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Synthesis of 4,8-Diarylcinnolines and Quinazolines with Potential Applications in Nonlinear Optics. Diazines. Part 28

V. Gautheron Chapoulaud, N. Plé, A. Turck and G. Quéguiner*

Laboratoire de Chimie Organique Fine et Hétérocyclique, UPRES-A 6014 IRCOF-INSA, B.P. 08, 76131 Mont St Aignan Cedex, France

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Abstract—New 4,8-diarylbenzodiazines have been synthesized using cross-coupling reactions and regioselective metalation at the *peri*-position C_8 of the benzene moiety of various cinnolines and quinazolines. Some of these compounds have been tested to assess their nonlinear optical properties.

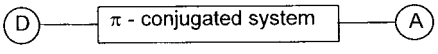
Introduction

For nearly 20 years, nonlinear optics (NLO) and electro-optics (EO) have received growing attention, because of their great importance in opto-electronic technology, e.g. optical telecommunications or computer optical signal processing.[1–9]

Development of more suitable NLO materials is nowadays greatly needed. One of the chosen solutions is the preparation of *organic* NLO components that have already shown numerous advantages compared to commercially available inorganic devices. Some of these advantages are an efficient tailorability and an extremely fast NLO response.[4–9]

The most investigated effects are the second-harmonic generation (SHG) and the Pockels effect. The molecular property responsible for these second-order optical effects is the first-order hyperpolarizability β.

Most of the organic compounds exhibiting high β values are basically dipolar and polarizable materials presenting a π-electronic conjugated system substituted by electron-donating (D) and electron-withdrawing (A) groups that lead to internal charge transfer (CT).



Amino and nitro groups are known to be respectively very strong electron-donating and electron-withdrawing substituents as indicated by their high Hammett σ values. They allow an asymmetric charge distribution, one of the conditions necessary to obtain efficient NLO compounds.[6]

As a matter of fact, famous examples resulting from that concept are *p*-aminonitrobenzene (pNA) and 4-*N*,*N*-dimethylamino-4′-nitrostilbene (DANS).

A polarized π-system can be generated by fusing or linearly connecting heteroaromatic systems of different electron densities. Moreover, the introduction of aromatic rings improves the transparency—nonlinearity trade-off and the thermal stability, these two factors being critical for electro-optical applications.[10–12]

The aromatic moieties investigated in this work are cinnolines and quinazolines disubstituted at the 4 and 8 positions by benzene rings bearing electron-donating or withdrawing groups or other heteroarenes such as thiophene.

In order to perform such a study, we have synthesized and characterized a number of 4,8-diarylcinnolines and quinazolines. The molecular first-order hyperpolarizability β of some of those compounds has been measured by Hyper-Rayleigh Scattering (HRS) in $CHCl_3$ at 1320 nm.

Results

The Pd-catalyzed cross-coupling reactions of arylboronic acids or aryl trialkylstannanes with haloarenes provide highly efficient and flexible methods to synthesize unsymmetrical heterobiaryls.[13–20] We have prepared numerous 4,8-diarylbenzodiazines by selective cross-coupling reactions involving 4-chlorocinnoline or quinazoline as starting materials. Indeed the carbon-chloride bond on diazine moiety is highly polarized thus allowing easy oxidative insertion of Pd(0). The following sequence of reactions is used as a general synthetic route (Scheme 1).

A first cross-coupling reaction under Suzuki conditions of various arylboronic acids with 4-chlorobenzodiazines was

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* Corresponding author. Tel.: +33-2-3552-29-00; fax: +33-2-3552-29-62; e-mail: guy.queguiner@insa-rouen.fr

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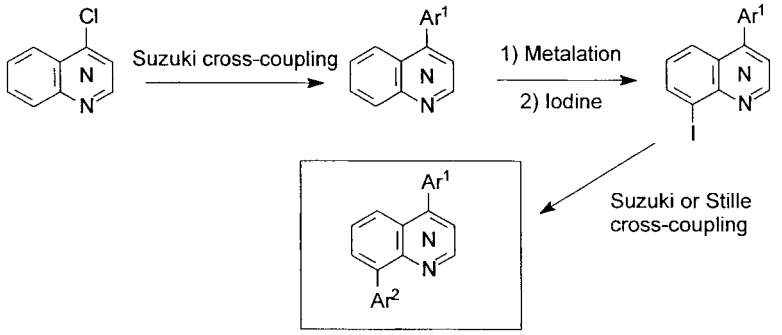
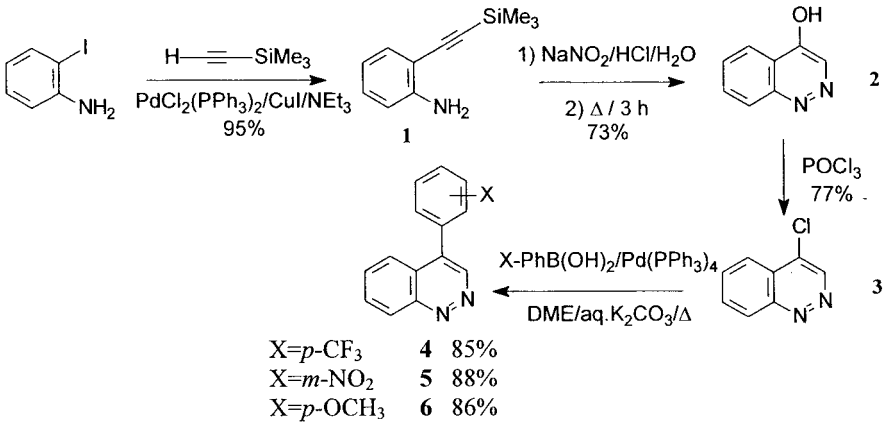


Scheme 1.



Scheme 2.

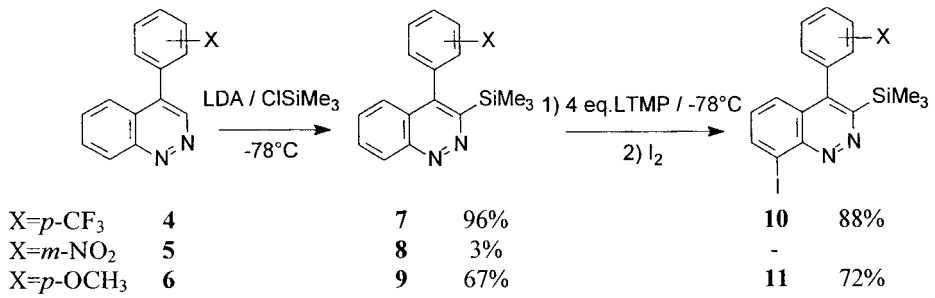
performed and afforded the corresponding 4-aryl derivatives.

In previous papers,[21–23] we have reported the unexpected lithiation and functionalization of the benzene moiety of various benzodiazines and more particularly of cinnolines and quinazolines. In these two cases, the exceptional reactivity towards metalation at the C_8 position, *peri* to the nitrogen atom, enabled us to form 4-aryl-8-lithiobenzodiazines, which were afterwards reacted with iodine to lead to 4-aryl-8-iodobenzodiazines. Another cross-coupling reaction afforded 4,8-diarylbenzodiazines.

