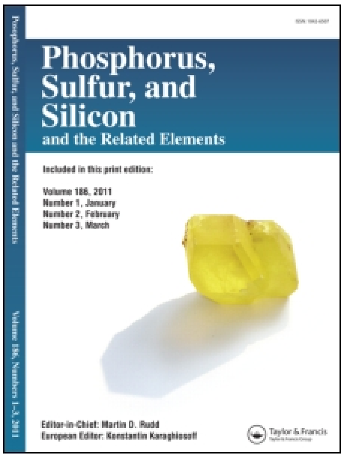

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UNPRECEDENTED OUTCOME OF BASE-PROMOTED NEBER REARRANGEMENT OF O-MESYLOXIME OF 2-ARYL-1,2,3,4-TETRAHYDRO-1-METHYLSUL FONYL-4-QUINOLONE- SYNTHESIS OF 4-AMINO-2-ARYLQUINOLINES

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UNPRECEDENTED OUTCOME OF BASE-PROMOTED NEBER REARRANGEMENT OF O-MESYLOXIME OF 2-ARYL-1,2,3,4-TETRAHYDRO-1-METHYLSULFONYL-4-QUINOLONE- SYNTHESIS OF 4-AMINO-2-ARYLQUINOLINES

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O-Mesyloximes derived from 2-aryl-1,2,3,4-tetrahydro-1-methylsulfonyl-4-quinolones react with sodium ethoxide in ethanol to afford the 4-amino-2-arylquinolines in high yield. No traces of the 3-amino-2-aryl-4-quinolones expected from the Neber rearrangement of the substrates were detected or isolated from the reaction mixture. The structures of the products were determined using a combination of ^{1}H NMR, ^{13}C NMR, IR and mass spectroscopic techniques.

Keywords: O-Mesyloxime 2-aryl-1; 2; 3; 4-tetrahydro-1-methylsulfonyl-4-quinolone derivatives; Neber rearrangement; 4-amino-2-arylquinolines

The unceasing interest in the synthesis and isolation of nitrogen-containing heterocyclic compounds such as quinolones and quinolines stems from their diverse chemistry and pharmacological activities especially as antimalarial agents.[1] Malaria remains one of the most infectious diseases in the world causing millions of deaths each year. The development of resistance against most commonly used drugs and the problems associated with the available drugs has led to increased need for new effective and safe analogues for the treatment of malaria.[2] We have previously reported iodine-methanol promoted oxidative aromatization of 2-aryl-1,2,3,4-tet-

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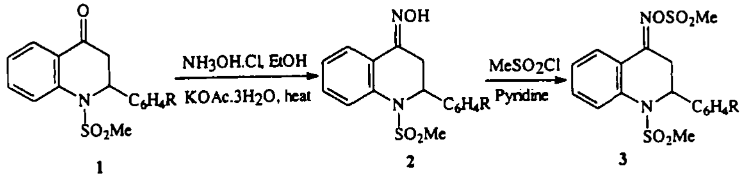
rahydro-4-quinolones to 2-aryl-4-methoxyquinolines.[3] Recently, we have reported the synthesis of 2-aryl-1,2,3,4-tetrahydro-1-methylsulfonyl-4-quinolones[4] and their conversion to benzodiazepine derivatives *via* azidotrimethylsilane-trifluoroacetic acid – mediated Schmidt rearrangement.[5] Flavanones, thiaflavanones and quinolones (azaflavanones) and their derivatives have been found to undergo carbonyl addition reactions with a variety of nitrogen nucleophiles to afford, for example, oximes and hydrazine derivatives.[6] As part of our continuing research on nitrogen-containing heterocyclic systems with potential biological activity, we became interested in the synthesis and further transformations of oximes derived from 2-aryl-1-methylsulfonyl-4-quinolones. The O-tosyloxime derivatives of thiaflavanone and thiaflavanone sulfone have been found to undergo metal(I) alkoxide – promoted Neber rearrangement to afford the corresponding α-aminoketones.[7] In this report, we describe the introduction of the amino group into the heterocyclic moiety of the 2-aryl-4-quinolones starting from the oximes derived from 2-aryl-1,2,3,4-tetrahydro-1-methylsulfonyl-4-quinolones.

