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Unprecedented access to functionalized pyrrolo [2,1-*a*]isoquinolines from the domino reaction of isoquinolinium ylides and electrophilic benzannulated heterocycles†

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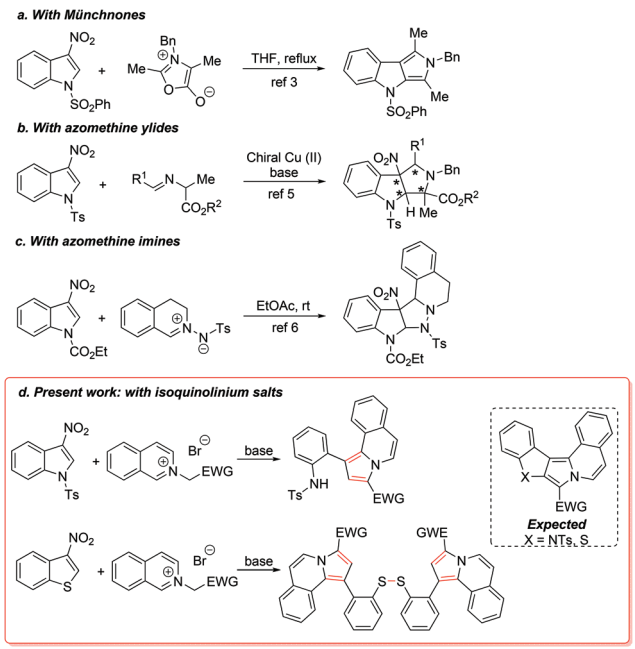
We have come across an unexpected reaction between electrophilic indoles and isoquinolinium methylides for accessing functionalized pyrrolo[2,1-*a*]isoquinolines. The reaction was found in general to yield the products in good yields. We also observed the formation of S–S-bridged bis-pyrrolo[2,1-*a*]isoquinolines from the reaction of 3-nitro benzothiophene and isoquinolinium methylides.

Introduction

Electrophilic benzannulated heterocycles, which exhibit unusual reactivity can be generated by installing electron-withdrawing substituents at precise positions.[1] In this way, an indole moiety can be made electrophilic by placing electron-withdrawing groups on the N-atom and C-2 or C-3 carbon atoms. The chemistry of electrophilic indoles was extensively investigated by several groups for the synthesis of functionalized (or fused) indoline/indole moieties.[2] Dipolar cycloaddition utilizing an electrophilic indole as the dipolarophile towards annulated heterocycles has been reported by different groups. The first of these reports came from Gribble's group in 1998 in which they synthesized pyrrolo[3,4-*b*]indoles *via* the dipolar cycloaddition of münchnones with an electrophilic indole (Scheme 1a).[3] Later, the same group also reported the reaction of azomethine ylides with electrophilic indoles, furnishing hexahydropyrrolo[3,4-*b*]indoles.[4] The asymmetric version of azomethine ylide addition to an electrophilic indole was independently reported by Arai and Stanley (Scheme 1b).[5] In 2017, Wang and co-workers reported the synthesis of five-ring-fused tetrahydroisoquinolines from azomethine imines and electrophilic indoles (Scheme 1c).[6] Our interest in the chemistry of electrophilic benzannulated heterocycles[7] made us devise dipolar cycloaddition reactions towards novel heteroacenes (Scheme 1d).

Heteroaromatic N-ylides are a class of dipoles which have been comprehensively studied for the generation of highly functionalized carbocycles and heterocycles.[8] In particular, isoquinolinium methylides have been utilized in dipolar cycloaddition reactions with several dipolarophiles, such as electron-deficient alkenes and alkynes to access fused



Scheme 1 Dipolar cycloadditions involving electrophilic benzannulated heterocycles.

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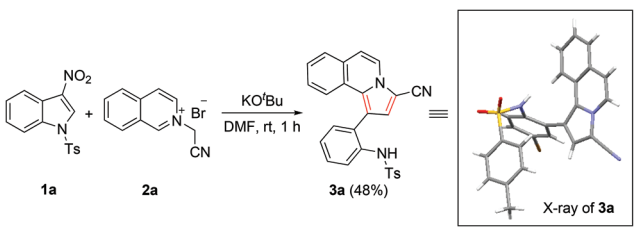
N-heterocyclic scaffolds.[9] The 1,3-dipolar cycloaddition of isoquinolinium methylides to nitrostyrenes has been reported previously. The first work in this line was published in 1990 when 1-nitro-2-phenyl-3-*R*-2,3-dihydrobenzo[*g*]indolizine was synthesized *via* the reaction between β-nitrostyrene and isoquinolinium methylide.[10] Later, Kucukdisli and Opatz reported the reaction of different heteroaromatic N-ylides (including isoquinolinium methylides) with β-nitrostyrene and found that aromatized products were obtained after the elimination of HNO_2.[11] In 2014, the dipolar cycloaddition of isoquinolinium methylides to 3-nitrochromenes was reported to furnish azadibenzo[*a*,*g*]fluorene derivatives.[12] Inspired by these reports on the dipolar cycloaddition of isoquinolinium methylides to nitrostyrenes, we hypothesized that the reactions of these heteroaromatic N-ylides with electrophilic benzannulated heterocycles would result in the development of novel heteroacenes (Scheme 1d).

Results and discussion

We commenced our studies by selecting *N*-tosyl-3-nitro indole **1a** and 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** as model substrates. Initially, **1a** (1.0 equiv.) and **2a** (1.1 equiv.) were treated in the presence of potassium *t*-butoxide (^{t}BuOK, 4.0 equiv.) in dimethylformamide (DMF) at room temperature for 1 h. Contrary to our expectation of the formation of a pentacene, as depicted in Scheme 1d, the 1,3-dipolar cycloaddition reaction between **1a** and **2a** resulted in the formation of functionalized pyrrolo[2,1-*a*]isoquinoline **3a** in 48% yield (Scheme 2). The structure of **3a** established by various spectroscopic analyses was further confirmed from X-ray crystallographic data.

Pyrrolo[2,1-*a*]isoquinoline moieties[13] are important fused N-heterocycles that are found in plenty of core structures of natural products, such as crispine A and B, trolline, lamellarins, and erythrina alkaloids, which are found to show interesting anticancer, antiviral and antibacterial activities.[14] Synthetic pyrrolo[2,1-*a*]isoquinolines have also been found to exhibit a plethora of biological properties, such as anticancer effects, multidrug resistance (MDR) reversal, estrogen receptor modulation, deoxyribonucleic acid (DNA) chelation, and antimicrobial, antiplatelet and anti-inflammatory effects.[15] In addition, these fused N-heterocycles have been utilized in developing different metal cation and organic sensors.[16] Two well-known strategies to access pyrrolo[2,1-*a*]isoquinolines are the annulation of appropriate rings to a substituted pyrrole or an N-functionalized isoquinoline.[13,15a,17] In 2019, Dong and Huang reported the synthesis of substituted indolizines from the reaction of chromones and pyridinium salts.[18] This reaction proceeded *via* a 1,3-dipolar cycloaddition-ring opening and aromatization cascade.

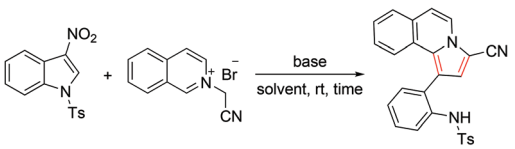


Scheme 2 1,3-Dipolar cycloaddition of an isoquinolinium methylide with an electrophilic indole.

Intrigued by the unexpected synthesis of the substituted pyrrolo[2,1-*a*]isoquinoline moiety, we went on with the optimization of the reaction conditions with **1a** and **2a** as substrates. Screening of different bases, such as ^{t}BuOK, ^{t}BuONa, NaOMe, Cs_2CO_3, K_2CO_3, Na_2CO_3, KOH, NaOH, LiOH, NaH and DIPEA (Table 1, entries 1–11) revealed that KOH was the most suitable base, furnishing the product in 54% yield. Then, we focused on the effect of different solvents on the reaction outcome (Table 1, entries 12–16). Among the screened solvents, DMF was found to be the most effective, giving the product in 54% yield. The yield of the reaction was found to decrease when the amount of base was decreased to 2.0 equivalents. In this case, the starting material was found to remain unreacted and no by-product was observed (Table 1, entry 19). Finally, we turned our attention towards the effect of substrate concentration on the reaction. To our delight, the use of 1.5 equivalents of **2a** increased the yield of **3a** to 88% (Table 1, entry 18).

