Tetrahedron 66 (2010) 3016–3023

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Detosylation of 3-amino-1-tosylindole-2-carbonitriles using DBU and thiophenol

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ARTICLE INFO

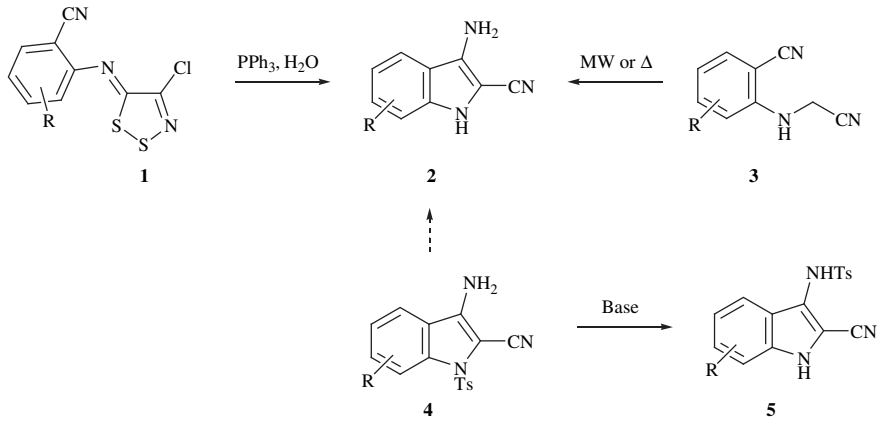
Article history:
Received 30 November 2009
Received in revised form 23 January 2010
Accepted 15 February 2010
Available online 18 February 2010

ABSTRACT

Attempted detosylation of the 3-amino-1-(*p*-tosylamino)indole-2-carbonitriles **4a–c** using either K_2CO_3 in EtOH or DBU in PhH at reflux gives unexpectedly the 3-(*N*-*p*-tosylamino)indole-2-carbonitriles **5a–c**, respectively in high yields. Nevertheless, treatment of 1-(*p*-tosylamino)indoles **4a–c** with thiophenol and DBU in PhH at reflux gives the detosylated 3-aminoindole-2-carbonitriles **5a–c**. Reaction mechanisms supporting the tosyl migration (**4**→**5**) and the reductive detosylation (**4**→**2**) are proposed. All new compounds are fully characterised.

1. Introduction

Indoles are important in both the biological and material sciences.[1] More specifically, several substituted 2-cyanoindoles are important intermediates in the synthesis of heteroaromatic molecules and biologically active compounds.[2,3] We recently developed two new routes to 3-aminoindole-2-carbonitriles **2**: The first a non classical route starting from 2-(4-chloro-1,2,3-dithiazolylidenamino)benzonitriles **1** on reaction with triphenylphosphine,[4] while the second was via a microwave assisted Thorpe–Ziegler cyclisation of the 2-(cyanomethylamino)benzonitriles **3**.[5] During these studies we pursued a synthesis of 3-aminoindole-2-carbonitriles **2** from the known 3-amino-1-tosylindole-2-carbonitrile **4**, however, detosylation proved difficult. Surprisingly our efforts to detosylate 3-amino-1-tosylindole-2-carbonitriles **4** in the presence of ethoxide at reflux in ethanol failed, while at higher temperatures (sealed tube) the unexpected 3-(*N*-tosyamino)indole-2-carbonitriles **5** were obtained in high yield (Scheme 1).



Scheme 1.

Since the tosyl group has been used as an indole N-protecting group numerous times and a popular method for detosylation involved treatment with alkali bases or alkoxides,[6,7] we found this migration to be curious and worthy of further study. Below we describe the difficulties encountered with the detosylation of 3-amino-1-tosylindole-2-carbonitrile **4** and provide a modified, high yielding process for a clean detosylation of 3-amino-1-tosylindole-2-carbonitrile that involves the use of thiophenol.

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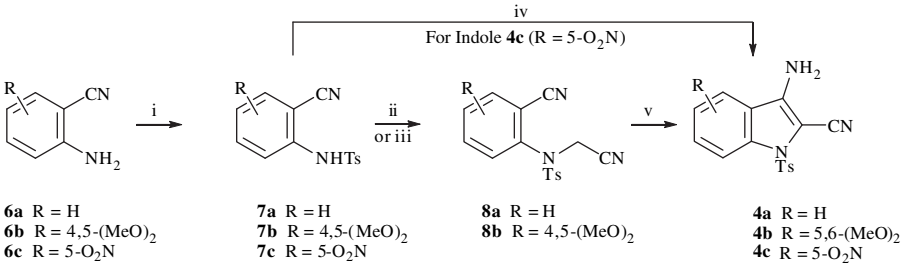
doi:10.1016/j.tet.2010.02.058

2. Results and discussion

Initially we re-investigated the synthesis of 3-amino-1-tosylindole-2-carbonitrile **4a** starting from anthranilonitrile **6a**.[8] This synthetic strategy was optimized to provide good yields of the parent, the 5,6-dimethoxy and the 5-nitro 3-amino-1-tosylindole-2-carbonitriles **4a**–**c** (Scheme 2).

During the investigation of this route to the 3-amino-1-tosylindole-2-carbonitriles **4a**–**c** some interesting observations were made:



Scheme 2. Reagents and conditions: (i) TsCl (1 equiv), C_5H_5N, 100 °C, 5 h, **7a** (5 h, 87%), **7b** (7 h, 80%) **7c** (36 h, 81%); (ii) $ClCH_2CN$ (1 equiv), K_2CO_3 (1 equiv), dry DMF, 100 °C, 70 min, (sealed tube) **8a** (70 min, 81%) **8b** (2 h, 73%); (iii) $ClCH_2CN$ (1 equiv), K_2CO_3 (1 equiv), dry DMF, MW (250 W), 12 PSI, **8a** (122 °C, 1 h, 86%) **8b** (100 °C, 10 min, 81%); (iv) $ClCH_2CN$ (1 mL), K_2CO_3 (2 equiv), 100 °C, **4c** (24 h, 40%), **6c**, (24 h, 46%); (v) K_2CO_3 (0.01 equiv), EtOH, **4a** (ca. 20 °C, 26 h, 96%), **4b** (78 °C, 30 h, 93%).

2.1. Cyanomethylation

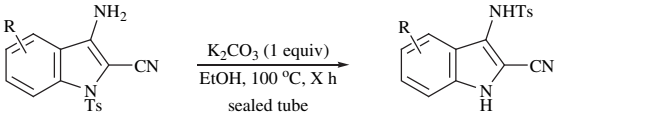
The direct cyanomethylation of anthranilonitrile **6a** using chloroacetonitrile could not be achieved and a prior N-monotosylation was needed.[8,9] Cyanomethylation of either 2-(*p*-tosylamino)benzonitrile **7a** or 4,5-dimethoxy-2-(*p*-tosylamino)-benzonitrile **7b** worked relatively well. When only 1 equiv of chloroacetonitrile was used, the cyanomethylation worked best in dry DMF and required at least 1 equiv of K_2CO_3. These reactions worked equally well using either conventional or microwave heating. In neat chloroacetonitrile or in EtOH, THF or DMF with excess chloroacetonitrile (120 equiv) at ca. 65 °C, quantitative yields of the cyanomethylated products **8a** and **8b** could be obtained with respect to the starting 2-(tosylamino)-benzonitriles **7a** and **7b**. Cyanomethylation of 5-nitro-2-(tosylamino)benzonitrile **7c** however, could not readily be controlled and heating 5-nitro-2-(tosylamino)benzonitrile **7c** in an excess of chloroacetonitrile at 100 °C in the presence of K_2CO_3 (2 equiv) for one day gave in moderate yield the cyclised 5-nitro-3-(tosylamino)indole-2-carbonitrile **4c** (40%) together with detosylated 2-amino-5-nitrobenzonitrile **6c** (46%).