RESULTS AND DISCUSSION

In analogy with the preparation of oxime derivatives of flavanones, thiaflavanones and quinolones, we converted the *N*-methylsulfonylquinolones **1** to the corresponding oxime derivatives **2** using hydroxylamine hydrochloride in ethanol in the presence of potassium acetate trihydrate (Scheme 1). The structures of systems **2** were determined using a combination of NMR (^1H and ^{13}C), IR and mass spectroscopic techniques and combustion analysis. The aliphatic regions of the ^1H NMR spectra of systems **2** are characterized by a double doublet at *ca.* δ 3.1 ppm, a doublet at *ca.* δ 3.9 ppm and a doublet at *ca.* δ 5.6 ppm, the first two multiplets corresponding to the nonequivalent methylene protons and the third to the methine proton. The significant chemical shift difference of the methylene proton signals *ca.* δ_H 0.8 ppm) compared to those of the precursors (*ca.* δ_H 0.1 ppm)[4] reflects the magnetic anisotropic effect of the oxime functionality and confirms *anti* configuration (relative to the A-ring) of the hydroxyl group.

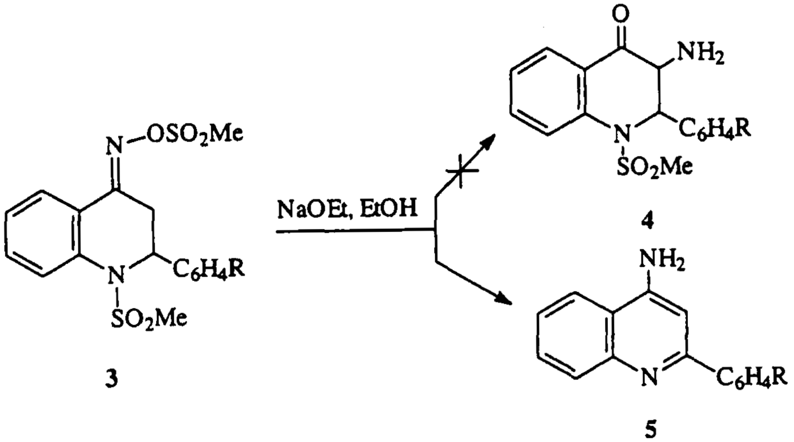
With the aim of preparing 3-amino-2-aryl-4-quinolones and in analogy with the reaction of O-tosyloxime derivatives of thiaflavanone and thiaflavanone sulfone with alkoxide bases,[7]we converted oximes **2** to the corre-



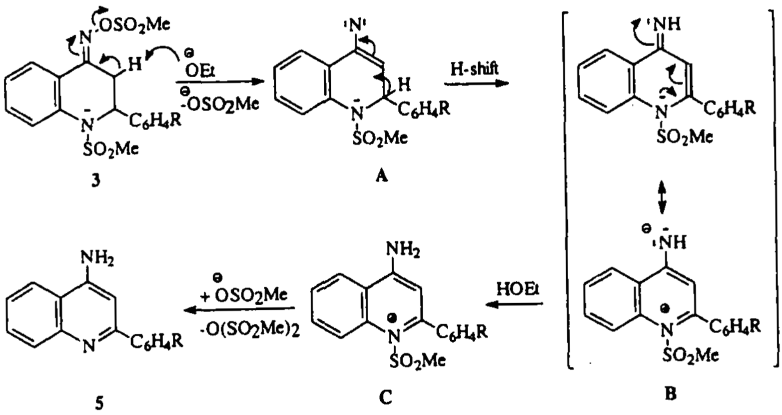
4'-R = H, (a); F, (b); Cl, (c); Br, (d) and OMe (e)