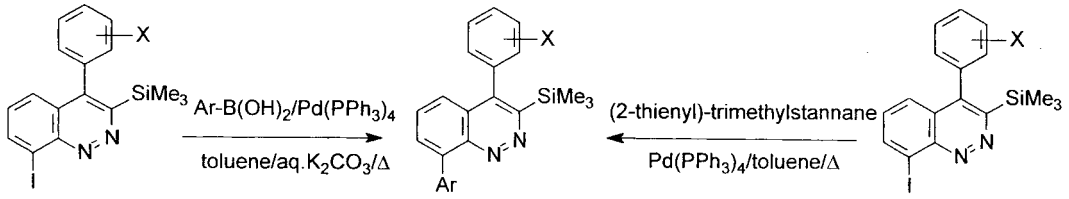
Synthesis of 4,8-diarylcinnolines

The starting 4-chlorocinnoline **3** was obtained by chlorination of the corresponding 4-hydroxycinnoline **2** synthesized in two steps from 2-iodoaniline.[21,24] The cross-coupling reaction was then carried out with various substituted arylboronic acids under Suzuki conditions, affording the related 4-arylcinnolines **4**–**6** in good yields (Scheme 2). This sequence provides a new route to cinnolines substituted at the 4 position by an aryl moiety, the latter being usually difficult to obtain by the standard Widman–Stoermer synthesis.[25,26]

In a previous paper, we have reported that treatment of 4-chlorocinnoline **3** with lithium 2,2,6,6-tetramethylpiperidide (LTMP) followed by reaction with iodine led to a mixture of 4-chloro-3-iodocinnoline and 4-chloro-3,8-diiodocinnoline.[21] This result reveals a higher reactivity towards metalation at C_3 than at C_8. In order to obtain only the monoiodo derivative at the C_8 position, the C_3



Scheme 3.



10	X=*p*-CF_3	Ar=*p*-$CH_3OC_6H_4$	**12**	60%[a]
	X=*p*-CF_3	Ar=*o*-thienyl	**13**	83%
11	X=*p*-OCH_3	Ar=*p*-$CF_3C_6H_4$	**14**	87%
	X=*p*-OCH_3	Ar=*m*-$NO_2C_6H_4$	**15**	72%[a]

(a) 25% of desilylated products **16** and **19** were isolated

10

Scheme 4.

position has to be protected by a substituent that would allow the iodination via metalation and could be easily removed after the cross-coupling reaction. The trimethylsilyl group has been chosen and introduced at the C_3 position by metalation of 4-arylcinnolines.

Treatment of compounds **4**–**6** with 1.1 equivalents of LDA (lithium diisopropylamide) as the metalating agent and trimethylsilyl chloride as the electrophile according to the 'in situ trapping technique'[27] led to compounds **7**–**9** (Scheme 3). Compounds **7** and **9** were obtained with good yields (respectively 96 and 67%) whereas silylation of compound **5** nearly failed. Only 3% of compound **8** was isolated, besides starting material and degradation products. This low yield could be explained by the reaction of the nitro group with the metalating agent to undergo oxido-reduction side reactions.[28,29] A further lithiation of compounds **7** and **9** with LTMP, followed by reaction with iodine, afforded the 8-iodo derivatives **10** (88%) and **11** (72%) (Scheme 3).

Cross-coupling reactions of various arylboronic acids or (2-thienyl)-trimethylstannane with compounds **10** and **11** have been performed, leading to 4,8-diaryl-3-trimethylsilyl-cinnolines **12**–**15** (Scheme 4).

Desilylation of compounds **12**–**15** has been carried out in THF with tetra-*n*-butylammonium fluoride (TBAF) and furnished the expected 4,8-diarylcinnolines **16**–**19** in good yields (66–95%) (Scheme 5).

In summary, 4,8-diarylcinnolines **16**–**19** were synthesized in five steps from 4-chlorocinnoline **3** with overall yields varying from 25 to 58%.

Synthesis of 4,8-diarylquinazolines

Following a similar synthetic route, we have prepared 4,8-diarylquinazolines starting from 4-chloro-6,7-dimethoxyquinazoline **20**.[30] The choice of this derivative was directed by the high reactivity and regioselectivity observed during lithiation at the C_8 position.[23] In this case, the presence of two methoxy groups on the benzene moiety makes it more reactive towards lithiation than the free C_2 position; thus the protection of this position was not needed.

As before, a first cross-coupling reaction of various arylboronic acids carried out with compound **20** afforded the related 4-aryl-6,7-dimethoxyquinazolines **21**–**23** in good yields (86–95%). These compounds were afterwards reacted with lithium alkylamides, then iodine as the electrophile to give 4-aryl-6,7-dimethoxy-8-iodoquinazolines **24** and **25**. It must be pointed out that, as for the related cinnolines, all attempts to lithiate compound **22** have failed, probably because of the presence of a nitro group. In this case, only starting material and degradation products were isolated.

A further cross-coupling reaction under Suzuki or Stille conditions completed the synthesis of 4,8-diaryl-6,7-dimethoxyquinazolines **26**–**30** (81–98%) (Scheme 6).

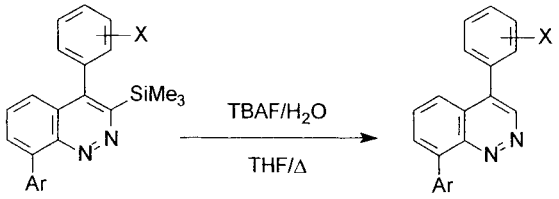
Measurements

The NLO measurements of the $\mu\beta$ values of compounds **14**, **26** and **29** are reported in Table 1. In this scalar product, μ is the ground-state dipole moment and β the vector part of the hyperpolarizability tensor of the molecule.

These preliminary results indicate that 4,8-diarylbenzodiazines have appreciable nonlinear optical properties, the quinazoline derivatives giving better results. Further and complete measurements will be performed with the other compounds.