2.2. Thorpe–Ziegler cyclisation

The ring closure of *N*-(2-cyanophenyl)-*N*-(*p*-tosyl)aminoacetonitriles **8a** and **8b** to afford the 3-amino-1-tosylindole-2-carbonitriles **4a** and **4b**, respectively, worked well in both DCM and EtOH and was dependent on the nature of the base. Weak amine bases such as pyridine and Et_3N failed to cyclise *N*-(2-cyanophenyl)-*N*-(*p*-tosyl)aminoacetonitrile **8a**, while DBU (0.5 equiv) in EtOH at ca. 20 °C for 1 h gave the indole **4a** in high yield (98%). The use of <0.5 equiv of DBU (0.25 equiv) in EtOH at ca. 20 °C for four days however, led to incomplete reaction. In EtOH the use of inorganic bases was superior; alkali metal bicarbonates, carbonates and hydroxide bases worked well, the stronger the base the faster the reaction. The use of only a catalytic quantity of K_2CO_3 (1 mol %) in EtOH at ca. 20 °C led to a near quantitative cyclisation in 26 h, while the use of either NaOH or Cs_2CO_3 (2 equiv) led to a quantitative conversion in ca. 1 min.

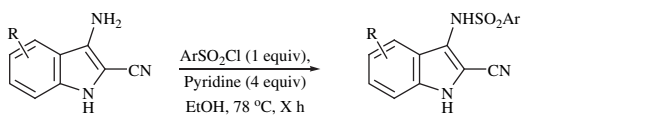
2.3. Detosylation

Rather surprisingly detosylating 3-amino-1-tosylindole-2-carbonitrile **4a** proved difficult. Acid treatment of the 1-tosylindole **4a** with either sulfuric acid 95%, or conc. HCl, or with HBr (48%) in the presence of phenol, or even glacial AcOH or *p*-TSA gave at first no reaction while prolonged heating led to highly coloured mixtures from which indigo and isoindigo could be tentatively identified (TLC). Reductive cleavage using $NaBH_4$ in MeOH, or $LiAlH_4$ in THF, or treatment with Li dust in THF or Na metal in liquid NH_3/THF also failed to provide the detosylated indole **2a**. Heating 3-amino-1-tosylindole-2-carbonitriles **4a**–**c** (0.06 mmol) in EtOH (1 mL) in the presence of K_2CO_3 (1 equiv) at reflux for 24 h gave only recovered starting materials but at ca. 100 °C (sealed tube), 3-(*N*-tosylamino)-indole-2-carbonitriles **5a**–**c** were isolated in good yields. In the absence of K_2CO_3, heating the reactions in EtOH at 100 °C (sealed tube) led to the recovery of unreacted 1-tosylindoles **4a**–**c**.

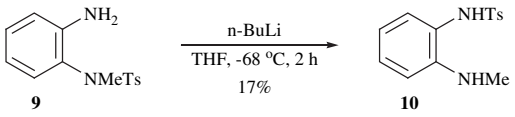


The isomerisation could also be achieved when 3-amino-1-tosylindole-2-carbonitrile **4a** was treated with DBU (0.2 equiv, 24 h, to 3 equiv, 1 h) in PhH at 80 °C however, during these reactions the mixtures became notably green in colour prior to affording 3-(*N*-tosylamino)indole-2-carbonitrile **5a** in 76–80% yields. The isomerisation could not be achieved when DBU was replaced by either pyridine, Et_3N or DMAP (1 equiv).

Furthermore, sulfonylation of 3-aminoindoles with TsCl,[10] or 4-aminobenzenesulfonyl chlorides[11] was reported to occur regioselectively on the exocyclic 3-amino to afford the 3-(*N*-sulfonylamino)indoles. Not surprisingly, treating pure samples of 3-aminoindole-2-carbonitriles **2a**–**c** with TsCl (1 equiv) and pyridine (4 equiv) in refluxing EtOH gave the 3-(*N*-tosylamino)indole-2-carbonitriles **5a**–**c** in 85, 86 and 82% yields, respectively while similar treatment of 3-aminoindole-2-carbonitrile **2a** with $PhSO_2Cl$ gave the 3-(*N*-benzenesulfonylamino)indole-2-carbonitrile **5d** in 88% yield.



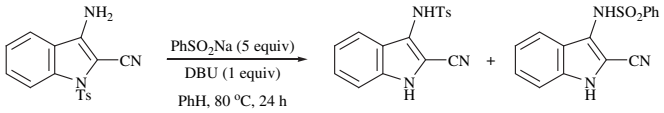
A pure sample of 3-(*N*-tosylamino)indole-2-carbonitrile **5a** treated with DBU in PhH at reflux or with K_2CO_3 in EtOH at reflux was stable, suffering neither isomerisation nor detosylation. To the best of our knowledge, only one example of a similar *N* to *N* tosyl migration has been reported on treating N^1-methyl-N^1-tosylbenzene-1,2-diamine **9** with BuLi to afford N^1-methyl-N^2-tosylbenzene-1,2-diamine **10** in low yield.[12]



9 **10**

2.3.1. Mechanistic rationale. The indole C-2 nitrile was expected to activate the C-3 amine towards deprotonation. In the presence of base, a direct tosyl metathesis could occur between the indole nitrogen at N1 and the C-3 amine via presumably an intermolecular route. However, when the 1-tosyindole **4a** was treated with primary aromatic amines or with the strongly nucleophilic secondary amine pyrrolidine (2 equiv) in EtOH or benzene at reflux no tosyl metathesis was observed and the starting 1-tosyindole **4a** could be recovered.

In light of this, we postulated that the migration involved a base catalyzed elimination of *p*-toluenesulfinate anion to afford the 2-cyano-3*H*-indol-3-imine **11**, which then trapped the sulfinate by-product (Scheme 3). DBU is known to promote elimination reactions.[13] The elimination of toluenesulfinate was partially supported when the reaction was repeated in the presence of sodium benzenesulfinate (fivefold excess) since a mixture of 3-(*N*-tosylamino)- and 3-(*N*-benzenesulfonylamino)indole-2-carbonitriles **5a** and **5d** (ca. 2:1 ratio by ^{1}H NMR) was obtained. Despite the fivefold excess of sodium benzenesulfinate, the major isomer was clearly the 3-tosylaminoindole **5a** suggesting a possible tight ion pairing.