With the optimized conditions in hand (1.0 equiv. of **1a**, 1.5 equiv. of **2a**, 4.0 equiv. of KOH, DMF, rt), we then explored the scope of the 1,3-dipolar cycloaddition of isoquinolinium

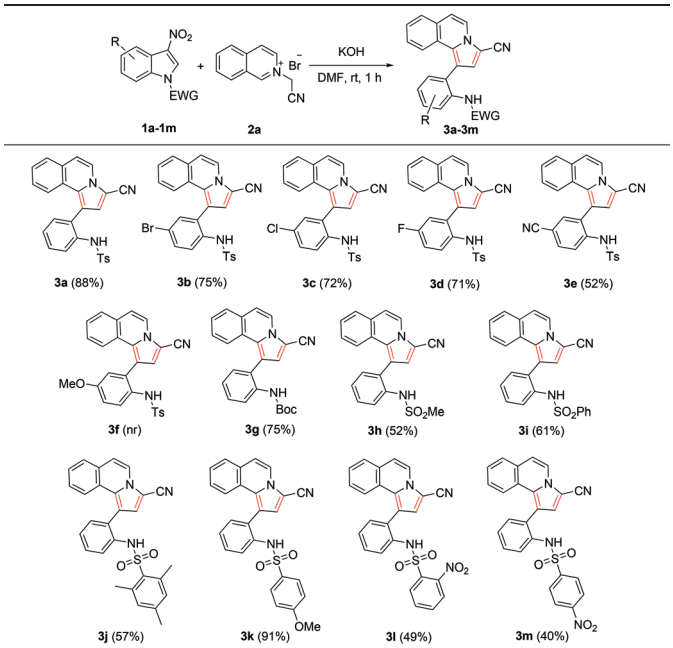
Table 1 Optimization studies[a]



Entry	Base	Solvent	Time (h)	Yield of **3a** (%)
1	^{t}BuOK	DMF	1	48
2	^{t}BuONa	DMF	1	21
3	NaOMe	DMF	1	—
4	Cs_2CO_3	DMF	1	37
5	K_2CO_3	DMF	1	16
6	Na_2CO_3	DMF	1	Trace
7	KOH	DMF	1	54
8	NaOH	DMF	1	49
9	LiOH	DMF	1	43
10	NaH	DMF	1	38
11	DIPEA	DMF	1	—
12	KOH	1,4-Dioxane	1	16
13	KOH	EtOH	1	—
14	KOH	CH_3CN	1	26
15	KOH	EtOAc	1	—
16	KOH	THF	1	22
17	KOH	DMF	12	61
18[b]	KOH	DMF	1	88
19[c]	KOH	DMF	1	10

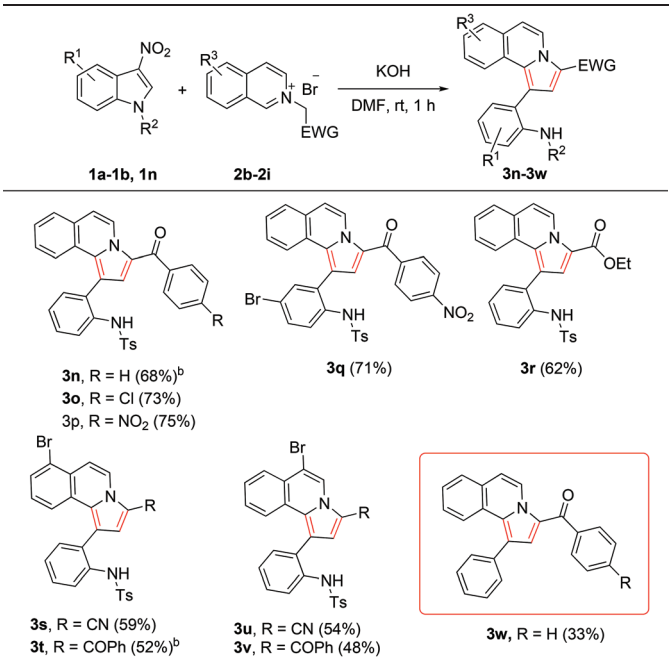
[a] Reaction conditions: **1a** (1.0 equiv., 0.16 mmol), **2a** (1.1 equiv.), base (4.0 equiv.), solvent (1.0 mL), rt. [b] **2a** (1.5 equiv.). [c] Base (2.0 equiv.).

Table 2 Generalization of 1,3-dipolar cycloaddition of isoquinolinium methylides with substituted electrophilic indoles[a]



[a] Reaction conditions: **1** (1.0 equiv., 100 mg), **2a** (1.5 equiv.), KOH (4.0 equiv.), DMF (0.16 M), rt, 1 h.

Table 3 Generalization of 1,3-dipolar cycloaddition reaction with various isoquinolinium bromides[a]



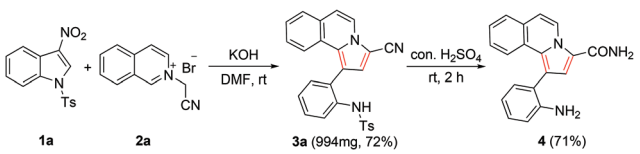
Reaction conditions: [a] **1** (1.0 equiv., 100 mg), **2a** (1.5 equiv.), KOH (4.0 equiv.), DMF (0.16 M), rt, 1 h. [b] 4 h.

methylides using different substituted electrophilic indoles, the results of which are summarized in Table 2. In this way, the generalization of different 3-nitro-indoles **1** with the model substrate 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** was studied. Reactions with halogens (Br, F, Cl)-substituted nitroindoles proceeded well, affording products **3b**, **3c** and **3d** in good yields. The dipolar cycloaddition of **2a** with 3-nitro-1-tosyl-1*H*-indole-5-carbonitrile afforded the corresponding substituted pyrrolo[2,1-*a*]isoquinoline **3e** in 52% yield. With an electron-releasing OMe-substituent (5-methoxy-3-nitro-1-tosyl-1*H*-indole), even after heating to reflux in DMF for a prolonged period of time, the reaction failed, which might be due to the reduced electrophilicity (**3f**). Next, the electron-withdrawing substituent on the N-atom of the indole was changed to Boc, in which case the expected product **3g** was isolated in 75% yield. The reactions with electrophilic indole substrates with SO_2Me and SO_2Ph on the N-atom afforded **3h** and **3i** in 52% and 61% yields. Finally, other sulfonyl substituents on the N-atom of the indole were found to influence the outcome of the reaction from which products **3j** to **3m** were obtained in moderate to excellent yields.

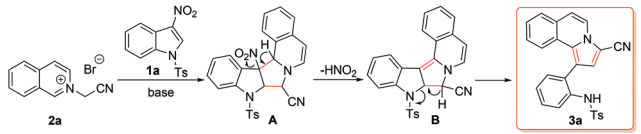
Further investigations were focused on evaluating the reactivity of different isoquinolinium bromides in the present dipolar cycloaddition with electrophilic indoles (Table 3). The reactions with isoquinolinium methylides **2b–2d** (with different substituents on the *para*-position of the phenyl ring) afforded the products **3n–3p** in good yields. The isoquinolinium methylides **2e** with an ethoxycarbonyl-group as the electron-withdrawing moiety also afforded the corresponding pyrrolo[2,1-*a*]isoquinoline **3r** in 62% yield. Finally, isoquinolinium bromides **2f–2i** prepared from 4-bromo isoquinoline and 5-bromo isoquinoline were tested for reactivity in the present transformation and products **3s–3v** were isolated from the reactions in satisfactory yields. *N*-Methyl-3-nitroindole led to the formation of pyrrolo[2,1-*a*] isoquinoline **3w**, wherein we observed the elimination of the *N*-methyl group.

We also attempted a gram-scale synthesis (starting from 1.0 g of **1a**) of pyrrolo[2,1-*a*]isoquinoline **3a**, and the compound was obtained in 72% yield (Scheme 3). Compound **3a** was then subjected to Ts-deprotection by treating it with concentrated H_2SO_4 for 2 hours, which furnished pyrrolo[2,1-*a*]isoquinoline **4**. In compound **4** not only was the Ts-group removed but the CN-moiety was also converted to the corresponding amide.

Based on our observations and on the reported literature,[10–12] we propose a plausible mechanism for the present domino dipolar cycloaddition-ring opening process that takes place during the reaction of electrophilic indole and



Scheme 3 Gram-scale reaction of **1a** with **2a** and *N*-Ts deprotection of pyrrolo[2,1-*a*]isoquinoline **3a**.

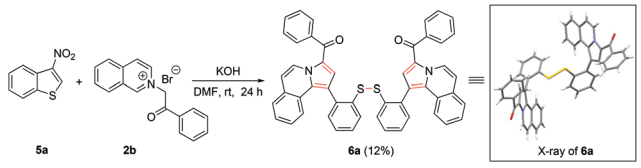


Scheme 4 Plausible mechanism for the synthesis of pyrrolo[2,1-*a*]isoquinoline **3**.

isoquinolinium methylide (Scheme 4). The first step is the deprotonation of the activated methylene group of the isoquinolinium salt by KOH to generate the corresponding N-ylide. This dipole then participates in a 1,3-dipolar cycloaddition with the dipolarophile, *N*-tosyl-3-nitroindole **1a** to generate the corresponding cycloadduct **A** (Scheme 4). Subsequent elimination of HNO_2 from **A** generates intermediate **B**, which upon aromatization results in a strain-induced cleavage of the C–N bond, furnishing the final product pyrrolo[2,1-*a*]isoquinoline **3a**.