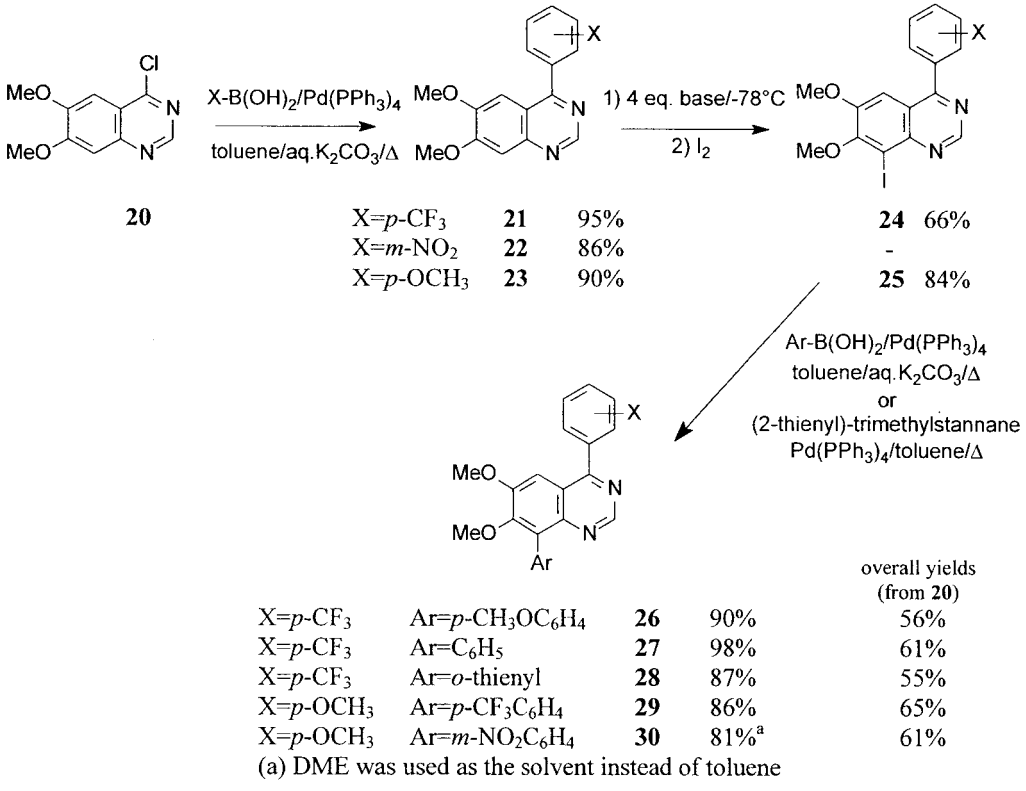
Conclusion

We have synthesized new 4,8-diarylbenzodiazines using cross-coupling reactions. The regioselective functionalization



12	X=*p*-CF_3	Ar=*p*-$CH_3OC_6H_4$	**16**	95%
13	X=*p*-CF_3	Ar=*o*-thienyl	**17**	87%
14	X=*p*-OCH_3	Ar=*p*-$CF_3C_6H_4$	**18**	66%
15	X=*p*-OCH_3	Ar=*m*-$NO_2C_6H_4$	**19**	76%

Scheme 5.



Scheme 6.

Table 1. Longest wavelength absorption maxima λ_{max}, transparency limits $\lambda_{cut\text{-}off}$ in $CHCl_3$ and $\mu\beta$ (HRS measurement at 1320 nm in $CHCl_3$)

Compound	λ_{max} (nm)	$\lambda_{cut\text{-}off}$ (nm)	$\mu\beta\times10^{-48}$ esu	μ (D)[a]
14	355	440	38	7.21
26	350	400	35	3.46
29	360	420	48	5.61

[a] μ Dipolar moment determined by the semi-empirical PM_3 method.

by iodine of the C_8 position of the benzene moiety of various cinnolines and quinazolines has been carried out by the metalation of this *peri* position. The nonlinear optical properties of some of these compounds have been measured and interesting and promising results have been observed. Synthesis of other new diarylbenzodiazines and measurements of their first-order hyperpolarizability β are in progress.

Experimental

Melting points were determined on a Kofler hot-stage. The ^1H, ^{13}C and ^{19}F NMR spectra were recorded in deuterochloroform on a Bruker AC 200 instrument. Microanalyses were performed on a Carlo Erba CHNOS 1160 apparatus. The IR spectra were obtained as potassium bromide pellets with a Perkin–Elmer FTIR 1650 spectrophotometer.

All reagents were of commercial quality and were purchased from Aldrich Chemical Co. or Acros. The Pd(0)-catalyst $Pd(PPh_3)_4$ was prepared according to the literature.[31] 4-Trifluoromethyl- and 4-methoxyphenylboronic acids were synthesized by halogen–metal exchange followed by reaction with trimethylborate from the commercially available 1-bromo-4-trifluoromethylbenzene or 1-bromo-4-methoxybenzene.

Procedure A for direct lithiation by lithium alkylamide (LTMP or LDA)

A solution of *n*-butyllithium (1.6 M or 2.5 M in hexane) was added to cold (−50°C), stirred and anhydrous tetrahydrofuran (15 mL) under an atmosphere of dry argon. Then 2,2,6,6-tetramethylpiperidine (TMPH) or diisopropylamine (DIPAH) was added. The mixture was warmed to 0°C. After 20 min, the temperature was lowered to −78°C and the benzodiazine dissolved in 5 mL of THF was added. After a time t_1 at −78°C, iodine was introduced and stirring was continued for a time t_2 at −78°C. Hydrolysis was then carried out using a solution of 35% aqueous hydrochloric acid, ethanol and tetrahydrofuran (1/4/5). At room temperature, the solution was made slightly basic with saturated sodium hydrogen carbonate solution and decolorized with sodium thiosulphate. After concentration, the residue was extracted with dichloromethane (3×15 mL). The combined organic extracts were dried over magnesium sulphate and evaporated. The crude product was purified by column chromatography on silica gel.

Procedure B for 'in situ trapping' metalation

The benzodiazine dissolved in 5 mL of THF and trimethylsilyl chloride were simultaneously introduced at −78°C into the solution containing the metalating agent (LTMP or LDA) prepared according to procedure A. The mixture

was then stirred for a time t at −78°C. The following steps are similar to procedure A.

General cross-coupling procedure C of arylboronic acid with halobenzodiazine

A mixture of the halobenzodiazine (2 mmol), the arylboronic acid (1.4 equiv.), $Pd(PPh_3)_4$ (0.05 equiv.), aqueous 2 M potassium carbonate (2 equiv.) and ethanol (1 mL) in degassed toluene or dimethoxyethane (15 mL) was heated under reflux and under nitrogen for 15–67 h. The reaction mixture was cooled, diluted with 15 mL of water and dichloromethane (1/1) and the organic layer separated. The aqueous layer was extracted with dichloromethane (3×15 mL), the combined organic extracts were dried over magnesium sulphate and evaporated. The crude product was purified by column chromatography on silica gel.

General cross-coupling procedure D of heteroaryl trialkylstannane with halobenzodiazine

A mixture of the halobenzodiazine (2 mmol), the heteroaryl trialkylstannane (1.2 equiv.) and $Pd(PPh_3)_4$ (0.05 equiv.) in degassed toluene (15 mL) was heated under reflux under nitrogen for 39–48 h. The following steps are similar to procedure C.

4-Chlorocinnoline (3). Into 50 mL of degassed triethylamine were successively introduced cuprous iodide (3.13 g, 0.36 equiv.), trimethylsilylacetylene (13 mL, 2 equiv.), after 10 min of stirring bis(triphenylphosphine) palladium dichloride (300 mg, 0.007 equiv.) and finally after 30 min of stirring, amino-2-iodobenzene (10 g, 45.6 mmol). The mixture was heated under reflux for 24 h, cooled and filtered. The filtrate was dried over magnesium sulphate and evaporated. Purification by column chromatography (silica gel, eluent: dichloromethane/petroleum ether (4/6)) afforded 8.15 g (95%) of (2′-aminophenyl)trimethylsilylacetylene **1** as a colorless oil; ^{1}H NMR ($CDCl_3$): δ 7.31 (d, J=8.2 Hz, 1H, H_3); 7.13 (dd, J=8.2 and 7.5 Hz, 1H); 6.68 (m, 2H, $2H_{arom}$); 4.24 (s, 2H, NH_2); 0.29 (s, 9H, $Si(CH_3)_3$).

