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Palladium-Catalyzed Cross-Coupling of 2-Chloroquinoxaline *N*-Oxides with Arylboronic Acids[‡]

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Keywords: Nitrogen heterocycles / *N*-oxides / Cross-coupling / Phosphane ligands / Density functional calculations

A selection of 2-chloro-substituted *O*-alkylquinoxaline *N*-oxides, easily accessible by the one-step annulation reaction of 4-fluoroaniline with 1,1,2-trichloro-2-nitroethylene and subsequent *O*-alkylation, was arylated at the chloronitrone unit in yields up to 96 %. This first efficient Pd-catalyzed Suzuki–Miyaura reaction of chloroquinoxaline *N*-oxides with arylboronic acids led to new 2-arylquinoxaline *N*-oxides. The scope and limitations of this arylation reaction were investigated, and the role of some sterically demanding boronic acids in the cross-coupling reaction was evaluated by means of DFT calculations. Additionally, the Pd-catalyzed *C*-arylation of the amide unit of selected quinoxalinone derivatives was accomplished.

Introduction

Since the first reported synthesis of quinoxaline in 1884 by O. Hinsberg[1] starting from *o*-phenylenediamine and glyoxal, numerous substituted members of this class of *N*-heterobicycles have been prepared in various ways.[2] Due to the broad spectrum of bioactivities, the quinoxaline *N*-oxides and *N*,*N*′-dioxides in particular became the focus of attention of many scientific groups. A subset of (hetero)-aryl-substituted *N*,*N*′-oxidized quinoxalines has especially promising biological properties. Among them, fluorophenyl-substituted *N*,*N*′-dioxide **1** shows selective antituberculotic activity against *M. tuberculosis* (Figure 1).[3]

Likewise, the phenylated ester derivative **2** inhibits the growth of certain strains of the malaria pathogen *P. falciparum* in micromolar concentrations,[4] whereas the thienyl-bearing *N*,*N*′-dioxide **3** shows good antitrypanosomal properties against the flagellate protozoan *T. cruzi*, which causes the Chagas disease.[5] In addition to their antimicrobial properties, some arylated quinoxaline *N*,*N*′-dioxides even possess antitumor or cancerostatic properties, such as sulfone Q39 (**4**), which is known to inhibit cell proliferation of certain human cancer cell lines at remarkably low concentrations.[6] The 6-chloro-2-(4-chlorophenyl)quinoxaline *N*,*N*′-dioxide (**5**) has been discussed as a hypoxia-selective antitumor agent.[7]

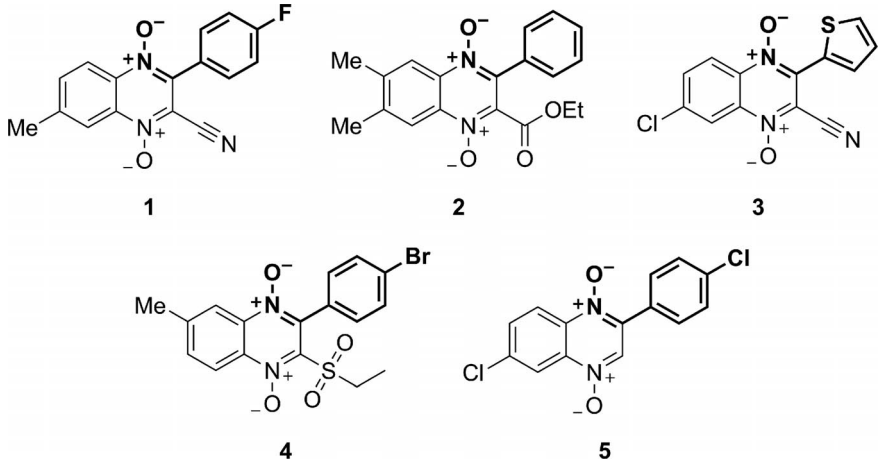

Figure 1. Bioactive aryl-substituted quinoxaline *N*,*N*′-dioxides.

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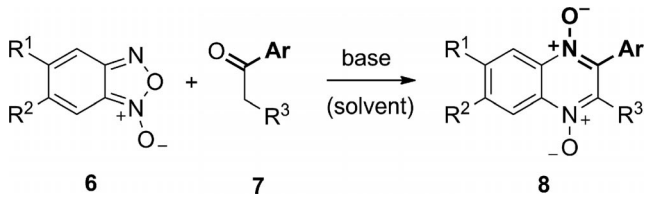
A general and versatile approach for the direct synthesis of aryl- and heteroaryl-substituted *N*,*N*′-dioxidized quinoxalines is the Beirut reaction of benzofurazan *N*-oxides (BFOs) **6** with appropriate nucleophiles, such as CH-acidic carbonyl compounds **7** in the presence of a base (Scheme 1).[8] The BFO derivatives for this reaction can be accessed by oxidation of the corresponding *o*-nitroanilines with sodium hypochlorite,[9] whereas most of the commonly used nucleophiles such as acetophenone (**7**; R^3 = H, Ar = Ph) are commercially available.

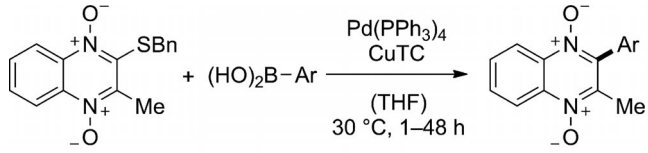


6 **7** **8**

Scheme 1. Beirut reaction for the synthesis of aryl-substituted quinoxaline *N*,*N*′-dioxides.

Among others, mono-*N*-oxidized arylquinoxalines can be accessed through the introduction of an aryl substituent by means of metal-catalyzed C–C coupling reactions. The synthetically most useful arylation reactions have been reported for the unsubstituted quinoxaline *N*-oxide (**9**), which was coupled with aryl chlorides,[10] arylsulfonylhydrazides,[11] sodium sulfinates,[12] aryl tosylates[13] and even non-activated arenes such as benzene[14] through palladium catalysis (Scheme 2).

Recently, Dahbi and Bisseret published a mild method for the palladium-catalyzed cross-coupling of a benzylsulfanyl-substituted quinoxaline *N*,*N*′-dioxide **11** with a broad range of arylboronic acids in the presence of an excess of copper(I) thiophene-2-carboxylate (CuTC) (Scheme 3).[15]

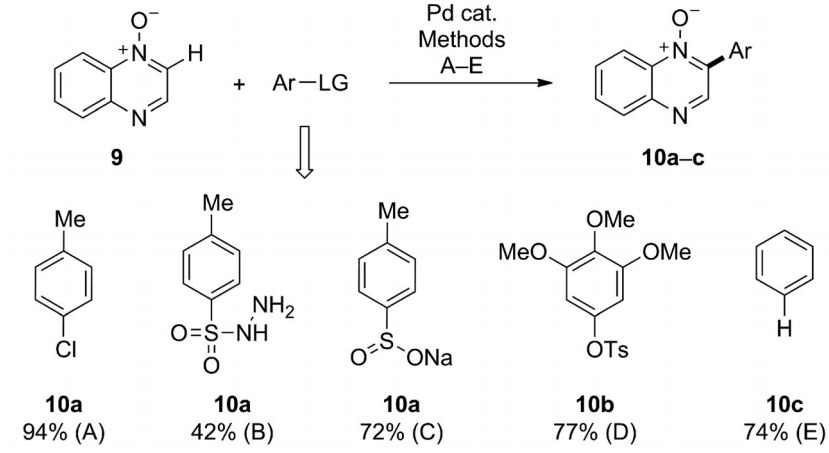


11 **12**

Scheme 3. Palladium-catalyzed cross-coupling of **11** with arylboronic acids.[15]

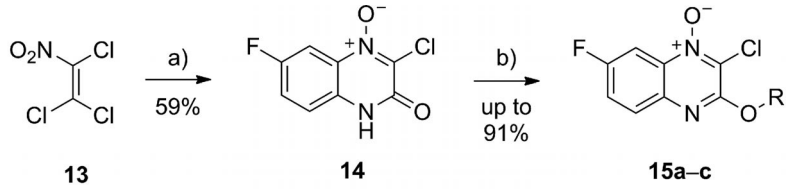
Despite their good results with the cross-coupling of the sulfanyl-substituted derivative **11**, C–C coupling of the analogous 2-chloro-substituted 3-methylquinoxaline-*N*,*N*′-dioxide with tolylboronic acid applying Suzuki–Miyaura conditions was not successful. To the best of our knowledge, the cross-coupling of a chloronitrone unit of quinoxaline *N*-oxides with boronic acids has not been accomplished to date. Therefore, due to our interest in fluorinated bioactive quinoxalines, as described previously, we planned to synthesize 2-chloro-substituted *O*-alkylquinoxaline *N*-oxides such as **15a**–**c** (Scheme 4). We started with the one-step annulation reaction of 4-fluoroaniline with 1,1,2-trichloro-2-nitroethylene (TCNiE, **13**)[16] and subsequent *O*-alkylation of the obtained quinoxalinone *N*-oxide **14** with different alcohols under adapted Mitsunobu conditions.[17]

Because of the easy and reliable synthetic access to the *O*-alkylated quinoxaline *N*-oxides **15a**–**c** and the previously described biological properties of several aryl-substituted *N*-oxides, we investigated the Suzuki–Miyaura reaction of the chloronitrone unit of our 2-chloroquinoxaline *N*-oxides with various arylboronic acids. The combination of this powerful type of cross-coupling reaction together with specially designed phosphine ligands is known to tolerate a broad variety of heterocycles and, additionally, to show wide functional group tolerance.



Reagents and conditions: (A) $Pd(OAc)_2$ (5 mol-%), $P(Cy)_3{\cdot}HBF_4$ (10 mol-%), Cs_2CO_3, (toluene), 130 °C, 24 h; (B) $Pd(OAc)_2$ (5 mol-%), $Cu(OAc)_2$, (1,4-dioxane/DMSO), 120 °C, 24 h; (C) $Pd(OAc)_2$ (5 mol%), TBAB (20 mol-%), $Cu(OAc)_2$, (1,4-dioxane/DMSO), 110 °C, 24 h; (D) $Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%), CsF, (toluene/*t*BuOH), 110 °C, 20 h; (E) $Pd(OAc)_2$, Ag_2CO_3, 130 °C, 16 h

Scheme 2. C–C coupling reactions of unsubstituted quinoxaline *N*-oxide (**9**) with substrates **10a**–**c**.[10–14]

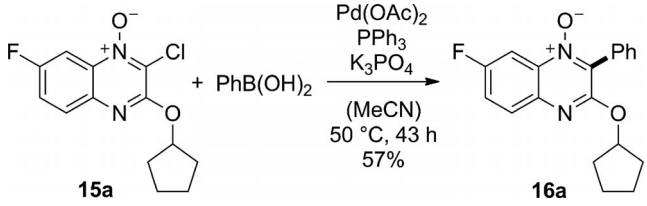


Reagents and conditions: (a) 4-fluoroaniline, NEt_3, (MeOH), 40 °C; (b) ROH, DEAD, PPh_3, (THF), 0 °C to 40 °C, R = cyclopentyl: 91% (**15a**) R = Et: 73% (**15b**), R = *i*Pr: 78% (**15c**).

Scheme 4. Synthesis of fluorinated 2-chloro-substituted *O*-alkylquinoxaline *N*-oxides **15a**–**c** starting from TCNiE (**13**) and 4-fluoroaniline.[17]

Results and Discussion

To establish reaction conditions for this C–C coupling we used 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**) as starting material, because it has good solubility and is easily accessible on a multigram scale with high yields. The first test reaction with phenylboronic acid under Suzuki–Miyaura cross-coupling conditions similar to a procedure developed by Fitzgerald, Liu and Mani[18] [$Pd(OAc)_2$, PPh_3, K_3PO_4, MeCN] allowed the corresponding phenylated *N*-oxide **16a** to be isolated in a promising yield (Scheme 5).



