123.4 (Ar–C_6), 122.9 (Ar–C_4), 46.3 (CH_2); *m/z* 231.0–233.0 $[M+H]^+$.

4.4. (2-Bromo-5-nitro-benzyl)-diethyl-amine 3

To a solution of 2-bromo-5-nitro-benzylamine **6** (0.65 g, 2.82 mmol) in CH_3CN (20 mL) was added NaOH (0.68 g, 6 equiv). After stirring the mixture at room temperature for 20 min, ethyl bromide (10 mL) was added and stirring was continued for 48 h at 40 °C. At room temperature, inorganic salts were filtered and the filtrate was evaporated. Saturated aqueous solution of $NaHCO_3$ (50 mL) was added and the aqueous layer was extracted with DCM (5×50 mL). The organic layers were then combined, dried over $MgSO_4$, and the solvent was evaporated. The residue was purified by TLC (Hex/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **3** as a yellow powder (0.57 g, 84% yield); R_f 0.7 (AcOEt/Cyh/NH_4OH, 3/7/0.2); mp=39–40 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.35 min; ^{1}H NMR ($CDCl_3$) δ 8.49 (1H, d, Ar–H_6, $^4J_{6,4}$=2.7 Hz), 7.94 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.7 Hz, $^4J_{4,6}$=2.7 Hz), 7.68 (1H, d, Ar–H_3, $^3J_{3,4}$=8.7 Hz), 3.67 (2H, s, CH_2), 2.61 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.07 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 133.2 (Ar–C_3), 125.0 (Ar–C_6), 122.5 (Ar–C_4), 57.1 (CH_2), 47.6 (2C, N–CH_2), 12.1 (2C, CH_3); *m/z* 287.1–289.1 $[M+H]^+$.

4.5. 1-(2-Bromo-5-nitro-benzyl)-pyrrolidine 4

To a solution of 2-bromo-5-nitro-benzylamine **6** (0.673 g, 2.91 mmol) in CH_3CN (125 mL) was added K_2CO_3 (2.01 g, 5 equiv). After stirring the mixture at room temperature for 20 min, 1,4-dibromobutane (0.52 mL, 1.5 equiv) was added and stirring was continued for 48 h at reflux. At room temperature, inorganic salts were filtered and the filtrate was evaporated. Saturated aqueous solution of $NaHCO_3$ (50 mL) was added and the aqueous layer was extracted with DCM (5×50 mL). The organic layers were then combined, dried over $MgSO_4$, and the solvent was evaporated. The residue was purified by TLC (Hex/AcOEt/NH_3, 8/2/0.2) to yield the expected compound **4** as a yellow-orange powder (0.61 g, 73% yield); R_f 0.6 (Cyh/AcOEt/NH_4OH, 8/2/0.2); mp=43–44 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.13 min; ^{1}H NMR ($CDCl_3$) δ 8.38 (1H, d, Ar–H_6, $^4J_{6,4}$=2.8 Hz), 7.95 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.7 Hz, $^4J_{4,6}$=2.8 Hz), 7.70 (1H, d, Ar–H_3, $^3J_{3,4}$=8.7 Hz), 3.78 (2H, s, CH_2), 2.61–2.65 (4H, m, N–CH_2), 1.83–1.88 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 133.5 (Ar–C_3), 125.0 (Ar–C_6), 122.8 (Ar–C_4), 59.3 (CH_2), 54.3 (2C, N–CH_2), 23.8 (2C, CH_2); *m/z* 285.0–287.0 $[M+H]^+$.

4.6. Reduction of nitro group: general procedure A

To a solution of nitro compound (1 equiv) in THF was added a solution of tin chloride (4 equiv) in THF with 1 M HCl (3 equiv). After stirring at reflux, the mixture was concentrated, alkalinized with $NaHCO_3$ (pH 8), and the aqueous layer was extracted with DCM (5×50 mL). The organic layers were then combined, dried over $MgSO_4$, the solvent was evaporated, and the residue was purified by TLC.

4.7. Aromatic substitution of 4-Cl group: general procedure B

To a solution of amine (1 equiv) in CH_3CN was added a solution of 4,7-dichloroquinoline (4,7-diClQuin) (1 equiv) in CH_3CN and 1 M HCl (1 equiv). After stirring at reflux, the mixture was concentrated and purified by TLC to yield the target compound.

4.8. Suzuki coupling: general procedure C

To a suspension of bromide (1 equiv), boronic acid (2 equiv), $Pd(OAc)_2$ (7.5%), P(*o*-tol)$_3$ (15%), and TBAB (20%) in toluene (3 mL) was added 2 M aqueous solution of Na_2CO_3 (1 mL) and EtOH (2 mL) under inert atmosphere. The reaction medium was heated to 65 °C and the evolution of the reaction was followed by TLC. The medium was evaporated, solubilized with aq satd $NaHCO_3$ (50 mL), and extracted with DCM (5×50 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by TLC to yield the expected compound.

4.9. Synthesis according to Scheme 3

4.9.1. 4-Bromo-3-diethylaminomethyl-phenylamine 7. Synthesized from compound **3** (408 mg, 1.42 mmol) and $SnCl_2$ (1.077 g) in HCl (4.26 mL) and THF (25 mL) according to general procedure A (reflux for 15 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **7** as a yellow oil (254 mg, 69% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 2.80 min; ^{1}H NMR ($CDCl_3$) δ 7.25 (1H, d, Ar–H_3, $^3J_{3,4}$=8.5 Hz), 6.97 (1H, d, Ar–H_6, $^4J_{6,4}$=2.9 Hz), 6.44 (1H, dd, Ar–H′, $^3J_{4,3}$=8.5 Hz, $^4J_{4,6}$=2.9 Hz), 3.67 (2H, s large, NH_2), 3.60 (2H, s, CH_2), 2.59 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.07 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 132.8 (Ar–C_3), 116.9 (Ar–C_6), 115.1 (Ar–C_4), 56.8 (CH_2), 47.1 (2C, N–CH_2), 11.7 (2C, CH_3); *m/z* 257.2–259.2 $[M+H]^+$.

4.9.2. 4-Bromo-3-pyrrolidin-1-ylmethyl-phenylamine 8. Synthesized from compound **4** (503 mg, 1.76 mmol) and $SnCl_2$ (1.338 g) in HCl (5.29 mL) and THF (80 mL) according to general procedure A (reflux for 6 h). The residue was

purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **8** as a yellow solid (339 mg, 75% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=57–58 °C; HPLC (C18—10 min) P_{HPLC} 97%, t_R 3.02 min; ^1H NMR ($CDCl_3$) δ 7.19 (1H, d, Ar–H_3, $^3J_{3,4}$=8.5 Hz), 6.82 (1H, d, Ar–H_6, $^4J_{6,4}$=2.9 Hz), 6.38 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.5 Hz, $^4J_{4,6}$=2.9 Hz), 3.63 (2H, s, CH_2), 2.58–2.64 (4H, m, N–CH_2), 1.70–1.82 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 133.1 (Ar–C_3), 117.1 (Ar–C_6), 115.4 (Ar–C_4), 59.5 (CH_2), 54.4 (2C, N–CH_2), 23.7 (2C, CH_2); *m/z* 255.1–257.1 $[M+H]^+$.

4.9.3. (4-Bromo-3-diethylaminomethyl-phenyl)-(7-chloro-quinolin-4-yl)-amine 1. Synthesized from compound **7** (242 mg, 0.94 mmol) and 4,7-diClQuin (186 mg) in HCl (0.94 mL) and CH_3CN (50 mL) according to general procedure B (reflux for 7 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **1** as a white solid (344 mg, 88% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=176–177 °C; HPLC (C18—10 min) P_{HPLC} 96%, t_R 3.49 min; HPLC (C18—40 min) P_{HPLC} 94%, t_R 14.91 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 13.93 min; ^1H NMR ($CDCl_3$) δ 8.53 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.00 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.92 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.55 (1H, d, Ar–H_6, $^4J_{6,4}$=2.7 Hz), 7.51 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.41 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.00–7.20 (1H, s large, NH), 7.05 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.7 Hz), 6.95 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.64 (2H, s, CH_2), 2.58 (4H, q, N–CH_2, ^3J=7.2 Hz), 1.03 (6H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 152.0 (Quin–C_2), 133.5 (Ar–C_3), 129.0 (Quin–C_8), 126.3 (Quin–C_6), 124.4 (Ar–C_6), 122.1 (Ar–C_4), 121.7 (Quin–C_5), 102.8 (Quin–C_3), 57.2 (CH_2), 47.5 (2C, N–CH_2), 12.2 (2C, CH_3); *m/z* 418.1–420.1 $[M+H]^+$.

4.9.4. (4-Bromo-3-pyrrolidin-1-ylmethyl-phenyl)-(7-chloro-quinolin-4-yl)-amine 2. Synthesized from compound **8** (429 mg, 1.29 mmol) and 4,7-diClQuin (256 mg) in HCl (1.3 mL) and CH_3CN (100 mL) according to general procedure B (reflux overnight). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **2** as a white solid (511 mg, 95% yield); R_f 0.9 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=155–156 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.50 min; HPLC (C18—40 min) P_{HPLC} 98%, t_R 14.80 min; HPLC (C4—40 min) P_{HPLC} 98%, t_R 13.75 min; ^1H NMR (MeOD) δ 8.35 (1H, d, Quin–H_2, $^3J_{2,3}$=5.5 Hz), 8.21 (1H, d, Quin–H_5, $^3J_{5,6}$=9.1 Hz), 7.81 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.56 (1H, d, Ar–H_3, $^3J_{3,4}$=8.5 Hz), 7.45 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.1 Hz, $^4J_{6,8}$=2.2 Hz), 7.43 (1H, d, Ar–H_6, $^4J_{6,4}$=2.7 Hz), 7.15 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.5 Hz, $^4J_{4,6}$=2.7 Hz), 6.92 (1H, d, Quin–H_3, $^3J_{3,2}$=5.5 Hz), 3.74 (2H, s, CH_2), 2.58–2.62 (4H, m, N–CH_2), 1.74–1.79 (4H, m, CH_2); ^{13}C NMR (MeOD) δ 151.3 (Quin–C_2), 133.5 (Ar–C_3), 126.6 (Quin–C_8), 125.7 (Quin–C_6), 125.1 (Ar–C_6), 123.5 (Quin–C_5), 123.2 (Ar–C_4), 102.0 (Quin–C_3), 59.3 (CH_2), 53.9 (2C, N–CH_2), 23.0 (2C, CH_2); *m/z* 416.2–418.2 $[M+H]^+$.

4.10. Synthesis according to Scheme 4

4.10.1. Diethyl-(4-nitro-biphenyl-2-ylmethyl)-amine 11a. Synthesized from compound **3** (100 mg, 0.348 mmol), phenylboronic acid (85 mg), $Pd(OAc)_2$ (6 mg), P(*o*-tol)$_3$ (16 mg), and TBAB (23 mg) according to general procedure C (reflux for 40 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11a** as a yellow oil (43 mg, 43% yield); R_f 0.5 (Cyh/AcOEt/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 95%, t_R 4.29 min; ^1H NMR ($CDCl_3$) δ 8.59 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.10 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 7.42–7.48 (3H, m, Ph), 7.35 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.29–7.33 (2H, m, Ph), 3.52 (2H, s, CH_2), 2.44 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.93 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 130.6 (Ar–C_3), 128.8 (2C, Ph), 128.2 (2C, Ph), 127.9 (Ph), 124.5 (Ar–C_6), 121.1 (Ar–C_4), 54.3 (CH_2), 46.9 (2C, N–CH_2), 11.8 (2C, CH_3); *m/z* 285.2 $[M+H]^+$.

4.10.2. Diethyl-(4′-methyl-4-nitro-biphenyl-2-ylmethyl)-amine 11b. Synthesized from compound **3** (200 mg, 0.696 mmol), 4-methylphenylboronic acid (189 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 16 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11b** as a yellow solid (161 mg, 78% yield); R_f 0.6 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=36–37 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.70 min; ^1H NMR ($CDCl_3$) δ 8.60 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.06 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.5 Hz), 7.33 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.26 (2H, m, Ph), 7.19 (2H, m, Ph), 3.55 (2H, s, CH_2), 2.45 (4H, q, N–CH_2, ^3J=7.1 Hz), 2.42 (3H, s, N–CH_3), 0.94 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 130.9 (Ar–C_3), 129.2 (2C, Ph), 129.0 (2C, Ph), 124.6 (Ar–C_6), 121.4 (Ar–C_4), 54.6 (CH_2), 47.2 (2C, N–CH_2), 21.4 (N–CH_3), 12.1 (2C, CH_3); *m/z* 299.2 $[M+H]^+$.

4.10.3. (4′-*tert*-Butyl-4-nitro-biphenyl-2-ylmethyl)-diethyl-amine 11c. Synthesized from compound **3** (200 mg, 0.696 mmol), 4-*tert*-butylphenylboronic acid (248 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 40 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11c** as a white solid (129 mg, 54% yield); R_f 0.7 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=91–92 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 5.68 min; ^1H NMR ($CDCl_3$) δ 8.59 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.09 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.5 Hz), 7.46 (2H, m, Ph, ^3J=8.0 Hz), 7.35 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.23 (2H, m, Ph, ^3J=8.0 Hz), 3.55 (2H, s, CH_2), 2.45 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.38 (9H, s, *t*-Bu), 0.94 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 130.7 (Ar–C_3), 128.5 (2C, Ph), 125.1 (2C, Ph), 124.4 (Ar–C_6), 121.1 (Ar–C_4), 54.3 (CH_2), 47.0 (2C, N–CH_2), 31.3 (3C, *t*-Bu), 11.9 (2C, CH_3); *m/z* 341.2 $[M+H]^+$.

4.10.4. Diethyl-(4-nitro-4′-trifluoromethyl-biphenyl-2-ylmethyl)-amine 11d. Synthesized from compound **3** (200 mg, 0.696 mmol), 4-(trifluoromethyl)-benzeneboronic acid (265 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 40 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11d** as a white solid (148 mg, 60% yield); R_f 0.5 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=36–37 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 5.09 min; ^1H NMR ($CDCl_3$) δ 8.59 (1H, d,

Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.14 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.3 Hz, $^4J_{4,6}$=2.4 Hz), 7.71 (2H, d, Ph, ^3J=8.0 Hz), 7.45 (2H, d, Ph, ^3J=8.0 Hz), 7.35 (1H, d, Ar–H_3, $^3J_{3,4}$=8.3 Hz), 3.51 (2H, s, CH_2), 2.45 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.93 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 130.8 (Ar–C_3), 129.5 (2C, Ph), 125.5 (2C, d, Ph, $^3J_{CH,F}$=3.9 Hz), 125.0 (Ar–C_6), 121.8 (Ar–C_4), 54.7 (CH_2), 47.0 (2C, N–CH_2), 11.8 (2C, CH_3); *m/z* 353.1 $[M+H]^+$.

4.10.5. Diethyl-(4′-methoxy-4-nitro-biphenyl-2-yl-methyl)-amine 11e. Synthesized from compound **3** (200 mg, 0.696 mmol), 4-methoxyphenylboronic acid (318 mg), $Pd(OAc)_2$ (18 mg), P(*o*-tol)$_3$ (48 mg), and TBAB (45 mg) according to general procedure C (reflux for 5 days). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11e** as a white solid (98 mg, 45% yield); R_f 0.5 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=59–60 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.52 min; ^{1}H NMR ($CDCl_3$) δ 8.59 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.08 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.5 Hz), 7.35 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.25 (2H, m, Ph), 6.98 (2H, m, Ph), 3.87 (3H, s, O–CH_3), 3.59 (2H, s, CH_2), 2.48 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.96 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 131.7 (Ar–C_3), 131.1 (2C, Ph), 125.6 (Ar–C_6), 122.3 (Ar–C_4), 114.7 (2C, Ph), 56.2 (O–CH_3), 55.3 (CH_2), 47.9 (2C, N–CH_2), 12.6 (2C, CH_3); *m/z* 315.3 $[M+H]^+$.