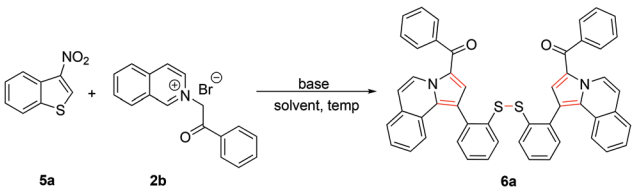
The unexpected domino transformation observed from the reaction of electrophilic indoles and isoquinolinium methylides prompted us to check the reactivity of electrophilic benzothiophenes. The initial experiment was performed by reacting 3-nitro benzothiophene **5a** with 2-(2-oxo-2-phenylethyl)isoquinolin-2-ium-bromide **2b** in the presence of KOH (2.0 equiv.) in DMF at room temperature. After 24 h, a bis-pyrrolo[2,1-*a*]isoquinoline **6a** linked with an S–S bond was isolated in 12% yield (Scheme 5). The structure of **6a** was established by various spectroscopic analyses and confirmed from X-ray crystallographic data.

The poor yield obtained for the synthesis of bis-pyrrolo[2,1-*a*]isoquinoline **6a** prompted us to optimize the reaction conditions with **5a** and **2b** as substrates. Increasing the equivalents of base and **2b** was found not to have a positive outcome on the reaction yield (Table 4, entries 2 and 3). A slight increase in the yield of **6a** was noted by carrying out the reaction at 60 °C (Table 4, entry 4). Screening of different bases, such as K_2CO_3, K_3PO_4, Na_2CO_3, Cs_2CO_3, NaOH, KOH and KO*t*Bu (Table 4, entries 4–10), revealed that K_3PO_4 was more efficient. Further screening of solvents showed that CH_3CN gave better results in comparison to other solvents, such as DMF, THF, EtOH, DMA, 1,4-dioxane or DMSO (Table 4, entries 7, 11–16). Also, performing the reaction in the presence of an oxidant, $Cu(OAc)_2{\cdot}H_2O$, was found to be less efficient (Table 4, entries 17 and 18). Finally, we carried out the reaction under an inert atmosphere to see whether the oxidation of intermediate thiol to an S–S bond bridged bis-pyrrolo[2,1-*a*]isoquinoline could be prevented (Table 4, entry 19). From this reaction, **6a** was isolated in low yield and we were not able to isolate the thiol or any other intermediates. Complete consumption of 3-nitrobenzothiophene **5a** was not observed in any of the reactions mentioned above.



Scheme 5 Synthesis of bis-pyrrolo[2,1-*a*]isoquinoline **6a** from 3-nitro benzothiophene and **2b**.

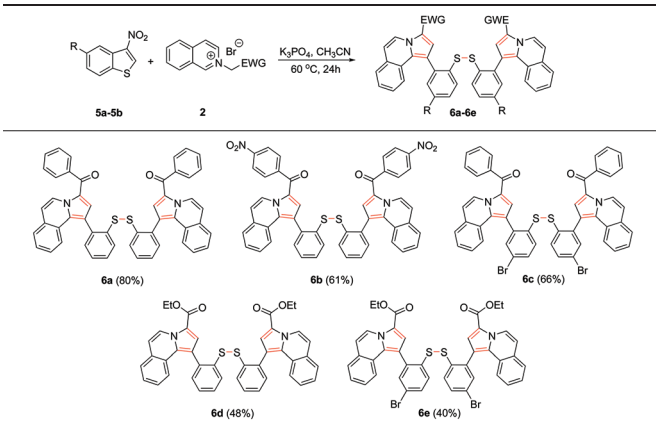
Table 4 Optimization studies[a]



Entry	Base	Solvent	Temp. (°C)	Yield of **6a** (%)
1	KOH	DMF	rt	12
2[b]	KOH	DMF	rt	10
3[c]	KOH	DMF	rt	10
4	KOH	DMF	60	14
5	^{t}BuOK	DMF	60	14
6	NaOH	DMF	60	10
7	K_3PO_4	DMF	60	29
8	K_2CO_3	DMF	60	14
9	Na_2CO_3	DMF	60	—
10	Cs_2CO_3	DMF	60	12
11	K_3PO_4	EtOH	60	—
12	K_3PO_4	THF	60	—
13	K_3PO_4	1,4-Dioxane	60	—
14	K_3PO_4	CH_3CN	60	80
15	K_3PO_4	DMA	60	14
16	K_3PO_4	DMSO	60	20
17	K_3PO_4, $Cu(OAc)_2{\cdot}H_2O$	DMF	60	Trace
18[d]	2,6-Lutidine, $Cu(OAc)_2{\cdot}H_2O$	DMF	60	Trace
19[e]	K_3PO_4	CH_3CN	60	20

[a] Reaction conditions: **5a** (1.0 equiv., 0.28 mmol), **2b** (1.5 equiv.), base (2.0 equiv.), solvent (1.0 mL), rt, 24 h. [b] Base (4.0 equiv.). [c] **2b** (3.0 equiv.). [d] Base (5.0 equiv.); $Cu(OAc)_2{\cdot}H_2O$ (1.5 equiv.). [e] Under an argon atmosphere.

Table 5 Generalization of 1,3-dipolar cycloaddition reaction of various isoquinolinium methylides with 3-nitro benzothiophene[a]



[a] Reaction conditions: **5** (1.0 equiv., 100 mg), **2** (1.5 equiv.), K_3PO_4 (2.0 equiv.), CH_3CN (0.28 M), 60 °C, 24 h.

With the optimized conditions in hand [1.0 equiv. of **5a**, 1.5 equiv. of **2b**, 2.0 equiv. of K_3PO_4, CH_3CN (1 ml), 60 °C], the scope of the reaction for the synthesis of bis-pyrrolo[2,1-*a*]isoquinoline was investigated (Table 5). The presence of a phenylethanone substitution on the isoquinolinium N-atom resulted in a better reaction, furnishing the corresponding S–S-bridged bis-pyrrolo[2,1-*a*]isoquinolines **6a–6c** in good to excellent yields. Reactions of isoquinolinium methylides **2e** with an ethoxycarbonyl group as the electron-withdrawing substituent afforded the corresponding products **6d** and **6e** in satisfactory yields. In all the reactions mentioned above, unreacted 3-nitrobenzothiophene **5a** was recovered.

Conclusions

In short, we have developed a domino reaction involving a 1,3-dipolar cycloaddition and a ring-opening between isoquinolinium ylides and electrophilic benzannulated heterocycles. This hitherto unknown methodology gives easy access to a series of highly functionalized pyrrolo[2,1-*a*] isoquinolines starting from different isoquinolinium methylides and 3-nitroindoles. In addition, we observed the formation of S–S-bridged bis-pyrrolo[2,1-*a*]isoquinolines from the reaction of 3-nitro benzothiophene and isoquinolinium methylides. We have also demonstrated the applicability of this cycloaddition reaction for the generation of pyrrolo[2,1-*a*] isoquinolines on the gram scale. Presently, we are currently looking at ways to synthesize pentacenes and dibenzazepines *via* site-selective C–H activation from the above obtained pyrrolo[2,1-*a*]isoquinolines, the details of which will be reported in due course.

Experimental

General experimental methods

All chemicals were of the best grade commercially available and were used without further purification. All solvents were purified according to the standard procedures; dry solvents were obtained according to the methods in the literature and stored over molecular sieves. Analytical thin-layer chromatography was performed on polyester sheets pre-coated with silica gel containing a fluorescent indicator (POLYGRAMSIL G/UV254). Gravity column chromatography was performed using neutral alumina, and mixtures of ethyl acetate hexanes were used for elution melting points which were determined using a calibrated digital melting point apparatus (Büchi 530 melting point apparatus). Infrared spectra were recorded on a Bruker FT-IR spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded using a Bruker Avance-300 (300 MHz for ^{1}H NMR, 75 MHz for $^{13}C\{^1H\}$ NMR) and Bruker AMX-500 (500 MHz for ^{1}H NMR, 125 MHz for $^{13}C\{^1H\}$ NMR) instruments. All spectra were measured at 300 K, unless otherwise specified. The chemical shifts δ are given in ppm and referenced to the external standard TMS or internal solvent standard. ^{1}H NMR coupling constants (J) are reported in Hertz (Hz) and multiplicities are indicated as follows s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets). Mass spectra were recorded with a ThermoFinnigan MAT95XL, a ThermoFisher Scientific LTQ Orbitrap Velos, and an Agilent 6890 gas chromatograph with a JMS-T100GC spectrometer or with an ESI/HRMS at 60 000 resolution using a Thermo Scientific Exactive mass spectrometer with orbitrap analyzer. Gas chromatographic analysis was performed using GCMS-TQ8030 SHIMADZU.