Scheme 5. Palladium-catalyzed cross-coupling of **15a** with phenylboronic acid under Suzuki–Miyaura conditions.

Our initial attempts to optimize the reaction either by increasing the temperature or the amount of base did not prove successful. We then applied a highly active catalyst system developed by Buchwald and Billingsley for the Suzuki–Miyaura cross-coupling of heteroaryl halides with heteroarylboronic acids [$Pd_2(dba)_3$ or $Pd(OAc)_2$, and the biphenyl-based monophosphine ligands SPhos (**17**), XPhos (**18**) or BrettPhos (**19**); Figure 2].[19]

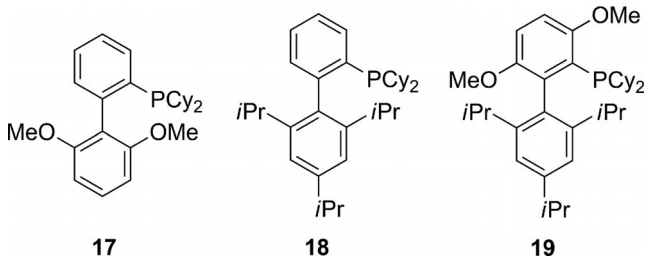


Figure 2. Structures of the biphenyl-based monophosphine ligands SPhos (**17**), XPhos (**18**), and BrettPhos (**19**).

Through the use of this system in a slightly modified procedure [$Pd(OAc)_2$, XPhos, K_3PO_4, 1,4-dioxane and water] at 100 °C, we were able to increase the yield of **16a** to 88% within a considerably shorter reaction time of 4 h.

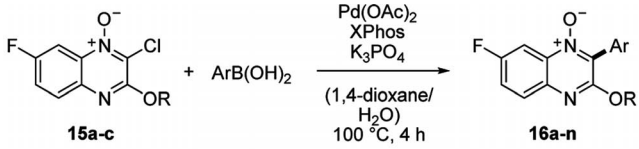
Additionally, we could successfully apply the optimized conditions for the cross-coupling of **15a** with phenylboronic acid to a number of substituted boronic acids and to two other *O*-alkylated quinoxaline *N*-oxides **15b** and **15c**, leading to 14 new arylated *N*-oxides (Table 1).

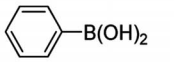
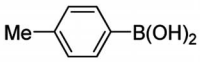
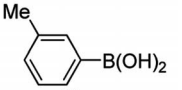
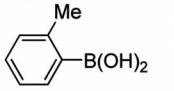
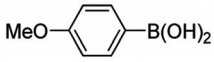
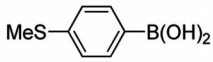
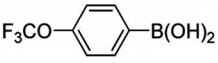
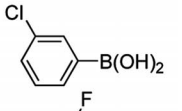
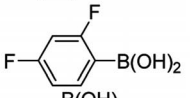
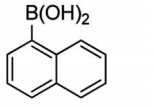
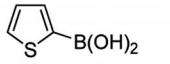
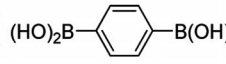
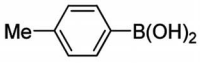
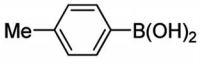
In general, the unsubstituted phenylboronic acid as well as electron-rich substrates such as 4-tolylboronic acid and bicyclic 1-naphthylboronic acid gave the best results for the three selected chloroquinoxaline *N*-oxides **15a**–**c** under the standard coupling conditions with very good yields up to 96%.

In contrast, arylboronic acids with electron-withdrawing substituents such as halogens, especially the (2,4-difluorophenyl)boronic acid, gave the corresponding coupled product **16i** in only poor yield. These arylboronic acids are known to undergo a competitive protodeboronation reaction. In the case of the 3-chlorophenylboronic acid, a consecutive reaction of the resulting product **16h** could be observed when 2.0 equiv. boronic acid was used. This problem was avoided by reducing the amount of the coupling substrate to 1.1 equiv., which led to the formation of the desired product in 60% yield.

Fortunately, the reaction conditions reported here even allowed the twofold cross-coupling of 1,4-phenylene-diboronic acid to give the 1,4-phenylene-bis(quinoxaline *N*-oxide) **16l**. The heterocyclic thienyl-2-boronic acid could also be converted into the corresponding thienyl-substituted *N*-oxide **16k**, but only in moderate yield (34%; a large amount of starting material was reisolated). The yield could be increased to 61% by extending the reaction time (8 h). To further improve the introduction of a thienyl-substituent into the quinoxaline *N*-oxide scaffold we investigated the reaction conditions of the interesting C–C coupling method developed by Burke, Knapp and Gillis, who used stable *N*-methyliminodiacetic acid (MIDA) boronates for the slow release of rather unstable boronic acids such as (2-thienyl)-boronic acid in situ.[20] By applying this procedure, we were able to isolate the thienyl-bearing *N*-oxide **16k** out of the reaction with the MIDA-protected boronate **20**, albeit in

Table 1. Cross-coupling of *O*-alkylated quinoxaline *N*-oxides under Suzuki–Miyaura conditions.[a]

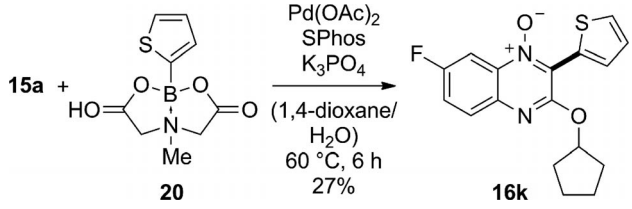


Entry	*N*-oxide	R	$ArB(OH)_2$	Product	Yield [%][b]
1	**15a**	*		**16a**	88
2	**15a**	*		**16b**	96
3	**15a**	*		**16c**	85
4	**15a**	*		**16d**	69
5	**15a**	*		**16e**	82
6	**15a**	*		**16f**	77
7	**15a**	*		**16g**	81
8	**15a**	*		**16h**	60[c]
9	**15a**	*		**16i**	23
10	**15a**	*		**16j**	89
11	**15a**	*		**16k**	34 / 61[d]
12	**15a**	*		**16l**	44[e]
13	**15b**	Et		**16m**	89
14	**15c**	*i*-Pr		**16n**	89

[a] Reaction conditions: $ArB(OH)_2$ (2.0 equiv.), $Pd(OAc)_2$ (5 mol-%), XPhos (10 mol-%), K_3PO_4 (3.0 equiv.). [b] Isolated yield after column chromatography. [c] $ArB(OH)_2$ (1.1 equiv.) was used. [d] Prolonged reaction time of 8 h. [e] Twofold cross-coupling product.

lower yield (27%) than in the reaction with unprotected boronic acid (Scheme 6).

In addition to the successfully used substrates for the cross-coupling reaction of the chloroquinoxaline *N*-oxides **15a**–**c**, some (hetero)arylboronic acids proved to be unsuitable as substrates under the chosen reaction conditions, such as (5-chloropyridin-2-yl)boronic acid or (2,6-dimethylphenyl)boronic acid (Figure 3).



Scheme 6. Cross-coupling of 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline 1-oxide (**15a**) with the MIDA-boronate of thienyl-2-boronic acid **20**.

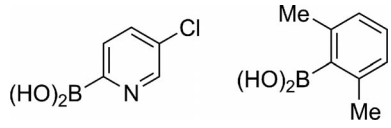


Figure 3. Unsuitable boronic acids for the examined Suzuki–Miyaura coupling reaction of chloroquinoxaline *N*-oxides.

Pyridinylboronic acids are also known to undergo fast competitive protodeboronation. In the case of the dimethylated substrate, the second methyl group in this electron-rich derivative, in comparison to the (2-tolyl)boronic acid used for the synthesis of **16d**, clearly prohibits the cross-coupling (69 vs. 0% yield). In general, Suzuki–Miyaura coupling reactions are known for their efficient formation of bis-*ortho*-substituted biaryls even under standard conditions. Under the applied reaction conditions of this paper, however, cross-coupling of a twofold *ortho*-substituted phenylboronic acid with **15a** did not succeed, although Buchwald et al. had reported the preparation of even tetrakis-*ortho*-substituted biaryls under similar conditions in good yields.[21] It remains unclear which step of the catalytic cycle is responsible for this lack of reaction. Therefore, we decided to study the steric influence of the tolylboronic acids by means of density functional theory (DFT) calculations. Rotational barriers of *ortho*-heteroatom-substituted biphenyls have been calculated this way to determine steric effects.[22] As an indicator of the steric hindrance of the introduced aryl moieties the rotational barriers of these aryl groups around the newly formed C–C bond were calculated (Figure 4).

Whereas the calculated rotational barriers for the 3- and 4-methylphenyl-substituted derivatives **16b** and **16c** are rather low (approximately 20 kJ/mol), the 2-tolyl-bearing *N*-oxide exhibits a considerably higher energy barrier (97 kJ/mol), indicating a certain steric hindrance of this aryl group, thus resulting in a decreased yield of compound **16d** (69%). Moreover, the inaccessible 2,6-dimethylphenyl-substituted *N*-oxide shows the highest rotational barrier (around 160 kJ/mol), which demonstrates the steric demand of this aryl substituent and gives a possible explanation for why the introduction of this group did not succeed. In addition, the calculated structure of this *N*-oxide clearly shows

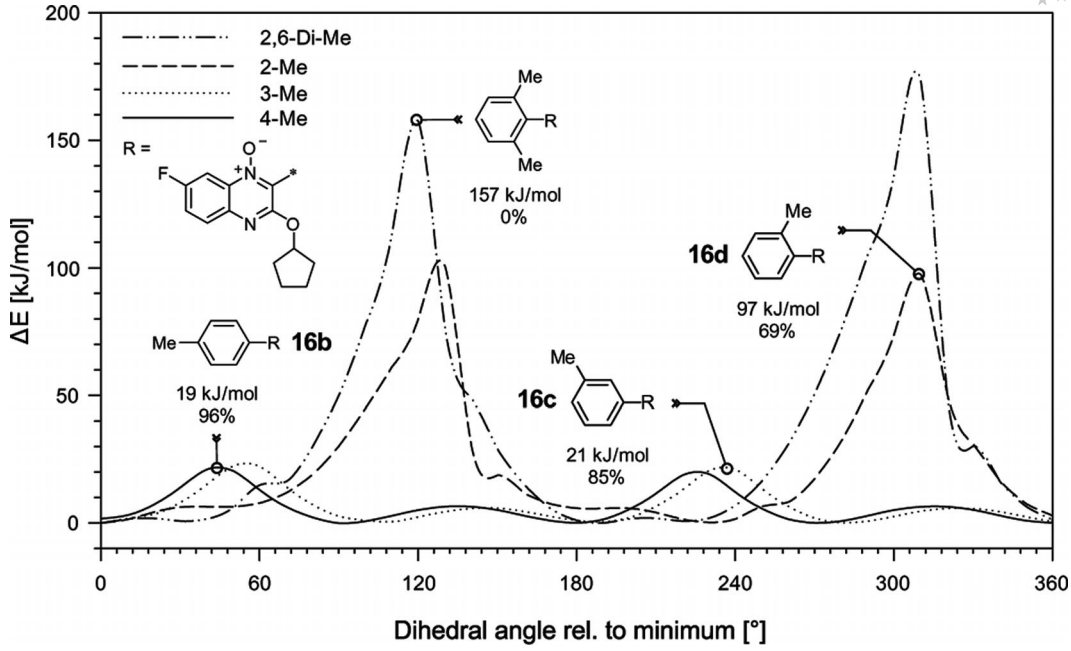


Figure 4. Calculated rotational barriers around the newly formed C–C bond for methylphenyl-substituted *O*-alkylquinoxaline *N*-oxides **16b**–**d** in comparison to the isolated yields (DFT functional: B3LYP, basis set: LACVP*).

the steric hindrance of the two methyl groups in the proximity of both the *N*-oxide moiety and the *O*-alkyl substituent (Figure 5).