4.10.6. 1-(2′-Diethylaminomethyl-4′-nitro-biphenyl-4-yl)-ethanone 11f. Synthesized from compound **3** (200 mg, 0.696 mmol), 4-acetylphenylboronic acid (228 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 40 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 7/3/0.2) to yield the expected compound **11f** as a white solid (89 mg, 39% yield); R_f 0.5 (Cyh/AcOEt/NH_4OH, 7/3/0.2); mp=96–97 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.16 min; ^{1}H NMR ($CDCl_3$) δ 8.58 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.12 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 8.06 (2H, m, Ph), 7.44 (2H, m, Ph), 7.37 (1H, d, Ar–H_3, $^4J_{3,4}$=8.4 Hz), 3.51 (2H, s, CH_2), 2.68 (3H, s, CO–CH_3), 2.44 (4H, q, N–CH_2, ^3J=7.2 Hz), 0.93 (4H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 130.5 (Ar–C_3), 129.3 (2C, Ph), 128.4 (2C, Ph), 124.7 (Ar–C_6), 121.5 (Ar–C_4), 54.7 (CH_2), 46.9 (2C, N–CH_2), 26.8 (CO–CH_3), 11.9 (2C, CH_3); *m/z* 327.2 $[M+H]^+$.

4.10.7. Diethyl-(4′-fluoro-4-nitro-biphenyl-2-ylmethyl)-amine 11g. Synthesized from compound **3** (200 mg, 0.696 mmol), 4-fluorophenylboronic acid (195 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 48 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11g** as a white solid (71 mg, 34% yield); R_f 0.5 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=42–43 °C; HPLC (C18—10 min) P_{HPLC} 97%, t_R 4.48 min; ^{1}H NMR ($CDCl_3$) δ 8.57 (1H, d, Ar–H_6, $^4J_{6,4}$=2.7 Hz), 8.12 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.7 Hz), 7.35 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.30 (2H, m, Ph), 7.13 (2H, m, Ph), 3.56 (2H, s, CH_2), 2.48 (4H, q, N–CH_2, ^3J=6.9 Hz), 0.95 (6H, t, CH_3, ^3J=6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 132.3 (Ar–C_3), 132.1 (2C, Ph, $^4J_{CH,F}$=8.4 Hz), 126.3 (Ar–C_6), 123.0 (Ar–C_4), 116.8 (2C, d, Ph, $^3J_{CH,F}$=21.3 Hz), 55.8 (CH_2), 48.3 (2C, N–CH_2), 12.9 (2C, CH_3); *m/z* 303.2 $[M+H]^+$.

4.10.8. Diethyl-(4-nitro-4′-thiophen-2-yl-biphenyl-2-yl-methyl)-amine 11h. Synthesized from compound **3** (200 mg, 0.696 mmol), 2-thiopheneboronic acid (267 mg), $Pd(OAc)_2$ (18 mg), P(*o*-tol)$_3$ (48 mg), and TBAB (45 mg) according to general procedure C (reflux for 5 days). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11h** as an orange solid (31 mg, 15% yield); R_f 0.5 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=40–41 °C; HPLC (C18—10 min) P_{HPLC} 96%, t_R 4.27 min; ^{1}H NMR ($CDCl_3$) δ 8.60 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.09 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.5 Hz, $^4J_{4,6}$=2.5 Hz), 7.53 (1H, d, Ar–H_3, $^4J_{3,4}$=8.5 Hz), 7.45 (1H, dd, Thio–H_5, $^3J_{5,4}$=5.1 Hz, $^4J_{5,3}$=1.2 Hz), 7.21 (1H, dd, Thio–H_3, $^3J_{3,4}$=3.6 Hz, $^4J_{3,5}$=1.2 Hz), 7.14 (1H, dd, Thio–H_4, $^3J_{4,3}$=3.6 Hz, $^3J_{4,5}$=5.1 Hz), 3.74 (2H, s, CH_2), 2.54 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.00 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 131.2 (Ar–C_3), 128.3 (Thio–C_3), 127.3 (Thio–C_4), 127.0 (Thio–C_5), 124.8 (Ar–C_6), 121.3 (Ar–C_4), 54.7 (CH_2), 46.7 (2C, N–CH_2), 11.5 (2C, CH_3); *m/z* 291.2 $[M+H]^+$.

4.10.9. Diethyl-(4′-furan-2-yl-4-nitro-biphenyl-2-yl-methyl)-amine 11i. Synthesized from compound **3** (200 mg, 0.696 mmol), 2-furaneboronic acid (195 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 5 days). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11i** as an yellow oil (35 mg, 16% yield); R_f 0.4 (Cyh/AcOEt/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.45 min; ^{1}H NMR ($CDCl_3$) δ 8.61 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.12 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2,5 Hz), 7.39–7.46 (1H, m, 4′-CH), 7.35 (1H, d, 3-CH, $^3J_{3,4}$=8.4 Hz), 7.23–7.28 (2H, m, 5′-CH, 6′-CH), 7.13–7.24 (1H, m, 3′-CH), 3.47 (2H, s, 7-CH_2), 2.42 (4H, qv, 2×9-CH_2, $^3J_{9,10}$=7.1 Hz), 0.91 (6H, t, 2×10-CH_3, $^3J_{10,9}$=7.1 Hz). 8.64 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.12 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.7 Hz, $^4J_{4,6}$=2.5 Hz), 7.81 (1H, d, Ar–H_3, $^4J_{3,4}$=8.7 Hz), 7.60 (1H, dd, Fur–H_5, $^3J_{5,4}$=1.8 Hz, $^4J_{5,3}$=0.5 Hz), 6.84 (1H, dd, Fur–H_3, $^3J_{3,4}$=3.4 Hz, $^4J_{3,5}$=0.5 Hz), 6.57 (1H, dd, Fur–H_4, $^3J_{4,3}$=3.4 Hz, $^3J_{4,5}$=1.8 Hz), 3.86 (2H, s, CH_2), 2.63 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.07 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 143.8 (Fur–C_5), 128.1 (Ar–C_3), 125.4 (Ar–C_6), 122.05 (Ar–C_4), 112.6 (Fur–C_3), 112.3 (Fur–C_4), 55.7 (CH_2), 47.4 (2C, N–CH_2), 11.9 (2C, CH_3); *m/z* 275.1 $[M+H]^+$.

4.10.10. Diethyl-(2′-fluoro-4-nitro-biphenyl-2-ylmethyl)-amine 11j. Synthesized from compound **3** (200 mg, 0.696 mmol), 2-fluorophenylboronic acid (195 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 54 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11g** as a white solid (35 mg, 16% yield); R_f 0.5 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=42–43 °C; HPLC (C18—10 min) P_{HPLC} 97%, t_R 4.48 min; ^{1}H NMR ($CDCl_3$) δ 8.61 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.12 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2,5 Hz), 7.39–7.46 (1H, m, Ph), 7.35 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.23–7.28 (2H, m, Ph), 7.13–7.24 (1H, m, Ph), 3.47 (2H, s, 7-CH_2),

2.42 (4H, qv, 2×9-CH_2, $^3J_{9,10}$=7.1 Hz), 0.91 (6H, t, 2×10-CH_3, $^3J_{10,9}$=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 131.3 (Ar–C_3), 131.1 (d, Ph–C_6, $^4J_{6,F}$=2.6 Hz), 130.5 (d, Ph–C_4, $^4J_{4,F}$=8.1 Hz), 124.5 (Ph–C_5), 124.4 (Ar–C_6), 121.5 (Ar–C_4), 115.9 (d, Ph–C_3, $^3J_{3',F}$=21.9 Hz), 54.5 (CH_2), 47.3 (2C, N–CH_2), 12.0 (2C, CH_3); *m/z* 303.2 $[M+H]^+$.

4.10.11. (4′-Chloro-4-nitro-biphenyl-2-ylmethyl)-diethyl-amine 11k. Synthesized from compound **3** (200 mg, 0.696 mmol), 4-chlorophenylboronic acid (218 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 16 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11k** as a yellow oil (143 mg, 64% yield); R_f 0.7 (Cyh/AcOEt/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.68 min; ^{1}H NMR ($CDCl_3$) δ 8.56 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.09 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.5 Hz), 7.43 (2H, m, Ph), 7.34 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.28 (2H, m, Ph), 3.53 (2H, s, CH_2), 2.46 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.94 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 131.5 (Ar–C_3), 131.1 (2C, Ph), 129.3 (2C, Ph), 125.5 (Ar–C_6), 122.2 (Ar–C_4), 55.3 (CH_2), 47.7 (2C, N–CH_2), 12.5 (2C, CH_3); *m/z* 319.2–321.2 $[M+H]^+$.

4.10.12. Diethyl-(2-methyl-5-nitro-benzyl)-amine 11l. To a suspension of compound **3** (200 mg, 0.697 mmol), methylboronic acid (84 mg, 1.5 equiv), $Pd(OAc)_2$ (24 mg, 0.15 equiv), P(*o*-tol)$_3$ (63 mg, 0.3 equiv), and K_2CO_3 (289 mg, 3 equiv) in THF (5 mL) was added water (0.5 mL) under inert atmosphere. The reaction medium was heated to 75 °C for 13 days. The medium was evaporated, solubilized with aq satd $NaHCO_3$ (50 mL), and extracted with DCM (5×50 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11l** as a yellow oil (105 mg, 68% yield); R_f 0.5 (AcOEt/Cyh/NH_4OH, 1/9/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.34 min; ^{1}H NMR ($CDCl_3$) δ 8.26 (1H, d, Ar–H_6, $^4J_{6,4}$=2.7 Hz), 7.97 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.7 Hz), 7.26 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 3.56 (2H, s, CH_2), 2.53 (4H, q, N–CH_2, ^3J=7.2 Hz), 2.44 (3H, s, CH_3), 1.04 (6H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 130.9 (Ar–C_3), 124.1 (Ar–C_6), 121.7 (Ar–C_4), 55.5 (CH_2), 47.2 (2C, CH_2), 19.6 (CH_3), 12.0 (2C, CH_3); *m/z* 223.2 $[M+H]^+$, 207.2 $[M+H–O]^+$.

4.10.13. Diethyl-(2-ethyl-5-nitro-benzyl)-amine 11m. To a suspension of compound **3** (200 mg, 0.697 mmol), ethylboronic acid (99 mg, 1.5 equiv), $Pd(OAc)_2$ (24 mg, 0.15 equiv), P(*o*-tol)$_3$ (63 mg, 0.3 equiv), and K_2CO_3 (289 mg, 3 equiv) in THF (5 mL) was added water (0.5 mL) under inert atmosphere. The reaction medium was heated to 75 °C for 13 days. The medium was evaporated, solubilized with aq satd $NaHCO_3$ (50 mL), and extracted with DCM (5×50 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **11m** as a yellow oil (112 mg, 68% yield); R_f 0.6 (Cyh/AcOEt/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 93%, t_R 3.82 min; ^{1}H NMR ($CDCl_3$) δ 8.31 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.01 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 7.30 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 3.60 (2H, s, CH_2), 2.81 (2H, q, Ar–CH_2, $^3J_{1',2'}$=7.5 Hz), 2.53 (4H, q, N–CH_2, ^3J=7.5 Hz), 1.25 (3H, t, CH_3, ^3J=7.5 Hz), 1.05 (6H, t, CH_3, ^3J=7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 129.2 (Ar–C_3), 124.4 (Ar–C_6), 121.9 (Ar–C_4), 57.9 (CH_2), 47.2 (2C, N–CH_2), 25.7 (Ar–CH_2), 14.7 (N–CH_3), 12.0 (2C, CH_3); *m/z* 237.3 $[M+H]^+$, 221.3 $[M+H–O]^+$.

4.10.14. 1-(4-Nitro-biphenyl-2-ylmethyl)-pyrrolidine 12a. Synthesized from compound **4** (150 mg, 0.526 mmol), phenylboronic acid (128 mg), $Pd(OAc)_2$ (9 mg), P(*o*-tol)$_3$ (24 mg), and TBAB (34 mg) according to general procedure C (reflux for 40 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 8/2/0.2) to yield the expected compound **12a** as a white solid (111 mg, 75% yield); R_f 0.6 (Cyh/AcOEt/NH_4OH, 8/2/0.2); mp=77 °C; HPLC (C18—10 min) P_{HPLC} 94%, t_R 4.49 min; ^{1}H NMR ($CDCl_3$) δ 8.48 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.10 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 7.35–7.48 (6H, m, Ar–H_3, Ph), 3.61 (2H, s, CH_2), 2.44–2.49 (4H, m, N–CH_2), 1.70–1.80 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.8 (Ar–C_3), 129.0 (2C, Ph), 128.3 (2C, Ph), 128.0 (Ph), 124.5 (Ar–C_6), 121.4 (Ar–C_4), 56.9 (CH_2), 53.8 (2C, N–CH_2), 23.6 (2C, CH_2); *m/z* 283.2 $[M+H]^+$.

4.10.15. 1-(4′-Methyl-4-nitro-biphenyl-2-ylmethyl)-pyrrolidine 12b. Synthesized from compound **4** (200 mg, 0.701 mmol), 4-methylphenylboronic acid (191 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 16 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **12b** as a white solid (149 mg, 71% yield); R_f 0.4 (Hex/AcOEt/NH_4OH, 9/1/0.2); mp=66–67 °C; HPLC (C18—10 min) P_{HPLC} 97%, t_R 4.84 min; ^{1}H NMR ($CDCl_3$) δ 8.47 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.11 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.5 Hz), 7.38 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.23–7.29 (4H, m, Ph), 3.61 (2H, s, CH_2), 2.45–2.49 (4H, m, N–CH_2), 2.39 (3H, s, CH_3), 1.73–1.82 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.9 (Ar–C_3), 129.0 (4C, Ph), 124.6 (Ar–C_6), 121.5 (Ar–C_4), 57.0 (CH_2), 53.9 (2C, N–CH_2), 23.6 (2C, CH_2), 21.3 (CH_3); *m/z* 297.1 $[M+H]^+$.

4.10.16. 1-(4′-Methyl-4-nitro-biphenyl-2-ylmethyl)-pyrrole 12′b. Isolated as a by-product (white solid, 12%); R_f 0.5 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=98 °C; HPLC (C18—10 min) P_{HPLC} 96%, t_R 7.93 min; ^{1}H NMR ($CDCl_3$) δ 8.15 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.3 Hz), 7.80 (1H, d, Ar–H_6, $^4J_{6,4}$=2.3 Hz), 7.42 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.29 (2H, d, Ph, ^3J=8.0 Hz), 7.15 (2H, d, Ph, ^3J=8.0 Hz), 6.53 (2H, m, Pyr–H_2), 6.18 (2H, m, Pyr–H_3), 5.05 (2H, s, N–CH_2), 2.44 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ 131.1 (Ar–C_3), 129.4 (2C, Ph), 128.4 (2C, Ph), 123.0 (Ar–C_6), 122.4 (Ar–C_4), 120.8 (2C, Pyr–C_2), 109.1 (2C, Pyr–C_2), 50.8 (CH_2), 21.1 (CH_3); *m/z* 293.2 $[M+H]^+$.