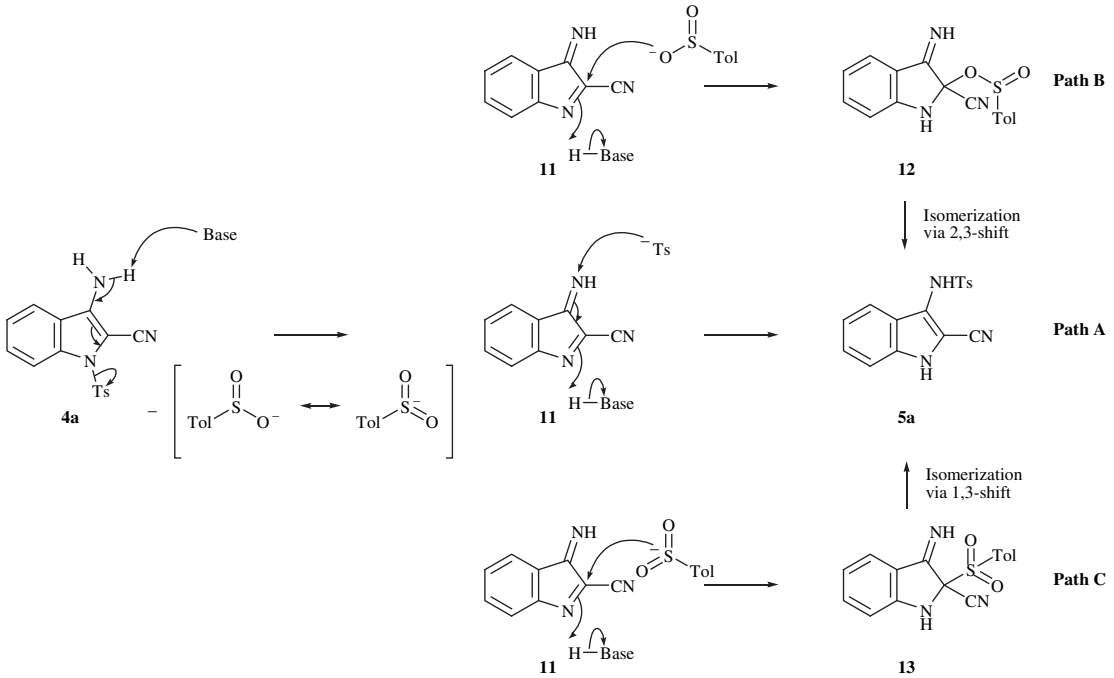


4a **5a** **5d**

Furthermore, under the reaction conditions both 3-aminoindole-2-carbonitrile **2a** and 3-(*N*-tosylamino)indole-2-carbonitrile **5a** were inert to sodium benzenesulfinate. The reaction supported that base treatment of 3-amino-1-tosylindole-2-carbonitrile **4a** released an intermediate, presumed to be the indolimine **11**, that reacted rapidly via an intermolecular fashion with the arylsulfinate anion formed.

Next we considered the recombination of the *p*-toluenesulfinate with the proposed intermediate 2-cyano-3*H*-indol-3-imine **11**. Since *p*-toluenesulfinates can be nucleophilic/reactive via oxygen or sulfur[14] several possibilities needed to be considered: the simplest (Path A) involved the direct addition of *p*-toluenesulfinate to the indolimine **11** in a manner that mimicked the Michael-type addition of nucleophiles to gramine derived 3-methylene-3*H*-indoles.[15] However, the conflicting local dipole of the exocyclic imine and lone pair repulsion from the imine nitrogen argued against this path. Path B, involved the addition of *p*-toluenesulfinate to the highly electrophilic indole C-2 position. Isomerization of the sulfinate ester **12** via either a concerted 2,3-sigmatropic rearrangement or via a stepwise ion pair process could give the 3-(*N*-tosylamino)indole **5**. Examples of the rearrangement of allylic sulfinate esters to the allylic sulfones are known,[16] tentatively supporting the proposed mechanism, however we were unable to find examples of an analogous rearrangement of iminoethyl sulfinate esters. Finally, Path C involved the addition of toluenesulfinate via its sulfur to the indole C-2 position to afford intermediate **13**, followed by a 1,3-shift to the exocyclic imine. Examples of these type of shifts have also been frequently reported.[17] Despite the prevalence of arylsulfinates to attack via sulfur, we tentatively favour Path B over Path C for two reasons: First a 2,3-shift would require a five-membered transition state while a 1,3-shift would required a less favourable four-membered transition state; and second, adduct **B** was less sterically crowded at the indole C-2 position than adduct **C**.

While the true nature of this migration requires further study, the above studies indicated that the base catalysed deprotection would require reductive conditions. The related 2-aryl-3*H*-indol-3-oximes have previously been reduced using Zn/HCl,[18] Pd/H_2,[19] Pt/H_2,[20] sodium hydrosulfite,[21] or ammonium sulfide,[22] and there have been two base catalysed detosylations reported that used



Scheme 3.

thiophenol,[23] however, despite the known reducing powers of thiophenol,[24] the authors did not mention the role of the mercaptans. Thiophenol facilitates the denosylation of 1-(*o*-, *p*-nitro substituted arylsulfonyl)indoles via *ipso* nucleophilic aromatic substitution on the nitroarenesulfonamide followed by elimination of the free indole, sulfur dioxide and a (phenyl)(*o*-, *p*-nitro-phenyl)sulfide.[25] In addition, thioglycolate has been used to detosylate indoles[26] but no support for a mechanism was presented.

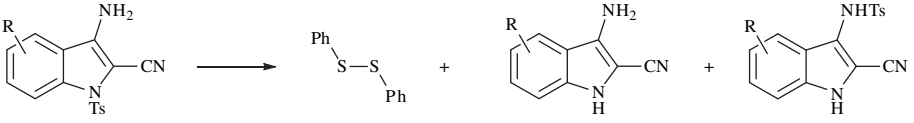
In our hands treating 3-amino-1-tosylindole-2-carbonitrile with DBU and PhSH (1–5 equiv) in an air atmosphere led to the isolation of detosylated 3-aminoindole-2-carbonitrile **2a** and the 3-(*N*-tosylamino)indole-2-carbonitrile **5a** together with a large quantity of diphenyl disulfide. Increasing the equivalents of PhSH (up to 5 equiv) led to formation of detosylated indole **2a** in high yield, however, a pure sample of 3-(*N*-tosylamino)indole-2-carbonitrile **5a** was stable to the reaction conditions suggesting the increased yield of detosylated indole **2a** did not arise from detosylation of the 3-(*N*-tosylamino)indole-2-carbonitrile **5a**. Oxidation of the thiophenol could have occurred owing to oxygen in the reaction mixture or in the air atmosphere. When the reaction was repeated under anaerobic conditions (degassed benzene under an argon atmosphere) the quantity of diphenyl disulfide recovered became nearly equimolar with respect to the free indole. This tentatively supported that thiophenol was reducing the 2-cyano-3*H*-indol-3-imine intermediate **11** to afford the desired 3-aminoindole-2-carbonitrile **2a**. On this basis the reaction was repeated with only 2–2.5 equiv of PhSH under argon and the reaction also came to completion with only traces of the migrated product. Finally, with these improved conditions both the dimethoxy and 5-nitro indoles **4b** and **4c** could be deprotected in high yields (Table 1).

2.3.2. Mechanistic rationale. Under these reaction conditions there was no trace of the possible diarylsulfide by-product phenyl(*p*-tolyl)sulfide. This was not surprising since in the absence of nitro substitution the tosylamide was not activated towards nucleophilic aromatic substitution. The possibility that the mercaptan attacked directly the sulfonamide sulfur to eliminate *S*-phenyl *p*-tolylthiosulfonate was also unlikely, since no trace of *S*-phenyl *p*-tolylthiosulfonate could be identified in the reaction mixture. A pure sample of *S*-phenyl *p*-tolylthiosulfonate was stable to the reaction conditions and also inert towards 3-aminoindole-2-carbonitrile **2a**. In light of our inability to detect either phenyl(*p*-tolyl)sulfide or *S*-phenyl *p*-tolylthiosulfonate in the reaction mixtures we proposed addition of thiophenol to the 2-cyano-3*H*-indol-3-imine **11** at the highly electrophilic indole C-2 position to afford intermediate **14**. Attack of a second mercaptan at the phenyl sulfide could eliminate the observed diphenyl disulfide and the 3-aminoindole-2-carbonitrile **2a** that was shown earlier to be inert to the toluenesulfinate by-product (Scheme 4).