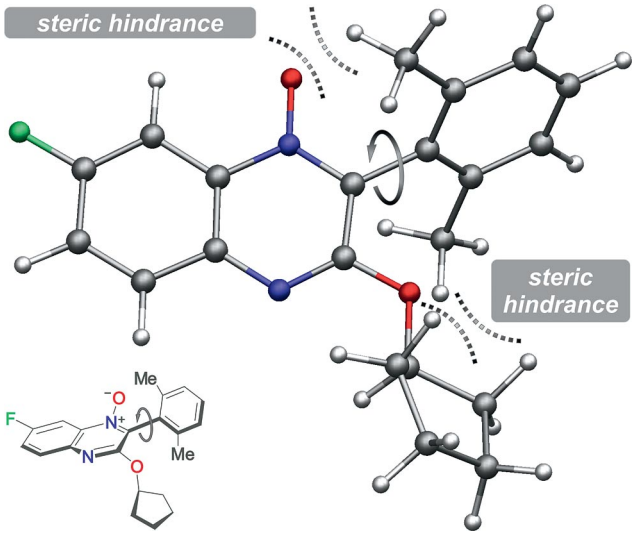
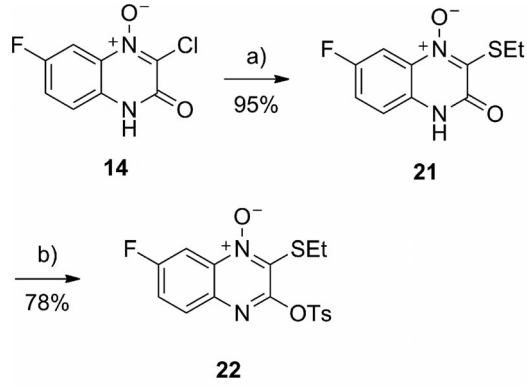


Figure 5. Calculated structure of the inaccessible 2,6-dimethylphenyl-substituted quinoxaline *N*-oxide.

According to a known procedure developed by Buchwald, Bhayana and Fors for the Suzuki–Miyaura coupling of C(sp^2)-tosylates such as 2-(tosyloxy)quinoxaline with hetero(aryl) boronic acids[23] in the presence of a highly efficient catalyst system with BrettPhos (**19**) as ligand, we decided to also investigate the arylation of the amide unit of our compounds after conversion into a tosylate. To avoid the favored cross-coupling reaction at the chloronitrone moiety, the ethylsulfanyl-substituted quinoxalinone *N*-oxide **21**, derived from the previously described reaction of the chlorinated analogue **14** with ethyl mercaptan,[17] was chosen as substrate.

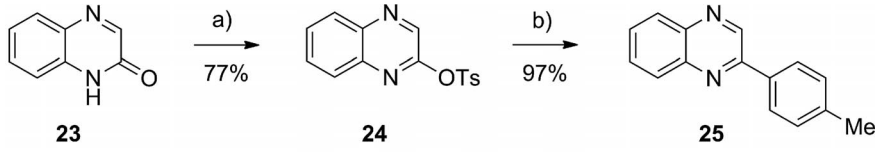
By deprotonation in the presence of sodium hydride and subsequent reaction with *p*-tosyl chloride, the amide could be converted into the corresponding tosylate **22** (Scheme 7).



Reagents and conditions: (a) EtSH, NaOEt, (EtOH), reflux;
(b) i: NaH, (DMF), 0 °C, 30 min; ii: *p*-TsCl, r.t., 1.5 h

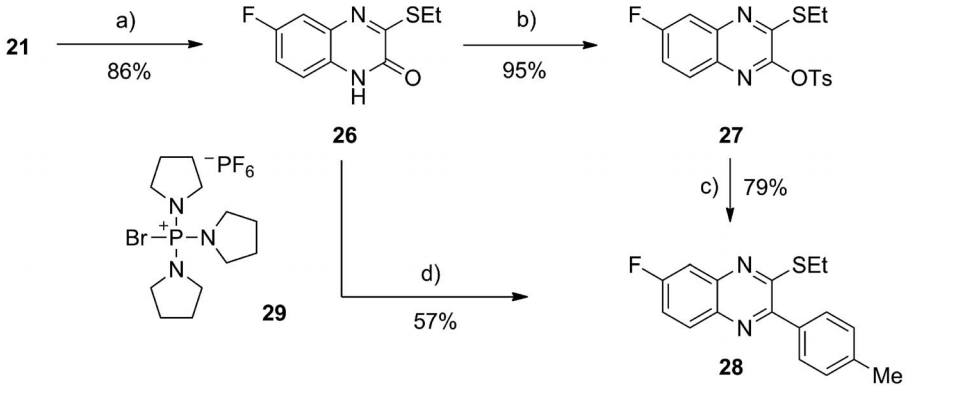
Scheme 7. Synthesis of the 3-(tosyloxy)quinoxaline *N*-oxide **22**.

Unfortunately, tosylate **22** did not react with the selected 4-tolylboronic acid under the conditions described in literature [2.0 equiv. $ArB(OH)_2$, 2 mol-% $Pd(OAc)_2$, 4 mol-% BrettPhos, 3.0 equiv. K_3PO_4, *t*-amyl alcohol or toluene as solvent, 110 °C]. Changing the reaction conditions did not lead to the desired arylated compound, which may be explained by a strong complexation of the palladium catalyst by substrate **22**, which may act as a bidentate ligand (*N*-oxide moiety, ethylsulfanyl substituent) towards the palladium center. Therefore, we decided to validate the reaction



Reagents and conditions: (a) i: NaH, (DMF), 0 °C, 30 min; ii: *p*-TsCl, r.t., 1.5 h; (b) 4-tolylboronic acid, $Pd(OAc)_2$ (4 mol-%), XPhos (8 mol-%), K_3PO_4, (toluene), 100 °C, 4 h

Scheme 8. Cross-coupling reaction of 2-tosyloxyquinoxaline (**24**) with (4-tolyl)boronic acid.



Reagents and conditions: (a) Lawesson's reagent, (THF), 40 °C, 2.5 h; (b) i: NaH, (DMF), 0 °C, 30 min; ii: *p*-TsCl, r.t., 2 h; (c) 4-tolylboronic acid, $Pd(OAc)_2$ (4 mol-%), XPhos (8 mol-%), K_3PO_4, (toluene), 100 °C, 14 h; (d) i: NEt_3, PyBroP **29**, (1,4-dioxane), r.t., 2 h; ii: 4-tolylboronic acid, 5 mol-% $PdCl_2(PPh_3)_2$, Na_2CO_3, H_2O, 100 °C, 4 h

Scheme 9. Cross-coupling reaction of 2-(tosyloxy)quinoxaline **27** with (4-tolyl)boronic acid.

conditions for the cross-coupling reaction of 4-tolylboronic acid with the unsubstituted 2-(*p*-tosyloxy)quinoxaline (**24**), which could be synthesized from 2-quinoxalinone (**23**) in 77% yield (Scheme 8). Under slightly modified conditions with XPhos as the ligand but similar to the procedure developed by Buchwald et al.,[23] we were able to obtain arylated quinoxaline **25** within a short reaction time (4 h) in excellent yield.

As a next step, the unoxidized derivative of tosylate **22** was chosen as a subject. Reduction of **21** was selectively accomplished by the use of Lawesson's reagent in 86% yield. The reduced species **26** was subsequently converted into tosylate **27** in almost quantitative yield (Scheme 9). The reduced tosylate **27** could be efficiently converted into the corresponding arylated fluoroquinoxaline **28** in 79% yield under the same conditions used for the synthesis of 2-(*p*-tolyl)quinoxaline (**25**) but with a prolonged reaction time (14 h). An interesting method for the direct C–C arylation of tautomerizable heterocycles such as 2-quinoxalinone (**23**) was reported by Kang and co-workers.[24] By tautomerizing the C=O bond of the amide unit in the presence of NEt_3 and subsequent reaction with bromo-tris-pyrrolidino phosphoniumhexafluorophosphate (PyBroP, **29**) a heterocyclic phosphonium salt was formed in situ, which was subsequently subjected to Suzuki–Miyaura coupling conditions yielding the unsubstituted tolylquinoxaline **25** in 94% yield.[24] Because of these promising results by Kang et al., we tried to apply the reported conditions to the ethylsulfanyl-substituted quinoxalinone *N*-oxide **21** but, again, the desired arylated product could neither be detected nor isolated, presumably again due to complexation of the palladium catalyst.

Therefore, the reduced fluoroquinoxalinone **26** was used as substrate and, in this case, the tolylated fluoroquinoxaline **28** could be isolated directly in 57% yield (Scheme 9). This experimental result supports the assumed complexation of the palladium catalyst by the quinoxaline *N*-oxides **21** and **22** via the *N*-oxide moiety and the sulfanyl group, which, as a consequence, is responsible for the infeasibility of the cross-coupling reaction of these derivatives under the chosen conditions.

Conclusions

A number of new 2-arylated *O*-alkylquinoxaline *N*-oxides **16a**–**n** were synthesized in yields up to 96% through cross-coupling of the chloronitrone unit of easily accessible quinoxaline *N*-oxides **15a**–**c** with arylboronic acids by employing a modified method of Buchwald et al. with XPhos as the ligand. To the best of our knowledge, this is the first successful Pd-catalyzed cross-coupling reaction of a chloronitrone unit of quinoxaline *N*-oxides with arylboronic acids. Furthermore, the steric influence of some boronic acids was evaluated by means of DFT calculations and compared to the yield of the reaction, giving a possible explanation for

the absence of the coupling reaction in the case of sterically demanding substrates. Additionally, arylation of the amide moiety of the sulfanyl-substituted quinoxalinone *N*-oxide **21** has been investigated. Possibly due to complexation of the palladium catalyst in the presence of both the sulfanyl group and the *N*-oxide moiety, the arylation of the amide function only proceeds when the corresponding reduced species are chosen as substrates.

Experimental Section

General: All chemicals and anhydrous DMF were obtained from commercial suppliers and used without further purification; anhydrous dioxane and toluene were distilled from sodium. TLC was performed on Merck aluminium-backed TLC plates (with silica gel 60 F_{254}) and flash chromatography was carried out on Macherey–Nagel silica gel 60 M (0.040–0.063 mm) with mixtures of petroleum ether (PE) and ethyl acetate (EtOAc) as eluents. The melting points were determined with a differential scanning calorimeter "DSC 6" by Perkin–Elmer. FTIR spectra were taken with a Bruker "Alpha-T" spectrometer (KBr pellets). ATR-IR spectra were measured on the same instrument with a Bruker "Alpha Platinum ATR" single reflection diamond ATR module. All NMR spectra were recorded with a Bruker NMR spectrometer "Avance III 600 MHz" at 25 °C. If not otherwise stated ^{1}H NMR spectra were measured at 600 MHz, and ^{1}H broadband-decoupled ^{13}C NMR and ^{13}C NMR DEPT-135 spectra at 150 MHz using $CDCl_3$ or [D_6]DMSO as solvent. The ^{15}N NMR spectra were measured at 61 MHz with nitromethane as internal standard (δ = 0.0 ppm). Chemical shifts δ are reported in ppm with the solvent residual peak used as the internal reference [$CDCl_3$: 7.26 ppm (^{1}H), 77.0 ppm (^{13}C); [D_6]DMSO: 2.49 ppm (^{1}H), 39.7 ppm (^{13}C)]. Mass spectra were measured with a Varian triple quadrupole mass spectrometer "320 MS" connected to a Varian gas chromatograph "450-GC" through direct exposure probe (DEP) using electronic ionization (EI at 20 or 70 eV). High-resolution mass spectra were recorded with a Waters mass spectrometer "VG Autospec" (EI), with a Waters mass spectrometer "Q-Tof Premier" coupled with a Waters "Acquity UPLC" (ESI) or with a Micromass mass spectrometer "LCT" coupled with a Waters "Alliance 2965 HPLC" (ESI) at the university of Hannover.