4.10.17. 1-(4′-*tert*-Butyl-4-nitro-biphenyl-2-ylmethyl)-pyrrolidine 12c. Synthesized from compound **4** (200 mg, 0.701 mmol), 4-*tert*-butylphenylboronic acid (250 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 16 h). The residue was purified by TLC (Hex/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **12c** as a white solid

(200 mg, 84% yield); R_f 0.4 (Hex/AcOEt/NH_4OH, 9/1/0.2); mp=45–47 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 5.82 min; ^1H NMR ($CDCl_3$) δ 8.48 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.11 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.5 Hz, $^4J_{4,6}$=2.4 Hz), 7.46 (2H, m, Ph), 7.39 (1H, d, Ar–H_3, $^3J_{3,4}$=8.5 Hz), 7.31 (2H, m, Ph), 3.64 (2H, s, CH_2), 2.47–2.51 (4H, m, N–CH_2), 1.74–1.82 (4H, m, CH_2), 1.38 (9H, s, *t*-Bu); ^{13}C NMR ($CDCl_3$) δ 130.7 (Ar–C_3), 128.6 (2C, Ph), 125.0 (2C, Ph), 124.4 (Ar–C_6), 121.3 (Ar–C_4), 56.8 (CH_2), 53.7 (2C, N–CH_2), 31.2 (3C, *t*-Bu), 23.4 (2C, CH_2); *m/z* 339.2 $[M+H]^+$.

4.10.18. 1-(4′-*tert*-Butyl-4-nitro-biphenyl-2-ylmethyl)-pyrrole 12′c. Isolated as a by-product (yellow solid, 63%); R_f 0.5 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=137 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 9.15 min; ^1H NMR ($CDCl_3$) δ 8.10 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.3 Hz), 7.75 (1H, d, Ar–H_6, $^4J_{6,4}$=2.3 Hz), 7.49 (2H, m, Ph), 7.40 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.21 (2H, m, Ph), 6.51 (2H, m, Pyr–H_2), 6.15 (2H, m, Pyr–H_3), 5.05 (2H, s, N–CH_2), 1.38 (9H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ 131.4 (Ar–C_3), 128.6 (2C, Ph), 125.9 (2C, Ph), 123.2 (Ar–C_6), 122.7 (Ar–C_4), 121.2 (2C, Pyr–C_2), 109.4 (2C, Pyr–C_3), 50.9 (CH_2), 31.6 (CH_3); *m/z* 335.4 $[M+H]^+$.

4.10.19. 1-(4-Nitro-4′-trifluoromethyl-biphenyl-2-ylmethyl)-pyrrolidine 12d. Synthesized from compound **4** (200 mg, 0.701 mmol), 4-trifluoromethylphenylboronic acid (266 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 16 h). The residue was purified twice by TLC (Hex/AcOEt/NH_4OH, 8/2/0.2 and then Cyh/DCM/NH_4OH, 3/7/0.2) to yield the expected compound **12d** as a yellow solid (162 mg, 66% yield); R_f 0.7 (Hex/AcOEt/NH_4OH, 8/2/0.2); mp=83–85 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 5.18 min; ^1H NMR ($CDCl_3$) δ 8.47 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.17 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 7.72 (2H, d, Ph, ^3J=8.5 Hz), 7.54 (2H, d, Ph, ^3J=8.5 Hz), 7.40 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 3.56 (2H, s, CH_2), 2.44–2.49 (4H, m, N–CH_2), 1.71–1.83 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.7 (Ar–C_3), 129.4 (2C, Ph), 125.2 (2C, d, Ph, $^3J_{CH,F}$=3.1 Hz), 124.8 (Ar–C_6), 121.7 (Ar–C_4), 56.9 (CH_2), 53.7 (2C, N–CH_2), 23.5 (2C, CH_2); *m/z* 351.2 $[M+H]^+$.

4.10.20. 1-(4-Nitro-4′-trifluoromethyl-biphenyl-2-ylmethyl)-pyrrole 12′d. Isolated as a by-product (white solid, 53%); R_f 0.8 (DCM/Cyh/NH_4OH, 7/3/0.2); mp=120 °C; HPLC (C18—10 min) P_{HPLC} 96%, t_R 7.97 min; ^1H NMR ($CDCl_3$) δ 8.22 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 7.88 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 7.74 (2H, d, Ph, ^3J=8.0 Hz), 7.43 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.36 (2H, d, Ph, ^3J=8.0 Hz), 6.47 (2H, m, Pyr–H_2), 6.17 (2H, m, Pyr–H_3), 5.01 (2H, s, N–CH_2); ^{13}C NMR ($CDCl_3$) δ 131.1 (Ar–C_3), 129.0 (2C, Ph), 125.7 (2C, Ph, $^3J_{H,F}$=3.2 Hz), 123.4 (Ar–C_6), 122.8 (Ar–C_4), 120.8 (2C, Pyr–C_2), 109.4 (2C, Pyr–C_3), 50.7 (CH_2); *m/z* 347.1 $[M+H]^+$.

4.10.21. 1-(4′-Methoxy-4-nitro-biphenyl-2-ylmethyl)-pyrrolidine 12e. Synthesized from compound **4** (200 mg, 0.701 mmol), 4-methoxyphenylboronic acid (320 mg), $Pd(OAc)_2$ (18 mg), P(*o*-tol)$_3$ (48 mg), and TBAB (45 mg) according to general procedure C (reflux for 5 days). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **12e** as a yellow oil (129 mg, 59% yield); R_f 0.4 (Cyh/AcOEt/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.54 min; ^1H NMR ($CDCl_3$) δ 8.45 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.08 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.5 Hz), 7.37 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.34 (2H, m, Ph), 6.98 (2H, m, Ph), 3.86 (3H, s, O–CH_3), 3.63 (2H, s, CH_2), 2.47–2.51 (4H, m, N–CH_2), 1.71–1.81 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.9 (Ar–C_3), 130.4 (2C, Ph), 124.7 (Ar–C_6), 121.5 (Ar–C_4), 113.7 (2C, Ph), 57.0 (CH_2), 55.3 (O–CH_3), 53.8 (2C, N–CH_2), 23.6 (2C, CH_2); *m/z* 313.3 $[M+H]^+$.

4.10.22. 1-(4′-Nitro-2′-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-ethanone 12f. Synthesized from compound **4** (200 mg, 0.701 mmol), 4-acetylphenylboronic acid (230 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 40 h). The residue was purified twice by TLC (Cyh/AcOEt/NH_4OH, 8/2/0.2 and then Cyh/AcOEt/NH_4OH, 7/3/0.2) to yield the expected compound **12f** as a yellow solid (158 mg, 70% yield); R_f 0.3 (Cyh/AcOEt/NH_4OH, 8/2/0.2); mp=104–105 °C; HPLC (C18—10 min) P_{HPLC} 97%, t_R 4.27 min; ^1H NMR ($CDCl_3$) δ 8.46 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.14 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 8.06 (2H, dd, Ph, ^3J=6.9 Hz, ^4J=1.5 Hz), 7.54 (2H, dd, Ph, ^3J=6.9 Hz, ^4J=1.8 Hz), 7.42 (1H, d, Ar–H_3, $^4J_{3,4}$=8.4 Hz), 3.59 (2H, s, CH_2), 2.68 (3H, s, CO–CH_3), 2.45–2.47 (4H, m, N–CH_2), 1.74–1.77 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.8 (Ar–C_3), 129.6 (2C, Ph), 128.4 (2C, Ph), 124.9 (Ar–C_6), 121.8 (Ar–C_4), 57.2 (CH_2), 54.0 (2C, N–CH_2), 26.8 (CO-CH_3), 23.8 (2C, CH); *m/z* 325.2 $[M+H]^+$.

4.10.23. 1-(4′-Fluoro-4-nitro-biphenyl-2-ylmethyl)-pyrrolidine 12g. Synthesized from compound **4** (200 mg, 0.701 mmol), 4-fluorophenylboronic acid (196 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 48 h). The residue was purified twice by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2 and then Cyh/AcOEt/NH_4OH, 8/2/0.2) to yield the expected compound **12g** as a white solid (81 mg, 38% yield); R_f 0.8 (Cyh/AcOEt/NH_4OH, 8/2/0.2); mp=78–79 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.46 min; ^1H NMR ($CDCl_3$) δ 8.53 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.15 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.5 Hz, $^4J_{4,6}$=2.4 Hz), 7.39 (1H, d, Ar–H_3, $^3J_{3,4}$=8.5 Hz), 7.37 (2H, m, Ph), 7.17 (2H, m, Ph), 3.71 (2H, s, CH_2), 2.57 (4H, m, N–CH_2), 1.78–1.83 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 131.1 (Ar–C_3), 130.9 (2C, Ph, $^3J_{CH,F}$=8.3 Hz), 125.1 (Ar–C_6), 122.1 (Ar–C_4), 115.5 (2C, Ph, $^2J_{CH,F}$=21.3 Hz), 56.6 (CH_2), 53.9 (2C, N–CH_2), 23.5 (2C, CH_2); *m/z* 301.3 $[M+H]^+$.

4.10.24. 1-(4-Nitro-4′-thiophen-2-yl-biphenyl-2-ylmethyl)-pyrrolidine 12h. Synthesized from compound **4** (200 mg, 0.701 mmol), 2-thiopheneboronic acid (270 mg), $Pd(OAc)_2$ (18 mg), P(*o*-tol)$_3$ (48 mg), and TBAB (45 mg) according to general procedure C (reflux for 140 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 8/2/0.2) to yield the expected compound **12h** as a yellow oil (86 mg, 43% yield); R_f 0.7 (Cyh/AcOEt/NH_4OH, 8/2/0.2); HPLC (C18—10 min) P_{HPLC} 97%, t_R 4.23 min; ^1H NMR ($CDCl_3$) δ 8.42 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 8.10 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.5 Hz, $^4J_{4,6}$=2.5 Hz), 7.58 (1H, d,

Ar–H_3, $^4J_{3,4}$=8.5 Hz), 7.46 (1H, dd, Thio–H_5, $^3J_{5,4}$=5.1 Hz, $^4J_{5,3}$=1.2 Hz), 7.36 (1H, dd, Thio–H_3, $^3J_{3,4}$=3.6 Hz, $^4J_{3,5}$= 1.2 Hz), 7.14 (1H, dd, Thio–H_4, $^3J_{4,3}$=3.6 Hz, $^3J_{4,5}$= 5.1 Hz), 3.79 (2H, s, CH_2), 2.57–2.61 (4H, m, N–CH_2), 1.76–1.85 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 131.4 (Ar–C_3), 129.0 (Thio–C_3), 127.7 (Thio–C_4), 127.7 (Thio–C_5), 125.3 (Ar–C_6), 122.0 (Ar–C_4), 57.5 (CH_2), 53.7 (2C, N–CH_2), 23.6 (2C, CH_2); *m/z* 289.2 $[M+H]^+$.

4.10.25. 1-(4′-Furan-2-yl-4-nitro-biphenyl-2-ylmethyl)-pyrrolidine 12i. Synthesized from compound **4** (200 mg, 0.701 mmol), 2-furaneboronic acid (236 mg), $Pd(OAc)_2$ (18 mg), P(*o*-tol)$_3$ (48 mg), and TBAB (45 mg) according to general procedure C (reflux for 140 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 8/2/0.2) to yield the expected compound **12i** as a yellow oil (76 mg, 40% yield); R_f 0.5 (Cyh/AcOEt/NH_4OH, 8/2/0.2); HPLC (C18—10 min) P_{HPLC} 96%, t_R 3.85 min; ^{1}H NMR ($CDCl_3$) δ 8.40 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.13 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.7 Hz, $^4J_{4,6}$=2.4 Hz), 7.85 (1H, d, Ar–H_3, $^4J_{3,4}$=8.7 Hz), 7.60 (1H, d, Fur–H_5, $^3J_{5,4}$=1.7 Hz), 6.96 (1H, d, Fur–H_3, $^3J_{3,4}$=3.4 Hz), 6.57 (1H, dd, Fur–H_4, $^3J_{4,3}$=3.4 Hz, $^3J_{4,5}$= 1.7 Hz), 3.85 (2H, s, CH_2), 2.60–2.64 (4H, m, N–CH_2), 1.78–1.87 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 143.9 (Fur–C_5), 128.0 (Ar–C_3), 125.6 (Ar–C_6), 122.3 (Ar–C_4), 113.1 (Fur–C_3), 112.4 (Fur–C_4), 58.4 (CH_2), 54.2 (2C, N–CH_2), 23.8 (2C, CH_2); *m/z* 273.2 $[M+H]^+$.

4.10.26. 1-(4′-Chloro-4-nitro-biphenyl-2-ylmethyl)-pyrrolidine 12k. Synthesized from compound **4** (200 mg, 0.701 mmol), 4-chlorophenylboronic acid (220 mg), $Pd(OAc)_2$ (12 mg), P(*o*-tol)$_3$ (32 mg), and TBAB (45 mg) according to general procedure C (reflux for 16 h). The residue was purified by TLC (Cyh/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **12k** as a white solid (129 mg, 58% yield); R_f 0.6 (Cyh/AcOEt/NH_4OH, 9/1/0.2); mp=107–108 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.17 min; ^{1}H NMR ($CDCl_3$) δ 8.44 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 8.12 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 7.36–7,44 (5H, m, Ph, Ar–H_3), 3.58 (2H, s, CH_2), 2.46–2.48 (4H, m, N–CH_2), 1.72–1.81 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 131.0 (Ar–C_3), 130.7 (2C, Ph), 128.7 (2C, Ph), 124.9 (Ar–C_6), 121.9 (Ar–C_4), 57.2 (CH_2), 54.0 (2C, N–CH_2), 23.8 (2C, CH_2); *m/z* 317.2 $[M+H]^+$.

4.10.27. 1-(2-Methyl-5-nitro-benzyl)-pyrrolidine 12l. To a suspension of compound **4** (200 mg, 0.701 mmol), methylboronic acid (63 mg, 1.5 equiv), $Pd(OAc)_2$ (24 mg, 0.15 equiv), P(*o*-tol)$_3$ (63 mg, 0.3 equiv), and K_2CO_3 (290 mg, 3 equiv) in THF (5 mL) was added water (0.5 mL) under inert atmosphere. The reaction medium was heated to 75 °C for 70 h. The medium was evaporated, solubilized with aq satd $NaHCO_3$(50 mL), and extracted with DCM (5×50 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by TLC (EP/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **12l** as a yellow oil (106 mg, 73% yield); R_f 0.5 (AcOEt/Cyh/NH_4OH, 1/9/0.2); HPLC (C18—10 min) P_{HPLC} >99%, t_R 3.28 min; ^{1}H NMR ($CDCl_3$) δ 8.14 (1H, d, Ar–H_6, $^4J_{6,4}$=2.7 Hz), 7.94 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.7 Hz, $^4J_{4,6}$=2.7 Hz), 7.21 (1H, d, Ar–H_3, $^3J_{3,4}$= 8,7 Hz), 3.59 (2H, s, CH_2), 2.45–2.52 (4H, m, N–CH_2), 2.39 (3H, s, CH_3), 1.70–1.81 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.8 (Ar–C_3), 123.8 (Ar–C_6), 121.8 (Ar–C_4), 57.7 (CH_2), 54.4 (2C, N–CH_2), 23.6 (2C, CH_2), 24.3 (1C, CH_3); *m/z* 221.1 $[M+H]^+$.