To a solution of the amino derivative **1** (2 g, 10.6 mmol) dissolved in 20 mL of water were cautiously added at 0°C 15 mL of a 6N aqueous hydrochloric acid solution, then, dropwise, 5 mL of an aqueous solution of sodium nitrite (1.1 g, 15.9 mmol), keeping the mixture temperature below 0°C. After 30 min, the mixture was heated under reflux for 3 h, cooled then neutralized with saturated aqueous sodium hydrogen carbonate solution. After concentration, the precipitate was filtered and washed with dichloromethane. 4-Hydroxycinnoline **2** (1.1 g, 73%) was obtained as a pale brown solid, mp 234–235°C (lit.[32]: 234°C).

A mixture of 4-hydroxycinnoline **2** (2 g, 13.7 mmol), phosphorus oxychloride (1.94 mL, 20.5 mmol) and anhydrous pyridine (0.33 mL, 4.1 mmol) dissolved in chlorobenzene (50 mL) was refluxed for 1 h. After cooling, concentration and neutralization with saturated aqueous potassium carbonate solution, the mixture was extracted with dichloromethane (3×15 mL). The combined organic layers were dried over magnesium sulphate and evaporated. Purification by flash column chromatography (silica gel, eluent: dichloromethane/ethyl acetate (8/2)) afforded 1.73 g (77%) of **3** as a yellow solid, mp 77–78°C (lit.[18]: 78°C); ^{1}H NMR ($CDCl_3$): δ 9.36 (s, 1H, H_3); 8.56 (d, J=8.3 Hz, 1H, H_8); 8.20 (d, J=7.8 Hz, 1H, H_5); 7.93 (m, 2H, $H_{6,7}$).

4-(4′-Trifluoromethylphenyl)cinnoline (4). Coupling of 4-trifluoromethylphenylboronic acid (1.4 equiv.) with **3** (328 mg, 2 mmol) according to the general procedure C (DME, t=44 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (6/4)) 466 mg (85%) of **4** as a yellow solid, mp 124–125°C; ^{1}H NMR ($CDCl_3$): δ 9.28 (s, 1H, H_3); 8.66 (d, J=8 Hz, 1H, H_8); 7.90 (m, 5H, $5H_{arom}$); 7.74 (m, 2H, $2H_{arom}$); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 3064, 1326, 1108, 770, 611 cm^{-1}. Anal. Calcd for $C_{15}H_9F_3N_2$ (274.24): C, 65.69; N, 10.22; H, 3.31. Found: C, 65.57; N, 10.14; H, 3.29.

4-(3′-Nitrophenyl)cinnoline (5). Coupling of 3-nitrophenylboronic acid (1.4 equiv.) with **3** (328 mg, 2 mmol) according to the general procedure C (DME, t=40 h) gave after purification by column chromatography (silica gel, eluent: dichloromethane/ethyl acetate (8/2)) 442 mg (88%) of **5** as a yellow solid, mp 182–183°C; ^{1}H NMR ($CDCl_3$): δ 9.30 (s, 1H, H_3); 8.69 (d, J=8.3 Hz, 1H, H_8); 8.46 (m, 2H, $2H_{PhNO_2}$); 7.90 (m, 5H, $5H_{arom}$); IR: ν 1523, 1352, 766, 691 cm^{-1}. Anal. Calcd for $C_{14}H_9N_3O_2$ (251.25): C, 66.93; N, 16.72; H, 3.61. Found: C, 66.85; N, 16.68; H, 3.87.

4-(4′-Methoxyphenyl)cinnoline (6). Coupling of 4-methoxyphenylboronic acid (1.4 equiv.) with **3** (328 mg, 2 mmol) according to the general procedure C (DME, t=16 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (5/5)) 406 mg (86%) of **6** as a yellow solid, mp 80–81°C; ^{1}H NMR ($CDCl_3$): δ 9.18 (s, 1H, H_3); 8.51 (d, J=8.4 Hz, 1H, H_8); 7.98 (d, J=8.2 Hz, 1H, H_5); 7.72 (m, 2H, $H_{6/7}$); 7.45 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 7.04 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 3.85 (s, 3H, OCH_3); IR: ν 3020, 1607, 1514, 1492, 1241, 838, 784 cm^{-1}. Anal. Calcd for $C_{15}H_{12}N_2O$ (236.27): C, 76.25; N, 11.86; H, 5.12. Found: C, 75.86; N, 11.67; H, 5.14.

4-(4′-Trifluoromethylphenyl)-3-trimethylsilylcinnoline (7). Metalation of **4** (860 mg, 3.14 mmol) according to procedure B with n-BuLi 1.6 M (1.1 equiv., 2.16 mL), DIPAH (1.2 equiv., 0.49 mL) and trimethylsilyl chloride (1.1 equiv., 0.48 mL), t=2 h, gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (6/4)) 1.04 g (96%) of **7** as a yellow solid, mp 97–98°C; ^{1}H NMR ($CDCl_3$): δ 8.58 (d, J=8.5 Hz, 1H, H_8); 7.82 (m, 3H, $2H_{PhCF_3}+H_{arom}$); 7.65 (td, J=8.5, 6.8 and 1.2 Hz, 1H, H_{arom}); 7.48 (d, J=8 Hz, 2H, $2H_{PhCF_3}$); 7.39 (d, J=8.5 Hz, 1H, H_5); 0.17 (s, 9H, $Si(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 2950, 1325, 1166, 1123, 834, 774, 616 cm^{-1}. Anal. Calcd for $C_{18}H_{17}F_3N_2Si$ (346.43): C, 62.41; N, 8.09; H, 4.95. Found: C, 62.33; N, 8.16; H, 4.67.

4-(3′-Nitrophenyl)-3-trimethylsilylcinnoline (8). Metalation of **5** (1.3 g, 5.18 mmol) according to procedure B

with *n*-BuLi 1.6 M (1.1 equiv., 3.6 mL), DIPAH (1.2 equiv., 0.82 mL) and trimethylsilyl chloride (1.1 equiv., 0.80 mL), t=4 h, gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (5/5)) 52 mg (3%) of **8** as a yellow solid, mp 112–113°C; ^{1}H NMR ($CDCl_3$): δ 8.68 (d, J=8.5 Hz, 1H, H_8); 8.42 (m, 1H, H_{PhNO_2}); 8.25 (m, 1H, H_{PhNO_2}); 7.96–7.66 (m, 4H, $4H_{arom}$); 7.38 (d, J=8.1 Hz, 1H, H_5); 0.17 (s, 9H, $Si(CH_3)_3$); IR: ν 1528, 1354, 841, 761 cm^{-1}. Anal. Calcd for $C_{17}H_{17}N_3O_2Si$ (323.43): C, 63.13; N, 12.99; H, 5.30. Found: C, 63.37; N, 12.76; H, 5.12.