All density-functional theory (DFT) calculations were carried out by using the Jaguar 7.7.107 software[25] running on Linux 2.6.18–238.el5 SMP (x86_64) on two AMD Phenom II X6 1090 T processor workstations (Beowulf-cluster) parallelized with OpenMPI. MM2 optimized structures were used as starting geometries. Complete geometry optimizations were carried out on the implemented LACVP* [Hay–Wadt effective core potential (ECP) basis on heavy atoms, N31G6* for all other atoms] basis set and with the B3LYP density functional. All calculated structures were proven to be true minima by the absence of imaginary frequencies. Plots were obtained by using Maestro 9.1.207, the graphical interface of Jaguar. Rotational barriers were calculated fully relaxed, fixing one torsion angle around the rotated bond, and optimizing all remaining degrees of freedom. Torsion angles were modified in steps of 10°.

Synthesis of 2-Aryl-Substituted *O*-Alkylquinoxaline *N*-Oxides 16a–n. General Procedure I: Under a nitrogen atmosphere in an oven-dried Schlenk tube equipped with a cooling finger, 2-chloroquinoxaline *N*-oxide (1.0 equiv.), boronic acid (2.0 equiv.), $Pd(OAc)_2$ (5 mol-%), XPhos (**19**, 10 mol-%) and K_3PO_4 (3.0 equiv.) were added, followed by evacuation of the reaction vessel and backfilling with nitrogen. Anhydrous 1,4-dioxane (4 mL) and degassed distilled water (0.1 mL) were added and the mixture was stirred for 4 h at 100 °C. Upon completion of the reaction, the cooled suspension was diluted with ethyl acetate (10–15 mL) and washed with saturated NaCl solution (5 mL) and water (5 mL). The organic phase was dried with Na_2SO_4 and the solvent was removed with a rotary evaporator. Finally, the obtained residue was purified by column chromatography and dried in vacuo.

3-(Cyclopentyloxy)-7-fluoro-2-phenylquinoxaline *N*-Oxide (16a): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), phenylboronic acid (129 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 20:1; 35 g silica gel) gave **16a** (151 mg, 0.466 mmol, 88%) as a pale-yellow solid; m.p. 76 °C, 299 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3064, 2959, 2872, 1621, 1586, 1552, 1505, 1450, 1427, 1413, 1374, 1341, 1314, 1290, 1278, 1235, 1188, 1158, 1121, 1101, 1074, 1051, 1025, 1001, 988, 972, 958, 951, 905, 890, 852, 825, 789, 770, 744, 722, 713, 691, 666, 637, 617, 583, 554, 508, 417 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.20 (dd, $J_{H,F}$ = 9.0, $J_{H,H}$ = 3.0 Hz, 1 H, 8-*H*), 7.84 (dd, $J_{H,H}$ = 9.2, $J_{H,F}$ = 5.1 Hz, 1 H, 5-*H*), 7.68–7.66 (m, 2 H, 10-*H*, 10′-*H*), 7.52–7.45 (m, 4 H, 6-*H*, 11-*H*, 11′-*H*, 12-*H*), 5.64–5.61 (m, 1 H, 13-*H*), 2.00–1.94 (m, 2 H, 14-*H*, 14′-*H*), 1.81–1.77 (m, 2 H, 14-*H*, 14′-*H*), 1.70–1.58 (m, 4 H, 15-H_2, 15′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 157.2 (o, C3), 137.8 (o, C4a), 134.7 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.7 (o, C2), 130.3 (+, 2 C, C10, C10′), 129.7 (+, C12), 129.6 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 127.9 (+, 2 C, C11, C11′), 127.7 (o, C9), 120.7 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 80.0 (+, C13), 32.6 (–, 2 C, C14, C14′), 23.7 (–, 2 C, C15, C15′) ppm. MS (EI, 70 eV): *m*/*z* (%) = 324 (65) [M]$^+$, 308 (4) [M – O]$^+$, 255 (67), 239 (33), 228 (100), 212 (34), 200 (60), 187 (9), 174 (7), 147 (5), 108 (46). HRMS (EI): *m*/*z* calcd. for $C_{19}H_{17}FN_2O_2$ [M]$^+$ 324.1274; found 324.1272.

3-(Cyclopentyloxy)-7-fluoro-2-(*p*-tolyl)quinoxaline *N*-Oxide (16b): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), (4-tolyl)-boronic acid (144 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 30:1; 35 g silica gel) gave **16b** (173 mg, 0.511 mmol, 96%) as a pale-yellow solid; m.p. 106 °C, 298 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3088, 3035, 2966, 2942, 2923, 2869, 1606, 1589, 1552, 1516, 1499, 1436, 1404, 1370, 1336, 1317, 1308, 1291, 1277, 1234, 1200, 1185, 1122, 1099, 1081, 1042, 1019, 966, 953, 933, 889, 870, 825, 797, 770, 762, 709, 617, 581, 554, 513, 418 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.20 (dd, $J_{H,F}$ = 9.1, $J_{H,H}$ = 2.9 Hz, 1 H, 8-*H*), 7.83 (dd, $J_{H,H}$ = 9.1, $J_{H,F}$ = 5.2 Hz, 1 H, 5-*H*), 7.59 (d, $J_{H,H}$ = 8.1 Hz, 2 H, 10-*H*, 10′-*H*), 7.45 (ddd, $J_{H,H}$ = 8.8, 2.9, $J_{H,F}$ = 8.1 Hz, 1 H, 6-*H*), 7.31 (d, $J_{H,H}$ = 8.1 Hz, 2 H, 11-*H*, 11′-*H*), 5.64–5.61 (m, 1 H, 14-*H*), 2.43 (s, 3 H, 13-H_3), 2.01–1.95 (m, 2 H, 15-*H*, 15′-*H*), 1.82–1.77 (m, 2 H, 15-*H*, 15′-*H*), 1.72–1.66 (m, 2 H, 16-*H*, 16′-*H*), 1.65–1.59 (m, 2 H, 16-*H*, 16′-*H*) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9 (o, d, $^1J_{C,F}$ = 247.6 Hz, C7), 157.2 (o, C3), 139.9 (o, C12), 137.6 (o, C4a), 134.8 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.9 (o, C2), 130.2 (+, 2 C, C10, C10′), 129.5 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 128.6 (+, 2 C, C11, C11′), 124.7 (o, C9), 120.5 (+, d, $^2J_{C,F}$ = 24.2 Hz, C6), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 79.9 (+, C14), 32.7 (–, 2 C, C15, C15′), 23.7 (–, 2 C, C16, C16′), 21.6 (+, C13) ppm. ^{15}N NMR (61 MHz, $CDCl_3$): δ = –83.6 (N1), –133.6 (N4) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (51) [M]$^+$, 322 (14) [M – O]$^+$, 269 (39), 254 (50), 242 (57), 226 (48), 213 (31), 202 (11), 137 (9), 120 (40), 105 (100). HRMS (EI): *m*/*z* calcd. for $C_{20}H_{19}FN_2O_2$ [M]$^+$ 338.1431; found 338.1429.

3-(Cyclopentyloxy)-7-fluoro-2-(*m*-tolyl)quinoxaline *N*-Oxide (16c): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), (3-tolyl)-boronic acid (144 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 15:1; 30 g silica gel) gave **16c** (152 mg, 0.449 mmol, 85%) as a colourless solid; m.p. 75 °C, 308 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3101, 2963, 2922, 2876, 2853, 1618, 1589, 1556, 1503, 1434, 1376, 1339, 1317, 1291, 1278, 1237, 1191, 1174, 1120, 1105, 1088, 1051, 999, 972, 958, 939, 912, 889, 865, 846, 817, 796, 759, 696, 631, 555, 535, 480, 414 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.21–8.19 (m, 1 H, 8-*H*), 7.85–7.83 (m, 1 H, 5-*H*), 7.49–7.48 (m, 1 H, 14-*H*), 7.46 (ddd, $J_{H,H}$ = 9.1, 2.8, $J_{H,F}$ = 7.8 Hz, 1 H, 6-*H*), 7.45–7.43 (m, 1 H, 12-*H*), 7.40–7.37 (m, 1 H, 11-*H*), 7.28–7.27 (m, 1 H, 10-*H*), 5.64–5.61 (m, 1 H, 16-*H*), 2.42 (s, 3 H, 15-H_3), 1.99–1.93 (m, 2 H, 17-*H*, 17′-*H*), 1.82–1.77 (m, 2 H, 17-*H*, 17′-*H*), 1.71–1.59 (m, 4 H, 18-H_2, 18′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 157.2 (o, C3), 137.7 (o, C4a), 137.5 (o, C13), 134.8 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.9 (o, C2), 130.7 (+, C14), 130.5 (+, C10), 129.5 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 127.8 (+, C11), 127.6 (o, C9), 127.3 (+, C12), 120.7 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 80.0 (+, C16), 32.7 (–, 2 C, C17, C17′), 23.7 (–, 2 C, C18, C18′), 21.5 (+, C15) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (42) $[M]^+$, 322 (14) $[M – O]^+$, 270 (73), 254 (68), 241 (100), 226 (85), 213 (68), 202 (33), 149 (9), 137 (12), 108 (63). HRMS (EI): *m*/*z* calcd. for $C_{20}H_{19}FN_2O_2$ $[M]^+$ 338.1431; found 338.1432.

3-(Cyclopentyloxy)-7-fluoro-2-(*o*-tolyl)quinoxaline *N*-Oxide (16d): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), (2-tolyl)-boronic acid (144 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 15:1; 30 g silica gel) gave **16d** (124 mg, 0.366 mmol, 69%) as a colourless solid; m.p. 78 °C, 311 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3111, 3077, 3026, 2971, 2955, 2869, 1626, 1589, 1552, 1505, 1433, 1409, 1384, 1371, 1333, 1313, 1293, 1278, 1235, 1213, 1185, 1164, 1127, 1097, 1051, 1039, 1029, 952, 931, 892, 872, 837, 822, 809, 769, 742, 722, 713, 636, 555, 537, 518, 488, 415 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.21 (dd, $J_{H,F}$ = 9.0, $J_{H,H}$ = 2.8 Hz, 1 H, 8-*H*), 7.88 (dd, $J_{H,H}$ = 9.1, $J_{H,F}$ = 5.2 Hz, 1 H, 5-*H*), 7.49 (ddd, $J_{H,H}$ = 9.1, 2.8, $J_{H,F}$ = 7.9 Hz, 1 H, 6-*H*), 7.40–7.38 (m, 1 H, 12-*H*), 7.35–7.34 (m, 1 H, 13-*H*), 7.32–7.29 (m, 1 H, 11-*H*), 7.24 (dd, $J_{H,H}$ = 7.7, 1.1 Hz, 1 H, 10-*H*), 5.62–5.59 (m, 1 H, 16-*H*), 2.16 (s, 3 H, 15-H_3), 1.97–1.91 (m, 2 H, 17-*H*, 17′-*H*), 1.75–1.69 (m, 2 H, 17-*H*, 17′-*H*), 1.61–1.55 (m, 4 H, 18-H_2, 18′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.8 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 157.6 (o, C3), 138.2 (o, C4a), 137.8 (o, C14), 134.8 (o, C2), 134.7 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 130.1 (+, C13), 129.6 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 129.6 (+, C12), 129.5 (+, C10), 128.0 (o, C9), 125.7 (+, C11), 120.7 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 79.8 (+, C16), 32.7 (–, C17), 32.6 (–, C17′), 23.6 (–, 2 C, C18, C18′), 19.3 (+, C15) ppm. MS (EI, 70 eV): *m*/*z* (%) = 338 (23) $[M]^+$, 323 (48) $[M – CH_3]^+$, 269 (6), 255 (100), 237 (20), 224 (23), 211 (16), 199 (11), 135 (11), 116 (12), 108 (35). HRMS (EI): *m*/*z* calcd. for $C_{20}H_{19}FN_2O_2$ $[M]^+$ 338.1431; found 338.1432.