4.10.28. 1-(2-Ethyl-5-nitro-benzyl)-pyrrolidine 12m. To a suspension of compound **4** (200 mg, 0.701 mmol), ethylboronic acid (77 mg, 1.5 equiv), $Pd(OAc)_2$ (24 mg, 0.15 equiv), P(*o*-tol)$_3$ (63 mg, 0.3 equiv), and K_2CO_3 (291 mg, 3 equiv) in THF (5 mL) was added water (0.5 mL) under inert atmosphere. The reaction medium was heated to 75 °C for 70 h. The medium was evaporated, solubilized with aq satd $NaHCO_3$ (50 mL), and extracted with DCM (5×50 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated. The residue was purified by TLC (pentane/AcOEt/NH_4OH, 9/1/0.2) to yield the expected compound **12m** as a yellow oil (79 mg, 48% yield); R_f 0.5 (pentane/AcOEt/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 94%, t_R 3.85 min; ^{1}H NMR ($CDCl_3$) δ 8.16 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 7.97 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 7.25 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 3.61 (2H, s, CH_2), 2.75 (2H, q, Ar–CH_2, ^3J=7.5 Hz), 2.43–2.51 (4H, m, N–CH_2), 1.67–1.78 (4H, m, CH_2), 1.18 (3H, t, CH_3, ^3J=7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 129.2 (Ar–C_3), 124.3 (Ar–C_6), 122.2 (Ar–C_4), 57.3 (CH_2), 54.5 (2C, N–CH_2), 25.7 (Ar–CH_2), 23.8 (2C, CH_2), 14.8 (CH_3); *m/z* 235.2 (M^++1), 219.1 $[M+H-O]^+$.

4.10.29. 2-Diethylaminomethyl-biphenyl-4-ylamine 13a. Synthesized from compound **11a** (43 mg, 0.150 mmol) and $SnCl_2$ (114 mg) in HCl (0.45 mL) and THF (15 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13a** as a yellow oil (29 mg, 76% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 97%, t_R 3.67 min; ^{1}H NMR ($CDCl_3$) δ 7.25–7.39 (5H, m, Ph), 7.05 (1H, d, Ar–H_6, $^4J_{6,4}$= 2.7 Hz), 7.02 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.61 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.7 Hz), 3.77 (2H, s large, NH_2), 3.51 (2H, s, CH_2), 2.47 (4H, q, N–CH_2, ^3J=7.2 Hz), 0.92 (6H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 130.8 (Ar–C_3), 129.7 (2C, Ph), 127.8 (2C, Ph), 126.3 (Ph), 115.6 (Ar–C_6), 113.5 (Ar–C_4), 54.2 (CH_2), 46.6 (2C, N–CH_2), 11.2 (2C, CH_3); *m/z* 255.3 $[M+H]^+$.

4.10.30. 2-Diethylaminomethyl-4′-methyl-biphenyl-4-ylamine 13b. Synthesized from compound **11b** (161 mg, 0.540 mmol) and $SnCl_2$ (408 mg) in HCl (1.62 mL) and THF (10 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13b** as a yellow oil (101 mg, 70% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.97 min; ^{1}H NMR ($CDCl_3$) δ 7.16 (4H, m, Ph), 7.03 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 6.99 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.57 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.5 Hz), 3.84 (2H, s large, NH_2), 3.48 (2H, s, CH_2), 2.45 (4H, q, N–CH_2, ^3J=7.1 Hz), 2.37 (3H, s, CH_3), 0.92 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 131.1 (Ar–C_3), 129.8 (2C, Ph), 128.8 (2C, Ph), 115.9 (Ar–C_6), 113.7 (Ar–C_4), 54.6 (CH_2), 47.0 (2C, N–CH_2), 21.4 (CH_3), 11.7 (2C, CH_3); *m/z* 269.3 $[M+H]^+$.

4.10.31. 4′-*tert*-Butyl-2-diethylaminomethyl-biphenyl-4-ylamine 13c. Synthesized from compound **11c** (128 mg,

0.375 mmol) and $SnCl_2$ (284 mg) in HCl (1.12 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13c** as a yellow oil (74 mg, 63% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 5.01 min; ^1H NMR ($CDCl_3$) δ 7.37 (2H, m, Ph), 7.20 (2H, m, Ph), 7.06 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 7.02 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.60 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.5 Hz), 3.92 (2H, s large, NH_2), 3.55 (2H, s, CH_2), 2.49 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.35 (9H, s, *t*-Bu), 0.92 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 131.9 (Ar–C_3), 130.2 (2C, Ph), 125.7 (2C, Ph), 116.6 (Ar–C_6), 114.5 (Ar–C_4), 55.1 (CH_2), 47.6 (2C, N–CH_2), 32.3 (3C, *t*-Bu), 11.9 (2C, CH_3); *m*/*z* 311.3 $[M+H]^+$.

4.10.32. 2-Diethylaminomethyl-4′-trifluoromethyl-biphenyl-4-ylamine 13d. Synthesized from compound **11d** (143 mg, 0.406 mmol) and $SnCl_2$ (308 mg) in HCl (1.22 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13d** as a yellow oil (86 mg, 66% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.68 min; ^1H NMR ($CDCl_3$) δ 7.61 (2H, d, Ph, $^3J_{3',2'}$=8 Hz), 7.40 (2H, d, Ph, $^3J_{2',3'}$=8 Hz), 7.06 (1H, d, Ar–H_6, $^4J_{6,4}$=2,4 Hz), 6.99 (1H, d, Ar–H_3, $^3J_{3,4}$=8,1 Hz), 6.63 (1H, dd, Ar–H_4, $^3J_{4,3}$=8,1 Hz, $^4J_{4,6}$=2,4 Hz), 4.13 (2H, s large, NH_2), 3.51 (2H, s, CH_2), 2.49 (4H, q, N–CH_2, ^3J=7,1 Hz), 0.92 (6H, t, CH_3, ^3J=7,1 Hz); ^{13}C NMR ($CDCl_3$) δ 130.9 (Ar–C_3), 130.0 (2C, Ph), 124.8 (2C, Ph, $^3J_{CH,F}$=3.0 Hz), 116.0 (Ar–C_6), 113.7 (Ar–C_4), 54.5 (1C, CH_2), 46.9 (2C, N–CH_2), 11.1 (2C, CH_3); *m*/*z* 323.2 $[M+H]^+$.

4.10.33. 2-Diethylaminomethyl-4′-methoxy-biphenyl-4-ylamine 13e. Synthesized from compound **11e** (98 mg, 0.312 mmol) and $SnCl_2$ (237 mg) in HCl (0.94 mL) and THF (10 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13e** as a yellow oil (46 mg, 53% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.60 min; ^1H NMR ($CDCl_3$) δ 7.18 (2H, m, Ph), 7.03 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.99 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.90 (2H, m, Ph), 6.60 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.70–4.00 (2H, s large, NH_2), 3.83 (3H, s, O–CH_3), 3.51 (2H, s, CH_2), 2.48 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.93 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 131.2 (Ar–C_3), 130.9 (2C, Ph), 115.9 (Ar–C_6), 113.8 (Ar–C_4), 113.5 (2C, Ph), 55.4 (O–CH_3), 54.5 (CH_2), 46.9 (2C, N–CH_2), 11.4 (2C, CH_3); *m*/*z* 285.3 $[M+H]^+$.

4.10.34. 1-(4′-Amino-2′-diethylaminomethyl-biphenyl-4-yl)-ethanone 13f. Synthesized from compound **11f** (89 mg, 0.272 mmol) and $SnCl_2$ (207 mg) in HCl (0.82 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13f** as a yellow oil (54 mg, 67% yield); R_f 0.7 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 96%, t_R 3.58 min; ^1H NMR ($CDCl_3$) δ 7.88 (2H, d, Ph, ^3J=8.1 Hz), 7.31 (2H, d, Ph, ^3J=8.1 Hz), 6.90–6.94 (2H, m, Ar–H_3, Ar–H_6), 6.54 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.80 (2H, s large, NH_2), 3.37 (2H, s, CH_2), 2.55 (3H, s, CO–CH_3), 2.35 (4H, q, N–CH_2, ^3J=6.9 Hz), 0.78 (6H, t, CH_3, ^3J=6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 129.9 (Ar–C_3), 129.1 (2C, Ph), 127.1 (2C, Ph), 115.0 (Ar–C_6), 112.6 (Ar–C_4), 53.8 (CH_2), 45.8 (2C, N–CH_2), 25.8 (CO-CH_2), 10.6 (2C, CH_3); *m*/*z* 297.3 $[M+H]^+$.

4.10.35. 2-Diethylaminomethyl-4′-fluoro-biphenyl-4-ylamine 13g. Synthesized from compound **11g** (70 mg, 0.233 mmol) and $SnCl_2$ (176 mg) in HCl (0.70 mL) and THF (25 mL) according to general procedure A (reflux for 5 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13g** as a yellow oil (42 mg, 66% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.77 min; ^1H NMR ($CDCl_3$) δ 7.21 (2H, m, Ph), 7.11 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 7.06 (2H, m, Ph), 6.99 (1H, d, Ar–H_3, $^3J_{3,4}$=8.2 Hz), 6.64 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.2 Hz, $^4J_{4,6}$=2.4 Hz), 4.40 (2H, s large, NH_2), 3.64 (2H, s, CH_2), 2.59 (4H, q, N–CH_2, ^3J=7.2 Hz), 0.96 (6H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 131.3 (2C, d, Ph, $^3J_{CH,F}$=7.6 Hz), 131.2 (Ar–C_3), 116.1 (Ar–C_6), 115.0 (2C, d, Ph, $^2J_{CH,F}$=21.0 Hz), 114.3 (Ar–C_4), 53.9 (CH_2), 46.4 (2C, N–CH_2), 10.5 (2C, CH_3); *m*/*z* 273.3 $[M+H]^+$.

4.10.36. 2-Diethylaminomethyl-4′-thiophen-2-yl-biphenyl-4-ylamine 13h. Synthesized from compound **11h** (77 mg, 0.264 mmol) and $SnCl_2$ (200 mg) in HCl (0.79 mL) and THF (25 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13h** as a yellow oil (29 mg, 43% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.67 min; ^1H NMR ($CDCl_3$) δ 7.27 (1H, dd, Thio–H_5, $^3J_{5,4}$=5.1 Hz, $^4J_{5,3}$=1.2 Hz), 7.16 (1H, d, Ar–H_3, $^4J_{3,4}$=8.2 Hz), 7.05 (1H, d, Ar–H_6, $^4J_{6,4}$=2.3 Hz), 7.04 (1H, dd, Thio–H_4, $^3J_{4,3}$=3.5 Hz, $^3J_{4,5}$=5.1 Hz), 6.96 (1H, dd, Thio–H_3, $^3J_{3,4}$=3.5 Hz, $^4J_{3,5}$=1.2 Hz), 6.58 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.2 Hz, $^4J_{4,6}$=2.5 Hz), 3.87 (2H, s large, NH_2), 3.65 (2H, s, CH_2), 2.56 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.99 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 132.1 (Ar–C_3), 127.1 (1C, C-4′), 126.7 (1C, C-3′), 124.9 (1C, C-5′), 116.0 (Ar–C_6), 113.7 (Ar–C_4), 54.7 (CH_2), 46.8 (2C, N–CH_2), 11.4 (2C, CH_3); *m*/*z* 261.3 $[M+H]^+$.

4.10.37. 2-Diethylaminomethyl-4′-furan-2-yl-biphenyl-4-ylamine 13i. Synthesized from compound **11i** (68 mg, 0.249 mmol) and $SnCl_2$ (189 mg) in HCl (0.75 mL) and THF (25 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13i** as a yellow oil (22 mg, 35% yield); R_f 0.2 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.24 min; ^1H NMR ($CDCl_3$) δ 7.44 (1H, dd, Fur–H_5, $^3J_{5,4}$=1.8 Hz, $^4J_{5,3}$=0.7 Hz), 7.34 (1H, d, Ar–H_3, $^4J_{3,4}$=8.3 Hz), 7.06 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 6.61 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.3 Hz, $^4J_{4,6}$=2.5 Hz), 6.45 (1H, dd, Fur–H_4, $^3J_{4,3}$= 3.2 Hz, $^3J_{4,5}$=1.8 Hz), 6.39 (1H, dd, Fur–H_3, $^3J_{3,4}$=3.2 Hz, $^4J_{3,5}$=0.7 Hz), 3.60–4.10 (2H, s large, NH_2), 3.79 (2H, s, CH_2), 2.64 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.05 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 141.2 (Fur–C_5), 129.8 (Ar–C_3), 116.1 (Ar–C_6), 113.9 (Ar–C_4), 111.2 (Fur–C_4),

107.4 (Fur–C_3), 55.0 (CH_2), 46.8 (2C, N–CH_2), 11.0 (2C, CH_3); *m/z* 245.2 $[M+H]^+$.

4.10.38. 2-Diethylaminomethyl-2′-fluoro-biphenyl-4-ylamine 13j. Synthesized from compound **11j** (91 mg, 0.301 mmol) and $SnCl_2$ (228 mg) in HCl (0.91 mL) and THF (25 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13j** as a yellow oil (53 mg, 65% yield); R_f 0.7 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.88 min; ^1H NMR ($CDCl_3$) δ 7.27–7.32 (1H, m, Ph–H_4), 7.18–7.26 (1H, m, Ph–H_5), 7.23–7.28 (1H, dd, Ph–H_6, $^3J_{6,5}$=7.2 Hz, $^4J_{6,4}$=1.1 Hz), 7.04–7.14 (2H, m, Ph–H_3, Ar–H_6), 6.98 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.61 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.93 (2H, s large, NH_2), 3.39 (2H, s, CH_2), 2.43 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.90 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 133.1 (d, Ph–C_5, $^3J_{5,F}$=2.9 Hz), 132.1 (Ar–C_3), 129.6 (d, Ph–C_4, $^3J_{4,F}$=7.5 Hz), 124.8 (d, Ph–C_6, $^3J_{6,F}$=2.8 Hz), 116.6 (Ar–C_3), 116.2 (d, Ph–C_3, $^2J_{3,F}$=22.6 Hz), 114.4 (Ar–C_4), 55.4 (CH_2), 47.8 (2C, N–CH_2), 12.4 (2C, CH_3); *m/z* 273.3 $[M+H]^+$.

4.10.39. 4′-Chloro-2-diethylaminomethyl-biphenyl-4-ylamine 13k. Synthesized from compound **11k** (143 mg, 0.449 mmol) and $SnCl_2$ (341 mg) in HCl (1.35 mL) and THF (25 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **13k** as a yellow solid (78 mg, 60% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=37–38 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.23 min; ^1H NMR ($CDCl_3$) δ 7.32 (2H, m, Ph), 7.20 (2H, m, Ph), 7.01 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 6.97 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.60 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.5 Hz), 3.95 (2H, s large, NH_2), 3.45 (2H, s, CH_2), 2.46 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.92 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 133.3 (2C, Ph), 131.3 (Ar–C_3), 128.2 (2C, Ph), 116.1 (Ar–C_6), 113.8 (Ar–C_4), 54.7 (CH_2), 46.8 (2C, N–CH_2), 11.5 (2C, CH_3); *m/z* 289.3–291.3 $[M+H]^+$.