Experimental procedure for the reaction between 3-nitro-*N*-tosyl indole and isoquinolinium salt

A mixture of 3-nitro-*N*-tosyl indole (1.0 equiv., 100 mg), isoquinolinium salt (1.5 equiv.) and KOH (4.0 equiv.) was weighed into a dry reaction tube. Dry DMF was added and the reaction mixture was stirred at room temperature. After completion of the reaction as indicated from the TLC, water was added and the aqueous layer was extracted three times with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was then purified by column chromatography (neutral alumina, eluent: mixtures of ethyl acetate/hexanes) to afford the corresponding products.

Synthesis and characterization of pyrrolo[2,1-*a*]isoquinolines (3a–3v)

***N*-(2-(3-Cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3a).** The general procedure was followed using 3-nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (118 mg, 0.47 mmol) and KOH (71 mg, 1.26 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3a** as a pale yellow solid (122 mg, 88%). Mp: 147–150 °C. IR (neat) ν_{max}: 3884, 3822, 3732, 3485, 3010, 2356, 1546, 1493, 1452, 1334, 1161, 1091, 903, 762 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, TMS): δ 8.09 (d, J = 7 Hz, 1H), 7.84 (d, J = 8.5 Hz, 1H), 7.68 (d, J = 7.5 Hz, 1H), 7.50–7.44 (m, 2H), 7.38 (d, J = 8.5 Hz, 2H), 7.25–7.21 (m, 2H), 7.17–7.13 (m, 3H), 7.10 (d, J = 8 Hz, 2H), 6.44 (s, 1H), 6.38 (s, 1H), 2.37 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 144.0, 136.2, 135.6, 131.6, 130.1, 129.7, 129.6, 128.6, 128.4, 128.1, 127.5, 127.0, 126.8, 125.4, 124.9, 122.8, 122.7, 122.5, 121.7, 114.6, 113.0, 112.9, 98.0, 21.6 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{26}H_{19}N_3NaO_2S$ 460.10902, found 460.11007.

***N*-(4-Bromo-2-(3-cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3b).** The general procedure was followed using 5-bromo-3-nitro-*N*-tosyl indole **1b** (100 mg, 0.25 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (95 mg, 0.38 mmol) and KOH (57 mg, 1.01 mmol) at rt for 1 h. Chromatography (eluent: 25% ethyl acetate in hexane) afforded the desired product **3b** as a brown solid (98 mg, 75%). Mp: 208–210 °C. IR (neat) ν_{max}: 3837, 3747, 3534, 3463, 3273, 2959, 2205, 1721, 1451, 1269, 1116, 1069, 885, 740 cm^{-1}. ^{1}H NMR (500 MHz, $(CD_3)_2CO$, TMS): δ 8.20 (d, J = 7.5 Hz, 1H), 8.13 (s, 1H), 7.85 (d, J = 8 Hz, 1H), 7.77 (d, J = 8.5 Hz, 1H), 7.71 (dd, J_1 = 9 Hz, J_2 = 1.5 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.51 (d, J

= 1.5 Hz, 1H), 7.44 (d, J = 8 Hz, 2H), 7.35 (d, J = 7.5 Hz, 1H), 7.29–7.24 (m, 2H), 7.17 (d, J = 7.5 Hz, 2H), 6.73 (s, 1H), 2.36 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $(CD_3)_2CO$): δ 143.7, 137.3, 136.1, 134.4, 132.2, 130.5, 130.4, 129.4, 128.6, 128.2, 127.9, 127.6, 126.8, 125.1, 124.9, 123.2, 122.8, 122.6, 117.5, 114.3, 112.6, 112.5, 97.8, 20.6 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{26}H_{18}BrN_3NaO_2S$ 538.01953, found 538.02063.

***N*-(4-Chloro-2-(3-cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3c).** The general procedure was followed using 5-chloro-3-nitro-*N*-tosyl indole **1c** (100 mg, 0.28 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (106 mg, 0.42 mmol) and KOH (64 mg, 1.14 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3c** as a yellow solid (96 mg, 72%). Mp: 190–192 °C. IR (neat) ν_{max}: 3839, 3751, 3570, 3481, 3265, 3239, 3142, 3048, 2952, 2207, 1595, 1490, 1327, 1160, 1087, 890, 778, 674 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.02 (d, J = 7.5 Hz, 1H), 7.72 (d, J = 9 Hz, 1H), 7.63 (d, J = 7.5 Hz, 1H), 7.42–7.37 (m, 2H), 7.29 (d, J = 8 Hz, 2H), 7.16–7.05 (m, 6H), 6.32 (s, 1H), 6.25 (s, 1H), 2.32 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 144.4, 135.9, 134.3, 131.4, 130.7, 130.1, 129.8, 129.7, 128.8, 128.6, 128.5, 128.3, 127.7, 127.0, 124.7, 123.1, 122.7, 122.5, 114.8, 112.6, 111.6, 98.3, 21.6 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{26}H_{18}ClN_3NaO_2S$ 494.07004, found 494.07205.

***N*-(2-(3-Cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)-4-fluorophenyl)-4-methylbenzenesulfonamide (3d).** The general procedure was followed using 5-flouro-3-nitro-*N*-tosyl-indole **1d** (100 mg, 0.29 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (111 mg, 0.44 mmol) and KOH (67 mg, 1.19 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3d** as a brown solid (97 mg, 71%). Mp: 172–174 °C. IR (neat) ν_{max}: 3869, 3805, 3714, 3622, 3479, 3326, 3190, 2214, 1546, 1453, 1324, 1154, 1087, 784, 662 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.07 (d, J = 7 Hz, 1H), 7.85–7.82 (m, 1H), 7.69 (d, J = 8 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.30 (d, J = 8 Hz, 2H), 7.25–7.17 (m, 3H), 7.15 (d, J = 7.5 Hz, 1H), 7.10 (d, J = 7.5 Hz, 2H), 6.94 (d, J = 8 Hz, 1H), 6.27 (s, 1H), 6.26 (s, 1H), 2.38 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.0, 159.1, 144.2, 135.9, 131.6, 131.6, 129.9, 129.7, 129.6, 128.8, 128.5, 128.3, 127.7, 127.0, 125.0, 124.9, 124.6, 122.6, 122.5, 122.4, 118.3, 118.1, 116.8, 116.6, 114.8, 112.7, 112.0, 98.1, 21.6 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{26}H_{18}FN_3NaO_2S$ 478.09960, found 478.10168.

***N*-(4-Cyano-2-(3-cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3e).** The general procedure was followed using 5-cyano-3-nitro-*N*-tosyl-indole **1e** (100 mg, 0.29 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (110 mg, 0.44 mmol) and KOH (66 mg, 1.17 mmol) at rt for 1 h. Chromatography (eluent: 25% ethyl acetate in hexane) afforded the desired product **3e** as a yellow solid (71 mg, 52%). Mp: 217–220 °C. IR (neat) ν_{max}: 3920, 3870, 3815, 3750, 3674, 3535, 3463, 2906, 2209, 1523, 1490, 1334, 1163, 901 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.13 (d, J = 7.5 Hz, 1H), 7.88 (d, J = 9 Hz, 1H), 7.72 (t, J = 7 Hz, 2H), 7.53–7.46 (m, 4H), 7.22–7.15 (m, 4H), 7.06 (d, J = 8.5 Hz, 1H), 6.76 (s, 1H), 6.69 (s, 1H), 2.40 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 144.8, 140.2, 135.6, 135.5, 133.6, 130.3, 129.9, 128.8, 128.6, 128.4, 127.8, 127.1, 126.4, 124.5, 124.1, 122.6, 122.6, 122.4, 122.0, 120.7, 119.8, 119.3, 118.0, 115.1, 112.4, 111.0, 110.0, 108.0, 102.7, 99.0, 21.6 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{27}H_{18}N_4NaO_2S$ 485.10427, found 485.10656.

***tert*-Butyl(2-(3-cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl) carbamate (3g).** The general procedure was followed using 3-nitro-*N*-Boc indole **1g** (100 mg, 0.38 mmol), 2-(cyanomethyl) isoquinolin-2-ium-bromide **2a** (143 mg, 0.57 mmol) and KOH (85 mg, 1.53 mmol) at rt for 1 h. Chromatography (eluent: 10% ethyl acetate in hexane) afforded the desired product **3g** as a colourless solid (110 mg, 75%). Mp: 157–160 °C. IR (neat) ν_{max}: 3804, 3586, 3533, 3506, 3365, 2992, 2359, 2326, 2206, 1717, 1513, 1452, 1151, 1021, 829, 763, 739, 702 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.14 (d, J = 8 Hz, 1H), 8.07(d, J = 7.5 Hz, 1H), 7.61 (d, J = 8 Hz, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.42–7.39 (m, 2H), 7.26–7.22 (m, 2H), 7.19 (s, 1H), 7.17 (s, 1H), 7.10–7.07 (m, 2H), 6.22 (s, 1H), 1.23 (s, 9H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 152.7, 137.1, 131.3, 130.1, 129.4, 128.6, 128.4, 128.0, 127.2, 125.4, 124.2, 123.5, 123.4, 123.2, 122.7, 119.8, 114.5, 114.3, 113.3, 98.2, 80.6, 28.1 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{24}H_{21}N_3NaO_2$ 406.15260, found 406.15397.