Another fraction afforded 880 mg (68%) of starting material.

4-(4′-Methoxyphenyl)-3-trimethylsilylcinnoline (9). Metalation of **6** (567 mg, 2.40 mmol) according to procedure B with *n*-BuLi 1.6 M (2.2 equiv., 3.30 mL), DIPAH (2.4 equiv., 0.76 mL) and trimethylsilyl chloride (2.2 equiv., 0.68 mL), t=2 h, gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (6/4)) 499 mg (67%) of **9** as a yellow solid, mp 115–116°C; ^{1}H NMR ($CDCl_3$): δ 8.50 (d, J=8.5 Hz, 1H, H_8); 7.77 (m, 1H, H_{arom}); 7.54 (m, 2H, $2H_{arom}$); 7.22 (d, J=8.6 Hz, 2H, $2H_{PhOCH_3}$); 7.04 (d, J=8.6 Hz, 2H, $2H_{PhOCH_3}$); 3.89 (s, 3H, OCH_3); 0.16 (s, 9H, $Si(CH_3)_3$); IR: ν 2954, 1607, 1514, 1248, 888, 834, 772 cm^{-1}. Anal. Calcd for $C_{18}H_{20}N_2OSi$ (308.45): C, 70.09; N, 9.08; H, 6.54. Found: C, 70.15; N, 9.02; H, 6.68.

8-Iodo-4-(4′-trifluoromethylphenyl)-3-trimethylsilylcinnoline (10). Metalation of **7** (154 mg, 0.45 mmol) according to procedure A with *n*-BuLi 1.6 M (4 equiv., 1.12 mL), TMPH (4.1 equiv., 0.31 mL), t_1=1 h, followed by reaction with iodine (2 equiv., 226 mg), t_2=2 h, gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (6/4)) 185 mg (88%) of **10** as a pale yellow solid, mp 179°C (decomp.); ^{1}H NMR ($CDCl_3$): δ 8.45 (dd, J=6 and 2 Hz, 1H, H_7); 7.83 (d, J=8 Hz, 2H, $2H_{PhCF_3}$); 7.47 (d, J=8 Hz, 2H, $2H_{PhCF_3}$); 7.36 (m, 2H, $H_{5/6}$); 0.17 (s, 9H, $Si(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 2960, 1322, 1174, 1131, 1066, 832, 618, 547 cm^{-1}. Anal. Calcd for $C_{18}H_{16}F_3IN_2Si$ (472.32): C, 45.77; N, 5.93; H, 3.41. Found: C, 45.88; N, 5.98; H, 3.56.

8-Iodo-4-(4′-methoxyphenyl)-3-trimethylsilylcinnoline (11). Metalation of **9** (120 mg, 0.39 mmol) according to procedure A with *n*-BuLi 1.6 M (4 equiv., 0.97 mL), TMPH (4.1 equiv., 0.28 mL), t_1=45 min, followed by reaction with iodine (2 equiv., 198 mg), t_2=1 h, gave after purification by column chromatography (silica gel, eluent: dichloromethane) 122 mg (72%) of **11** as a yellow solid, mp 144–145°C; ^{1}H NMR ($CDCl_3$): δ 8.39 (d, J=7.2 Hz, 1H, H_7); 7.51 (d, J=8.5 Hz, 1H, H_5); 7.29 (dd, J=8.5 and 7.2 Hz, 1H, H_6); 7.20 (d, J=8.6 Hz, 2H, $2H_{PhOCH_3}$); 7.04 (d, J=8.6 Hz, 2H, $2H_{PhOCH_3}$); 3.91 (s, 3H, OCH_3); 0.18 (s, 9H, $Si(CH_3)_3$); IR: ν 1605, 1514, 1248, 1024, 835, 773 cm^{-1}. Anal. Calcd for $C_{18}H_{19}IN_2OSi$ (434.35): C, 49.77; N, 6.45; H, 4.41. Found: C, 49.82; N, 6.41; H, 4.40.

8-(4′-Methoxyphenyl)-4-(4′-trifluoromethylphenyl)-3-trimethylsilylcinnoline (12). Coupling of 4-methoxyphenylboronic acid (1.4 equiv.) with **10** (945 mg, 2 mmol) according to the general procedure C (toluene, t=40 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (8/2)) 543 mg (60%) of **12** as a yellow solid, mp 188–189°C; ^{1}H NMR ($CDCl_3$): δ 7.82 (m, 4H, $4H_{PhCF_3}$); 7.68 (m, 1H, H_6); 7.49 (m, 3H, $2H_{PhOCH_3}+H_7$); 7.33 (dd, J=8.4 and 1.3 Hz, 1H, H_5); 7.08 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 3.90 (s, 3H, OCH_3); 0.16 (s, 9H, $Si(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 2956, 1607, 1326, 1248, 1176, 1121, 840 cm^{-1}. Anal. Calcd for $C_{25}H_{23}F_3N_2OSi$ (452.55): C, 66.35; N, 6.19; H, 5.12. Found: C, 66.22; N, 6.02; H, 5.01.

Another fraction afforded 190 mg (25%) of desilylated product **16**.

8-(2′-Thienyl)-4-(4′-trifluoromethylphenyl)-3-trimethylsilylcinnoline (13). Coupling of (2-thienyl)-trimethylstannane (1.2 equiv.) with **10** (945 mg, 2 mmol) according to the general procedure D (toluene, t=48 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (8/2)) 711 mg (83%) of **13** as a yellow solid, mp 161–162°C; ^{1}H NMR ($CDCl_3$): δ 8.14 (d, J=7.6 Hz, 1H, H_7); 7.97 (d, J=3.6 Hz, 1H, $H_{3'thienyl}$); 7.83 (d, J=8.1 Hz, 2H, $2H_{PhCF_3}$); 7.65 (dd, J=8.2 and 7.6 Hz, 1H, H_6); 7.58 (d, J=5.1 Hz, 1H, $H_{5'thienyl}$); 7.50 (d, J=8.1 Hz, 2H, $2H_{PhCF_3}$); 7.26 (m, 2H, $2H_{arom}$); 0.18 (s, 9H, $Si(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 1326, 1122, 833 cm^{-1}. Anal. Calcd for $C_{22}H_{19}F_3N_2SSi$ (428.55): C, 61.66; N, 6.54; H, 4.47; S, 7.48. Found: C, 61.91; N, 6.25; H, 4.53; S, 7.62.