4.10.40. 3-Diethylaminomethyl-4-methyl-phenylamine 13l. Synthesized from compound **11l** (105 mg, 0.473 mmol) and $SnCl_2$ (359 mg) in HCl (1.42 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9/1/0.2) to yield compound **13l** as a yellow oil (51 mg, 56% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 87%, t_R 0.64–2.31 min; ^1H NMR ($CDCl_3$) δ 6.90 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.78 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.49 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.55 (2H, s large, NH_2), 3.44 (2H, s, CH_2), 2.53 (4H, q, N–CH_2, ^3J=7.2 Hz), 2.22 (3H, s, CH_3), 1.04 (4H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 130.9 (Ar–C_3), 116.7 (Ar–C_6), 113.7 (Ar–C_4), 55.6 (CH_2), 47.1 (2C, N–CH_2), 18.6 (CH_3), 11.8 (2C, CH_3); *m/z* 193.2 $[M+H]^+$.

4.10.41. 3-Diethylaminomethyl-4-ethyl-phenylamine 13m. Synthesized from compound **11m** (112 mg, 0.475 mmol) and $SnCl_2$ (360 mg) in HCl (1.43 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9/1/0.2) to yield compound **13m** as a yellow oil (68 mg, 69% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 88%, t_R 0.64–2.49 min; ^1H NMR ($CDCl_3$) δ 6.94 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.80 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.52 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.0 Hz, $^4J_{4,6}$=2.4 Hz), 3.50 (2H, s large, NH_2), 3.46 (2H, s, CH_2), 2.60 (2H, q, Ar–CH_2, ^3J=7.5 Hz), 2.51 (4H, q, N–CH_2, ^3J=7.2 Hz), 1.15 (3H, t, CH_3, ^3J=7.5 Hz), 1.03 (3H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 129.4 (Ar–C_3), 116.7 (Ar–C_6), 114.0 (Ar–C_4), 55.1 (CH_2), 47.1 (2C, N–CH_2), 24.9 (Ar–CH_2), 15.8 (CH_3), 11.9 (2C, CH_3); *m/z* 207.3 (M^++1).

4.10.42. 2-Pyrrolidin-1-ylmethyl-biphenyl-4-ylamine 14a. Synthesized from compound **12a** (104 mg, 0.367 mmol) and $SnCl_2$ (279 mg) in HCl (1.10 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14a** as a yellow oil (70 mg, 75% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.42 min; ^1H NMR ($CDCl_3$) δ 7.13–7.27 (5H, m, Ph), 6.95 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.88 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.52 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.74 (2H, s large, NH_2), 3.46 (2H, s, CH_2), 2.35–2.39 (4H, m, N–CH_2), 1.61–1.66 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.0 (Ar–C_3), 128.9 (2C, Ph), 126.9 (2C, Ph), 125.3 (Ph), 114.8 (Ar–C_6), 112.6 (Ar–C_4), 56.3 (CH_2), 53.0 (2C, N–CH_2), 22.5 (2C, CH_2); *m/z* 253.3 $[M+H]^+$.

4.10.43. 4′-Methyl-2-pyrrolidin-1-ylmethyl-biphenyl-4-ylamine 14b. Synthesized from compound **12b** (149 mg, 0.501 mmol) and $SnCl_2$ (380 mg) in HCl (1.50 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14b** as a yellow oil (95 mg, 71% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.94 min; ^1H NMR ($CDCl_3$) δ 7.21 (2H, m, Ph), 7.16 (2H, m, Ph), 7.02 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.94 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.58 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.75 (2H, s large, NH_2), 3.53 (2H, s, CH_2), 2.43–2.47 (4H, m, N–CH_2), 2.37 (3H, s, CH_3), 1.69–1.76 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 131.9 (Ar–C_3), 130.7 (2C, Ph), 129.6 (2C, Ph), 116.7 (Ar–C_6), 114.5 (Ar–C_4), 58.3 (CH_2), 54.9 (2C, N–CH_2), 24.5 (2C, CH_2); *m/z* 267.2 $[M+H]^+$.

4.10.44. 4′-*tert*-Butyl-2-pyrrolidin-1-ylmethyl-biphenyl-4-ylamine 14c. Synthesized from compound **12c** (200 mg, 0.591 mmol) and $SnCl_2$ (448 mg) in HCl (1.78 mL) and THF (25 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14c** as a yellow oil (135 mg, 74% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9/1/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.96 min; ^1H NMR ($CDCl_3$) δ 7.36 (2H, m, Ph), 7.26 (2H, m, Ph), 7.03 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.95 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.56 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.60–3.90 (2H, s large, NH_2), 3.56 (2H, s, CH_2), 2.44–2.47 (4H, m, N–CH_2), 1.71–1.74 (4H, m, CH_2), 1.35 (9H, s, *t*-Bu); ^{13}C NMR ($CDCl_3$) δ 131.3 (Ar–C_3), 129.6

(2C, Ph), 125.0 (2C, Ph), 115.9 (Ar–C_6), 113.7 (Ar–C_4), 57.6 (CH_2), 54.2 (2C, N–CH_2), 31.7 (3C, *t*-Bu), 23.7 (2C, CH_2); *m/z* 309.3 $[M+H]^+$.

4.10.45. 2-Pyrrolidin-1-ylmethyl-4′-trifluoromethyl-biphenyl-4-ylamine 14d. Synthesized from compound **12d** (178 mg, 0.507 mmol) and $SnCl_2$ (385 mg) in HCl (1.52 mL) and THF (25 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14d** as a yellow oil (116 mg, 71% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.57 min; ^1H NMR ($CDCl_3$) δ 7.61 (2H, d, Ph, ^3J=8.0 Hz), 7.48 (2H, d, Ph, ^3J=8.0 Hz), 7.02 (1H, d, Ar–H_3, $^3J_{3,4}$=8.2 Hz), 6.93 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.61 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.70–3.90 (2H, s large, NH_2), 3.48 (2H, s, CH_2), 2.42–2.47 (4H, m, N–CH_2), 1.67–1.77 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 131.8 (Ar–C_3), 130.9 (2C, Ph), 125.6 (2C, d, Ph, $^3J_{CH,F}$=3.8 Hz), 116.9 (Ar–C_6), 114.5 (Ar–C_4), 58.3 (CH_2), 54.8 (2C, N–CH_2), 24.3 (2C, CH_2); *m/z* 321.1 $[M+H]^+$.

4.10.46. 4′-Methoxy-2-pyrrolidin-1-ylmethyl-biphenyl-4-ylamine 14e. Synthesized from compound **12e** (129 mg, 0.412 mmol) and $SnCl_2$ (313 mg) in HCl (1.24 mL) and THF (25 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14e** as a yellow oil (66 mg, 56% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.57 min; ^1H NMR ($CDCl_3$) δ 7.22 (2H, m, Ph), 7.02 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.96 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.90 (2H, m, Ph), 6.60 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 4.06 (2H, s large, NH_2), 3.83 (3H, s, O–CH_3), 3.61 (2H, s, CH_2), 2.51–2.54 (4H, m, N–CH_2), 1.72–1.76 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 131.2 (Ar–C_3), 131.0 (2C, Ph), 116.0 (Ar–C_6), 114.1 (Ar–C_4), 113.6 (2C, Ph), 57.2 (CH_2), 55.4 (O–CH_3), 54.0 (2C, N–CH_2), 23.5 (2C, CH_2); *m/z* 283.2 $[M+H]^+$.

4.10.47. 1-(4′-Amino-2′-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-ethanone 14f. Synthesized from compound **12f** (158 mg, 0.488 mmol) and $SnCl_2$ (370 mg) in HCl (1.47 mL) and THF (25 mL) according to general procedure A (reflux for 4 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14f** as a yellow oil (102 mg, 71% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.46 min; ^1H NMR ($CDCl_3$) δ 7.96 (2H, m, Ph), 7.46 (2H, m, Ph), 7.05 (1H, d, Ar–H_3, $^4J_{3,4}$=8.2 Hz), 6.95 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.63 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.2 Hz, $^4J_{4,6}$=2.4 Hz), 4.05 (2H, s large, NH_2), 3.54 (2H, s, CH_2), 2.63 (3H, s, CO–CH_3), 2.45–2.50 (4H, m, N–CH_2), 1.71–1.78 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.8 (Ar–C_3), 129.9 (2C, Ph), 128.0 (2C, Ph), 116.0 (Ar–C_6), 113.7 (Ar–C_4), 57.3 (CH_2), 53.8 (2C, N–CH_2), 26.6 (CO–CH_2), 23.4 (2C, CH_2); *m/z* 295.3 $[M+H]^+$.

4.10.48. 4′-Fluoro-2-pyrrolidin-1-ylmethyl-biphenyl-4-ylamine 14g. Synthesized from compound **12g** (78 mg, 0.258 mmol) and $SnCl_2$ (196 mg) in HCl (0.84 mL) and THF (25 mL) according to general procedure A (reflux for 2 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14g** as a yellow oil (39 mg, 55% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 97%, t_R 3.72 min; ^1H NMR ($CDCl_3$) δ 7.27 (2H, m, Ph), 7.06 (2H, m, Ph), 7.01 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.97 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.63 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 4.18 (2H, s large, NH_2), 3.61 (2H, s, CH_2), 2.49–2.58 (4H, m, N–CH_2), 1.70–1.84 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 131.6 (2C, d, Ph, $^3J_{CH,F}$=7.4 Hz), 131.4 (Ar–C_3), 116.2 (Ar–C_6), 115.2 (2C, d, Ph, $^2J_{CH,F}$=20.9 Hz), 114.3 (Ar–C_4), 57.3 (CH_2), 54.2 (2C, N–CH_2), 23.6 (2C, CH_2); *m/z* 271.3 $[M+H]^+$.

4.10.49. 2-Pyrrolidin-1-ylmethyl-4′-thiophen-2-ylbiphenyl-4-ylamine 14h. Synthesized from compound **12h** (86 mg, 0.299 mmol) and $SnCl_2$ (277 mg) in HCl (0.90 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14h** as a yellow oil (50 mg, 65% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.56 min; ^1H NMR ($CDCl_3$) δ 7.17 (1H, dd, Thio–H_5, $^3J_{5,4}$=5.1 Hz, $^4J_{5,3}$=1.5 Hz), 7.11 (1H, d, Ar–H_3, $^4J_{3,4}$=8.1 Hz), 6.98 (1H, dd, Thio–H_3, $^3J_{3,4}$=3.6 Hz, $^4J_{3,5}$=1.5 Hz), 6.96 (1H, dd, Thio–H_4, $^3J_{4,3}$=3.6 Hz, $^3J_{4,5}$=5.1 Hz), 6.83 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.49 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.4 Hz), 3.73 (2H, s large, NH_2), 3.55 (2H, s, CH_2), 2.43–2.47 (4H, m, N–CH_2), 1.63–1.76 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 132.1 (Ar–C_3), 127.1 (Thio–C_4), 126.7 (Thio–C_3), 124.8 (Thio–C_5), 116.2 (Ar–C_6), 113.7 (Ar–C_4), 57.8 (CH_2), 54.1 (2C, N–CH_2), 23.7 (2C, CH_2); *m/z* 259.2 $[M+H]^+$.

4.10.50. 4′-Furan-2-yl-2-pyrrolidin-1-ylmethyl-biphenyl-4-ylamine 14i. Synthesized from compound **12i** (76 mg, 0.278 mmol) and $SnCl_2$ (211 mg) in HCl (0.84 mL) and THF (25 mL) according to general procedure A (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14i** as a yellow oil (30 mg, 44% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.05 min; ^1H NMR ($CDCl_3$) δ 7.44 (1H, dd, Fur–H_5, $^3J_{5,4}$=1.8 Hz, $^4J_{5,3}$=0.9 Hz), 7.41 (1H, d, Ar–H_3, $^4J_{3,4}$=8.4 Hz), 6.90 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 6.61 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 6.96 (1H, dd, Fur–H_3, $^3J_{3,4}$=3.3 Hz, $^4J_{3,5}$=0.9 Hz), 6.57 (1H, dd, Fur–H_4, $^3J_{4,3}$=3.3 Hz, $^3J_{4,5}$=1.8 Hz), 3.95 (2H, s large, NH_2), 3.73 (2H, s, CH_2), 2.57–2.62 (4H, m, N–CH_2), 1.77–1.81 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 140.9 (Fur–C_5), 129.3 (Ar–C_3), 116.1 (Ar–C_6), 113.6 (Ar–C_4), 111.1 (Fur–C_4), 107.3 (Fur–C_3), 57.9 (CH_2), 53.9 (2C, N–CH_2), 23.4 (2C, CH_2); *m/z* 243.2 $[M+H]^+$.

4.10.51. 4′-Chloro-2-pyrrolidin-1-ylmethyl-biphenyl-4-ylamine 14k. Synthesized from compound **12k** (129 mg, 0.407 mmol) and $SnCl_2$ (309 mg) in HCl (1.23 mL) and THF (10 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14k** as a yellow oil (69 mg, 59% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.17 min; ^1H NMR ($CDCl_3$) δ 7.32 (2H, m, Ph), 7.26 (2H, m, Ph), 6.99 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 6.92 (1H, d, Ar–H_6,

$^4J_{6,4}$=2.5 Hz), 6.60 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.5 Hz), 3.90 (2H, s large, NH_2), 3.50 (2H, s, CH_2), 2.44–2.49 (4H, m, N–CH_2), 1.68–1.77 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 131.3 (2C, Ph), 131.1 (Ar–C_3), 128.2 (2C, Ph), 116.2 (Ar–C_6), 113.9 (Ar–C_4), 57.5 (CH_2), 54.1 (2C, N–CH_2), 23.6 (2C, CH_2); *m/z* 287.2–289.2 $[M+H]^+$.

4.10.52. 4-Methyl-3-pyrrolidin-1-ylmethyl-phenylamine 14l. Synthesized from compound **12l** (100 mg, 0.453 mmol) and $SnCl_2$ (343 mg) in HCl (1.36 mL) and THF (10 mL) according to general procedure A (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14l** as a yellow oil (69 mg, 44% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 99%, t_R 0.65–2.26 min; ^{1}H NMR ($CDCl_3$) δ 6.83 (1H, d, Ar–H_3, $^3J_{3,4}$=7.9 Hz), 6.64 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 6.40 (1H, dd, Ar–H_4, $^3J_{4,3}$=7.9 Hz, $^4J_{4,6}$=2.5 Hz), 3.44 (2H, s, CH_2), 2.43–2.49 (4H, m, N–CH_2), 2.14 (3H, s, Ar–CH_3), 1.65–1.93 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 130.9 (Ar–C_3), 116.4 (Ar–C_6), 113.8 (Ar–C_4), 58.0 (CH_2), 54.6 (2C, N–CH_2), 23.7 (2C, CH_2), 18.5 (Ar–CH_3); *m/z* 191.2 $[M+H]^+$.

4.10.53. 4-Ethyl-3-pyrrolidin-1-ylmethyl-phenylamine 14m. Synthesized from compound **12m** (64 mg, 0.271 mmol) and $SnCl_2$ (206 mg) in HCl (0.82 mL) and THF (20 mL) according to general procedure A (reflux for 6 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield compound **14m** as a yellow oil (35 mg, 63% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); HPLC (C18—10 min) P_{HPLC} 91%, t_R 0.65–2.82 min; ^{1}H NMR ($CDCl_3$) δ 6.95 (1H, d, Ar–H_3, $^3J_{3,4}$=8.0 Hz), 6.71 (1H, d, Ar–H_6, $^4J_{6,4}$=2.5 Hz), 6.54 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.0 Hz, $^4J_{4,6}$=2.5 Hz), 3.57 (2H, s, CH_2), 3.35–3.55 (2H, large signal, NH_2), 2.60 (2H, q, Ar–CH_2, ^3J=7.5 Hz), 2.52–2.57 (4H, m, N–CH_2), 1.74–1.83 (4H, m, CH_2), 1.15 (3H, t, CH_3, ^3J=7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 129.3 (Ar–C_3), 116.2 (Ar–C_6), 113.7 (Ar–C_4), 57.3 (CH_2), 54.2 (2C, N–CH_2), 24.9 (Ar–CH_2), 23.3 (2C, CH_2), 15.6 (CH_3); *m/z* 205.1 $[M+H]^+$.