***N*-(2-(3-Cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)methanesulfonamide (3h).** The general procedure was followed using 1-(methylsulfonyl)-3-nitro-1*H*-indole **1h** (100 mg, 0.42 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (155 mg, 0.62 mmol) and KOH (93 mg, 1.66 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3h** as a colourless solid (78 mg, 52%). Mp: 167–169 °C. IR (neat) ν_{max}: 3884, 3769, 3688, 3546, 3478, 3269, 2903, 2206, 1569, 1485, 1385, 1326, 1157, 1101, 969, 768 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.08 (d, J = 7.5 Hz, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.64 (d, J = 8 Hz, 1H), 7.47 (t, J = 8 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H), 7.35 (d, J = 8 Hz, 1H), 7.31 (d, J = 7.5 Hz, 1H), 7.24–7.19 (m, 2H), 7.12–7.10 (m, 2H), 6.22 (s, 1H), 2.78 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 136.0, 132.2, 130.2, 128.7, 128.6, 128.4, 127.8, 125.4, 125.0, 124.9, 122.9, 122.7, 122.7, 118.8, 114.9, 112.9, 112.8, 98.6, 39.9 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{20}H_{15}N_3NaO_2S$ 384.07772, found 384.07822.

***N*-(2-(3-Cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)benzenesulfonamide (3i).** The general procedure was followed using 3-nitro-1-(phenylsulfonyl)-1*H*-indole **1i** (100 mg, 0.33 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (124 mg, 0.50 mmol) and KOH (74 mg, 1.32 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3i** as a colourless solid (85 mg, 61%). Mp: 203–205 °C. IR (neat) ν_{max}: 3870, 3848, 3726, 3675, 3536, 3451, 3301, 3260, 2876, 2355, 2196, 1576, 1487, 1445, 1386, 1329, 1159, 1092, 896 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.02 (d, J = 7 Hz, 1H), 7.77 (d, J = 8 Hz, 1H), 7.61 (d, J = 8 Hz, 1H), 7.45–7.38 (m, 5H), 7.28–7.25 (m, 1H), 7.19–7.11 (m, 5H), 7.08 (d, J = 8 Hz, 1H), 6.31 (s, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 139.0, 135.4, 133.1, 131.7, 130.1, 129.8,

129.0, 128.7, 128.4, 128.2, 127.6, 127.0, 126.9, 125.5, 124.9, 122.8, 122.6, 122.5, 121.7, 114.7, 112.9, 98.1 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{25}H_{17}N_3NaO_2S$ 446.09337, found 446.09430.

***N*-(2-(3-Cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-2,4,6-trimethylbenzenesulfonamide (3j).** The general procedure was followed using 1-(mesitylsulfonyl)-3-nitro-1*H*-indole **1j** (100 mg, 0.29 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (109 mg, 0.44 mmol) and KOH (65 mg, 1.16 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3j** as a colourless solid (77 mg, 57%). Mp: 213–215 °C. IR (neat) ν_{max}: 3895, 3788, 3669, 3636, 3531, 3436, 3300, 3123, 2922, 2794, 2340, 2207, 1573, 1485, 1441, 1330, 1258, 1156, 1011, 791 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.02 (d, J = 7 Hz, 1H), 7.66 (d, J = 8.5 Hz, 1H), 7.61 (d, J = 8 Hz, 1H), 7.41–7.38 (m, 2H), 7.19–7.18 (m, 2H), 7.15–7.13 (m, 2H), 7.07 (d, J = 7 Hz, 1H), 6.59 (s, 1H), 6.57 (s, 2H), 6.45 (s, 1H), 2.11 (s, 3H), 2.04 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 142.4, 138.8, 135.3, 133.9, 131.8, 131.6, 129.9, 129.5, 128.6, 128.4, 128.2, 128.0, 127.5, 125.9, 124.9, 123.8, 122.9, 122.6, 122.4, 114.6, 113.7, 112.9, 98.1, 22.8, 21.0 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{28}H_{23}N_3NaO_2S$ 488.14032, found 488.14207.

***N*-(2-(3-Cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methoxybenzenesulfonamide (3k).** The general procedure was followed using 1-((4-methoxyphenyl)sulfonyl)-3-nitro-1*H*-indole **1k** (100 mg, 0.30 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (112 mg, 0.45 mmol) and KOH (68 mg, 1.20 mmol) at rt for 1 h. Chromatography (eluent: 25% ethyl acetate in hexane) afforded the desired product **3k** as a brown solid (125 mg, 91%). Mp: 183–185 °C. IR (neat) ν_{max}: 3838, 3728, 3675, 3644, 3459, 3217, 2319, 1700, 1543, 1402, 1324, 1153, 1091, 1019, 892, 836, 785, 660 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.02 (d, J = 7.5 Hz, 1H), 7.77 (d, J = 8.5 Hz, 1H), 7.60 (d, J = 8 Hz, 1H), 7.43–7.34 (m, 4H), 7.17–7.15 (m, 2H), 7.10–7.06 (m, 3H), 6.68 (d, J = 8.5 Hz, 2H), 6.43 (s, 1H), 6.30 (s, 1H), 3.75 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 163.2, 135.6, 131.6, 130.6, 129.8, 129.2, 128.6, 128.4, 128.1, 127.5, 126.7, 125.3, 124.9, 122.9, 122.7, 122.5, 121.5, 114.7, 114.1, 113.0, 55.6 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{26}H_{19}N_3NaO_3S$ 476.10393, found 476.10366.

***N*-(2-(3-Cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-2-nitrobenzenesulfonamide (3l).** The general procedure was followed using 3-nitro-1-((2-nitrophenyl)sulfonyl)-1*H*-indole **1l** (100 mg, 0.29 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (108 mg, 0.43 mmol) and KOH (64 mg, 1.15 mmol) at rt for 1 h. Chromatography (eluent: 25% ethyl acetate in hexane) afforded the desired product **3l** as a yellow solid (66 mg, 49%). Mp: 132–135 °C. IR (neat) ν_{max}: 3865, 3803, 3680, 3605, 3453, 3112, 2203, 1635, 1582, 1532, 1400, 1349, 1173, 1121, 898, 850, 777, 733 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 7.94 (d, J = 7 Hz, 1H), 7.84 (d, J = 8 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.58 (d, J = 8 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.45–7.38 (m, 3H), 7.36–7.33 (m, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.23–7.19 (m, 2H), 7.04–7.00 (m, 3H), 6.42 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 147.1, 135.0, 133.7, 132.9, 132.4, 131.5, 130.5, 130.2, 129.8, 129.0, 128.6, 128.5, 128.0, 127.7, 126.9, 125.5, 125.1, 124.9, 122.5, 122.2, 114.6, 113.5, 112.8 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{25}H_{16}N_4NaO_4S$ 491.07845, found 491.07918.

***N*-(2-(3-Cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-nitrobenzenesulfonamide (3m).** The general procedure was followed using 3-nitro-1-((4-nitrophenyl)sulfonyl)-1*H*-indole **1m** (100 mg, 0.29 mmol), 2-(cyanomethyl)isoquinolin-2-ium-bromide **2a** (108 mg, 0.43 mmol) and KOH (65 mg, 1.15 mmol) at rt for 1 h. Chromatography (eluent: 25% ethyl acetate in hexane) afforded the desired product **3m** as a yellow solid (54 mg, 40%). Mp: 209–212 °C. IR (neat) ν_{max}: 3825, 3711, 3630, 3484, 3187, 2364, 1562, 1520, 1338, 1156, 862, 754, 679 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.03 (d, J = 7.5 Hz, 1H), 7.80–7.76 (m, 3H), 7.55 (d, J = 7.5 Hz, 1H), 7.49–7.44 (m, 3H), 7.31 (t, J = 7.5 Hz, 1H), 7.24–7.19 (m, 2H), 7.05 (d, J = 7.5 Hz, 1H), 6.95 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 8.5 Hz, 1H), 6.82 (s, 1H), 6.64 (s, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 149.8, 144.8, 134.5, 132.0, 130.1, 130.0, 128.3, 128.2, 128.2, 127.9, 127.7, 127.3, 126.3, 124.7, 123.8, 122.6, 122.4, 122.3, 122.2, 114.8, 112.8, 112.6, 98.5 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{25}H_{16}N_4NaO_4S$ 491.07845, found 491.08002.