3. Conclusions

3-Amino-1-tosylindole-2-carbonitriles **4a–c** supporting both NO_2 and MeO substituents on the benzo fusion on treatment with either DBU or K_2CO_3 suffer a tosyl migration to afford 3-(*N*-tosylamino)indole-2-carbonitriles **5a–c** in high yield. This migration can be thwarted in either anaerobic or aerobic conditions in the presence of thiophenol (2–2.5 or 5 equiv, respectively), to give the detosylated indoles **2a–c**. Tosylation of 3-aminoindole-2-carbonitriles **2a–c** gave exclusively the 3-tosylaminoindole-2-carbonitriles **5a–c**, respectively.

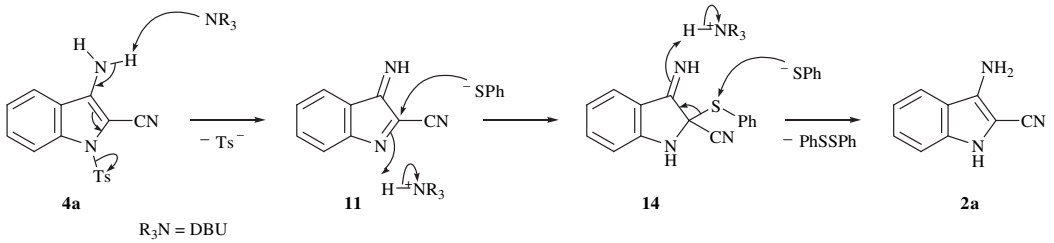
Table 1
Deprotection of the 3-amino-1-tosylindole-2-carbonitriles **4a–c** (0.06 mmol) using DBU and PhSH in PhH (2 mL) at 80 °C



4a-c **2a-c** **5a-c**

R	DBU (equiv)	PhSH (equiv)	Time (h)	Yields (%)		
				PhSSPh[b]	**2**	**5**
H	1	1	26	62	**2a** (27)	**5a** (71)
H	1	2	24	95	**2a** (40)	**5a** (57)
H	1	3	18	144	**2a** (60)	**5a** (39)
H	1	4	14	183	**2a** (85)	**5a** (8)
H	1	5	12	248	**2a** (92)	—
H	1	5[a]	24	104	**2a** (88)	—
H	1	2[a]	17	85	**2a** (89)	**5a** (6–4)
H	1	2.5[a]	14	93	**2a** (88)	**5a** (trace)
H	0.5	5	24	183	**2a** (80)	—
H	0.2	5	32	243	**2a** (90)	—
5,6-$(MeO)_2$	1	5	24	230	**2b** (88)	—
5-O_2N	1	5	1	240	**2c** (90)	—
5,6-$(MeO)_2$	1	2[a]	25	91	**2b** (86)	—
5-O_2N	1	2[a]	3	95	**2c** (89)	—

[a] Dry and degassed PhH was used, and the rxn took place under Argon.
[b] Yield calculated based on the need for 2×PhSH for the deprotection of 1×tosylindole.



4a **11** **14** **2a**

R_3N = DBU

Scheme 4.

4. Experimental

4.1. General methods and materials

DMF was freshly distilled from Na_2SO_4 under argon. Benzene was freshly distilled from CaH_2 under argon. Reactions were protected from atmospheric moisture by $CaCl_2$ drying tubes. Anhydrous Na_2SO_4 was used for drying organic extracts, and all volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial glass backed thin layer chromatography (TLC) plates (Merck Kieselgel 60 F_{254}). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography[27] was used throughout for all non-TLC scale chromatographic separations using Merck Silica Gel 60 (less than 0.063 mm). A CEM Discover Microwave Reactor was used for microwave experiments. Chemglass heavy wall cylindrical pressure vessels (15 mL) with a Teflon bushing as a pressure seal were used for the sealed tube studies. Melting points were determined using a PolyTherm-A, Wagner & Munz, Koefler-Hotstage Microscope apparatus or where noted using a TA Instruments DSC Q1000 with samples hermetically sealed in aluminium pans under an argon atmosphere; using heating rates of 5 °C/min. Solvents used for recrystallization are indicated after the melting point. UV spectra were obtained using a Perkin–Elmer Lambda-25 UV/vis spectrophotometer and inflections are identified by the abbreviation 'inf'. IR spectra were recorded on a Shimadzu FTIR-NIR Prestige-21 spectrometer with a Pike *Miracle* Ge ATR accessory and strong, medium and weak peaks are represented by s, m and w, respectively. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 machine (at 300 and 75 MHz, respectively). ^{13}C NMR *C*H assignments were supported by DEPT-135 NMR experiments. Deuterated solvents were used for homonuclear lock and the signals are referenced to the deuterated solvent peaks. Low resolution (EI) mass spectra were recorded on a Shimadzu Q2010 GC–MS with direct inlet probe.

4.1.1. 2-(p-Tosylamino)benzonitrile ***7a***. To a stirred solution of 2-aminobenzonitrile **6a** (1.0 g, 8.47 mmol) in pyridine (10 mL) at ca. 20 °C and protected with $CaCl_2$ drying tube, was added *p*-TsCl (1.61 g, 8.47 mmol, 1 equiv). The mixture then was heated to ca. 100 °C for 5 h until no starting material remained (TLC). The mixture was allowed to cool to ca. 20 °C, diluted with DCM (20 mL) and washed with 5% HCl (4×20 mL). The organic layer was separated and dried to give the title compound **7a** (2.0 g, 87%) as colourless plates, mp (DSC) onset: 133 °C, peak max: 135 °C (lit.,[8] 133–134 °C) (from cyclohexane/EtOH); λ_{max}(DCM)/nm 231 (log ϵ 4.21), 241 inf (4.07), 275 inf (3.21), 294 (3.39); ν_{max}/cm^{-1} 3472w, 3364w, 3212w (NH), 2230m (C≡N), 1597m, 1578m, 1495s, 1431m, 1335s, 1298m, 1290m, 1159s, 1094s, 916s, 822m, 806s, 762s, 719m; δ_H(300 MHz; $CDCl_3$) 7.73–7.69 (3H, m, Ar *H*), 7.55 (1H, dd, *J* 7.9, 7.9, 1.5, Ph *H*), 7.47 (1H, dd, *J* 7.8, 1.5, Ph *H*), 7.26 (2H, d, *J* 8.1, Tos *H*-3/5), 7.17 (1H, ddd, *J* 7.6, 7.6, 1.0, Ph *H*), 7.11 (1H, br s, N*H*), 2.39 (3H, s, CH_3); δ_C(75 MHz; $CDCl_3$) 144.6, 139.2, 135.4, 134.1 (*C*H), 132.8 (*C*H), 129.9 (*C*H), 127.3 (*C*H), 125.1 (*C*H), 121.8 (*C*H), 115.7 (*C*≡N), 104.3 (*C*C≡N), 21.5 (*C*H$_3$); *m*/*z* (EI) 272 (M$^+$, 32%), 207 (2), 155 (56), 139 (2), 91 ($C_7H_7^+$, 100), 77 (2), 65 (24), 51 (3) identical to an authentic sample.