4.10.54. (7-Chloro-quinolin-4-yl)-(2-diethylaminomethyl-biphenyl-4-yl)-amine 9a. Synthesized from compound **13a** (29 mg, 0.113 mmol) and 4,7-diClQuin (22 mg) in HCl (0.11 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 3 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9a** as a white solid (32 mg, 68% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=174–175 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.25 min; HPLC (C18—40 min) P_{HPLC} 99%, t_R 17.62 min; HPLC (C4—40 min) P_{HPLC} 97%, t_R 17.20 min; ^{1}H NMR ($CDCl_3$) δ 8.56 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.02 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.93 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.65 (1H, s, Ar–H_6), 7.31–7.45 (6H, m, Quin–H_6, Ph), 7.24–7.26 (2H, m, Ar–H_3, Ar–H_4), 7.07 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 7.01 (1H, s large, NH), 3.52 (2H, s, CH_2), 2.45 (4H, q, N–CH_2, ^3J=7.2 Hz), 0.92 (4H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 151.8 (Quin–C_2), 130.9 (Ar–C_3), 129.4 (2C, Ph), 128.8 (Quin–C_8), 128.0 (2C, Ph), 126.9 (Ph), 125.9 (Quin–C_6), 123.1 (Ar–C_6), 121.3 (Quin–C_5), 120.2 (Ar–C_4), 102.4 (Quin–C_3), 54.3 (CH_2), 46.8 (2C, N–CH_2), 11.6 (2C, CH_3); *m/z* 416.3–418.3 $[M+H]^+$.

4.10.55. (7-Chloro-quinolin-4-yl)-(2-diethylaminomethyl-4′-methyl-biphenyl-4-yl)-amine 9b. Synthesized from compound **13b** (101 mg, 0.376 mmol) and 4,7-diClQuin (74 mg) in HCl (0.38 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 5 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9b** as a yellow solid (158 mg, 79% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=174–175 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.44 min; HPLC (C18—40 min) P_{HPLC} 99%, t_R 18.81 min; HPLC (C4—40 min) P_{HPLC} 99%, t_R 18.26 min; ^{1}H NMR ($CDCl_3$) δ 8.48 (1H, d, Quin–H_2, $^3J_{2,3}$=5.5 Hz), 8.07 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.95 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.65 (1H, d, Ar–H_6, $^4J_{6,4}$=1.5 Hz), 7.33 (1H, dd, Quin–H_6, $^3J_{6,5}$=8.9 Hz, $^4J_{6,8}$=2.1 Hz), 7.18–7.26 (6H, m, Ph, Ar–H_3, Ar–H_4), 7.03 (1H, d, Quin–H_3, $^3J_{3,2}$=5.5 Hz), 3.56 (2H, s, CH_2), 2.45 (4H, q, N–CH_2, ^3J=7.1 Hz), 2.40 (3H, s, CH_3), 0.90 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.5 (Quin–C_2), 131.0 (Ar–C_3), 129.3 (2C, Ph), 128.8 (2C, Ph), 128.1 (Quin–C_8), 125.8 (Quin–C_6), 123.5 (Ar–C_6), 122.3 (Quin–C_5), 20.7 (Ar–C_4), 102.3 (Quin–C_3), 54.3 (CH_2), 46.8 (2C, N–CH_2), 21.2 (CH_3), 11.5 (2C, CH_3); *m/z* 430.4–432.4 $[M+H]^+$.

4.10.56. (4′-*tert*-Butyl-2-diethylaminomethyl-biphenyl-4-yl)-(7-chloro-quinolin-4-yl)-amine 9c. Synthesized from compound **13c** (74 mg, 0.237 mmol) and 4,7-diClQuin (45 mg) in HCl (0.24 mL) and CH_3CN (15 mL) according to general procedure B (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9c** as a white solid (93 mg, 83% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=213–214 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 5.01 min; HPLC (C18—40 min) P_{HPLC} 99%, t_R 21.62 min; HPLC (C4—40 min) P_{HPLC} 99%, t_R 21.07 min; ^{1}H NMR ($CDCl_3$) δ 8.56 (1H, d, Quin–H_2, $^3J_{2,3}$=5.3 Hz), 8.03 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.91 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.63 (1H, d, Ar–H_6, $^4J_{6,4}$=2.1 Hz), 7.46 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.42 (2H, d, Ph, ^3J=6.6 Hz), 7.23–7.28 (4H, m, Ph, Ar–H_3, Ar–H_4), 7.07 (1H, d, Quin–H_3, $^3J_{3,2}$=5.3 Hz), 6.83 (1H, s large, NH), 3.55 (2H, s, CH_2), 2.46 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.38 (9H, s, *t*-Bu), 0.93 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 152.1 (Quin–C_2), 131.2 (Ar–C_3), 129.2 (2C, Ph), 129.1 (Quin–C_8), 126.1 (Quin–C_6), 125.1 (2C, Ph), 123.3 (Ar–C_6), 121.4 (Quin–C_5), 120.3 (Ar–C_4), 102.6 (Quin–C_3), 54.5 (CH_2), 47.1 (2C, N–CH_2), 31.5 (3C, *t*-Bu), 11.9 (2C, CH_3); *m/z* 472.3–474.3 $[M+H]^+$.

4.10.57. (7-Chloro-quinolin-4-yl)-(2-diethylaminomethyl-4′-trifluoromethyl-biphenyl-4-yl)-amine 9d. Synthesized from compound **13d** (86 mg, 0.267 mmol) and 4,7-diClQuin (53 mg) in HCl (0.27 mL) and CH_3CN (15 mL) according to general procedure B (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9d** as a white solid (108 mg, 84% yield); R_f 0.7 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=214–215 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.65 min; HPLC (C18—40 min) P_{HPLC} 99%, t_R 19.67 min; HPLC (C4—40 min)

P_{HPLC} 99%, t_R 19.56 min; ^{1}H NMR ($CDCl_3$) δ 8.58 (1H, d, Quin–H_2, $^3J_{2,3}$=5.3 Hz), 8.04 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.92 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.68 (2H, d, Ph, ^3J=7.9 Hz), 7.62 (1H, d, Ar–H_6, $^4J_{6,4}$=1.7 Hz), 7.45–7.49 (3H, m, Quin–H_6, Ph), 7.22–7.28 (2H, m, Ar–H_3, Ar–H_4), 7.09 (1H, d, Quin–H_3, $^3J_{3,2}$=5.3 Hz), 6.84 (1H, s large, NH), 3.49 (2H, s, CH_2), 2.44 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.92 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.9 (Quin–C_2), 130.8 (Ar–C_3), 129.7 (2C, Ph), 128.9 (Quin–C_8), 126.1 (Quin–C_6), 124.9 (2C, Ph, $^3J_{CH,F}$=3.6 Hz), 123.1 (Ar–C_6), 121.2 (Quin–C_5), 120.1 (Ar–C_4), 102.6 (Quin–C_3), 54.6 (CH_2), 46.7 (2C, N–CH_2), 11.7 (2C, CH_3); *m/z* 484.3–486.2 $[M+H]^+$.

4.10.58. (7-Chloro-quinolin-4-yl)-(2-diethylaminomethyl-4′-methoxy-biphenyl-4-yl)-amine 9e. Synthesized from compound **13e** (46 mg, 0.162 mmol) and 4,7-diClQuin (32 mg) in HCl (0.17 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 5 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9e** as a yellow solid (66 mg, 91% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=155–156 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.30 min; HPLC (C18—40 min) P_{HPLC} 98%, t_R 18.08 min; HPLC (C4—40 min) P_{HPLC} 99%, t_R 17.44 min; ^{1}H NMR ($CDCl_3$) δ 8.52 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.00 (1H, d, Quin–H_5, $^3J_{5,6}$=8.9 Hz), 7.98 (1H, d, Quin–H_8, $^4J_{8,6}$=2.2 Hz), 7.63 (1H, d, Ar–H_6, $^4J_{6,4}$=1.4 Hz), 7.62 (1H, dd, Quin–H_6, $^3J_{6,5}$=8.9 Hz, $^4J_{6,8}$=2.2 Hz), 7.21–7.27 (4H, m, Ph, Ar–H_3, Ar–H_4), 7.04 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 6.96 (2H, d, Ph, $^3J_{3,4}$=8.2 Hz), 3.86 (3H, s, O–CH_3), 3.59 (2H, s, CH_2), 2.50 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.93 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.7 (Quin–C_2), 131.2 (Ar–C_3), 130.9 (2C, Ph), 128.5 (Quin–C_8), 126.0 (Quin–C_6), 123.5 (Ar–C_6), 121.9 (Quin–C_5), 120.7 (Ar–C_4), 113.6 (2C, Ph), 102.4 (Quin–C_3), 55.3 (O–CH_3), 54.3 (CH_2), 46.8 (2C, N–CH_2), 11.3 (2C, CH_3); *m/z* 446.3–448.3 $[M+H]^+$.

4.10.59. 1-[4′-(7-Chloro-quinolin-4-ylamino)-2′-diethylaminomethyl-biphenyl-4-yl]-ethanone 9f. Synthesized from compound **13f** (54 mg, 0.184 mmol) and 4,7-diClQuin (36 mg) in HCl (0.19 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 5 h). The residue was purified by TLC (DCM/NH_4OH, 10/0.2) to yield the expected compound **9f** as a white solid (54 mg, 64% yield); R_f 0.4 (DCM/NH_4OH, 10/0.2); mp=141–142 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.13 min; HPLC (C18—40 min) P_{HPLC} 98%, t_R 17.09 min; HPLC (C4—40 min) P_{HPLC} 98%, t_R 16.42 min; ^{1}H NMR ($CDCl_3$) δ 8.46 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.01 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.90 (2H, m, Ph), 7.86 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.59 (1H, d, Ar–H_6, $^4J_{6,4}$=2.1 Hz), 7.36 (2H, m, Ph), 7.31 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.22 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.2 Hz, $^4J_{4,6}$=2.3 Hz), 7.16 (1H, d, Ar–H_3, $^3J_{3,4}$=8.2 Hz), 6.98 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.49 (2H, s, CH_2), 2.53 (3H, s, CO–CH_2), 2.38 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.80 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 152.4 (Quin–C_2), 131.8 (Ar–C_3), 130.7 (2C, Ph), 129.1 (Quin–C_8), 129.1 (2C, Ph), 126.8 (Quin–C_6), 124.4 (Ar–C_6), 123.3 (Quin–C_5), 121.5 (Ar–C_4), 103.5 (Quin–C_3), 55.5 (CH_2), 47.6 (2C, N–CH_2), 27.5 (1C, C-6′), 12.0 (2C, CH_3); *m/z* 458.3–460.3 $[M+H]^+$.

4.10.60. 7-Chloro-*N*-(2-((diethylamino)methyl)-4′-fluorobiphenyl-4-yl)quinolin-4-amine 9g. Synthesized from compound **13g** (40 mg, 0.148 mmol) and 4,7-diClQuin (29 mg) in HCl (0.15 mL) and CH_3CN (15 mL) according to general procedure B (reflux for 8 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9g** as a white solid (42 mg, 66% yield); R_f 0.7 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=167–168 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.08 min; HPLC (C18—40 min) P_{HPLC} >99%, t_R 17.92 min; HPLC (C4—40 min) P_{HPLC} 98%, t_R 17.50 min; ^{1}H NMR ($CDCl_3$) δ 8.57 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.03 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.95 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.63 (1H, d, Ar–H_6, $^4J_{6,4}$=2.1 Hz), 7.47 (1H, d, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.23–7.33 (4H, m, Ph, Ar–H_3, Ar–H_4), 7.14 (2H, m, Ph), 7.07 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.60 (2H, s, CH_2), 3.49 (1H, s, NH), 2.54 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.96 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.7 (Quin–C_2), 131.0 (Ar–C_3), 130.9 (2C, d, Ph, $^4J_{CH,F}$=8.0 Hz), 128.7 (Quin–C_8), 126.0 (Quin–C_6), 123.1 (Ar–C_6), 121.3 (Quin–C_5), 120.3 (Ar–C_4), 115.0 (2C, d, Ph, $^3J_{CH,F}$=21.2 Hz), 102.4 (Quin–C_3), 54.1 (CH_2), 46.6 (2C, N–CH_2), 11.0 (2C, CH_3); *m/z* 434.3–436.3 $[M+H]^+$.

4.10.61. (7-Chloro-quinolin-4-yl)-(2-diethylaminomethyl-4′-thiophen-2-ylbiphenyl-4-yl)-amine 9h. Synthesized from compound **13h** (29 mg, 0.113 mmol) and 4,7-diClQuin (22 mg) in HCl (0.11 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 4 h). The residue was purified by TLC (DCM/NH_4OH, 10/0.2) to yield the expected compound **9h** as a orange solid (41 mg, 87% yield); R_f 0.6 (DCM/NH_4OH, 10/0.2); mp=154–155 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.92 min; HPLC (C18—40 min) P_{HPLC} 99%, t_R 17.36 min; HPLC (C4—40 min) P_{HPLC} 97%, t_R 10.79 min; ^{1}H NMR ($CDCl_3$) δ 8.53 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.03 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.98 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.66 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 7.35–7.41 (3H, m, Ar–H_3, Quin–H_6, Thio–H_5), 7.25 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 7.05–7.13 (3H, m, Thio–H_3, Thio–H_4, Quin–H_3), 3.76 (2H, s, CH_2), 2.58 (4H, q, N–CH_2, ^3J=7.2 Hz), 0.98 (6H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 151.5 (Quin–C_2), 132.2 (Ar–C_3), 128.5 (Quin–C_8), 127.4 (2C, Thio–C_3, Thio–C_4), 126.3 (Thio–C_5), 125.8 (Quin–C_6), 123.4 (Ar–C_6), 122.1 (Quin–C_5), 120.5 (Ar–C_4), 102.8 (Quin–C_3), 54.6 (CH_2), 46.9 (2C, N–CH_2), 11.2 (2C, CH_3); *m/z* 422.3–424.3 $[M+H]^+$.