3-(Cyclopentyloxy)-7-fluoro-2-(4-methoxyphenyl)quinoxaline *N*-Oxide (16e): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), (4-methoxyphenyl)boronic acid (161 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 20:1; 35 g silica gel) gave **16e** (155 mg, 0.437 mmol, 82%) as a pale-yellow solid; m.p. 107 °C, 301 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3097, 3012, 2962, 2941, 2872, 2837, 1608, 1576, 1552, 1516, 1500, 1469, 1439, 1409, 1370, 1341, 1317, 1301, 1287, 1258, 1237, 1184, 1177, 1124, 1098, 1047, 1029, 955, 892, 868, 825, 800, 770, 621, 557, 547, 528, 418 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.20–8.18 (m, 1 H, 8-*H*), 7.83–7.81 (m, 1 H, 5-*H*), 7.72–7.70 (m, 2 H, 10-*H*, 10′-*H*), 7.44 (ddd, $J_{H,H}$ = 9.1, 2.8, $J_{H,F}$ = 7.8 Hz, 1 H, 6-*H*), 7.03–7.00 (m, 2 H, 11-*H*, 11′-*H*), 5.64–5.61 (m, 1 H, 14-*H*), 3.88 (s, 3 H, 13-H_3), 2.01–1.95 (m, 2 H, 15-*H*, 15′-*H*), 1.83–1.78 (m, 2 H, 15-*H*, 15′-*H*), 1.73–1.60 (m, 4 H, 16-H_2, 16′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 160.5 (o, C12), 157.2 (o, C3), 137.4 (o, C4a), 134.8 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.5 (o, C2), 132.1 (+, 2 C, C10, C10′), 129.5 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 120.4 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 119.6 (o, C9), 113.3 (+, 2 C, C11, C11′), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 80.0 (+, C14), 55.3 (+, C13), 32.7 (–, 2 C, C15, C15′), 23.7 (–, 2 C, C16, C16′) ppm. MS (EI, 70 eV): *m*/*z* (%) = 354 (100) $[M]^+$, 338 (18) $[M – O]^+$, 285 (47), 270 (49), 258 (19), 242 (30), 227 (21), 215 (18), 199 (18), 187 (10), 135 (14), 120 (15), 105 (30). HRMS (EI): *m*/*z* calcd. for $C_{20}H_{19}FN_2O_3$ $[M]^+$ 354.1380; found 354.1381.

3-(Cyclopentyloxy)-7-fluoro-2-[4-(methylthio)phenyl]quinoxaline *N*-Oxide (16f): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), 4-(methylthiophenyl)boronic acid (178 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 10:1; 35 g silica gel) gave **16f** (151 mg, 0.408 mmol, 77%) as a yellow solid; m.p. 99 °C, 281 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3099, 3062, 2956, 2935, 2866, 1618, 1591, 1553, 1502, 1434, 1414, 1402, 1370, 1340, 1316, 1290, 1268, 1235, 1184, 1121, 1099, 1042, 1014, 953, 892, 869, 823, 780, 647, 554, 514, 418 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.19 (dd, $J_{H,F}$ = 9.1, $J_{H,H}$ = 2.9 Hz, 1 H, 8-*H*), 7.83 (dd, $J_{H,H}$ = 9.1, $J_{H,F}$ = 5.2 Hz, 1 H, 5-*H*), 7.66–7.64 (m, 2 H, 10-*H*, 10′-*H*), 7.47–7.44 (m, 1 H, 6-*H*), 7.35–7.33 (m, 2 H, 11-*H*, 11′-*H*), 5.64–5.61 (m, 1 H, 14-*H*), 2.54 (s, 3 H, 13-H_3), 2.01–1.95 (m, 2 H, 15-*H*, 15′-*H*), 1.83–1.78 (m, 2 H, 15-*H*, 15′-*H*), 1.72–1.60 (m, 4 H, 16-H_2, 16′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 157.1 (o, C3), 141.1 (o, C12), 137.6 (o, C4a), 134.8 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.2 (o, C2), 130.8 (+, 2 C, C10, C10′), 129.5 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 125.0 (+, 2 C, C11, C11′), 123.9 (o, C9), 120.6 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 80.0 (+, C14), 32.7 (–, 2 C, C15, C15′), 23.7 (–, 2 C, C16, C16′), 15.2 (+, C13) ppm. MS (EI, 70 eV): *m*/*z* (%) = 370 (41) $[M]^+$, 354 (39) $[M – O]^+$, 302 (20), 286 (100), 258 (61), 243 (45), 210 (12), 199 (11), 149 (52), 119 (40), 108 (30). HRMS (EI): *m*/*z* calcd. for $C_{20}H_{19}FN_2O_2S$ $[M]^+$ 370.1151; found 370.1149.

3-(Cyclopentyloxy)-7-fluoro-2-[4-(trifluoromethoxy)phenyl]quinoxaline *N*-Oxide (16g): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), [4-(trifluoromethoxy)phenyl]boronic acid (219 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 15:1; 30 g silica gel) gave **16g** (175 mg, 0.429 mmol, 81%) as an orange solid; m.p. 121 °C, 292 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3099, 3067, 3052, 2968, 2879, 1623, 1606, 1592, 1553, 1512, 1500, 1436, 1410, 1367, 1344, 1313, 1291, 1263, 1228, 1187, 1171, 1158, 1124, 1114, 1098, 1044, 1021, 956, 921, 890, 875, 866, 845, 829, 806, 782, 713, 674, 644, 557, 538, 510, 419 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.18 (dd, $J_{H,F}$ = 9.0, $J_{H,H}$ = 2.8 Hz, 1 H, 8-*H*), 7.85 (dd, $J_{H,H}$ = 9.1, $J_{H,F}$ = 5.2 Hz, 1 H, 5-*H*), 7.77–7.74 (m, 2 H, 10-*H*, 10′-*H*), 7.48 (ddd, $J_{H,H}$ = 9.1, 2.8, $J_{H,F}$ = 7.8 Hz, 1 H, 5-*H*), 7.35–7.33 (m, 2 H, 11-*H*, 11′-*H*), 5.65–5.62 (m, 1 H, 14-*H*), 2.02–1.96 (m, 2 H, 15-*H*, 15′-*H*), 1.81–1.77 (m, 2 H, 15-*H*, 15′-

H), 1.70–1.61 (m, 4 H, 16-H_2, 16′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.0 (o, d, $^1J_{C,F}$ = 249.8 Hz, C7), 156.9 (o, C3), 149.9 (o, C12), 137.9 (o, C4a), 134.7 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 132.4 (o, C2), 132.3 (+, 2 C, C10, C10′), 129.7 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 126.2 (o, C9), 121.0 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 120.4 (o, q, $^1J_{C,F}$ = 258.6 Hz, C13), 120.1 (+, 2 C, C11, C11′), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 80.3 (+, C14), 32.7 (–, 2 C, C15, C15′), 23.7 (–, 2 C, C16, C16′) ppm. MS (EI, 70 eV): *m*/*z* (%) = 408 (45) $[M]^+$, 392 (9) $[M – O]^+$, 339 (99) $[M – CF_3]^+$, 323 (52) $[M – OCF_3]^+$, 312 (51), 296 (45), 284 (18), 255 (31), 243 (18), 227 (23), 215 (45), 199 (27), 189 (29), 161 (9), 149 (9), 108 (100). HRMS (EI): *m*/*z* calcd. for $C_{20}H_{16}F_4N_2O_3$ $[M]^+$ 408.1097; found 408.1096.

2-(3-Chlorophenyl)-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-Oxide (16h): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), (3-chlorophenyl)boronic acid (91 mg, 0.584 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 15:1; 30 g silica gel) gave **16h** (115 mg, 0.321 mmol, 60%) as a colourless solid; m.p. 85 °C, 301 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3108, 3064, 2969, 2953, 2872, 1619, 1593, 1586, 1568, 1552, 1505, 1442, 1402, 1373, 1341, 1334, 1314, 1306, 1290, 1264, 1237, 1191, 1167, 1127, 1107, 1079, 1052, 1034, 998, 985, 978, 956, 935, 908, 898, 879, 845, 826, 806, 787, 770, 749, 719, 689, 667, 641, 535, 418 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.18 (dd, $J_{H,F}$ = 9.0, $J_{H,H}$ = 2.8 Hz, 1 H, 8-*H*), 7.85 (dd, $J_{H,H}$ = 9.1, $J_{H,F}$ = 5.2 Hz, 1 H, 5-*H*), 7.68 (s, 1 H, 14-*H*), 7.59–7.57 (m, 1 H, 10-*H*), 7.50–7.46 (m, 1 H, 6-*H*), 7.45–7.42 (m, 2 H, 11-*H*, 12-*H*), 5.65–5.62 (m, 1 H, 15-*H*), 2.00–1.94 (m, 2 H, 16-*H*, 16′-*H*), 1.82–1.79 (m, 2 H, 16-*H*, 16′-*H*), 1.71–1.61 (m, 4 H, 17-H_2, 17′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.0 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 156.8 (o, C3), 137.9 (o, C4a), 134.7 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.8 (o, C9), 132.3 (o, C2), 130.5 (+, C14), 129.8 (+, C12), 129.7 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 129.4 (o, C13), 129.1 (+, C11), 128.6 (+, C10), 121.1 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 80.3 (+, C15), 32.7 (–, 2 C, C16, C16′), 23.6 (–, 2 C, C17, C17′) ppm. MS (EI, 70 eV): *m*/*z* (%) = 358 (8) $[M]^+$, 342 (2) $[M – O]^+$, 291 (27), 274 (20), 262 (47), 255 (100), 246 (21), 234 (14), 227 (58), 210 (13), 199 (41), 149 (6), 139 (11), 108 (53). HRMS (EI): *m*/*z* calcd. for $C_{19}H_{16}ClFN_2O_2$ $[M]^+$ 358.0884; found 358.0882.