4-(4′-Methoxyphenyl)-8-(4′-trifluoromethylphenyl)-3-trimethylsilylcinnoline (14). Coupling of 4-trifluoromethylphenylboronic acid (1.4 equiv.) with **11** (869 mg, 2 mmol) according to the general procedure C (toluene, t=40 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (6/4)) 787 mg (87%) of **14** as a yellow solid, mp 188–189°C; ^{1}H NMR ($CDCl_3$): δ 7.92 (m, 2H, $2H_{arom}$); 7.69 (m, 5H, $5H_{arom}$); 7.30 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 7.09 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 3.94 (s, 3H, OCH_3); 0.18 (s, 9H, $Si(CH_3)_3$); ^{19}F NMR ($CDCl_3$): δ −62.7; IR: ν 1609, 1516, 1324, 1250, 1123, 837 cm^{-1}. Anal. Calcd for $C_{25}H_{23}F_3N_2OSi$ (452.55): C, 66.35; N, 6.19; H, 5.12. Found: C, 66.63; N, 5.90; H, 5.15.

4-(4′-Methoxyphenyl)-8-(3′-nitrophenyl)-3-trimethylsilylcinnoline (15). Coupling of 3-nitrophenylboronic acid (1.4 equiv.) with **11** (869 mg, 2 mmol) according to the general procedure C (toluene, t=40 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (5/5)) 619 mg (72%) of **15** as an orange solid, mp 115–116°C; ^{1}H NMR ($CDCl_3$): δ 8.61 (s, 1H, H_{PhNO_2}); 8.32 (d, J=8.2 Hz, 1H, H_{PhNO_2}); 8.20 (d, J=7.7 Hz, 1H, H_7); 7.82 (m, 1H, H_{arom}); 7.62 (m, 3H, $3H_{arom}$); 7.28 (d, J=8.6 Hz, 2H, $2H_{PhOCH_3}$); 7.09 (d, J=8.6 Hz, 2H, $2H_{PhOCH_3}$); 3.94 (s, 3H, OCH_3); 0.18 (s, 9H, $Si(CH_3)_3$); IR: ν 1526, 1350, 1249, 839, 740 cm^{-1}. Anal. Calcd for $C_{24}H_{23}N_3O_3Si$ (429.55): C, 67.11; N, 9.78; H, 5.40. Found: C, 67.18; N, 9.67; H, 5.42.

Another fraction afforded 179 mg (25%) of desilylated product **19**.

8-(4′-Methoxyphenyl)-4-(4′-trifluoromethylphenyl)cinnoline (16). TBAF (1 M in THF, excess, 2 mL) and H_2O (1 mL) were added to **12** (120 mg, 0.27 mmol) dissolved in 10 mL of THF. The mixture was then gently refluxed for 22 h, cooled and diluted with 10 mL of water. After separation of the organic layer, the aqueous layer was extracted with dichloromethane (3×20 mL). The combined organic layers were dried over magnesium sulphate and concentrated. Purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (6/4)) afforded 96 mg (95%) of **16** as a yellow solid, mp 221–222°C; ^{1}H NMR ($CDCl_3$): δ 9.28 (s, 1H, H_3); 7.89–7.70 (m, 9H, $4H_{PhCF_3}+2H_{PhOCH_3}+H_{5/6/7}$); 7.09 (d, J=8.6 Hz, 2H, $2H_{PhOCH_3}$); 3.91 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 55.57 (OCH_3), 113.97, 114.33, 123.19, 123.71, 125.47, 126.10, 126.15, 127.89, 130.46, 130.59, 130.95, 131.06, 131.78, 132.41, 132.48 (Ph and Ar), 144.07 (C-3), 159.92 (Ph or Ar);); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 1606, 1509, 1323, 1246, 1174, 1134, 1067, 851, 829, 789 cm^{-1}. Anal. Calcd for $C_{22}H_{15}F_3N_2O$ (380.37): C, 69.47; N, 7.36; H, 3.97. Found: C, 69.80; N, 7.03; H, 4.17.

8-(2′-Thienyl)-4-(4′-trifluoromethylphenyl)cinnoline (17). TBAF (1 M in THF, 1.2 equiv., 0.7 mL) and H_2O (1 mL) were added to **13** (250 mg, 0.58 mmol) dissolved in 10 mL of THF. The mixture was then gently refluxed for 24 h. The following treatments are similar to compound **16**. Purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (8/2)) afforded 181 mg (87%) of **17** as a yellow solid, mp 191–192°C; ^{1}H NMR ($CDCl_3$): δ 9.30 (s, 1H, H_3); 8.18 (m, 1H, H_{arom}); 7.97–7.59 (m, 8H, $8H_{arom}$); 7.23 (m, 1H, $1H_{arom}$); ^{13}C NMR ($CDCl_3$) δ 123.29, 124.89, 126.34, 126.39, 127.42, 128.80, 129.05, 130.09, 130.71, 132.12, 134.88 (Ph and Ar), 144.72 (C-3); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 1324, 1120, 844, 701 cm^{-1}. Anal. Calcd for $C_{19}H_{11}F_3N_2S$ (356.37): C, 64.04; N, 7.86; H, 3.11; S, 9.00. Found: C, 64.36; N, 7.57; H, 3.11; S, 8.87.

Another fraction gave 33 mg (13%) of starting material.

4-(4′-Methoxyphenyl)-8-(4′-trifluoromethylphenyl)cinnoline (18). TBAF (1 M in THF, 1.7 equiv., 1 mL) and H_2O (1 mL) were added to **14** (260 mg, 0.58 mmol) dissolved in 10 mL of THF. The mixture was then gently refluxed for 24 h. The following treatments are similar to compound **16**. Purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (7/3)) afforded 145 mg (66%) of **18** as a yellow solid, mp 206–207°C; ^{1}H NMR ($CDCl_3$): δ 9.32 (s, 1H, H_3); 8.11 (dd, J=7.6 and 2.2 Hz, 1H, H_7); 7.94–7.77 (m, 6H, $6H_{arom}$); 7.56 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 7.14 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 3.94 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 55.56 (OCH_3), 114.81, 125.74, 125.22, 125.40, 126.57, 130.902, 131.18, 131.44, 131.51, 134.87, 140.55, 142.00 (Ph and Ar), 145.01 (C-3), 148.18, 160.83 (Ph or Ar); ^{19}F NMR ($CDCl_3$): δ −62.8; IR: ν 1602, 1328, 1127, 1111, 1069, 841, 830, 787 cm^{-1}. Anal. Calcd for $C_{22}H_{15}F_3N_2O$ (380.37): C, 69.47; N, 7.36; H, 3.97. Found: C, 69.69; N, 7.14; H, 4.06.

Another fraction gave 89 mg (34%) of starting material.

4-(4′-Methoxyphenyl)-8-(3′-nitrophenyl)cinnoline (19). TBAF (1 M in THF, 3 equiv., 0.8 mL) and H_2O (1 mL) were added to **15** (120 mg, 0.28 mmol) dissolved in 10 mL of THF. The mixture was then gently refluxed for 20 h. The following treatments are similar to compound **16**. Purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (5/5)) afforded 76 mg (76%) of **19** as a yellow solid, mp 205–206°C; ^{1}H NMR ($CDCl_3$): δ 9.34 (s, 1H, H_3); 8.64 (s, 1H, H_{PhNO_2}); 8.34 (d, J=7.8 Hz, 1H, H_{arom}); 8.16 (m, 2H, $2H_{arom}$); 7.88 (m, 2H, $2H_{arom}$); 7.71 (dd, J=8 and 7.8 Hz, 1H, H_{arom}); 7.56 (d, J=8.2 Hz, 2H, $2H_{PhOCH_3}$); 7.15 (d, J=8.2 Hz, 2H, $2H_{PhOCH_3}$); 3.95 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 55.89 (OCH_3), 115.06, 116.07, 123.15, 126.08, 126.63, 129.94, 131.15, 131.46, 131.67, 137.76, 140.25 (Ph and Ar), 145.37 (C-3), 148.35, 161.09, 167.86, 168.04 (Ph and Ar); IR: ν 1608, 1532, 1352, 1250, 837, 787, 700 cm^{-1}. Anal. Calcd for $C_{21}H_{15}N_3O_3$ (357.37): C, 70.58; N, 11.76; H, 4.23. Found: C, 70.73; N, 11.55; H, 4.26.