***N*-(2-(3-Benzoylpyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3n).** The general procedure was followed using 3-nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 2-(2-oxo-2-phenylethyl)isoquinolin-2-ium-bromide **2b** (156 mg, 0.47 mmol) and KOH (71 mg, 1.26 mmol) at rt for 4 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3n** as a yellow solid (111 mg, 68%). Mp: 223–226 °C. IR (neat) ν_{max}: 3843, 3741, 3633, 3438, 3251, 2371, 1608, 1487, 1436, 1334, 1231, 1159, 905, 871, 807 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.59 (d, J = 7.5 Hz, 1H), 7.78–7.76 (m, 3H), 7.64 (d, J = 8 Hz, 1H), 7.54–7.52 (m, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.42–7.36 (m, 2H), 7.24 (s, 1H), 7.21–7.19 (m, 2H), 7.15–7.11 (m, 3H), 7.04 (t, J = 7.5 Hz, 1H), 6.73 (d, J = 8 Hz, 2H), 6.65 (s, 1H), 6.46 (s, 1H), 2.07 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 185.4, 143.7, 140.2, 136.0, 135.7, 132.7, 131.7, 131.5, 129.6, 129.5, 129.3, 129.2, 128.4, 128.0, 127.8, 127.2, 127.0, 127.0, 126.8, 125.5, 125.0, 124.6, 124.0, 123.4, 120.5, 114.3, 113.1, 21.4 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + H)^+$ calcd for $C_{32}H_{25}N_2O_3S$ 517.15804, found 517.15996.

***N*-(2-(3-(4-Chlorobenzoyl)pyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3o).** The general procedure was followed using 3-nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 2-(2-(4-chlorophenyl)-2-oxoethyl)isoquinolin-2-ium bromide **2c** (172 mg, 0.47 mmol) and KOH (71 mg, 1.26 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3o** as a yellow solid (127 mg, 73%). Mp: 215–218 °C. IR (neat) ν_{max}: 3837, 3750, 3478, 3247, 2360, 1606, 1433, 1365, 1331, 1155, 1084, 900, 804 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.54 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 8.5 Hz, 1H), 7.71 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 8 Hz, 1H), 7.43–7.36 (m, 4H), 7.26 (d, J = 8 Hz, 2H), 7.20–7.12 (m, 4H), 7.05 (t, J = 7.5 Hz, 1H), 6.74 (d, J = 7.5 Hz, 2H), 6.60 (s,

1H), 6.44 (s, 1H), 2.11 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 183.9, 143.8, 138.5, 137.8, 136.0, 135.7, 133.0, 131.7, 130.5, 129.6, 129.3, 128.7, 128.2, 127.9, 127.1, 127.0, 126.7, 125.4, 125.0, 124.5, 123.7, 123.4, 120.5, 114.5, 113.3, 21.4 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{32}H_{33}ClN_2NaO_3S$ 573.10101, found 573.10307.

4-Methyl-*N*-(2-(3-(4-nitrobenzoyl)pyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)benzenesulfonamide (3p). The general procedure was followed using 3-nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 2-(2-(4-nitrophenyl)-2-oxoethyl)isoquinolin-2-ium bromide **2d** (177 mg, 0.47 mmol) and KOH (71 mg, 1.26 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3p** as a bright yellow solid (134 mg, 75%). Mp: 199–203 °C. IR (neat) ν_{max}: 3876, 3831, 3798, 3717, 3573, 3463, 3404, 3229, 2348, 1740, 1650, 1587, 1523, 1440, 1333, 1161, 1086, 798, 704 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.61 (d, J = 7.5 Hz, 1H), 8.30 (d, J = 8.5 Hz, 2H), 7.91 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 8 Hz, 1H), 7.68 (d, J = 8 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 8 Hz, 2H), 7.20–7.19 (m, 2H), 7.16–7.11 (m, 2H), 7.05 (t, J = 7.5 Hz, 1H), 6.79 (d, J = 8 Hz, 2H), 6.73 (s, 1H), 6.45 (s, 1H), 2.12 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 182.7, 149.3, 145.6, 143.8, 136.1, 135.7, 133.7, 131.7, 129.9, 129.8, 129.4, 128.5, 128.1, 127.3, 127.2, 127.0, 126.5, 125.4, 124.9, 124.4, 124.6, 123.6, 123.2, 120.1, 115.1, 114.0, 21.4 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{32}H_{23}N_3NaO_5S$ 584.12506, found 584.12785.

***N*-(4-Bromo-2-(3-(4-nitrobenzoyl)pyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4 methylbenzene sulfonamide (3q).** The general procedure was followed using 5-bromo-3-nitro-*N*-tosyl indole **1b** (100 mg, 0.25 mmol), 2-(2-(4-nitrophenyl)-2-oxoethyl)isoquinolin-2-ium bromide **2d** (142 mg, 0.38 mmol) and KOH (57 mg, 1.01 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3q** as a yellow solid (115 mg, 71%). Mp: 250–252 °C. IR (neat) ν_{max}: 3937, 3870, 3792, 3726, 3597, 3560, 3527, 3396, 3337, 3238, 3043, 2927, 1729, 1694, 1589, 1518, 1468, 1435, 1334, 1163, 802, 702 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.59 (d, J = 7.5 Hz, 1H), 8.31 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8 Hz, 2H), 7.69 (d, J = 7.5 Hz, 1H), 7.60 (d, J = 9 Hz, 1H), 7.49–7.46 (m, 2H), 7.34 (s, 1H), 7.28 (s, 1H), 7.21–7.19 (m, 2H), 7.16–7.10 (m, 2H), 6.81 (d, J = 7.5 Hz, 2H), 6.69 (s, 1H), 6.42 (s, 1H), 2.14 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 182.8, 149.4, 145.4, 144.0, 135.9, 135.0, 134.3, 133.5, 132.7, 129.9, 129.8, 129.5, 128.7, 128.5, 128.3, 127.3, 127.1, 127.0, 125.4, 124.1, 123.6, 123.5, 123.4, 121.5, 117.6, 115.2, 112.4, 21.4 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{32}H_{22}BrN_3NaO_5S$ 662.03558, found 662.03709.

Ethyl 1-(2-(4-methylphenylsulfonamido)phenyl)pyrrolo[2,1-*a*]isoquinoline-3-carboxylate (3r). The general procedure was followed using 3-nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 2-(2-ethoxy-2-oxoethyl)isoquinolin-2-ium-bromide **2e** (140 mg, 0.47 mmol) and KOH (71 mg, 1.26 mmol) at rt for 1 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3r** as a colourless solid (95 mg, 62%). Mp: 125–126 °C. IR (neat) ν_{max}: 3904, 3831, 3700, 3437, 3267, 2837, 1684, 1544, 1493, 1447, 1380, 1332, 1290, 1203, 1158, 1079, 954, 902, 790, 742 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.23 (d, J = 7.5 Hz, 1H), 7.77 (d, J = 8.5 Hz, 1H), 7.56 (d, J = 8 Hz, 1H), 7.38–7.30 (m, 2H), 7.27 (d, J = 8 Hz, 2H), 7.18–7.10 (m, 2H), 7.04 (d, J = 8 Hz, 1H), 7.00–6.95 (m, 2H), 6.87–6.86 (m, 3H), 6.54 (s, 1H), 4.35 (q, J = 7 Hz, 2H,), 2.19 (s, 3H), 1.37 (t, J = 7 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.1, 143.6, 136.0, 135.5, 131.7, 131.1, 130.3, 129.4, 129.3, 128.5, 127.7, 127.6, 127.4, 127.0, 127.0, 127.0, 125.0, 125.0, 124.6, 122.9, 122.0, 120.8, 116.3, 113.5, 112.3, 60.3, 21.6, 14.6 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{28}H_{24}N_2NaO_4S$ 507.13490, found 507.13644.

***N*-(2-(7-Bromo-3-cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3s).** The general procedure was followed using 3-nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 5-bromo-2-(cyanomethyl)isoquinolin-2-ium-bromide **2f** (156 mg, 0.47 mmol) and KOH (71 mg, 1.26 mmol) at rt for 1 h. Chromatography (eluent: 10% ethyl acetate in hexane) afforded the desired product **3s** as a colourless solid (96 mg, 59%). Mp: 74–76 °C. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.13 (d, J = 7.5 Hz, 1H), 7.82 (d, J = 8.5 Hz, 1H), 7.69 (d, J = 8 Hz, 1H), 7.56 (d, J = 7.5 Hz, 1H), 7.50–7.46 (m, 1H), 7.36 (d, J = 8 Hz, 2H), 7.24–7.14 (m, 3H), 7.08 (d, J = 8 Hz, 2H), 6.98 (t, J = 8 Hz, 1H), 6.50 (s, 1H), 6.40 (s, 1H), 2.37 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 144.1, 136.1, 135.5, 131.9, 131.5, 130.0, 129.6, 129.3, 129.0, 127.6, 127.0, 126.5, 126.4, 125.5, 123.7, 123.4, 122.5, 122.1, 121.8, 113.8, 113.2, 112.5, 98.3, 21.6 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + Na)^+$ calcd for $C_{26}H_{18}BrN_3NaO_2S$ 538.01953, found 538.02089.