4.1.2. 4,5-Dimethoxy-2-(p-tosylamino)benzonitrile ***7b***. Similar treatment of 2-amino-4,5-dimethoxybenzonitrile **6b** (1.0 g, 5.62 mmol) with *p*-TsCl gave after 7 h the *title compound* **7b** (1.49 g, 80%) as colourless prisms, mp 192–193 °C (from cyclohexane/EtOH); (Found: C, 57.9; H, 4.9; N, 8.4. $C_{16}H_{16}N_2O_4S$ requires C, 57.8; H, 4.85; N, 8.4%); λ_{max}(DCM)/nm 242 (log ϵ 2.87), 268 inf (2.80), 301 (2.57); ν_{max}/cm^{-1} 3254m (NH), 2224w (C≡N), 1514s, 1396m, 1354s, 1333m, 1275s, 1223s, 1202m, 1169s, 1110m, 1090m, 999s, 893s, 862s, 816s; δ_H(300 MHz; $CDCl_3$) 7.64 (2H, d, *J* 8.4, Tos *H*-2/6), 7.24 (2H, d, *J* 9.0, Tos *H*-3/5), 7.23 (1H, s, Ph *H*-3 or 6), 6.98 (1H, br s, N*H*), 6.80 (1H, s, Ph *H*-3 or 6), 3.93 (3H, s, CH_3O), 3.81 (3H, s, CH_3O), 2.39 (3H, s, CH_3); δ_C(75 MHz; $CDCl_3$) 153.5, 147.0, 144.6, 135.2, 134.2, 129.8 (*C*H), 127.3 (*C*H), 116.1 (*C*≡N), 112.9 (*C*H), 107.3 (*C*H), 96.7 (*C*C≡N), 56.4 (*C*H$_3$O), 56.2 (*C*H$_3$O), 21.6 (*C*H$_3$); *m*/*z* (EI) 332 (M$^+$, 45%), 177 ($C_7H_7SO_2^+$, 100), 150 (19), 135 (8), 120 (4), 107 (3), 104 (3), 91 ($C_7H_7^+$, 27), 77 (7), 68 (9), 65 (23), 53 (1).

4.1.3. 5-Nitro-2-(p-tosylamino)benzonitrile ***7c***. Similar treatment of 2-amino-5-nitrobenzonitrile **6c** (1.0 g, 6.17 mmol) with *p*-TsCl (1.18 g, 6.17 mmol, 1 equiv) gave after 36 h the *title compound* **7c** (1.58 g, 81%) as light yellow cotton-like fibres, mp 159–160 °C (lit.,[28] 165.5–167 °C); λ_{max}(DCM)/nm 229 (log ϵ 3.31), 237 inf (3.25), 302 (3.10); ν_{max}/cm^{-1} 3217w (NH), 3188w, 3075w, 2239w (C≡N), 1585m, 1531m, 1493m, 1416m, 1344s, 1287m, 1169s, 1082m, 924m, 878s, 795m, 745m; δ_H(300 MHz; $CDCl_3$) 8.39 (1H, d, *J* 2.4, Ph *H*-6), 8.36 (1H, d, *J* 9.2, 2.6, Ph *H*-4), 7.86 (1H, d, *J* 9.0, Ph *H*-3), 7.82 (2H, d, *J* 8.4, Tos *H*-2/6), 7.68 (1H, br s, N*H*), 7.34 (2H, d, *J* 8.1, Tos *H*-3/5), 2.42 (3H, s, CH_3); δ_C(75 MHz; $CDCl_3$) 145.8, 144.8, 142.9, 134.8, 130.3 (*C*H), 129.3 (*C*H), 128.7 (*C*H), 127.4 (*C*H), 118.6 (*C*H), 113.9 (*C*≡N), 102.3 (*C*C≡N), 21.65 (*C*H$_3$); *m*/*z* (EI)%, 317 (M$^+$, 12%), 156 (5), 155 (57), 91 (100), 89 (7), 65 (26).

4.1.4. N-(2-Cyanophenyl)-N-(p-tosyl)aminoacetonitrile ***8a***. To a stirred mixture of 2-(*p*-tosylamino)benzonitrile **7a** (50 mg, 0.18 mmol) in DMF (2 mL) and K_2CO_3 (25 mg, 0.18 mmol, 1 equiv) at ca. 20 °C, chloroacetonitrile was added (11 μL, 0.18 mmol, 1 equiv). The reaction tube was then sealed and the mixture was heated to ca. 100 °C for 70 min, until no starting material remained (TLC). The mixture was allowed to cool to ca. 20 °C, diluted with DCM (10 mL) and washed with water (4×10 mL). The organic layer was separated and dried to give the title compound **8a** (48 mg, 81%) as colourless cotton-like fibres, mp 82–83 °C (lit.,[8] 81–82 °C) (from cyclohexane/DCM); λ_{max}(DCM)/nm 220 inf (log ϵ 2.91), 231 (3.42), 275 inf (2.34), 282 inf (2.21); ν_{max}/cm^{-1} 2239w (C≡N), 1491m, 1449m, 1362s, 1169s, 1117m, 1086m, 856s, 814m, 785m, 766m, 741m; δ_H(300 MHz; $CDCl_3$) 7.72 (1H, dd, *J* 9.0, 1.8, Ph *H*), 7.68–7.62 (3H, m, Ar *H*), 7.54 (1H, ddd, *J* 7.5, 7.5, 1.2, Ph *H*), 7.44 (1H, dd, *J* 8.1, 0.6, Ph *H*), 7.34 (2H, d, *J* 8.1, Tos *H*-3/5), 4.62 (2H, s, CH_2), 2.45 (3H, s, CH_3); δ_C(75 MHz; $CDCl_3$) 145.5, 140.0, 134.3 (*C*H), 134.0 (*C*H), 134.0, 131.0 (*C*H), 130.2 (*C*H), 130.1 (*C*H), 128.1 (*C*H), 115.4, 114.5, 114.2, 39.1 (N*C*H$_2$), 21.7 (*C*H$_3$); *m*/*z* (EI) 311 (M$^+$, 12%), 284 (3), 155 (75), 129 (7), 103 (8), 102 (9), 91 ($C_7H_7^+$, 100), 76 (3), 65 (25), 51 (5) identical to an authentic sample.

4.1.5. N-(2-Cyano-4,5-dimethoxyphenyl)-N-(p-tosyl)aminoacetonitrile ***8b***. Similar treatment of 4,5-dimethoxy-2-[(*p*-tosylamino)]benzonitrile **7b** (50 mg, 0.15 mmol) with chloroacetonitrile gave after 2 h the *title compound* **8b** (43 mg, 73%) as colourless needles, mp 191–192 °C (from cyclohexane/DCM); (Found: C, 58.3; H, 4.6; N, 11.3. $C_{18}H_{17}N_3O_4S$ requires C, 58.2; H, 4.6; N, 11.3%); λ_{max}(DCM)/nm 242 (log ϵ 2.93), 261 (2.87), 269 (2.86), 274 inf (2.83), 297 inf (2.51); ν_{max}/cm^{-1} 2272w (C≡N), 1599m, 1522m, 1360s, 1275m, 1225m, 1164s, 1134m, 1090m, 1076m, 1015m, 968m, 876m, 860m, 816m, 781m; δ_H(300 MHz; $CDCl_3$) 7.68 (2H, d, *J* 8.4, Tos *H*-2/6), 7.34 (2H, d, *J* 8.1, Tos *H*-3/5), 7.02 (1H, s, Ph *H*-3 or 6), 6.90 (1H, s, Ph *H*-3 or 6), 4.61 (2H, s, CH_2), 3.91 (3H, s, CH_3O), 3.84 (3H, s, CH_3O) 2.45 (3H, s, CH_3); δ_C(75 MHz; $CDCl_3$) 153.0, 149.9, 145.4, 134.2, 134.1, 130.0 (*C*H), 128.2 (*C*H), 115.7 (*C*≡N), 114.6 (*C*≡N), 114.3 (*C*H), 113.8 (*C*H), 105.5 (*C*C≡N), 56.4 (*C*H$_3$O), 39.3 (*C*H$_2$), 21.7 (*C*H$_3$); *m*/*z* (EI) 371 (M$^+$, 18%), 216 ($C_7H_7SO_2^+$, 100), 200 (1), 189 (41), 174 (3), 155 (5), 147 (3), 119 (2), 104 (3), 91 ($C_7H_7^+$, 28), 77 (2), 65 (12).