3-(Cyclopentyloxy)-2-(2,4-difluorophenyl)-7-fluoroquinoxaline *N*-Oxide (16i): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), (2,4-difluorophenyl)boronic acid (168 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 30:1; 35 g silica gel) gave **16i** (44 mg, 0.122 mmol, 23%) as a pale-yellow solid; m.p. 108 °C, 180 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3111, 3081, 3064, 2973, 2876, 1618, 1596, 1586, 1556, 1515, 1496, 1436, 1422, 1379, 1340, 1316, 1291, 1271, 1250, 1233, 1188, 1144, 1122, 1108, 1091, 1042, 962, 952, 905, 889, 845, 829, 782, 772, 736, 724, 710, 621, 611, 594, 555, 527, 508, 477, 468, 451, 415 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.18 (dd, $J_{H,F}$ = 9.0, $J_{H,H}$ = 3.0 Hz, 1 H, 8-*H*), 7.87 (dd, $J_{H,H}$ = 9.2, $J_{H,F}$ = 5.1 Hz, 1 H, 5-*H*), 7.54–7.48 (m, 2 H, 6-*H*, 14-*H*), 7.05–7.01 (m, 1 H, 13-*H*), 6.99–6.96 (m, 1 H, 11-*H*), 5.64–5.61 (m, 1 H, 15-*H*), 2.00–1.93 (m, 2 H, 16-*H*, 16′-*H*), 1.81–1.74 (m, 2 H, 16-*H*, 16′-*H*), 1.69–1.58 (m, 4 H, 17-H_2, 17′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.1 (o, dd, $^1J_{C,F}$ = 252.0, $^3J_{C,F}$ = 12.1 Hz, C12), 161.1 (o, dd, $^1J_{C,F}$ = 254.2, $^3J_{C,F}$ = 12.1 Hz, C10), 160.9 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 157.2 (o, C3), 138.4 (o, C4a), 134.6 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 132.8 (+, dd, $^3J_{C,F}$ = 11.0, $^3J_{C,F}$ = 5.0 Hz, C14), 129.8 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 129.0 (o, C2), 121.2 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 112.5 (+, dd, $^2J_{C,F}$ = 15.4, $^4J_{C,F}$ = 3.3 Hz, C9), 111.5 (+, dd, $^2J_{C,F}$ = 22.0, $^4J_{C,F}$ = 3.3 Hz, C13), 104.9 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 104.4 (+, t, $^2J_{C,F}$ = 25.3 Hz, C11), 80.2 (+, C15), 32.7 (–, C16), 32.6 (–, C16′), 23.7 (–, C17), 23.6 (–, C17′) ppm. MS (EI, 70 eV): *m*/*z* (%) = 360 (88) $[M]^+$, 344 (3) $[M – O]^+$, 292 (100), 272 (87), 264 (67), 248 (57), 236 (34), 228 (17), 216 (38), 197 (9), 141 (52), 130 (9), 120 (9), 108 (94). HRMS (EI): *m*/*z* calcd. for $C_{19}H_{15}F_3N_2O_2$ $[M]^+$ 360.1086; found 360.1088.

3-(Cyclopentyloxy)-7-fluoro-2-(naphthalen-1-yl)quinoxaline *N*-Oxide (16j): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), (1-naphthyl)boronic acid (183 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); column chromatography (PE/EtOAc, 10:1, 35 g silica gel) gave **16j** (177 mg, 0.473 mmol, 89%) as a pale-yellow solid; m.p. 138 °C, 283 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3104, 3039, 2958, 2941, 2909, 2869, 1621, 1591, 1552, 1499, 1465, 1434, 1379, 1346, 1311, 1293, 1254, 1230, 1194, 1170, 1121, 1091, 1058, 1044, 1032, 999, 969, 953, 893, 878, 839, 823, 799, 774, 697, 653, 535, 531, 482, 414 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.24 (dd, $J_{H,F}$ = 8.9, $J_{H,H}$ = 2.7 Hz, 1 H, 8-*H*), 8.00 (d, $J_{H,H}$ = 8.2 Hz, 1 H, 12-*H*), 7.95–7.92 (m, 2 H, 5-*H*, 14-*H*), 7.61 (dd, $J_{H,H}$ = 8.2, 7.2 Hz, 1 H, 11-*H*), 7.57–7.55 (m, 1 H, 10-*H*), 7.55–7.50 (m, 2 H, 6-*H*, 15-*H*), 7.45–7.41 (m, 1 H, 16-*H*), 7.34 (dd, $J_{H,H}$ = 8.4, 0.8 Hz, 1 H, 17-*H*), 5.63–5.60 (m, 1 H, 19-*H*), 1.93–1.83 (m, 2 H, 20-*H*, 20′-*H*), 1.71–1.57 (m, 2 H, 20-*H*, 20′-*H*), 1.52–1.38 (m, 4 H, 21-H_2, 21′-H_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 158.0 (o, C3), 138.4 (o, C4a), 134.8 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.7 (o, C2), 133.5 (o, C13), 130.8 (o, C18), 130.2 (+, C12), 129.7 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 128.7 (+, C14), 128.4 (+, C10), 126.6 (+, C16), 126.1 (+, 2 C, C9, C15), 125.2 (+, C11), 124.5 (+, C17), 121.0 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 105.0 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 79.9 (+, C19), 32.6 (–, C20), 32.5 (–, C20′), 23.5 (–, 2 C, C21, C21′) ppm. MS (EI, 70 eV): *m*/*z* (%) = 374 (54) $[M]^+$, 358 (13) $[M – O]^+$, 305 (48), 289 (62), 261 (48), 250 (68), 153 (25), 140 (21), 127 (57), 115 (50), 108 (18). HRMS (ESI): *m*/*z* calcd. for $C_{23}H_{19}FN_2O_2$ $[M + H]^+$ 375.1509; found 375.1509.

3-(Cyclopentyloxy)-7-fluoro-2-(thiophen-2-yl)quinoxaline *N*-Oxide (16k): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), (thiophen-2-yl)boronic acid (136 mg, 1.061 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (338 mg, 1.592 mmol); reaction time: 8 h; column chromatography (PE/EtOAc, 30:1, 35 g silica gel) gave **16k** (106 mg, 0.321 mmol, 60%) as a yellow solid; m.p. 121 °C, 274 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3145, 3094, 3078, 2953, 2868, 1613, 1593, 1553, 1505, 1497, 1470, 1437, 1423, 1403, 1384, 1346, 1311, 1290, 1243, 1228, 1198, 1178, 1124, 1091, 1078, 1067, 1028, 998, 951, 903, 875, 858, 848, 825, 777, 743, 714, 697, 669, 647, 618, 565, 551, 508, 422 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.75 (dd, $J_{H,H}$ = 4.2, 1.0 Hz, 1 H, 12-*H*), 8.24 (dd, $J_{H,F}$ = 9.0, $J_{H,H}$ = 2.9 Hz, 1 H, 8-*H*), 7.80 (dd, $J_{H,H}$ = 9.0, $J_{H,F}$ = 5.3 Hz, 1 H, 5-*H*), 7.67 (dd, $J_{H,H}$ = 5.1, 1.0 Hz, 1 H, 10-*H*), 7.41 (ddd, $J_{H,H}$ = 9.0, 2.9, $J_{H,F}$ = 7.8 Hz, 1 H, 6-*H*), 7.32 (dd, $J_{H,H}$ = 5.1, 4.2 Hz, 1 H, 11-*H*), 5.88–5.85 (m, 1 H, 13-*H*), 2.18–2.12 (m, 2 H, 14-*H*, 14′-*H*), 2.09–2.03 (m, 2 H, 14-*H*, 14′-*H*), 1.96–1.89 (m, 2 H, 15-*H*, 15′-*H*), 1.81–1.74 (m, 2 H, 15-*H*, 15′-*H*) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.2 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 155.2 (o, C3), 134.8 (o, C4a), 133.5 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.3 (+, C12), 130.8 (+, C10), 129.2 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 129.1 (o, C2), 128.8 (o, C9), 126.7 (+, C11), 119.8 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 104.6 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 81.0 (+, C13), 32.9 (–, 2 C, C14, C14′), 24.0 (–, 2 C, C15, C15′) ppm. MS (EI, 70 eV): *m*/*z* (%) = 330 (100) $[M]^+$, 314 (12) $[M – O]^+$, 262 (69), 246

(39), 234 (75), 218 (38), 205 (21), 192 (23), 180 (15), 173 (13), 161 (11), 149 (14), 129 (11), 120 (15), 111 (69). HRMS (EI): *m*/*z* calcd. for $C_{17}H_{15}FN_2O_2S$ $[M]^+$ 330.0838; found 330.0839.

2,2′-(1,4-Phenylene)bis[3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-Oxide] (16l): Following general procedure I: 2-chloro-3-(cyclopentyloxy)-7-fluoroquinoxaline *N*-oxide (**15a**; 150 mg, 0.531 mmol), benzene-1,4-diboronic acid (352 mg, 2.122 mmol), XPhos (25.0 mg, 0.053 mmol), $Pd(OAc)_2$ (6.0 mg, 0.027 mmol) and K_3PO_4 (676 mg, 3.180 mmol); column chromatography (PE/EtOAc, 8:1 → 5:1; 30 g silica gel) gave **16l** (67 mg, 0.117 mmol, 44%) as a pale-yellow solid; m.p. 245 °C, 290 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3102, 2961, 2872, 1623, 1591, 1550, 1500, 1439, 1407, 1366, 1340, 1314, 1296, 1273, 1237, 1185, 1122, 1097, 1036, 955, 868, 836, 820, 783, 553, 528, 418 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.22 (dd, $J_{H,F}$ = 9.0, $J_{H,H}$ = 2.9 Hz, 2 H, 8-*H*, 8′-*H*), 7.87–7.85 (m, 6 H, 5-*H*, 5′-*H*, 10-*H*, 10′-*H*, 10′′-*H*, 10′′′-*H*), 7.48 (ddd, $J_{H,H}$ = 9.1, 2.9, $J_{H,F}$ = 7.8 Hz, 2 H, 6-*H*, 6′-*H*), 5.67–5.65 (m, 2 H, 11-*H*, 11′-*H*), 2.03–1.97 (m, 4 H, 12-*H*, 12′-*H*, 12′′-*H*, 12′′′-*H*), 1.85–1.80 (m, 4 H, 12-*H*, 12′-*H*, 12′′-*H*, 12′′′-*H*), 1.74–1.68 (m, 4 H, 13-*H*, 13′-*H*, 13′′-*H*, 13′′′-*H*), 1.66–1.61 (m, 4 H, 13-*H*, 13′-*H*, 13′′-*H*, 13′′′-*H*) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.0 (o, d, $^1J_{C,F}$ = 249.8 Hz, 2 C, C7, C7′), 157.1 (o, 2 C, C3, C3′), 137.8 (o, 2 C, C4a, C4a′), 134.8 (o, d, $^3J_{C,F}$ = 11.0 Hz, 2 C, C8a, C8a′), 133.1 (o, 2 C, C2, C2′), 130.0 (+, 4 C, C10, C10′, C10′′, C10′′′), 129.6 (+, d, $^3J_{C,F}$ = 8.8 Hz, 2 C, C5, C5′), 129.0 (o, 2 C, C9, C9′), 120.9 (+, d, $^2J_{C,F}$ = 25.3 Hz, 2 C, C6, C6′), 105.0 (+, d, $^2J_{C,F}$ = 27.5 Hz, 2 C, C8, C8′), 80.2 (+, 2 C, C11, C11′), 32.7 (–, 4 C, C12, C12′, C12′′, C12′′′), 23.8 (–, 4 C, C13, C13′, C13′′, C13′′′) ppm. MS (EI, 70 eV): *m*/*z* (%) = 570 (4) $[M]^+$, 554 (8) $[M – O]^+$, 538 (33) $[M – O – O]^+$, 485 (4), 470 (9), 434 (5), 417 (8), 402 (100), 390 (8), 374 (29), 346 (35), 239 (12), 215 (16), 202 (14), 152 (25), 108 (39). HRMS (EI): *m*/*z* calcd. for $C_{32}H_{28}F_2N_4O_4$ $[M]^+$ 570.2079; found 570.2074.