4.10.62. (7-Chloro-quinolin-4-yl)-(2-diethylaminomethyl-4′-furan-2-yl-biphenyl-4-yl)-amine 9i. Synthesized from compound **13i** (22 mg, 0.088 mmol) and 4,7-diClQuin (18 mg) in HCl (0.09 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 4 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9i** as a yellow solid (26 mg, 73% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=146–147 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.73 min; HPLC (C18—40 min) P_{HPLC} 96%, t_R 16.48 min; HPLC (C4—40 min) P_{HPLC} 96%, t_R 10.05 min; ^{1}H NMR ($CDCl_3$) δ 8.53 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 7.99 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.98 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.66 (1H, d, Ar–H_6,

$^4J_{6,4}$=2.2 Hz), 7.60 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.52 (1H, d, Fur–H_5, $^3J_{5,4}$=1.8 Hz), 7.40 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.27 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.2 Hz), 7.05 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 6.56 (1H, d, Fur–H_3, $^3J_{3,4}$=3.3 Hz), 6.51 (1H, dd, Fur–H_4, $^3J_{4,3}$=3.3 Hz, $^3J_{4,5}$=1.8 Hz), 3.87 (2H, s, CH_2), 2.65 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.05 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.6 (Quin–C_2), 142.0 (Fur–C_5), 129.4 (Ar–C_3), 128.5 (Quin–C_8), 126.2 (Quin–C_6), 123.2 (Ar–C_6), 121.9 (Quin–C_5), 120.4 (Ar–C_4), 111.5 (Fur–C_4), 109.0 (Fur–C_3), 102.9 (Quin–C_3), 55.1 (CH_2), 47.0 (2C, N–CH_2), 11.2 (2C, CH_3); *m/z* 406.3–408.3 $[M+H]^+$.

4.10.63. 7-Chloro-*N*-(2-((diethylamino)methyl)-2′-fluorobiphenyl-4-yl)quinolin-4-amine 9j. Synthesized from compound **13j** (53 mg, 0.196 mmol) and 4,7-diClQuin (39 mg) in HCl (0.20 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9g** as a white solid (70 mg, 82% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=180–181 °C; HPLC (C18—10 min) P_{HPLC} 95%, t_R 4.12 min; HPLC (C18—40 min) P_{HPLC} >99%, t_R 17.87 min; HPLC (C4—40 min) P_{HPLC} 96%, t_R 17.37 min; ^{1}H NMR ($CDCl_3$) δ 8.58 (1H, d, Quin–H_2, $^3J_{2,3}$=5.3 Hz), 8.03 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.93 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.66 (1H, d, Ar–H_6, $^4J_{6,4}$=1.9 Hz), 7.46 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6'',8''}$=2.1 Hz), 7.34–7.42 (1H, m, Ph), 7.22–7.30 (4H, m, Ph, Ar–H_3, Ar–H_4), 7.15–7.09 (1H, m, Ph), 7.12 (1H, d, Quin–H_3, $^3J_{3,2}$=5.3 Hz), 6.85–7.05 (1H, s large, NH), 3.49 (2H, s, CH_2), 2.44 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.92 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.7 (Quin–C_2), 131.4 (Ph–C_5), 131.1 (Ar–C_3), 129.1 (d, Ph–C_4, $^3J_{4,F}$=7.4 Hz), 128.7 (Quin–C_8), 126.9 (Quin–C_6), 123.8 (d, Ph–C_6, $^3J_{6,F}$=3.5 Hz), 122.4 (Ar–C_6), 121.1 (Quin–C_5), 119.7 (Ar–C_4), 115.2 (d, Ph–C_3, $^2J_{3,F}$=22.2 Hz), 102.5 (Quin–C_3), 54.1 (CH_2), 46.8 (2C, N–CH_2), 11.4 (2C, CH_3); *m/z* 434.0–436.0 $[M+H]^+$.

4.10.64. (4′-Chloro-2-diethylaminomethyl-biphenyl-4-yl)-(7-chloro-quinolin-4-yl)-amine 9k. Synthesized from compound **13k** (78 mg, 0.269 mmol) and 4,7-diClQuin (53 mg) in HCl (0.27 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 5 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9k** as a white solid (109 mg, 90% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=179–180 °C; HPLC (C18—10 min) P_{HPLC} 97%, t_R 4.51 min; HPLC (C18—40 min) P_{HPLC} 99%, t_R 19.07 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 18.51 min; ^{1}H NMR ($CDCl_3$) δ 8.50 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.05 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.96 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.62 (1H, d, Ar–H_6, $^4J_{6,4}$=2.2 Hz), 7.35–7.41 (3H, m, Ph, Quin–H_6), 7.18–7.29 (3H, m, Ph, Ar–H_4), 7.20 (1H, d, Ar–H_3, $^3J_{3,4}$=8.2 Hz), 7.04 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.50 (2H, s, CH_2), 3.49 (1H, s, NH), 2.46 (4H, q, N–CH_2, ^3J=7.1 Hz), 0.91 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.7 (Quin–C_2), 131.2 (Ar–C_3), 131.1 (2C, Ph), 128.5 (2C, Ph), 128.4 (Quin–C_8), 126.2 (Quin–C_6), 123.8 (Ar–C_6), 122.4 (Quin–C_5), 120.9 (Ar–C_4), 102.7 (Quin–C_3), 54.7 (CH_2), 47.0 (2C, N–CH_2), 11.7 (2C, CH_3); *m/z* 450.2 $[M+H]^+$.

4.10.65. (7-Chloro-quinolin-4-yl)-(3-diethylaminomethyl-4-methyl-phenyl)-amine 9l. Synthesized from compound **13l** (51 mg, 0.263 mmol) and 4,7-diClQuin (52 mg) in HCl (0.27 mL) and CH_3CN (25 mL) according to general procedure B (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9l** as a white-yellow solid (92 mg, 98% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=151–152 °C; HPLC (C18—10 min) P_{HPLC} 93%, t_R 4.19 min; HPLC (C18—40 min) P_{HPLC} 93%, t_R 14.84 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 13.92 min; ^{1}H NMR ($CDCl_3$) δ 8.45 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 7.97 (1H, d, Quin–H_5, $^3J_{5,6}$=8.9 Hz), 7.95 (1H, d, Quin–H_8, $^4J_{8',6'}$=2.0 Hz), 7.25–7.55 (1H, s large, NH), 7.34 (1H, d, Ar–H_6, $^4J_{6,4}$=2.2 Hz), 7.33 (1H, dd, Quin–H_6, $^3J_{6,5}$=8.9 Hz, $^4J_{6,8}$=2.0 Hz), 7.14 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 7.08 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.2 Hz), 6.85 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.50 (2H, s, CH_2), 2.51 (4H, q, N–CH_2, ^3J=7.2 Hz), 2.34 (3H, s, Ar–CH_3), 1.01 (6H, t, CH_3, ^3J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 151.6 (Quin–C_2), 131.1 (Ar–C_3), 128.4 (Quin–C_8), 125.7 (Quin–C_6), 124.2 (Ar–C_6), 121.9 (Quin–C_5), 121.5 (Ar–C_4), 101.8 (Quin–C_3), 55.3 (CH_2), 47.0 (2C, N–CH_2), 18.8 (Ar–CH_3), 11.7 (2C, CH_3); *m/z* 354.3–356.3 $[M+H]^+$.

4.10.66. (7-Chloro-quinolin-4-yl)-(3-diethylaminomethyl-4-ethyl-phenyl)-amine 9m. Synthesized from compound **13m** (68 mg, 0.328 mmol) and 4,7-diClQuin (65 mg) in HCl (0.33 mL) and CH_3CN (25 mL) according to general procedure B (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **9m** as a white-yellow solid (117 mg, 97% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=167–168 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.51 min; HPLC (C18—40 min) P_{HPLC} 95%, t_R 15.71 min; HPLC (C4—40 min) P_{HPLC} 99%, t_R 14.88 min; ^{1}H NMR ($CDCl_3$) δ 8.45 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 7.99 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.95 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.40–7.70 (1H, s large, NH), 7.39 (1H, d, Ar–H_6, $^4J_{6,4}$=2.1 Hz), 7.32 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.18 (1H, d, Ar–H_3, $^3J_{3,4}$=7.5 Hz), 7.12 (1H, dd, Ar–H_4, $^3J_{4,3}$=7.5 Hz, $^4J_{4,6}$=2.1 Hz), 6.88 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.53 (2H, s, CH_2), 2.71 (2H, q, Ar–CH_2, ^3J=7.5 Hz), 2.50 (4H, q, N–CH_2, ^3J=7.1 Hz), 1.23 (3H, t, CH_3, ^3J=7.5 Hz), 1.00 (6H, t, CH_3, ^3J=7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 151.4 (Quin–C_2), 129.4 (Ar–C_3), 128.2 (Quin–C_8), 125.6 (Quin–C_6), 124.3 (Ar–C_6), 121.9 (Quin–C_5), 121.6 (Ar–C_4), 101.8 (Quin–C_3), 54.7 (CH_2), 46.9 (2C, N–CH_2), 24.9 (Ar–CH_2), 15.1 (CH_3), 11.7 (2C, CH_3); *m/z* 368.2–370.2 $[M+H]^+$.

4.10.67. (7-Chloro-quinolin-4-yl)-(2-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-amine 10a. Synthesized from compound **14a** (70 mg, 0.277 mmol) and 4,7-diClQuin (55 mg) in HCl (0.28 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10a** as a white solid (105 mg, 91% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=183–184 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.04 min; HPLC (C18—40 min) P_{HPLC} 98%, t_R 17.58 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 16.92 min; ^{1}H NMR ($CDCl_3$) δ 8.45 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 7.91 (1H,

d, Quin–H_5, $^3J_{5,6}$=8.7 Hz), 7.89 (1H, d, Quin–H_8, $^4J_{8,6}$=2.4 Hz), 7.45 (1H, d, Ar–H_6, $^4J_{6,4}$=1.2 Hz), 7.19–7.37 (8H, m, Quin–H_6, Ar–H_4, Ar–H_3, Ph), 7.07 (1H, s large, NH), 6.96 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.51 (2H, s, CH_2), 2.36–2.38 (4H, m, N–CH_2), 1.60–1.64 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 151.3 (Quin–C_2), 130.3 (Ar–C_3), 128.7 (2C, Ph), 128.0 (Quin–C_8), 127.2 (2C, Ph), 126.3 (Ph), 125.2 (Quin–C_6), 122.5 (Ar–C_6), 121.0 (Quin–C_5), 119.9 (Ar–C_4), 101.7 (Quin–C_3), 56.2 (CH_2), 53.1 (2C, N–CH_2), 22.8 (2C, CH_2); *m/z* 414.3–416.3 $[M+H]^+$.

4.10.68. (7-Chloro-quinolin-4-yl)-(4′-methyl-2-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-amine 10b. Synthesized from compound **14b** (95 mg, 0.356 mmol) and 4,7-diClQuin (71 mg) in HCl (0.36 mL) and CH_3CN (25 mL) according to general procedure B (reflux for 4 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10b** as a white solid (143 mg, 94% yield); R_f 0.7 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=174–175 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.33 min; HPLC (C18—40 min) P_{HPLC} 99%, t_R 18.74 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 18.10 min; ^{1}H NMR ($CDCl_3$) δ 8.56 (1H, d, Quin–H_2, $^3J_{2,3}$=5.3 Hz), 8.02 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.91 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.53 (1H, d, Ar–H_6, $^4J_{6,4}$=1.5 Hz), 7.44 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.22–7.30 (6H, m, Ar–H_3, Ar–H_3, Ph), 7.05 (1H, d, Quin–H_3, $^3J_{3,2}$=5.3 Hz), 6.94 (1H, s large, NH), 3.62 (2H, s, CH_2), 2.46–2.49 (4H, m, N–CH_2), 2.42 (3H, s, CH_3), 1.69–1.80 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 152.1 (Quin–C_2), 131.3 (Ar–C_3), 129.6 (2C, Ph), 129.1 (Quin–C_8), 128.9 (2C, Ph), 126.2 (Quin–C_6), 123.5 (Ar–C_6), 121.5 (Quin–C_5), 120.7 (Ar–C_4), 102.6 (Quin–C_3), 57.3 (CH_2), 54.2 (2C, N–CH_2), 23.6 (2C, CH_2), 21.3 (CH_3); *m/z* 428.1–430.1 $[M+H]^+$.

4.10.69. (4′-*tert*-Butyl-2-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-(7-chloro-quinolin-4-yl)-amine 10c. Synthesized from compound **14c** (135 mg, 0.439 mmol) and 4,7-diClQuin (87 mg) in HCl (0.44 mL) and CH_3CN (25 mL) according to general procedure B (reflux for 4 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10c** as a white solid (200 mg, 97% yield); R_f 0.7 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=206–207 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 5.05 min; HPLC (C18—40 min) P_{HPLC} 99%, t_R 21.49 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 20.92 min; ^{1}H NMR ($CDCl_3$) δ 8.57 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.03 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.91 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.54 (1H, d, Ar–H_6, $^4J_{6,4}$=2.0 Hz), 7.42–7.48 (3H, m, Ph, Quin–H_6), 7.24–7.34 (4H, m, Ph, Ar–H_3, Ar–H_4), 7.06 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 6.89 (1H, s large, NH), 3.65 (2H, s, CH_2), 2.49–2.54 (4H, m, N–CH_2), 1.73–1.78 (4H, m, CH_2), 1.39 (9H, s, *t*-Bu); ^{13}C NMR ($CDCl_3$) δ 152.0 (Quin–C_2), 131.2 (Ar–C_3), 129.2 (2C, Ph), 129.0 (Quin–C_8), 126.1 (Quin–C_6), 125.0 (2C, Ph), 123.3 (Ar–C_6), 121.3 (Quin–C_5), 120.5 (Ar–C_4), 102.5 (Quin–C_3), 57.1 (CH_2), 54.0 (2C, N–CH_2), 31.4 (3C, *t*-Bu), 23.5 (2C, CH_2); *m/z* 470.2–472.2 $[M+H]^+$.

4.10.70. (7-Chloro-quinolin-4-yl)-(2-pyrrolidin-1-ylmethyl-4′-trifluoromethyl-biphenyl-4-yl)-amine 10d. Synthesized from compound **14d** (116 mg, 0.361 mmol) and 4,7-diClQuin (72 mg) in HCl (0.36 mL) and CH_3CN (25 mL) according to general procedure B (reflux for 16 h). The residue was purified by TLC (DCM/NH_4OH, 10/0.2) to yield the expected compound **10d** as a white solid (164 mg, 94% yield); R_f 0.3 (DCM/NH_4OH, 10/0.2); mp=203–204 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 5.05 min; HPLC (C18—40 min) P_{HPLC} 98%, t_R 19.67 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 19.46 min; ^{1}H NMR ($CDCl_3$) δ 8.59 (1H, d, Quin–H_2, $^3J_{2,3}$=5.3 Hz), 8.04 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.93 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.69 (2H, d, Ph, ^3J=8.1 Hz), 7.53–7.57 (3H, m, Ph, Ar–H_6), 7.47 (1H, dd, Quin–H_6, $^3J_{6,5}$=9 Hz, $^4J_{6,8}$=2.1 Hz), 7.26–7.30 (2H, m, Ar–H_3, Ar–H_4), 7.08 (1H, d, Quin–H_3, $^3J_{3,2}$=5.3 Hz), 6.93 (1H, s large, NH), 3.56 (2H, s, CH_2), 2.47–2.55 (4H, m, N–CH_2), 1.73–1.79 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 152.1 (Quin–C_2), 131.2 (Ar–C_3), 130.1 (2C, Ph), 129.2 (Quin–C_8), 126.4 (Quin–C_6), 125.2 (2C, Ph), 123.5 (Ar–C_6), 121.5 (Quin–C_5), 120.6 (Ar–C_4), 103.0 (Quin–C_3), 57.4 (CH_2), 54.1 (2C, N–CH_2), 23.7 (2C, CH_2); *m/z* 482.0–484.0 $[M+H]^+$.