6,7-Dimethoxy-4-(4′-trifluoromethylphenyl)quinazoline (21). Coupling of 4-trifluoromethylphenylboronic acid (1.4 equiv.) with **20**[27] (450 mg, 2 mmol) according to the general procedure C (toluene, t=40 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (5/5)) 635 mg (95%) of **21** as a white solid, mp 187–188°C; ^{1}H NMR ($CDCl_3$): δ 9.20 (s, 1H, H_2); 7.86 (m, 4H, $4H_{PhCF_3}$); 7.40 (s, 1H, H_{arom}); 7.20 (s, 1H, H_{arom}); 4.08 (s, 3H, OCH_3); 3.91 (s, 3H, OCH_3); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 1617, 1505, 1328, 1140, 1105, 847 cm^{-1}. Anal. Calcd for $C_{17}H_{13}F_3N_2O_2$ (334.30): C, 61.08; N, 8.38; H, 3.92. Found: C, 61.37; N, 8.12; H, 4.22.

6,7-Dimethoxy-4-(3′-nitrophenyl)quinazoline (22). coupling of 3-nitrophenylboronic acid (1.4 equiv.) with **20**[27] (450 mg, 2 mmol) according to the general procedure C (toluene, t=24 h) gave after purification by column chromatography (silica gel, eluent: ethyl acetate/ethanol (9/1)) 535 mg (86%) of **22** as a white solid, mp 234–235°C; ^{1}H NMR ($CDCl_3$): δ 9.24 (s, 1H, H_2); 8.70 (s, 1H, H_{PhNO_2}); 8.44 (d, J=8.4 Hz, 1H, H_{PhNO_2}); 8.17 (d, J=7.8 Hz, 1H, H_{PhNO_2}); 7.79 (dd, J=7.8 and 8.4 Hz, 1H, H_{PhNO_2}); 7.44 (s, 1H, H_{arom}); 7.22 (s, 1H, H_{arom}); 4.11 (s, 3H, OCH_3); 3.93 (s, 3H, OCH_3); IR: ν 1534, 1504, 1349, 1238, 859, 690 cm^{-1}. Anal. Calcd for $C_{16}H_{13}N_3O_4$ (311.30): C, 61.73; N, 13.50; H, 4.21. Found: C, 61.86; N, 13.21; H, 4.40.

6,7-Dimethoxy-4-(4′-methoxyphenyl)quinazoline (23). Coupling of 4-methoxyphenylboronic acid (1.4 equiv.) with **20**[27] (450 mg, 2 mmol) according to the general procedure C (toluene, t=38 h) gave after purification by column chromatography (silica gel, eluent: ethyl acetate) 533 mg (90%) of **23** as a pale yellow solid, mp 144–145°C; ^{1}H NMR ($CDCl_3$): δ 9.12 (s, 1H, H_2); 7.72 (d, J=8.4 Hz, 2H, $2H_{PhOCH_3}$); 7.33, 7.32 (2×s, 2H, $H_{5/8}$); 7.05 (d, J=8.4 Hz, 2H, $2H_{PhOCH_3}$); 4.03 (s, 3H, OCH_3); 3.88, 3.87 (2×s, 6H, 2×OCH_3); IR: ν 1608, 1504, 1258, 1237, 1176, 1137, 1026, 860, 832 cm^{-1}. Anal. Calcd for $C_{17}H_{16}N_2O_3$ (296.33): C, 68.91; N, 9.45; H, 5.44. Found: C, 69.25; N, 9.11; H, 5.46.

6,7-Dimethoxy-8-iodo-4-(4′-trifluoromethylphenyl)quinazoline (24). Metalation of **21** (100 mg, 0.30 mmol) according

to procedure A with *n*-BuLi 1.6 M (4 equiv., 0.75 mL), DIPAH (4.1 equiv., 0.16 mL), t_1=1 h, followed by reaction with iodine (2 equiv., 152 mg), t_2=2 h, gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (6/4)) 91 mg (66%) of **24** as a pale yellow solid, mp 172–173°C; ^{1}H NMR ($CDCl_3$): δ 9.35 (s, 1H, H_2); 7.87 (m, 4H, $4H_{PhCF_3}$); 7.29 (s, 1H, H_5); 3.92 (s, 3H, OCH_3); 3.86 (s, 3H, OCH_3); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 2938, 1323, 1150, 800, 605, 559 cm^{-1}. Anal. Calcd for $C_{17}H_{12}F_3IN_2O_2$ (460.19): C, 44.37; N, 6.09; H, 2.63. Found: C, 44.21; N, 6.21; H, 2.67.

Another fraction gave 18 mg (18%) of starting material.

6,7-Dimethoxy-8-iodo-4-(4′-methoxyphenyl)quinazoline (25). Metalation of **23** (100 mg, 0.34 mmol) according to procedure A with *n*-BuLi 1.6 M (4 equiv., 0.86 mL), TMPH (4.1 equiv., 0.24 mL), t_1=1 h, followed by reaction with iodine (2.5 equiv., 215 mg), t_2=2 h, gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (4/6)) 119 mg (84%) of **25** as a beige solid, mp 154–155°C; ^{1}H NMR ($CDCl_3$): δ 9.30 (s, 1H, H_2); 7.74 (d, J=8.8 Hz, 2H, $2H_{PhOCH_3}$); 7.45 (s, 1H, H_5); 7.08 (d, J=8.8 Hz, 2H, $2H_{PhOCH_3}$); 4.02 (s, 3H, OCH_3); 3.91 (s, 6H, 2×OCH_3); IR: ν 1606, 1474, 1249, 1071, 1034, 798 cm^{-1}. Anal. Calcd for $C_{17}H_{15}IN_2O_3$ (422.22): C, 48.36; N, 6.63; H, 3.58. Found: C, 48.46; N, 6.53; H, 3.82.