3-Ethoxy-7-fluoro-2-(*p*-tolyl)quinoxaline *N*-Oxide (16m): Following general procedure I: 2-chloro-3-ethoxy-7-fluoroquinoxaline *N*-oxide (**15b**; 150 mg, 0.618 mmol), (4-tolyl)boronic acid (168 mg, 1.236 mmol), XPhos (29.0 mg, 0.062 mmol), $Pd(OAc)_2$ (6.9 mg, 0.031 mmol) and K_3PO_4 (394 mg, 1.855 mmol); column chromatography (PE/EtOAc, 10:1; 35 g silica gel) gave **16m** (165 mg, 0.553 mmol, 89%) as a pale-yellow solid; m.p. 159 °C, 317 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3089, 2992, 2968, 2951, 2903, 1622, 1609, 1593, 1573, 1548, 1518, 1500, 1466, 1436, 1409, 1386, 1370, 1340, 1311, 1291, 1280, 1237, 1187, 1130, 1102, 1074, 1047, 1026, 961, 876, 866, 833, 822, 799, 772, 760, 701, 624, 558, 511, 425 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.20 (dd, $J_{H,F}$ = 9.1, $J_{H,H}$ = 2.9 Hz, 1 H, 8-*H*), 7.84 (dd, $J_{H,H}$ = 9.1, $J_{H,F}$ = 5.2 Hz, 1 H, 5-*H*), 7.61–7.60 (m, 2 H, 10-*H*, 10′-*H*), 7.47 (ddd, $J_{H,H}$ = 9.1, 2.9, $J_{H,F}$ = 7.8 Hz, 1 H, 6-*H*), 7.34–7.32 (m, 2 H, 11-*H*, 11′-*H*), 4.54 (q, $J_{H,H}$ = 7.0 Hz, 2 H, 14-H_2), 2.44 (s, 3 H, 13-H_3), 1.38 (t, $J_{H,H}$ = 7.0 Hz, 3 H, 15-H_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 161.0 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 157.5 (o, C3), 140.0 (o, C12), 137.5 (o, C4a), 135.0 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 133.6 (o, C2), 130.2 (+, 2 C, C10, C10′), 129.5 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 128.8 (+, 2 C, C11, C11′), 124.6 (o, C9), 120.7 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 105.0 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 63.4 (–, C14), 21.6 (+, C13), 14.3 (+, C15) ppm. MS (EI, 70 eV): *m*/*z* (%) = 298 (37) $[M]^+$, 282 (16) $[M – O]^+$, 269 (33) $[M – CH_2CH_3]^+$, 253 (16), 241 (14), 226 (30), 210 (16), 202 (14), 186 (7), 149 (8), 120 (43), 108 (69), 91 (100). HRMS (EI): *m*/*z* calcd. for $C_{17}H_{15}FN_2O_2$ $[M]^+$ 298.1118; found 298.1118.

7-Fluoro-3-isopropoxy-2-(*p*-tolyl)quinoxaline *N*-Oxide (16n): Following general procedure I: 2-chloro-7-fluoro-3-isopropoxyquinoxaline *N*-oxide (**15c**; 150 mg, 0.584 mmol), (4-tolyl)boronic acid (159 mg, 1.169 mmol), XPhos (28.0 mg, 0.058 mmol), $Pd(OAc)_2$ (6.6 mg, 0.029 mmol) and K_3PO_4 (372 mg, 1.753 mmol); column chromatography (PE/EtOAc, 10:1; 30 g silica gel) gave **16n** (163 mg, 0.522 mmol, 89%) as a pale-yellow solid; m.p. 123 °C, 311 °C (dec.). IR (ATR): $\tilde{\nu}$ = 3099, 3039, 2974, 2928, 2874, 2867, 1615, 1607, 1589, 1549, 1516, 1497, 1471, 1464, 1450, 1433, 1407, 1384, 1362, 1340, 1325, 1310, 1290, 1277, 1232, 1186, 1177, 1146, 1119, 1103, 1095, 1041, 1020, 957, 945, 916, 888, 865, 837, 819, 802, 768, 724, 709, 698, 661, 654, 638, 621, 579, 555, 532, 521, 515, 485, 432, 411, 405 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 8.20 (dd, $J_{H,F}$ = 9.1, $J_{H,H}$ = 2.9 Hz, 1 H, 8-*H*), 7.82 (dd, $J_{H,H}$ = 9.1, $J_{H,F}$ = 5.2 Hz, 1 H, 5-*H*), 7.60 (d, $J_{H,H}$ = 8.1 Hz, 2 H, 10-*H*, 10′-*H*), 7.45 (ddd, $J_{H,H}$ = 9.1, 2.9, $J_{H,F}$ = 7.8 Hz, 1 H, 6-*H*), 7.32 (d, $J_{H,H}$ = 8.1 Hz, 2 H, 11-*H*, 11′-*H*), 7.32 (d, $J_{H,H}$ = 8.1 Hz, 2 H, 11-*H*, 11′-*H*), 5.52 (sept, $J_{H,H}$ = 6.2 Hz, 1 H, 14-*H*), 2.44 (s, 3 H, 13-H_3), 1.36 (d, $J_{H,H}$ = 6.2 Hz, 6 H, 15-H_3, 15′-H_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 160.9 (o, d, $^1J_{C,F}$ = 248.7 Hz, C7), 157.1 (o, C3), 139.9 (o, C12), 137.7 (o, C4a), 134.8 (o, d, $^3J_{C,F}$ = 9.9 Hz, C8a), 133.8 (o, C2), 130.4 (+, 2 C, C10, C10′), 129.4 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 128.7 (+, 2 C, C11, C11′), 124.7 (o, C9), 120.6 (+, d, $^2J_{C,F}$ = 24.2 Hz, C6), 105.0 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 70.5 (+, C14), 21.8 (+, C15, C15′), 21.7 (+, C13) ppm. MS (EI, 70 eV): *m*/*z* (%) = 312 (100) $[M]^+$, 296 (9) $[M – O]^+$, 269 (75), 253 (37), 242 (72), 226 (43), 213 (64), 205 (89), 175 (13), 134 (10), 108 (63). HRMS (EI): *m*/*z* calcd. for $C_{18}H_{17}FN_2O_2$ $[M]^+$ 313.1352; found 313.1354.

3-(Ethylthio)-6-fluoroquinoxalin-2(1*H*)-one (26): To a stirred suspension of 3-(ethylsulfanyl)-6-fluoroquinoxalin-2(1*H*)-one *N*-oxide (**21**; 200 mg, 0.832 mmol) in anhydrous THF (5 mL), Lawesson's reagent (337 mg, 0.832) was added under a nitrogen atmosphere. The mixture was stirred for 2.5 h at 40 °C, then the solvent was removed in vacuo and the residue was purified by column chromatography (PE/EtOAc, 10:1; 30 g silica gel) to give **26** (161 mg, 0.718 mmol, 86%) as a pale-yellow solid; m.p. 247 °C. IR (KBr): $\tilde{\nu}$ = 3078, 3054, 3032, 3011, 2978, 2955, 2925, 2895, 2868, 2815, 2736, 1676 (C=O), 1639, 1613, 1526, 1495, 1467, 1433, 1406, 1379, 1343, 1258, 1147, 1118, 1079, 1055, 972, 878, 866, 853, 810, 759, 634, 607, 581, 438 cm^{-1}. ^1H NMR (600 MHz, $[D_6]$DMSO): δ = 12.51 (br. s, 1 H, N*H*), 7.43 (dd, $J_{H,F}$ = 9.4, $J_{H,H}$ = 2.6 Hz, 1 H, 5-*H*), 7.31–7.25 (m, 2 H, 7-*H*, 8-*H*), 3.08 (q, $J_{H,H}$ = 7.5 Hz, 2 H, 9-H_2), 1.30 (t, $J_{H,H}$ = 7.5 Hz, 3 H, 10-H_3) ppm. ^{13}C NMR (150 MHz, $[D_6]$DMSO): δ = 162.4 (o, C3), 158.2 (o, d, $^1J_{C,F}$ = 239.9 Hz, C6), 152.7 (o, C2), 132.7 (o, d, $^3J_{C,F}$ = 11.0 Hz, C4a), 126.9 (o, C8a), 117.0 (+, d, $^3J_{C,F}$ = 9.9 Hz, C8), 116.1 (+, d, $^2J_{C,F}$ = 24.2 Hz, C7), 112.3 (+, d, $^2J_{C,F}$ = 23.1 Hz, C5), 23.2 (–, C9), 13.8 (+, C10) ppm. MS (EI, 70 eV): *m*/*z* (%) = 224 (56) $[M]^+$, 198 (51), 190 (39), 170 (42), 163 (24), 140 (32), 135 (33), 108 (100). HRMS (EI): *m*/*z* calcd. for $C_{10}H_9FN_2OS$ $[M]^+$ 224.0420; found 224.0421.

Synthesis of Tosylated Quinoxalines 22, 24 and 27. General Procedure II: To a stirred suspension of sodium hydride (60 wt.-% in mineral oil, 1.1 equiv.) in anhydrous DMF under a nitrogen atmosphere at room temp., the corresponding quinoxalinone (1.0 equiv.) was gradually added. The mixture was stirred until hydrogen gas evolution ceased, then *p*-TsCl (1.1 equiv.) was added and the resulting solution was stirred at room temp. for 1.5 to 2.0 h. After completion of the reaction the product was purified in the described manner.

2-(Ethylthio)-7-fluoro-3-(tosyloxy)quinoxaline *N*-Oxide (22): Following general procedure II: NaH (60 wt.-%, 92 mg, 2.29 mmol), 3-(ethylsulfanyl)-6-fluoroquinoxalin-2(1*H*)-one *N*-oxide (**21**; 500 mg, 2.08 mmol) in anhydrous DMF (10 mL), *p*-TsCl (436 mg, 2.29 mmol); reaction time: 1.5 h; purification: After dilution with Et_2O (50 mL) the organic phase was washed with brine (20 mL) and H_2O (3 × 15 mL). The organic phase was dried with Na_2SO_4

and the solvent was removed in vacuo, then the residue was purified by column chromatography (PE/EtOAc, 3:1; 50 g silica gel) to give **22** (644 mg, 1.63 mmol, 78%) as a pale-yellow solid; m.p. 108 °C, 203 °C (dec.). IR (ATR): $\tilde{\nu}$ = 3094, 2991, 2943, 2883, 1617, 1597, 1496, 1458, 1448, 1408, 1383, 1372, 1352, 1310, 1293, 1280, 1242, 1207, 1192, 1178, 1123, 1093, 1079, 1048, 1021, 971, 892, 871, 845, 839, 812, 798, 776, 765, 752, 728, 701, 680, 668, 651, 603, 580, 555, 537, 500, 469, 462, 433, 413 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.09 (dd, $J_{H,F}$ = 8.8, $J_{H,H}$ = 2.8 Hz, 1 H, 8-*H*), 8.06–8.04 (m, 2 H, 12-*H*, 12′-*H*), 7.85 (dd, $J_{H,H}$ = 9.1, $J_{H,F}$ = 5.1 Hz, 1 H, 5-*H*), 7.48 (ddd, $J_{H,H}$ = 9.1, 2.8, $J_{H,F}$ = 7.7 Hz, 1 H, 6-*H*), 7.41–7.40 (m, 2 H, 13-*H*, 13′-*H*), 3.35 (q, $J_{H,H}$ = 7.4 Hz, 2 H, 9-H_2), 2.48 (s, 3 H, 15-H_3), 1.29 (t, $J_{H,H}$ = 7.4 Hz, 3 H, 10-H_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.8 (o, d, $^1J_{C,F}$ = 254.2 Hz, C7), 152.0 (o, C3), 146.1 (o, C14), 137.0 (o, d, $^3J_{C,F}$ = 11.0 Hz, C8a), 135.7 (o, C2), 135.4 (o, C4a), 133.6 (o, C11), 131.1 (+, d, $^3J_{C,F}$ = 8.8 Hz, C5), 129.7 (+, 2 C, C13, C13′), 129.2 (+, 2 C, C12, C12′), 121.2 (+, d, $^2J_{C,F}$ = 25.3 Hz, C6), 104.0 (+, d, $^2J_{C,F}$ = 27.5 Hz, C8), 26.6 (–, C9), 21.8 (+, C15), 15.1 (+, C10) ppm. MS (EI, 20 eV): *m*/*z* (%) = 394 (3) $[M]^+$, 377 (27) $[M - OH]^+$, 304 (13), 223 (25), 196 (18), 190 (12), 155 (100). HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{15}FN_2O_4S_2$ $[M + H]^+$ 395.0536; found 395.0537.