4.1.6. 3-Amino-1-(p-tosyl)indole-2-carbonitrile ***4a***. To a stirred solution of *N*-(2-cyanophenyl)-*N*-(*p*-tosyl)aminoacetonitrile **8a** (100 mg, 0.32 mmol) in EtOH (2 mL) at ca. 20 °C, was added K_2CO_3 (0.4 mg, 3.2×10^{-3} mmol, 0.01 equiv). The reaction mixture was left to stir for 26 h until no starting material remained (TLC). The

mixture was then diluted with DCM (15 mL) and washed with water (4×20 mL). The organic layer was separated and dried to give the title compound **4a** (96 mg, 96%) as light orange needles, mp (DSC) onset: 203 °C, peak max: 205 °C (lit.,[8] 195.5–196.5 °C) (from cyclohexane/EtOH); λ_{max}(DCM)/nm 231 (log ϵ 4.35), 247 inf (4.25), 270 inf (3.95), 277 inf (3.93), 297 (4.04), 319 (4.10); ν_{max}/cm^{-1} 3447m (NH_2), 3348m (NH), 3260w, 3240w, 2208s (C≡N), 1653s, 1597m, 1568m, 1364s, 1184m, 1169s, 1153m, 1115m, 1086s, 974m, 810m, 770s, 752s; δ_H(300 MHz; $CDCl_3$) 8.18 (1H, d, *J* 8.7, indole *H*-4), 7.72 (2H, d, *J* 8.4, Tos *H*-2/6), 7.54 (1H, ddd, *J* 7.8, 7.8, 1.2, indole *H*-5), 7.40 (1H, d, *J* 7.5, indole *H*-7), 7.31 (1H, ddd, *J* 7.5, 7.5, 0.9, indole *H*-6), 7.18 (2H, d, *J* 8.1, Tos *H*-3/5), 4.49 (2H, br s, NH_2), 2.33 (3H, s, CH_3); δ_C(75 MHz; DMSO-d_6) one peak overlapping 148.1, 145.5, 137.2, 131.4, 129.9 (*C*H), 126.7 (*C*H), 124.7 (indole *C*H), 123.7, 120.8 (indole *C*H), 115.9 (indole *C*H), 114.4 (*C*≡N), 84.3 (*C*C≡N), 20.95 (CH_3); *m*/*z* (EI) 311 (M^+, 11%), 156 (100), 129 (21), 102 (13), 91 ($C_7H_7^+$, 15), 76 (5), 65 (9), 51 (5) identical to an authentic sample.

4.1.7. 3-Amino-5,6-dimethoxy-1-(p-tosyl)indole-2-carbonitrile ***4b***. Similar treatment of *N*-(2-cyano-4,5-dimethoxyphenyl)-*N*-(*p*-tosyl)aminoacetonitrile **8b** (100 mg, 0.27 mmol) gave after 30 h the *title compound* **4b** (93 mg, 93%) as light yellow needles, mp 209–210 °C (from cyclohexane/EtOH); (Found C, 58.3; H, 4.6; N, 11.2. $C_{18}H_{17}N_3O_4S$ requires C, 58.2; H, 4.6; N, 11.3%); λ_{max}(DCM)/nm 230 (log ϵ 2.34), 269 (2.23), 277 (2.23), 312 (2.28), 324 inf (2.22); ν_{max}/cm^{-1} 3466w (NH_2), 3372w, 3352m (NH), 3265w, 2185m (C≡N), 1649m, 1570m, 1485s, 1437m, 1364s, 1298s, 1229s, 1188m, 1176m, 1171m, 1159s, 1090m, 1013s, 918m, 849m, 816m, 770m; δ_H(300 MHz; DMSO-d_6) 7.58 (2H, d, *J* 8.1, Tos *H*-2/6), 7.51 (1H, s, indole *H*-4), 7.37 (1H, s, indole *H*-7), 7.32 (2H, d, *J* 8.1, Tos *H*-3/5), 6.79 (2H, br s, NH_2), 3.92 (3H, s, CH_3O), 3.73 (3H, s, CH_3O) 2.29 (3H, s, CH_3); δ_C(75 MHz; DMSO-d_6) 151.3, 148.7, 147.5, 145.3, 132.1, 131.2, 129.8 (*C*H), 126.9 (*C*H), 116.1, 114.9, 101.8 (*C*H), 99.0 (*C*H), 83.3 (*C*C≡N), 55.8 (CH_3O), 55.6 (CH_3O), 21.0 (CH_3); *m*/*z* (EI) 371 (M^+, 8%), 216 ($C_7H_8SO_2^+$, 100), 200 (2), 189 (2), 172 (6), 158 (4), 143 (2), 121 (3), 116 (3), 103 (3), 91 ($C_7H_7^+$, 14), 78 (3), 65 (13), 51 (4).

4.1.8. 3-Amino-5-nitro-1-(p-tosyl)indole-2-carbonitrile ***4c***. To a stirred mixture of 5-nitro-2-(*p*-tosylamino)benzonitrile **7c** (100 mg, 0.315 mmol) in chloroacetonitrile (1 mL) at ca. 20 °C was added K_2CO_3 (87 mg, 0.63 mmol, 2 equiv). The mixture heated to ca. 100 °C for 24 h, until no starting material remained (TLC). The mixture was allowed to cool to ca. 20 °C, diluted with DCM (10 mL) and washed with water (4×10 mL). The organic layer was separated, dried, adsorbed onto silica and chromatography (hexane/DCM, 2:8) gave 2-amino-5-nitrobenzo-carbonitrile **6c** (23.1 mg, 45%) as light yellow dust, mp (DSC) onset: 207 °C, peak max: 208 °C (lit.,[29] 210–211 °C), R_f (hexane/DCM, 2:1) 0.66; identical to an authentic sample. Further elution (DCM 100%) gave the *title compound* **4c** (45 mg, 40%) as yellow fibres, mp 236–237 °C (from cyclohexane/EtOH); R_f (DCM) 0.30; (Found C, 53.8; H, 3.2; N, 15.65. $C_{16}H_{12}N_4O_4S$ requires C, 53.9; H, 3.4; N, 15.7%); λ_{max}(DCM)/nm 233 (log ϵ 3.43), 287 (3.50), 326 inf (3.04), 338 inf (2.91); ν_{max}/cm^{-1} 3458m (NH_2), 3375s, 3102w, 2207m (C≡N), 1632m, 1612m, 1593m, 1524s, 1477m, 1383s, 1342s, 1285m, 1256s, 1192s, 1175s, 1088m, 1070m, 982m, 903m, 891m, 837m, 822m, 810s, 739m, 702s; δ_H(300 MHz; $CDCl_3$) 8.41 (1H, s, indole *H*-4), 8.37 (1H, d, *J* 2.1, indole *H*-7), 8.30 (1H, dd, *J* 8.7, 1.2, indole *H*-6), 7.77 (2H, d, *J* 8.4, Tos *H*-2/6), 7.28 (2H, d, *J* 7.8, Tos *H*-3/5), 2.36 (3H, s, CH_3); δ_C(75 MHz; $CDCl_3$) 147.0, 144.4, 139.7, 136.2, 133.5, 130.6 (*C*H), 127.5 (*C*H), 124.4 (*C*H), 123.7, 122.6, 116.5 (*C*H), 116.2 (*C*H), 112.4 (*C*≡N), 21.8 (CH_3); *m*/*z* (EI) 356 (M^+, 21%), 202 (13), 201 ($C_7H_8SO_2^+$, 100), 156 (7), 155 (55), 128 (16), 116 (3), 102 (8), 101 (14), 92 (19), 91 (87), 77 (5), 76 (6), 75 (7), 65 (33).