6,7-Dimethoxy-8-(4′-methoxyphenyl)-4-(4′-trifluoromethylphenyl)quinazoline (26). Coupling of 4-methoxyphenylboronic acid (1.4 equiv.) with **24** (920 mg, 2 mmol) according to the general procedure C (toluene, t=67 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (6/4)) 793 mg (90%) of **26** as a beige solid, mp 182–183°C; ^{1}H NMR ($CDCl_3$): δ 9.25 (s, 1H, H_2); 7.91 (m, 4H, $4H_{PhCF_3}$); 7.46 (d, J=8.8 Hz, 2H, $2H_{PhOCH_3}$); 7.32 (s, 1H, H_5); 7.08 (d, J=8.8 Hz, 2H, $2H_{PhOCH_3}$); 3.94 (s, 3H, OCH_3); 3.90 (s, 3H, OCH_3); 3.71 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 55.88, 56.43, 61.75 (OCH_3), 106.28, 114.67, 121.28, 123.05, 126.81, 129.071, 130.12, 131.64, 135.92, 137.94, 148.39 (Ph and Ar), 153.39 (C-2), 153.84, 161.58 (Ph and Ar); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 2939, 1465, 1323, 1244, 1159, 1121, 848 cm^{-1}. Anal. Calcd for $C_{24}H_{19}F_3N_2O_3$ (440.42): C, 65.45; N, 6.36; H, 4.35. Found: C, 65.36; N, 6.43; H, 4.36.

6,7-Dimethoxy-8-phenyl-4-(4′-trifluoromethylphenyl)-quinazoline (27). Coupling of phenylboronic acid (1.4 equiv.) with **24** (920 mg, 2 mmol) according to the general procedure C (toluene, t=44 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (8/2)) 804 mg (98%) of **27** as a pale brown solid, mp 167–168°C; ^{1}H NMR ($CDCl_3$): δ 9.25 (s, 1H, H_2); 7.91 (m, 4H, $4H_{PhCF_3}$); 7.52 (m, 5H, $5H_{Ph}$); 7.34 (s, 1H, H_5); 3.95 (s, 3H, OCH_3); 3.72 (s, 3H, OCH_3); ^{19}F NMR ($CDCl_3$): δ −62.9; IR: ν 2938, 1600, 1474, 1407, 1325, 1244, 1113, 852, 815, 753 cm^{-1}. Anal. Calcd for $C_{23}H_{17}F_3N_2O_2$ (410.39): C, 67.31; N, 6.83; H, 4.18. Found: C, 67.08; N, 6.77; H, 4.19.

6,7-Dimethoxy-8-(2′-thienyl)-4-(4′-trifluoromethylphenyl)-quinazoline (28). Coupling of (2-thienyl)-trimethylstannane (1.2 equiv.) with **24** (920 mg, 2 mmol) according to the general procedure D (toluene, t=39 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (8/2)) 725 mg (87%) of **28** as a yellow solid, mp 135–136°C; ^{1}H NMR ($CDCl_3$): δ 9.32 (s, 1H, H_2); 7.89 (m, 4H, $4H_{PhCF_3}$); 7.80 (dd, J=3.6 and J=1 Hz, 1H, $H_{3'thienyl}$); 7.58 (dd, J=5.2 and J=1 Hz, 1H, $H_{5'thienyl}$); 7.28 (s, 1H, H_5); 7.25 (dd, J=5.2 and J=3.6 Hz, 1H, $H_{4'thienyl}$); 3.94 (s, 3H, OCH_3); 3.87 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 56.23, 61.06 (OCH_3), 103.87, 120.93, 125.87, 125.92, 126.73, 127.91, 130.19, 130.95, 141.49, 146.68 (Ph and Ar), 153.05 (C-2), 153.82, 163.7 (Ph and Ar); ^{19}F NMR ($CDCl_3$): δ −63; IR: ν 2944, 1467, 1327, 1167, 1121, 694 cm^{-1}. Anal. Calcd for $C_{21}H_{15}F_3N_2O_2S$ (416.42): C, 60.57; N, 6.73; H, 3.63. Found: C, 60.84; N, 6.46; H, 4.02.

6,7-Dimethoxy-4-(4′-methoxyphenyl)-8-(4′-trifluoromethylphenyl)quinazoline (29). Coupling of 4-trifluoromethylphenylboronic acid (1.4 equiv.) with **25** (844 mg, 2 mmol) according to the general procedure C (toluene, t=52 h) gave after purification by column chromatography (silica gel, eluent: petroleum ether/ethyl acetate (5/5)) 758 mg (86%) of **29** as a beige solid, mp 161–162°C; ^{1}H NMR ($CDCl_3$): δ 9.18 (s, 1H, H_2); 7.81 (d, J=8.8 Hz, 2H, $2H_{PhOCH_3}$); 7.79 (d, J=8.1 Hz, 2H, $2H_{PhCF_3}$); 7.64 (d, J=8.1 Hz, 2H, $2H_{PhCF_3}$); 7.55 (s, 1H, H_5); 7.12 (d, J=8.8 Hz, 2H, $2H_{PhOCH_3}$); 3.97 (s, 3H, OCH_3); 3.93 (s, 3H, OCH_3); 3.74 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 55.87, 56.39, 61.64 (OCH_3), 105.86, 114.63, 125.22, 125.27, 130.45, 131.62, 131.88, 138.14, 145.38 (Ph and Ar), 153.41 (C-2), 153.79, 161.52, 165.96 (Ph and Ar); ^{19}F NMR ($CDCl_3$): δ −62.7; IR: ν 1607, 1474, 1397, 1332, 1114 cm^{-1}. Anal. Calcd for $C_{24}H_{19}F_3N_2O_3$ (440.42): C, 65.45; N, 6.36; H, 4.35. Found: C, 65.75; N, 6.06; H, 4.48.

6,7-Dimethoxy-4-(4′-methoxyphenyl)-8-(3′-nitrophenyl)-quinazoline (30). Coupling of 3-nitrophenylboronic acid (1.4 equiv.) with **25** (844 mg, 2 mmol) according to the general procedure C (DME, t=44 h) gave after purification by column chromatography (silica gel, eluent: dichloromethane/ethyl acetate (7/3)) 676 mg (81%) of **30** as a beige solid, mp 229–230°C; ^{1}H NMR ($CDCl_3$): δ 9.17 (s, 1H, H_2); 8.42 (s, 1H, H_{PhNO_2}); 8.32 (d, J=8.2 Hz, 1H, H_{PhNO_2}); 7.86 (d, J=7.7 Hz, 1H, H_{PhNO_2}); 7.80 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 7.69 (dd, J=8.2 and 7.7 Hz, 1H, H_{PhNO_2}); 7.57 (s, 1H, H_5); 7.13 (d, J=8.7 Hz, 2H, $2H_{PhOCH_3}$); 3.98 (s, 3H, OCH_3); 3.94 (s, 3H, OCH_3); 3.78 (s, 3H, OCH_3); ^{13}C NMR ($CDCl_3$) δ 53.15, 56.36, 61.61 (OCH_3), 95.61, 104.08, 108.87, 126.12, 128.23, 130.41, 131.24, 149.99 (Ph and Ar), 153.59 (C-2); IR: ν 1607, 1528, 1475, 1407, 1348, 1251, 1175, 1036, 812 cm^{-1}. Anal. Calcd for $C_{23}H_{19}N_3O_5$ (417.42): C, 66.18; N, 10.07; H, 4.59. Found: C, 66.55; N, 9.72; H, 4.76.

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