***N*-(2-(3-Benzoyl-7-bromopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3t).** The general procedure was followed using 3 -nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 5-bromo-2-(2-oxo-2-phenylethyl)isoquinolin-2-ium bromide **2g** (192 mg, 0.47 mmol) and KOH (71 mg, 1.26 mmol) at rt for 4 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3t** as a yellow solid (98 mg, 52%). Mp: 243–247 °C. IR (neat) ν_{max}: 3916, 3877, 3804, 3670, 3529, 3444, 2957, 2450, 1727, 1673, 1618, 1334, 1162, 911, 867, 787 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.62 (d, J = 7.5 Hz, 1H), 7.79–7.75 (m, 3H), 7.64 (d, J = 7.5 Hz, 1H), 7.55–7.53 (m, 2H), 7.46 (t, J = 7.5 Hz, 2H), 7.40–7.37 (m,1H), 7.25 (d, J = 8 Hz, 2H), 7.17–7.11 (m, 3H), 6.86 (t, J = 8 Hz, 1H), 6.74 (d, J = 8 Hz, 2H), 6.71 (s, 1H), 6.42 (s, 1H), 2.08 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 185.5, 143.8, 139.9, 136.0, 135.6, 131.8, 131.8, 131.7, 131.6, 129.7, 129.3, 129.2, 128.6, 128.4, 128.2, 127.0, 127.0, 126.7, 126.1, 125.1, 124.0, 122.8, 122.0, 120.8, 113.7, 112.8, 21.4 ppm. HRMS (ESI-Orbitrap) *m*/*z*: $(M + H)^+$ calcd for 617.05050, found 617.05084.

***N*-(2-(6-Bromo-3-cyanopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3u).** The general procedure was followed using 3-nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 4-bromo-2-(cyanomethyl)isoquinolin-2-ium-bromide **2h** (156 mg, 0.47 mmol) and KOH (70 mg, 1.26 mmol) at rt for 1 h. Chromatography (eluent: 10% ethyl acetate in hexane) afforded the desired product **3u** as a yellow solid (88 mg, 54%). Mp: 167–170 °C. IR (neat) ν_{max}: 3917, 3847,

3803, 3619, 3448, 3227, 2204, 1591, 1489, 1434, 1331, 1159, 1086, 915, 811 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.37 (s, 1H), 8.04 (d, J = 8 Hz, 1H), 7.84 (d, J = 8.5 Hz, 1H), 7.56–7.53 (m, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.37 (d, J = 7.5 Hz, 2H), 7.28–7.21 (m, 4H), 7.09 (d, J = 7.5 Hz, 2H), 6.46 (s, 2H), 2.38 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 144.0, 136.2, 135.6, 131.5, 129.9, 129.5, 129.4, 128.6, 127.3, 127.2, 127.0, 126.4, 125.4, 125.0, 123.6, 123.1, 122.9, 121.8, 113.6, 112.4, 110.8, 98.0, 21.6 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{26}H_{18}BrN_3NaO_2S$ 538.01953, found 538.02112.

***N*-(2-(3-Benzoyl-6-bromopyrrolo[2,1-*a*]isoquinolin-1-yl)phenyl)-4-methylbenzenesulfonamide (3v).** The general procedure was followed using 3-nitro-*N*-tosyl indole **1a** (100 mg, 0.32 mmol), 4-bromo-2-(2-oxo-2-phenylethyl)isoquinolin-2-ium bromide **2i** (192 mg, 0.47 mmol) and KOH (71 mg, 1.26 mmol) at rt for 4 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **3v** as a yellow solid (90 mg, 48%). Mp: 230–234 °C. IR (neat) ν_{max}: 3878, 3744, 3638, 3557, 3492, 3264, 3059, 1744, 1708, 1649, 1613, 1428, 1335, 1160, 1089, 980, 903, 814, 762, 727 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.92 (s, 1H), 8.02 (d, J = 8 Hz, 1H), 7.77–7.74 (m, 3H), 7.53 (t, J = 7 Hz, 1H), 7.50–7.43 (m, 3H), 7.38 (t, J = 7.5 Hz, 1H), 7.24 (d, J = 8 Hz, 2H), 7.19–7.12 (m, 3H), 7.08 (t, J = 7.5 Hz, 1H), 6.72 (d, J = 8 Hz, 2H), 6.67 (s, 1H), 6.43 (s, 1H), 2.07 (s, 3H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 185.4, 143.8, 139.8, 136.0, 135.6, 131.8, 131.7, 131.6, 129.7, 129.3, 129.2, 128.7, 128.5, 128.2, 126.9, 126.9, 126.9, 126.6, 126.6, 125.2, 124.5, 123.8, 123.5, 120.9, 113.5, 110.6, 21.5 ppm. HRMS (ESI-Orbitrap) m/z: $(M + H)^+$ calcd for$C_{32}H_{23}BrN_2NaO_sS$ 617.05050, found 617.05255.

Phenyl(1-phenylpyrrolo[2,1-*a*]isoquinolin-3-yl)methanone (3w). The general procedure was followed using 3-nitro-*N*-methyl indole **1n** (100 mg, 0.57 mmol), 2-(2-oxo-2-phenylethyl)isoquinolin-2-ium-bromide **2b** (279 mg, 0.85 mmol) and KOH (128 mg, 2.28 mmol) at rt for 1 h. Chromatography (eluent: 5% ethyl acetate in hexane) afforded the desired product **3w** as a yellow solid (65 mg, 33%). Mp: 183–185 °C. IR (neat) ν_{max}: 3700, 3643, 3531, 3557, 3358, 2328, 1911, 1764, 1730, 1598, 1566, 1443, 1393, 1364, 1331, 1282, 1195, 902, 790, 747, 718 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.30 (d, J = 8 Hz, 1H), 8.19 (d, J = 7.5 Hz, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.59–7.55 (m, 2H), 7.52 (d, J = 8 Hz, 2H), 7.19 (t, J = 7 Hz, 1H), 7.15–7.13 (m, 3H), 7.09–7.04 (m, 6H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 187.6, 139.7, 138.1, 135.8, 134.8, 131.2, 130.1, 129.8, 128.9, 127.9, 127.7, 127.7, 127.5, 126.9, 126.6, 125.3, 124.7, 123.4, 122.0, 113.0, 103.6 ppm. HRMS (ESI-Orbitrap) m/z: $(M + H)^+$ calcd for$C_{25}H_{18}NO$ 348.13829, found 348.13923.

Synthesis and characterization of 4

The compound **3a** (100 mg, 0.23 mmol) was treated with concentrated H_2SO_4 (2.0 equiv.) at room temperature for 2 hours. After completion of the reaction as indicated from the TLC, the reaction mixture was cooled and quenched by drop-wise addition of saturated $NaHCO_3$ solution and the aqueous layer extracted three times with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue was then purified by column chromatography (50% ethyl acetate in hexane) to afford the pyrrolo[2,1-*a*]isoquinoline **4** as a brown solid (49 mg, 71%). Analytical data of **4**: Mp: 118–120 °C. ^1H NMR (500 MHz, $(CD_3)_2CO$, TMS): δ 9.45 (d, J = 7.5 Hz, 1H), 7.64 (d, J = 8 Hz, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.28 (t, J = 7.5 Hz, 1H), 7.24 (s, 1H), 7.13 (t, J = 7.5 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 7.02 (d, J = 7.5 Hz, 1H), 6.95 (d, J = 8 Hz, 1H), 6.75 (d, J = 8 Hz, 1H), 6.60 (t, J = 7 Hz, 1H), 4.28 (s, 2H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $(CD_3)_2CO$): δ 163.3, 146.7, 131.2, 129.0, 128.7, 128.1, 127.0, 126.6, 126.5, 126.0, 125.2, 123.4, 121.3, 118.7, 118.5, 116.8, 115.7, 115.1, 114.6, 112.0 ppm. HRMS (ESI-Orbitrap) m/z: $(M + H)^+$ calcd for $C_{19}H_{16}N_3O$ 302.12879, found 302.12991.

Experimental procedure for the reaction between 3-nitrobenzothiophene and isoquinolinium salt

A mixture of 3-nitrobenzothiophene (1.0 equiv., 100 mg), isoquinolinium salt (1.5 equiv.) and K_3PO_4 (2.0 equiv.) was weighed into a dry reaction tube. Dry CH_3CN was added and allowed to stir at 60 °C for 24 h. After completion of the reaction, the solvent was removed under vacuum. The residue was then purified by column chromatography (silica gel, eluent: mixtures of ethyl acetate/hexanes) to afford the corresponding products.