4.1.9. 3-(p-Tosylamino)indole-2-carbonitrile ***5a***. To a stirred solution of 3-amino-1-(*p*-tosyl)indole-2-carbonitrile **4a** (20 mg, 0.06 mmol) in EtOH (1 mL) at ca. 20 °C was added K_2CO_3 (9 mg, 0.06 mmol, 1 equiv). The reaction vessel was sealed, and heated at 100 °C (bath temperature). The reaction mixture was left to stir for 5 h until no starting material remained (TLC). The mixture was diluted with DCM (15 mL) and washed with water (4×20 mL) to remove the K_2CO_3. The organic layer was separated and dried to give the *title compound* **5a** (25.7 mg, 65%) as a colourless cotton-like fibres, mp 234–235 °C (from cyclohexane/EtOH); (Found: C, 61.7; H, 4.2; N, 13.4. $C_{16}H_{13}N_3O_2S$ requires C, 61.7; H, 4.2; N, 13.5%); λ_{max}(DCM)/nm 231 (log ϵ 4.50), 289 (4.23), 313 inf (3.75); ν_{max}/cm^{-1} 3358m and 3310m (NH), 2228m (C≡N), 1366m, 1346s, 1310s, 1250m, 1182m, 1157s, 1090m, 893m, 814s, 748s; δ_H(300 MHz; DMSO-d_6) 12.33 (1H, br s, N*H*Ts), 10.19 (1H, br s, N*H*), 7.52 (2H, d, *J* 8.1, Tos *H*-2/6), 7.35 (1H, d, *J* 8.4, indole *H*-4), 7.29–7.22 (3H, m, Ar *H*), 7.12 (1H, d, *J* 8.1, indole *H*-7), 6.96 (1H, dd, *J* 7.5, 7.5, indole *H*-6), 2.33 (3H, s, CH_3); δ_C(75 MHz; DMSO-d_6) 143.2, 136.8, 135.3, 129.5 (*C*H), 126.8 (*C*H), 125.8 (indole *C*H), 122.4, 121.6, 120.7 (indole *C*H), 119.4 (indole *C*H), 112.9 (*C*≡N), 112.4 (indole *C*H), 103.9 (*C*C≡N), 20.9 (CH_3); *m*/*z* (EI) 311 (M^+, 23%), 156 (100), 129 (20), 102 (11), 91 ($C_7H_7^+$, 7), 76 (4), 65 (5).

4.1.10. 5,6-Dimethoxy-3-(p-tosylamino)indole-2-carbonitrile ***5b***. Similar treatment of 3-amino-5,6-dimethoxy-1-(*p*-tosyl)indole-2-carbonitrile **4b** (20 mg, 0.05 mmol) gave after 3 h the *title compound* **5b** (29 mg, 79%) as a colourless cotton-like fibres, mp 214–215 °C (from cyclohexane/EtOH); (Found: C, 58.3; H, 4.6; N, 11.3. $C_{18}H_{17}N_3O_4S$ requires C, 58.2; H, 4.6; N, 11.3%); λ_{max}(DCM)/nm 230 (log ϵ 4.45), 296 inf (4.23), 307 inf (4.27), 318 (4.31), 330 inf (4.22); ν_{max}/cm^{-1} 3362m and 3271m (NH), 2833, 2218m (C≡N), 1487m, 1379m, 1339s, 1319s, 1260s, 1246m, 1227m, 1204m, 1161s, 1117m, 1092s, 1016m, 947w, 887m, 849m, 816s, 758m, 750m; δ_H(300 MHz; DMSO-d_6) 12.02 (1H, br s, N*H*Ts), 9.97 (1H, br s, N*H*), 7.54 (2H, d, *J* 8.1, Tos *H*-2/6), 7.30 (2H, d, *J* 8.1, Tos *H*-3/5), 6.75 (1H, s, indole *H*-4 or 7), 6.20 (1H, s, indole *H*-4 or 7), 3.76 (3H, s, CH_3O), 3.46 (3H, s, CH_3O), 2.33 (3H, s, CH_3); δ_C(75 MHz; DMSO-d_6) 150.0, 145.8, 143.1, 137.1, 130.4, 129.5 (*C*H), 126.9 (*C*H), 121.4, 115.3, 113.5 (*C*≡N), 102.1 (*C*C≡N), 99.0 (indole *C*H), 94.1 (indole *C*H), 55.4 (OCH_3), 55.0 (OCH_3), 20.9 (CH_3); *m*/*z* (EI) 371 (M^+, 21%), 216 ($M^+-C_7H_7O_2S$, 100), 200 (3), 189 (7), 173 (4), 163 (4), 155 (4), 144 (3), 130 (2), 104 (3), 91 (14), 77 (4), 65 (9).

4.1.11. 5-Nitro-3-(p-tosyl)aminoindole-2-carbonitrile ***5c***. Similar treatment of 3-amino-5-nitro-1-(*p*-tosyl)indole-2-carbonitrile **4c** (20 mg, 0.056 mmol) gave after 1 h the *title compound* **5c** (17 mg, 85%) as colourless plates, mp 264–265 °C (from cyclohexane/EtOH); (Found C, 54.0; H, 3.4; N, 15.7. $C_{16}H_{12}N_4O_4S$ requires C, 53.9; H, 3.4; N, 15.72%); λ_{max}(DCM)/nm 226 (log ϵ 4.06), 263 inf (4.13), 265 (4.14), 268 (4.11), 272 (4.09); ν_{max}/cm^{-1} 3375m (NH), 3258, 2232 (C≡N), 1533m, 1485m, 1404m, 1339s, 1157s, 1088m, 897m, 814m, 777m, 735s; δ_H(300 MHz; DMSO-d_6) 13.13 (1H, br s, N*H*Ts), 10.42 (1H, br s, N*H*), 8.08 (1H, dd, *J* 6.6, 2.3, indole *H*-6), 7.86 (1H, d, *J* 2.1, indole *H*-4), 7.57 (1H, d, *J* 9.0, indole *H*-7), 7.51 (2H, d, *J* 8.4, Tos *H*-2/6), 7.28 (2H, d, *J* 8.1 Tos *H*-3/5), 2.29 (3H, s, CH_3); δ_C(75 MHz; DMSO-d_6) 143.7, 141.8, 137.6, 136.0, 129.6 (*C*H), 126.8 (*C*H), 123.9, 121.4, 120.3 (indole *C*H), 116.8 (indole *C*H), 113.7 (indole *C*H), 111.8 (*C*≡N), 107.5 (*C*C≡N), 20.8 (CH_3); *m*/*z* (EI) 356 (M^+, 28%), 201 (80), 155 (64), 148 (3), 128 (13), 116 (4), 101 (17), 91 (100), 75 (13), 65 (40), 51 (8).

4.2. Preparation of 3-(*p*-tosylamino)indole-2-carbonitrile 5a from 3-amino-1-(*p*-tosyl)indole-2-carbonitrile 4a using DBU: (typical procedure)

To a stirred solution of DBU (3 μL, 0.019 mmol, 0.2 equiv) in dry PhH at ca. 20 °C, was added 3-amino-1-tosylindole-2-carbonitrile **4a** (30 mg, 0.096 mmol). The reaction mixture was left to stir for 24 h at reflux until no starting material remained (TLC). The reaction mixture was then allowed to cool to ca. 20 °C, adsorbed onto silica and chromatography (hexane/*tert*-butyl ether, 50:50) gave 3-

(*p*-tosylamino)indole-2-carbonitrile **5a** in (30 mg, 76%) as a colourless cotton-like fibres, mp 234–235 °C (from cyclohexane/EtOH) identical to that described above.