2-(Tosyloxy)quinoxaline (24): Following general procedure II: NaH (60 wt.-%, 151 mg, 3.76 mmol), 2-quinoxalinone (**23**; 500 mg, 3.42 mmol) in anhydrous DMF (5 mL), *p*-TsCl (665 mg, 3.49 mmol); reaction time: 1.5 h; purification: After dilution with brine (20 mL) the organic phase was extracted with Et_2O (3× 20 mL). The combined organic phases were dried with Na_2SO_4 and the solvent was removed in vacuo, then the residue was purified by column chromatography (PE/EtOAc, 3:1; 50 g silica gel) to give **24** (795 mg, 2.65 mmol, 77%) as a colourless solid; m.p. 100 °C, 305 °C (dec.). IR (ATR): $\tilde{\nu}$ = 3102, 3033, 2926, 1597, 1575, 1569, 1496, 1401, 1378, 1362, 1338, 1311, 1292, 1265, 1213, 1199, 1190, 1172, 1129, 1121, 1088, 1016, 991, 982, 966, 917, 907, 877, 846, 815, 804, 793, 769, 703, 670, 648, 633, 615, 578, 548, 540, 532, 526, 485, 481, 452, 417, 411 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.65 (s, 1 H, 3-*H*), 8.11–8.09 (m, 1 H, 5-*H*), 8.03–8.01 (m, 2 H, 10-*H*, 10′-*H*), 7.91–7.89 (m, 1 H, 8-*H*), 7.78–7.73 (m, 2 H, 6-*H*, 7-*H*), 7.38 (dd, $J_{H,H}$ = 8.5, 0.6 Hz, 2 H, 11-*H*, 11′-*H*), 2.46 (s, 3 H, 13-H_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 150.9 (o, C2), 145.9 (o, C12), 141.2 (o, C4a), 139.7 (o, C8a), 139.1 (+, C3), 133.3 (o, C9), 131.1 (+, C7), 129.8 (+, 2 C, C11, C11′), 129.7 (+, C6), 129.1 (+, C5), 129.0 (+, 2 C, C10, C10′), 128.5 (+, C8), 21.7 (+, C13) ppm. MS (CI): *m*/*z* (%) = 301 (4) $[M + H]^+$, 236 (100), 208 (16), 155 (23), 145 (9), 91 (20).

2-(Ethylthio)-7-fluoro-3-(tosyloxy)quinoxaline (27): Following general procedure II: NaH (60 wt.-%, 64 mg, 1.605 mmol), 3-(ethylthio)-6-fluoroquinoxalin-2(1*H*)-one (**26**; 300 mg, 1.338 mmol) in anhydrous DMF (5 mL), *p*-TsCl (281 mg, 1.472 mmol); reaction time: 2.0 h; purification: After dilution with Et_2O (15 mL) the organic phase was washed with brine (5 mL) and H_2O (3× 5 mL). The organic phase was dried with Na_2SO_4 and the solvent was removed in vacuo to give **27** (479 mg, 1.266 mmol, 95%) as a pale-yellow solid; m.p. 114 °C, 302 °C (dec.). IR (ATR): $\tilde{\nu}$ = 3094, 2977, 2932, 1619, 1595, 1582, 1552, 1497, 1448, 1387, 1371, 1299, 1282, 1259, 1230, 1215, 1192, 1174, 1136, 1116, 1091, 1065, 1056, 1017, 983, 967, 960, 890, 865, 833, 811, 797, 775, 758, 744, 718, 698, 688, 662, 623, 613, 606, 580, 545, 532, 519, 496, 485, 474, 444, 429, 415, 406 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.10–8.08 (m, 2 H, 10-*H*, 10′-*H*), 7.79 (dd, $J_{H,H}$ = 9.2, $J_{H,F}$ = 5.7 Hz, 1 H, 8-*H*), 7.54 (dd, $J_{H,F}$ = 9.2, $J_{H,H}$ = 2.8 Hz, 1 H, 5-*H*), 7.40–7.39 (m, 2 H, 11-*H*, 11′-*H*), 7.34 (ddd, $J_{H,H}$ = 9.2, 2.8, $J_{H,F}$ = 8.1 Hz, 1 H, 7-*H*), 3.27 (q, $J_{H,H}$ = 7.3 Hz, 2 H, 14-H_2), 2.47 (s, 3 H, 13-H_3), 1.41 (t, $J_{H,H}$ = 7.3 Hz, 3 H, 15-H_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.6 (o, d, $^1J_{C,F}$ = 250.9 Hz, C6), 151.6 (o, C2), 147.7 (o, d, $^4J_{C,F}$ = 3.3 Hz, C8a), 145.9 (o, C12), 141.9 (o, d, $^3J_{C,F}$ = 13.2 Hz, C4a), 133.7 (o, C3), 133.6 (o, C9), 129.8 (+, d, $^3J_{C,F}$ = 9.9 Hz, C8), 129.7 (+, 2 C, C11, C11′), 129.2 (+, 2 C, C10, C10′), 118.1 (+, d, $^2J_{C,F}$ = 25.3 Hz, C7), 111.6 (+, d, $^2J_{C,F}$ = 23.1 Hz, C5), 23.9 (–, C14), 21.8 (+, C13), 13.7 (+, C15) ppm. MS (EI, 70 eV): *m*/*z* (%) = 378 (13) $[M]^+$, 314 (13), 236 (12), 223 (86), 191 (16), 167 (100), 155 (22), 140 (11), 108 (22). HRMS (ESI): *m*/*z* calcd. for $C_{17}H_{15}FN_2O_3S_2$ $[M + H]^+$ 379.0586; found 379.0583.

C–C Coupling of (Tosyloxy)quinoxalines. General Procedure III:[23] Under a nitrogen atmosphere, an oven-dried Schlenk tube equipped with a cooling finger was filled with the tosyloxyquinoxaline (1.0 equiv.), boronic acid (2.0 equiv.), $Pd(OAc)_2$ (4 mol-%), XPhos (**19**; 8 mol-%) and K_3PO_4 (3.0 equiv.) followed by evacuation of the reaction vessel and backfilling with nitrogen. Anhydrous toluene was then added and the mixture was stirred at 100 °C for the appropriate time. After completion of the reaction, the cooled suspension was diluted with ethyl acetate (5 mL) and washed with saturated NaCl solution (5 mL) and water (5–10 mL). The organic phase was dried with Na_2SO_4 and the solvent was removed with a rotary evaporator. Finally, the obtained residue was purified by column chromatography and dried in vacuo.

2-(*p*-Tolyl)quinoxaline (25): Following general procedure III: 2-tosyloxyquinoxaline (**24**; 450 mg, 1.5 mmol), (4-tolyl)boronic acid (408 mg, 3.0 mmol), XPhos (57.0 mg, 0.12 mmol), $Pd(OAc)_2$ (13.0 mg, 0.06 mmol) and K_3PO_4 (955 mg, 4.5 mmol) in anhydrous toluene (8 mL); column chromatography (PE/EtOAc, 30:1; 100 g silica gel) gave **25** (319 mg, 1.448 mmol, 97%) as a colourless solid; m.p. 97 °C. IR (KBr): $\tilde{\nu}$ = 3056, 3028, 3016, 2922, 2859, 1613, 1578, 1545, 1489, 1467, 1450, 1430, 1310, 1288, 1276, 1264, 1231, 1213, 1185, 1137, 1125, 1045, 1015, 956, 933, 830, 753, 714, 670, 607, 555, 487, 478, 408 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.31 (s, 1 H, 3-*H*), 8.15–8.13 (m, 1 H, 8-*H*), 8.11–8.09 (m, 3 H, 5-*H*, 10-*H*, 10′-*H*), 7.78–7.75 (m, 1 H, 7-*H*), 7.74–7.71 (m, 1 H, 6-*H*), 7.37 (dd, $J_{H,H}$ = 7.9, 0.6 Hz, 2 H, 11-*H*, 11′-*H*), 2.45 (s, 3 H, 13-H_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 151.8 (o, C2), 143.3 (+, C3), 142.3 (o, C8a), 141.4 (o, C4a), 140.5 (o, C12), 134.0 (o, C9), 130.2 (+, C7), 129.9 (+, 2 C, C11, C11′), 129.5 (+, C8), 129.3 (+, C6), 129.1 (+, C5), 127.4 (+, 2 C, C10, C10′), 21.4 (+, C13) ppm. MS (EI, 70 eV): *m*/*z* (%) = 220 (100) $[M]^+$, 205 (6) $[M - CH_3]^+$, 193 (21), 178 (4), 165 (9), 116 (7), 110 (9).

3-(Ethylthio)-6-fluoro-2-(*p*-tolyl)quinoxaline (28): Following general procedure III: 2-(ethylthio)-7-fluoro-3-(tosyloxy)quinoxaline (**27**; 378 mg, 1.0 mmol), (4-tolyl)boronic acid (272 mg, 2.0 mmol), XPhos (38.0 mg, 0.08 mmol), $Pd(OAc)_2$ (9.0 mg, 0.04 mmol) and K_3PO_4 (637 mg, 3.0 mmol) in anhydrous toluene (6 mL); column chromatography (PE/EtOAc, 30:1; 30 g silica gel) gave **28** (237 mg, 0.794 mmol, 79%) as a pale-yellow solid; m.p. 107 °C. IR (KBr): $\tilde{\nu}$ = 3078, 3052, 3031, 2963, 2930, 2869, 1616, 1566, 1538, 1510, 1487, 1443, 1413, 1382, 1347, 1316, 1306, 1286, 1257, 1225, 1211, 1185, 1154, 1118, 1092, 1051, 1025, 992, 969, 855, 840, 830, 815, 787, 774, 757, 726, 712, 626, 614, 567, 507, 478, 424, 411 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03–8.01 (m, 1 H, 8-*H*), 7.67–7.66 (m, 2 H, 11-*H*, 11′-*H*), 7.59–7.57 (m, 1 H, 5-*H*), 7.38 (ddd, $J_{H,H}$ = 9.1, 2.8, $J_{H,F}$ = 8.2 Hz, 1 H, 7-*H*), 7.34–7.32 (m, 2 H, 10-*H*, 10′-*H*), 3.27 (q, $J_{H,H}$ = 7.5 Hz, 2 H, 14-H_2), 2.45 (s, 3 H, 13-H_3), 1.40 (t, $J_{H,H}$ = 7.5 Hz, 3 H, 15-H_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 162.8 (o, d, $^1J_{C,F}$ = 250.9 Hz, C6), 157.0 (o, C3), 152.9 (o, C2), 142.2 (o, d, $^3J_{C,F}$ = 13.2 Hz, C4a), 139.9 (o, C12), 136.4 (o, C8a), 134.2 (o, C9), 131.1 (+, d, $^3J_{C,F}$ = 9.9 Hz, C8), 129.2 (+, 2 C, C11, C11′), 128.9 (+, 2 C, C10, C10′), 117.8 (+, d, $^2J_{C,F}$ = 25.3 Hz, C7), 111.4

(+, d, $^2J_{C,F}$ = 20.9 Hz, C5), 25.1 (–, C14), 21.5 (+, C13), 13.8 (+, C15) ppm. MS (EI, 70 eV): *m/z* (%) = 298 (25) $[M]^+$, 283 (16) $[M - CH_3]^+$, 269 (21) $[M - CH_2CH_3]^+$, 255 (9), 237 (6), 214 (5), 180 (96), 152 (45), 124 (27), 120 (42), 105 (100). HRMS (EI): *m/z* calcd. for $C_{17}H_{15}FN_2S$ $[M]^+$ 298.0940; found 298.0942.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H and ^{13}C NMR spectra.

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