Synthesis and characterization of bis-pyrrolo[2,1-*a*] isoquinolines (6a–6e)

(1,1′-(Disulfanediylbis(2,1-phenylene))bis(pyrrolo[2,1-*a*]isoquinoline-3,1-diyl))bis(phenylmethanone) (6a). The general procedure was followed using 3-nitrobenzo[*b*]thiophene **5a** (100 mg, 0.56 mmol), 2-(2-oxo-2-phenylethyl)isoquinolin-2-ium-bromide **2b** (275 mg, 0.84 mmol) and K_3PO_4 (237 mg, 1.12 mmol) at 60 °C for 24 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **6a** as a yellow solid (169 mg, 80%). Mp: 249–252 °C. IR (neat) ν_{max}: 3945, 3846, 3779, 3682, 3538, 2961, 2363, 1728, 1613, 1414, 1331, 1227, 1168, 1121, 1072, 1031, 965, 932, 871, 791, 756, 727, 688 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.61 (dd, J_1 = 7.5 Hz, J_2 = 1 Hz, 2H), 7.80–7.77 (m, 4H), 7.63 (t, J = 7 Hz, 2H), 7.47–7.42 (m, 5H), 7.41–7.37 (m, 7H), 7.25–7.20 (m, 3H), 7.17–7.14 (m, 3H), 7.12–7.05 (m, 6H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 185.6, 185.5, 140.5, 140.4, 137.1, 137.1, 134.4, 134.4, 132.8, 132.7, 131.3, 131.3, 129.7, 129.6, 129.2, 128.9, 128.9, 128.2, 127.9, 127.8, 127.8, 127.6, 127.5, 127.0, 126.9, 126.5, 126.4, 125.7, 125.7, 125.5, 125.4, 125.2, 125.1, 124.0, 123.7, 123.7, 116.4, 114.0 ppm. HRMS (ESI-Orbitrap) m/z: $(M + H)^+$ calcd for $C_{50}H_{33}N_2O_2S_2$ 757.19780, found 757.20007.

(1,1′-(Disulfanediylbis(2,1-phenylene))bis(pyrrolo[2,1-*a*]isoquinoline-3,1-diyl))bis((4-nitrophenyl)methanone) (6b). The general procedure was followed using 3-nitrobenzo[*b*]thiophene **5a** (100 mg, 0.56 mmol), 2-(2-(4-nitrophenyl)-2-oxoethyl) isoquinolin-2-ium-bromide **2d** (312 mg, 0.84 mmol) and K_3PO_4 (237 mg, 1.12 mmol) at 60 °C for 24 h. Chromatography (eluent: 20% ethyl acetate in hexane) afforded the desired product **6b** as a yellow solid (145 mg, 61%). Mp: 290–292 °C.

IR (neat) ν_{max}: 3900, 3822, 3722, 3650, 3430, 2959, 2918, 2336, 1727, 1616, 1519, 1334, 1282, 1119, 1072, 853, 798, 729, 697 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.62 (d, J = 7.5 Hz, 2H), 8.26–8.24 (m, 4H), 7.93–7.90 (m, 4H), 7.69 (t, J = 7 Hz, 2H), 7.50–7.36 (m, 7H), 7.27–7.23 (m, 3H), 7.17–7.06 (m, 8H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 182.8, 182.7, 149.2, 145.9, 145.9, 137.0, 137.0, 134.0, 133.9, 133.8, 133.7, 131.3, 129.9, 129.1, 129.1, 128.5, 128.4, 127.9, 127.9, 127.8, 127.8, 127.2, 127.1, 126.7, 126.7, 125.6, 125.5, 125.0, 124.9, 124.1, 123.5, 123.1, 123.0, 117.2, 117.2, 114.7 ppm. HRMS (ESI-Orbitrap) m/z: $(M + H)^+$ calcd for $C_{25}H_{15}N_2O_3S$ 847.16795, found 847.16754.

(1,1′-(Disulfanediylbis(3-bromo-6,1phenylene))bis(pyrrolo[2,1-*a*]isoquinoline-3,1 diyl))bis(phenylmethanone) (6c). The general procedure was followed using 5-bromo-3-nitrobenzo[*b*]thiophene **5b** (100 mg, 0.39 mmol), 2-(2-oxo-2-phenylethyl)isoquinolin-2-ium-bromide **2b** (191 mg, 0.58 mmol) and K_3PO_4 (165 mg, 0.78 mmol) at 60 °C for 24 h. Chromatography (eluent: 10% ethyl acetate in hexane) afforded the desired product **6c** as a light yellow solid (117 mg, 66%). Mp: 230–232 °C. IR (neat) ν_{max}: 3952, 3803, 3390, 3072, 2958, 2922, 2357, 1722, 1606, 1572, 1457, 1328, 1279, 1118, 1070, 938, 868, 791, 742, 687 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.60 (d, J = 7.5 Hz, 2H), 7.78 (t, J = 7 Hz, 4H), 7.70–7.66 (m, 2H), 7.50–7.46 (m, 3H), 7.44–7.39 (m, 8H), 7.33 (d, J = 8 Hz, 1H), 7.26–7.22 (m, 2H), 7.18–7.05 (m, 8H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 185.6, 185.6, 140.3, 140.2, 136.4, 136.4, 136.3, 133.9, 132.6, 132.4, 131.9, 131.8, 131.5, 129.7, 129.6, 129.2, 128.3, 128.3, 128.2, 128.2, 127.7, 127.6, 127.5, 127.5, 127.4, 127.3, 127.2, 127.1, 125.7, 125.6, 124.9, 124.8, 123.9, 123.8, 123.7, 120.4, 120.4, 114.9, 114.9, 114.2, 114.2 ppm. HRMS (ESI-Orbitrap) m/z: $(M + H)^+$ calcd for $C_{50}H_{31}Br_2N_2O_2S_2$ 915.01677, found 915.01770.

Diethyl1,1′-(disulfanediylbis(2,1-phenylene))bis(pyrrolo[2,1-*a*]isoquinoline-3-carboxylate)(6d). The general procedure was followed using 3-nitrobenzo[*b*]thiophene **5a** (100 mg, 0.56 mmol), 2-(2-ethoxy-2-oxoethyl)isoquinolin-2-ium-bromide **2e** (248 mg, 0.84 mmol) and K_3PO_4 (237 mg, 1.12 mmol) at 60 °C for 24 h. Chromatography (eluent: 5% ethyl acetate in hexane) afforded the desired product **6d** as a colourless solid (93 mg, 48%). Mp: 248–250 °C. IR (neat) ν_{max}: 3898, 3841, 3732, 3598, 3357, 2917, 2846, 2312, 1738, 1477, 1444, 1374, 1331, 1203, 1074, 693, 665 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.26 (d, J = 7.5 Hz, 2H), 7.60–7.58 (m, 2H), 7.48–7.46 (m, 1H), 7.42 (dd, J_1 = 8 Hz, J_2 = 1 Hz, 1H), 7.39–7.32 (m, 6H), 7.23–7.20 (m, 2H), 7.18–7.10 (m, 6H), 6.99 (d, J = 7.5 Hz, 2H), 4.36–4.29 (m, 4H), 1.36–1.32 (m, 6H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4, 161.4, 137.1, 137.0, 134.6, 131.3, 131.2, 131.1, 128.8, 128.7, 128.6, 128.5, 127.5, 127.4, 127.2, 126.9, 126.8, 126.3, 126.3, 125.6, 125.6, 125.3, 125.2, 124.8, 124.8, 123.5, 122.6, 115.9, 115.9, 115.6, 115.6, 60.2, 14.5 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{42}H_{32}N_2NaO_4S_2$ 715.16957, found 715.17230.

Diethyl 1,1′-(disulfanediylbis(3-bromo-6,1-phenylene))bis(pyrrolo[2,1-a]isoquinoline-3-carboxylate) (6e). The general procedure was followed using 5-bromo-3-nitrobenzo[*b*]thiophene **5b** (100 mg, 0.39 mmol), 2-(2-ethoxy-2-oxoethyl)isoquinolin-2-ium-bromide **2e** (172 mg, 0.58 mmol) and K_3PO_4 (165 mg, 0.78 mmol) at 60 °C for 24 h. Chromatography (eluent: 10% ethyl acetate in hexane) afforded the desired product **6e** as a colourless solid (66 mg, 40%). Mp: 237–240 °C. IR (neat) ν_{max}: 3911, 3840, 3754, 3681, 3603, 3564, 3263, 3130, 2361, 1691, 1457, 1375, 1340, 1214, 1077, 801, 745, 691, 638 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 9.26 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 2H), 7.64–7.60 (m, 2H), 7.43–7.38 (m, 4H), 7.34–7.31 (m, 2H), 7.28–7.27 (m, 2H), 7.22–7.14 (m, 6H), 7.03–7.00 (m, 2H), 4.37–4.29 (m, 4H),1.36–1.32 (m, 6H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.3, 161.2, 136.7, 136.3, 136.3, 133.9, 133.9, 131.8, 131.7, 131.1, 130.9, 128.6, 128.6, 127.6, 127.6, 127.5, 127.5, 127.4, 127.1, 127.0, 125.3, 125.2, 124.8, 124.8, 123.2, 122.4, 122.3, 120.3, 120.3, 116.2, 116.1, 114.2, 114.1, 113.4, 113.4, 60.3, 60.3, 14.5, 14.5 ppm. HRMS (ESI-Orbitrap) m/z: $(M + Na)^+$ calcd for $C_{42}H_{30}Br_2N_2NaO_4S_2$ 872.98855, found 872.98987.

Conflicts of interest

There are no conflicts to declare.

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