4.3. Preparation of 3-(*p*-tosylamino)indole-2-carbonitrile 5a from 3-aminoindole-2-carbonitrile 2a and *p*-TsCl: (typical procedure)

To a stirred solution of 3-aminoindole-2-carbonitrile **2a** (20 mg, 0.06 mmol) and pyridine (21 μL, 0.24 mmol, 4 equiv) in EtOH (2 mL) at ca. 20 °C, was added *p*-TsCl (11 mg, 0.06 mmol, 1 equiv). The reaction mixture was heated at reflux for 5 h until no starting material remained (TLC). The mixture was diluted with DCM (15 mL) and washed with 5% HCl (4×20 mL) to remove pyridine. The organic layer was separated and dried to give 3-(*p*-tosylamino)indole-2-carbonitrile **5a** (34 mg, 85%) identical to that described above.

*4.3.1. 3-(Benzesulfonylamino)indole-2-carbonitrile **5d**.* Similar treatment of 3-aminoindole-2-carbonitrile **2a** (20 mg, 0.06 mmol) gave after 12 h the *title compound* **5d** (16 mg, 88%) as a light yellow cotton-like fibres, mp 230–231 °C (from cyclohexane/EtOH); (Found C, 60.6; H, 3.7; N, 14.1. $C_{15}H_{11}N_3O_2S$ requires C, 60.6; H, 3.7; N, 14.1%); λ_{max}(DCM)/nm 208 (log ϵ 3.50), 223 (3.61), 289 (3.29), 305 inf (3.02), 317 inf (2.76); ν_{max}/cm^{-1} 3360m and 3306m (NH), 2228m (C≡N), 1450m, 1366m, 1344m, 1308m, 1167s, 1159s, 1094m, 895m, 745s, 721m; δ_H(300 MHz; DMSO-d_6) 12.36 (1H, br s, N*H*SO$_2$Ph), 10.27 (1H, br s, N*H*), 7.66–7.58 (3H, m, Ph *H*), 7.51–7.45 (2H, m, Ph *H*), 7.36 (1H, d, *J* 8.4, indole *H*-4 or 7), 7.25 (1H, dd, *J* 7.5, 7.4, indole *H*-5 or 6), 7.07 (1H, d, *J* 8.1, indole *H*-4 or 7), 6.95 (1H, dd, *J* 7.7, 7.35, indole *H*-5 or 6); δ_C(75 MHz; DMSO-d_6) 139.5, 135.3, 132.9 (*C*H), 129.1 (*C*H), 126.7 (*C*H), 125.8 (*C*H), 122.5, 121.4, 120.8 (*C*H), 119.3 (*C*H), 112.8 (*C*≡N), 112.4 (*C*H), 104.1 (*CC*≡N); *m*/*z* (EI) 297 (M$^+$, 16%), 287 (4), 156 (PhSO$_2$N$^+$, 100), 129 (30), 103 (25), 77 (19), 76 (14), 51 (17).

4.4. Reaction of 3-amino-1-(*p*-tosyl)indole-2-carbonitrile 4a with sodium phenylsulfinate

To a stirred solution of DBU (10 μL, 0.06 mmol, 1 equiv) and sodium benzene-sulfinate (49 mg, 0.3 mmol, 5 equiv) in dry benzene (2 mL) at ca. 20 °C and protected with $CaCl_2$ drying tube, 3-amino-1-(*p*-tosyl)indole-2-carbonitrile **4a** (20 mg, 0.06 mmol) was added. The reaction mixture was then heated to ca. 80 °C for 24 h, until no starting material remained (TLC). The reaction mixture was then allowed to cool to ca. 20 °C, adsorbed onto silica and chromatography (DCM/*tert*-butyl methyl ether, 50:50) gave a mixture of 3-(*N*-tosylamino)- and 3-(*N*-benzenesulfonylamino)indole-2-carbonitriles **5a** and **5b** (ratio by ^{1}H NMR ca. 2:1).

*4.4.1. 3-Aminoindole-2-carbonitrile **2a** (aerobic conditions, see Table 1).* To a stirred solution of DBU (10 μL, 0.06 mmol, 1 equiv) and thiophenol (31 μL, 0.30 mmol, 5 equiv) in distilled benzene (2 mL) at ca. 20 °C and protected with $CaCl_2$ drying tube, 3-amino-1-(*p*-tosyl)indole-2-carbonitrile **4a** (20 mg, 0.06 mmol) was added. The reaction mixture was then heated to ca. 80 °C for 12 h, until no starting material remained (TLC). The reaction mixture was then allowed to cool to ca. 20 °C, adsorbed onto silica and chromatography (hexane) gave diphenyl disulfide (32 mg, 248%) as colourless needles, mp 60–61 °C (from cyclohexane). Further elution (hexane/*tert*-butyl methyl ether, 50:50) gave the title compound **2a** (21 mg, 92%) as light yellow cotton-like fibres, mp 172–173 °C (lit.,[4] 172–173 °C) (from cyclohexane/EtOH) identical to an authentic sample.

*4.4.2. 3-Amino-5,6-dimethoxyindole-2-carbonitrile **2b**.* Similar treatment of 3-amino-5,6-dimethoxy-1-(*p*-tosyl)indole-2-carbonitrile **4b** (20 mg, 0.05 mmol) gave after 24 h the title compound **2b** (10 mg, 88%) as yellow needles, mp 194–195 °C (lit.,[5] 194–195 °C) (from cyclohexane/EtOH) identical to an authentic sample.

*4.4.3. 3-Amino-5-nitroindole-2-carbonitrile **2c**.* Similar treatment of 3-amino-5-nitro-1-(*p*-tosyl)indole-2-carbonitrile **4c** (20 mg, 0.056 mmol) gave after 1 h the title compound **2c** (10 mg, 90%) as red cotton-like fibres, mp 310–311 °C (lit.,[4] 310–311 °C) (from benzene) identical to an authentic sample.

*4.4.4. 3-Aminoindole-2-carbonitrile **2a** (Anaerobic conditions, see Table 1).* To a stirred solution of DBU (10 μL, 0.06 mmol, 1 equiv) and thiophenol (31 μL, 0.30 mmol, 5 equiv) in distilled and degassed benzene (2 mL) at ca. 20 °C under argon atmosphere, 3-amino-1-(*p*-tosyl)indole-2-carbonitrile **4a** (20 mg, 0.06 mmol) was added. The reaction mixture was then heated to ca. 80 °C for 24 h, until no starting material remained (TLC). The reaction mixture was then allowed to cool to ca. 20 °C, adsorbed onto silica and chromatography (hexane) gave diphenyl disulfide (14 mg, 104%) as colourless needles, mp 60–61 °C (from cyclohexane). Further elution (hexane/*tert*-butyl methyl ether, 50:50) gave the title compound **2a** (8 mg, 88%) as light yellow cotton-like fibres, mp 172–173 °C (lit.,[4] 172–173 °C) (from cyclohexane/EtOH) identical to an authentic sample.

Acknowledgements

The authors wish to thank the Cyprus Research Promotion Foundation [Grant No. ΤΕΧΝΟΛΟΓΙΑ/ΘΕΠΙΣ/0308(ΒΕ)/08] and the following organisations in Cyprus for generous donations of chemicals and glassware: the State General Laboratory, the Agricultural Research Institute and the Ministry of Agriculture. Furthermore, we thank the A.G. Leventis Foundation for helping to establish the NMR facility in the University of Cyprus.

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