4.10.71. (7-Chloro-quinolin-4-yl)-(4′-methoxy-2-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-amine 10e. Synthesized from compound **14e** (66 mg, 0.232 mmol) and 4,7-diClQuin (46 mg) in HCl (0.24 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10e** as a white solid (97 mg, 94% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=160–161 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 4.16 min; HPLC (C18—40 min) P_{HPLC} 98%, t_R 18.03 min; HPLC (C4—40 min) P_{HPLC} 99%, t_R 17.31 min; ^{1}H NMR ($CDCl_3$) δ 8.52 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 7.98–8.01 (2H, m, Quin–H_5, Quin–H_8), 7.52 (1H, s, Ar–H_6), 7.25–7.32 (3H, m, Quin–H_6, Ph), 7.25–7.27 (2H, m, Ar–H_3, Ar–H_4), 7.02 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 6.95 (2H, d, Ph, ^3J=8.7 Hz), 3.86 (3H, s, O–CH_3), 3.63 (2H, s, CH_2), 2.50 (4H, m, N–CH_2), 1.72 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 151.6 (Quin–C_2), 131.1 (Ar–C_3), 130.5 (2C, Ph), 128.4 (Quin–C_8), 125.8 (Quin–C_6), 123.5 (Ar–C_6), 121.8 (Quin–C_5), 120.8 (Ar–C_4), 113.5 (2C, Ph), 102.3 (Quin–C_3), 56.9 (CH_2), 55.2 (CH_3), 53.8 (2C, N–CH_2), 23.3 (2C, CH_2); *m/z* 444.3–446.3 $[M+H]^+$.

4.10.72. 1-[4′-(7-Chloro-quinolin-4-ylamino)-2′-pyrrolidin-1-ylmethyl-biphenyl-4-yl]-ethanone 10f. Synthesized from compound **14f** (102 mg, 0.345 mmol) and 4,7-diClQuin (68 mg) in HCl (0.35 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10f** as a yellow solid (135 mg, 91% yield); R_f 0.5 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=207–208 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.87 min; HPLC (C18—40 min) P_{HPLC} 93%, t_R 17.12 min; HPLC (C4—40 min) P_{HPLC} 99%, t_R 16.33 min; ^{1}H NMR ($CDCl_3$) δ 8.43 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 8.04 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.92 (2H, d, Ph, $^3J_{3',2'}$=8.3 Hz), 7.87 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.54 (1H, d, Ar–H_6, $^4J_{6,4}$=2.0 Hz), 7.41 (2H, d, Ph, $^3J_{2',3'}$=8.3 Hz), 7.33 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.29 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.3 Hz, $^4J_{4,6}$=2.1 Hz), 7.22 (1H, d, Ar–H_3, $^3J_{3,4}$=8.3 Hz), 6.99 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.66 (2H, s, CH_2), 2.54 (3H, s, CO–CH_3), 2.51–2.54 (4H,

m, N–CH_2), 1.66–1.69 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 150.6 (Quin–C_2), 130.3 (Ar–C_3), 129.0 (2C, Ph), 127.5 (2C, Ph), 127.3 (Quin–C_8), 125.1 (Quin–C_6), 122.6 (Ar–C_6), 121.7 (Quin–C_5), 120.2 (Ar–C_4), 101.9 (Quin–C_3), 55.6 (CH_2), 52.9 (2C, N–CH_2), 25.7 (CO–CH_3), 22.4 (2C, CH_2); *m/z* 456.4–458.4 $[M+H]^+$.

4.10.73. (4′-Chloro-2-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-(7-chloro-quinolin-4-yl)-amine 10k. Synthesized from compound **14k** (69 mg, 0.239 mmol) and 4,7-diClQuin (47 mg) in HCl (0.24 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 5 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10k** as a white solid (102 mg, 95% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=194–195 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 4.51 min; HPLC (C18—40 min) P_{HPLC} 94%, t_R 19.14 min; HPLC (C4—40 min) P_{HPLC} 98%, t_R 18.36 min; ^{1}H NMR ($CDCl_3$) δ 8.55 (1H, d, Quin–H_2, $^3J_{2,3}$=5.3 Hz), 8.01 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.96 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.50 (1H, d, Ar–H_6, $^4J_{6,4}$=1.6 Hz), 7.33–7.44 (5H, m, Quin–H_6, Ph), 7.26–7.30 (2H, m, Ar–H_3, Ar–H_4), 7.05 (1H, d, Quin–H_3, $^3J_{3,2}$=5.3 Hz), 3.57 (2H, s, CH_2), 2.46–2.50 (4H, m, N–CH_2), 1.72–1.76 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 151.5 (Quin–C_2), 131.1 (Ar–C_3), 130.9 (2C, Ph), 128.4 (2C, Ph), 128.2 (Quin–C_8), 126.0 (Quin–C_6), 123.5 (Ar–C_6), 122.2 (Quin–C_5), 120.8 (Ar–C_4), 102.5 (Quin–C_3), 56.8 (CH_2), 53.9 (2C, N–CH_2), 23.3 (2C, CH_2); *m/z* 448.2–450.2 $[M+H]^+$.

4.10.74. (7-Chloro-quinolin-4-yl)-(4′-fluoro-2-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-amine 10g. Synthesized from compound **14g** (39 mg, 0.142 mmol) and 4,7-diClQuin (28 mg) in HCl (0.14 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10g** as a white solid (54 mg, 88% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=187–188 °C; HPLC (C18—10 min) P_{HPLC} 97%, t_R 4.13 min; HPLC (C18—40 min) P_{HPLC} 94%, t_R 17.91 min; HPLC (C4—40 min) P_{HPLC} 97%, t_R 17.37 min; ^{1}H NMR ($CDCl_3$) δ 8.57 (1H, d, Quin–H_2, $^3J_{2,3}$=5.3 Hz), 8.03 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.90 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.63 (1H, m, Ar–H_6), 7.46 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.35–7.41 (2H, m, Ph), 7.26–7.29 (2H, m, Ar–H_3, Ar–H_4), 7.08–7.15 (2H, m, Ph), 7.06 (1H, d, Quin–H_3, $^3J_{3,2}$=5.3 Hz), 6.84 (1H, s large, NH), 3.55 (2H, s, CH_2), 2.46–2.48 (4H, m, N–CH_2), 1.73–1.81 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 152.1 (Quin–C_2), 131.3 (2C, Ph), 131.2 (Ar–C_3), 129.2 (Quin–C_8), 126.3 (Quin–C_6), 123.6 (Ar–C_6), 121.4 (Quin–C_5), 120.7 (Ar–C_4), 115.1 (2C, d, Ph, $^2J_{CH,F}$=21.1 Hz), 102.7 (Quin–C_3), 57.5 (CH_2), 54.2 (2C, N–CH_2), 23.7 (2C, CH_2); *m/z* 432.0–434.0 $[M+H]^+$.

4.10.75. (7-Chloro-quinolin-4-yl)-(2-pyrrolidin-1-ylmethyl-4′-thiophen-2-ylbiphenyl-4-yl)-amine 10h. Synthesized from compound **14h** (50 mg, 0.194 mmol) and 4,7-diClQuin (38 mg) in HCl (0.20 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 18 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10h** as an orange solid (73 mg, 90% yield); R_f 0.7 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=135–136 °C; HPLC (C18—10 min) P_{HPLC} 99%, t_R 3.88 min; HPLC (C18—40 min) P_{HPLC} >99%, t_R 12.97 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 10.48 min; ^{1}H NMR ($CDCl_3$) δ 8.52 (1H, d, Quin–H_2, $^3J_{2,3}$=5.1 Hz), 7.99 (1H, d, Quin–H_5, $^3J_{5,6}$=11.1 Hz), 7.98 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.49 (1H, d, Ar–H_6, $^4J_{6,4}$=2.1 Hz), 7.43 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 7.36 (1H, dd, Quin–H_6, $^3J_{6,5}$=11.1 Hz, $^4J_{6,8}$=2.1 Hz), 7.35 (1H, dd, Thio–H_5, $^3J_{5,4}$=5.1 Hz, $^4J_{5,3}$=1.2 Hz), 7.24 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.1 Hz), 7.18 (1H, dd, Thio–H_3, $^3J_{3,4}$=3.6 Hz, $^4J_{3,5}$=1.2 Hz), 7.09 (1H, dd, Thio–H_4, $^3J_{4,3}$=3.6 Hz, $^3J_{4,5}$=5.1 Hz), 7.03 (1H, d, Quin–H_3, $^3J_{3,2}$=5.1 Hz), 3.71 (2H, s, CH_2), 2.54 (4H, m, N–CH_2), 1.68–1.79 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 151.5 (Quin–C_2), 131.8 (Ar–C_3), 128.3 (Quin–C_8), 127.2 (Thio–C_3), 127.1 (Thio–C_4), 125.8 (Quin–C_6), 125.5 (Thio–C_5), 123.4 (Ar–C_6), 121.8 (Quin–C_5), 120.4 (Ar–C_4), 102.6 (Quin–C_3), 57.3 (CH_2), 53.7 (2C, N–CH_2), 23.3 (2C, CH_2); *m/z* 420.2–422.2 $[M+H]^+$.

4.10.76. (7-Chloro-quinolin-4-yl)-(4′-furan-2-yl-2-pyrrolidin-1-ylmethyl-biphenyl-4-yl)-amine 10i. Synthesized from compound **14i** (30 mg, 0.122 mmol) and 4,7-diClQuin (24 mg) in HCl (0.12 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 16 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10i** as an orange solid (47 mg, 94% yield); R_f 0.6 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=66–67 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.64 min; HPLC (C18—40 min) P_{HPLC} >99%, t_R 12.02 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 9.69 min; ^{1}H NMR ($CDCl_3$) δ 8.44 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 7.91 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.89 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.57 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.43 (1H, dd, Fur–H_5, $^3J_{5,4}$=1.8 Hz, $^4J_{5,3}$=0.7 Hz), 7.39 (1H, d, Ar–H_6, $^4J_{6,4}$=2.2 Hz), 7.29 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.19 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.2 Hz), 6.93 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 6.57 (1H, dd, Fur–H_3, $^3J_{3,4}$=3.4 Hz, $^4J_{3,5}$=0.7 Hz), 6.43 (1H, dd, Fur–H_4, $^3J_{4,3}$=3.4 Hz, $^3J_{4,5}$=1.8 Hz), 3.75 (2H, s, CH_2), 2.55 (4H, m, N–CH_2), 1.70–1.73 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 150.6 (Quin–C_2), 140.9 (Fur–C_5), 128.0 (Ar–C_3), 127.5 (Quin–C_8), 125.0 (Quin–C_6), 122. 6 (Ar–C_6), 120.8 (Quin–C_5), 119.6 (Ar–C_4), 110.5 (Fur–C_4), 108.1 (Fur–C_3), 101.7 (Quin–C_3), 56.8 (1C CH_2), 52.9 (2C, N–CH_2), 22.4 (2C, CH_2); *m/z* 404.2–406.2 $[M+H]^+$.

4.10.77. (7-Chloro-quinolin-4-yl)-(4-methyl-3-pyrrolidin-1-ylmethyl-phenyl)-amine 10l. Synthesized from compound **14l** (61 mg, 0.323 mmol) and 4,7-diClQuin (64 mg) in HCl (0.33 mL) and CH_3CN (10 mL) according to general procedure B (reflux for 4 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9/1/0.2) to yield the expected compound **10l** as a white solid (107 mg, 95% yield); R_f 0.4 (DCM/MeOH/NH_4OH, 9.5/0.5/0.2); mp=140–141 °C; HPLC (C18—10 min) P_{HPLC} >99%, t_R 3.56 min; HPLC (C18—40 min) P_{HPLC} 93%, t_R 14.92 min; HPLC (C4—40 min) P_{HPLC} >99%, t_R 13.77 min; ^{1}H NMR ($CDCl_3$) δ 8.35 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 7.93 (1H, d, Quin–H_5, $^3J_{5,6}$=8.9 Hz), 7.87 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.70–7.40 (1H, s large, NH), 7.25 (1H, dd, Quin–H_6, $^3J_{6,5}$=8.9 Hz, $^4J_{6,8}$=2.1 Hz), 7.20 (1H, d, Ar–H_6,

$^4J_{6,4}$=2.1 Hz), 7.09 (1H, d, Ar–H_3, $^3J_{3,4}$=8.1 Hz), 7.04 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.1 Hz, $^4J_{4,6}$=2.1 Hz), 6.76 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.51 (2H, s, CH_2), 2.41–2.48 (4H, m, N–CH_2), 2.28 (3H, s, Ar–CH_3), 1.67–1.74 (4H, m, CH_2); ^{13}C NMR ($CDCl_3$) δ 151.7 (Quin–C_2), 131.3 (Ar–C_3), 128.3 (Quin–C_8), 125.8 (Quin–C_6), 124.4 (Ar–C_6), 122.2 (Quin–C_5), 121.9 (Ar–C_4), 101.9 (Quin–C_3), 57.9 (CH_2), 54.5 (2C, N–CH_2), 23.7 (2C, CH_2), 18.9 (Ar–CH_3); *m/z* 352.3–354.3 $[M+H]^+$.

4.10.78. (7-Chloro-quinolin-4-yl)-(4-ethyl-3-pyrrolidin-1-ylmethyl-phenyl)-amine 10m. Synthesized from compound **14m** (35 mg, 0.170 mmol) and 4,7-diClQuin (34 mg) in HCl (0.17 mL) and CH_3CN (20 mL) according to general procedure B (reflux for 3 h). The residue was purified by TLC (DCM/MeOH/NH_4OH, 9.5/0.5/0.2) to yield the expected compound **10m** as a white-yellow solid (57 mg, 91% yield); R_f 0.7 (AcOEt/MeOH/NH_4OH, 9.5/0.5/0.2); mp=143–144 °C; HPLC (C18—10 min) P_{HPLC} 98%, t_R 3.79 min; HPLC (C18—40 min) P_{HPLC} 94%, t_R 15.77 min; HPLC (C4—40 min) P_{HPLC} 99%, t_R 14.75 min; ^{1}H NMR ($CDCl_3$) δ 8.36 (1H, d, Quin–H_2, $^3J_{2,3}$=5.4 Hz), 7.87 (1H, d, Quin–H_8, $^4J_{8,6}$=2.1 Hz), 7.85 (1H, d, Quin–H_5, $^3J_{5,6}$=9.0 Hz), 7.27 (1H, dd, Quin–H_6, $^3J_{6,5}$=9.0 Hz, $^4J_{6,8}$=2.1 Hz), 7.21 (1H, d, Ar–H_6, $^4J_{6,4}$=2.4 Hz), 7.11 (1H, d, Ar–H_3, $^3J_{3,4}$=8.4 Hz), 7.06 (1H, dd, Ar–H_4, $^3J_{4,3}$=8.4 Hz, $^4J_{4,6}$=2.4 Hz), 6.78 (1H, d, Quin–H_3, $^3J_{3,2}$=5.4 Hz), 3.54 (2H, s, CH_2), 2.63 (2H, q, Ar–CH_2, ^3J=7.5 Hz), 2.38–2.47 (4H, m, N–CH_2), 1.63–1.73 (4H, m, CH_2), 1.14 (3H, t, CH_3, ^3J=7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 153.2 (Quin–C_2), 131.0 (Ar–C_3), 129.6 (Quin–C_8), 127.2 (Quin–C_6), 125.0 (Ar–C_6), 123.0 (Ar–C_4), 122.4 (Quin–C_5), 103.2 (Quin–C_3), 57.9 (CH_2), 55.6 (2C, N–CH_2), 25.9 (Ar–CH_2), 24.6 (2C, CH_2), 16.7 (CH_3); *m/z* 366.2–368.2 $[M+H]^+$.

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