SCHEME 1

sponding *anti* O-mesyloximes **3** (Scheme 1). Oximes **2** were treated with methanesulfonyl chloride in pyridine to afford products **3** in appreciable yields (> 70%). The presence of an additional methyl signal at *ca.* δ_H 3.2 ppm and *ca.* δ_C 36.6 ppm, and the absence of the hydroxyl proton signal in the ^{1}H NMR and IR spectra of systems **3** distinguish them from the corresponding precursors **2** and confirm mesyl incorporation. Systems **3** were, in turn, subjected to sodium ethoxide in ethanol with the aim of effecting the Neber rearrangement to afford the corresponding 3-amino-2-aryl-4-quinolones **4**. At the outset of this investigation and in analogy with the Neber rearrangement of analogous thiaflavanone and thiaflavanone sulfone[7] we had expected to obtain the 3-amino-2-aryl-4-quinolones **4** (Scheme 2). However, application of these reaction conditions to systems **3** led in each case to the isolation in high yield (> 80%) of a single product found by ^{1}H NMR and ^{13}C NMR spectroscopy to be lacking the aliphatic proton and carbon signals and to comprise solely of the aromatic proton and carbon signals. In addition to the expected A- and B-ring proton signals, their ^{1}H NMR spectra are characterized by the presence of a singlet at *ca.* δ 7.1 ppm corresponding to the C-3 proton and a broad singlet integrating for two protons. The latter corresponds to the amino group and its presence was also confirmed by a broad IR absorption band at *ca.* ν_{max} 3000 – 3400 cm^{-1}. The absence of the aliphatic proton and carbon signals in the spectra of these products distinguish them from the corresponding precursors and rule out the possibility of the expected 3-amino-4-quinolone derivatives **4**. The structures of the products were unambiguously determined using a combination of ^{1}H NMR, ^{13}C NMR, IR and mass spectroscopic techniques as those of 4-amino-2-arylquinolines **5**. Their experimentally determined accurate m/z values represent, in each case, closest fit consistent with the structures of 4-amino-2-arylquinolines **5**.



SCHEME 2



SCHEME 3

The formation of the 4-amino-2-arylquinolines **5** can be explained by the mechanism shown in Scheme 3. The reaction presumably begins with the abstraction of the acidic C-3 proton by sodium ethoxide followed by the loss of the mesylate ion to form a nitrene intermediate **A**. Formation of the latter is consistent with the mechanism previously proposed by House and Berkowitz for the Neber rearrangement of the open chain tosylates.[8] Intermediate **A** instead of undergoing intramolecular cyclization to afford an azirine intermediate in analogy with the Neber reaction of thiaflavanone and thiaflavanone sulfone oximes,[7] presumably undergoes prototropic shift to afford conjugated intermediate **B**. Conjugative effects and subsequent protonation of the latter by the solvent presumably afford intermediate **C**, which would then lose 1-methanesulfonyl fragment probably as methanesulfonic anhydride to yield 4-amino-2-arylquinoline **5**. The proposed mechanism fits well with the results shown in Scheme 2 and this observation represents, as far as we are aware unprecedented outcome of attempted metal(I) alkoxide-promoted Neber rearrangement reaction of O-sulfonyloxime derivatives of flavanone analogues. Further studies on the scope and limitations of this reaction are currently in progress.

The oxime derivatives **2** and **3** and the 4-amino-2-arylquinolines **5** prepared in this work are suitable substrates for further studies of chemical transformation and biological activity. Several oximes bearing aromatic or heterocyclic rings, for example, are reported to exhibit activities against fungal plant pathogens or abilities to reactivate acetylcholinesterase inhibited by organophosphates.[9] On the other hand, the quinoline nucleus is present in several natural compounds and in some pharmacologically active substances including inhibitors of tirosine kinase PDY-RTK.[10]

EXPERIMENTAL

Melting points were recorded on a Thermocouple digital melting point apparatus and are uncorrected. For column chromatography, Merck kieselgel 60 (0.063 – 0.200 mm) was used as stationary phase. IR spectra were recorded as KBr pellets using Hitachi 270 – 30 Infrared spectrophotometer. NMR spectra were obtained using a Varian Gemini 200 MHz spectrometer, and the chemical shifts calibrated using TMS or solvent signals. High- and low-resolution mass spectra were recorded at Cape Technikon Mass Spectrometry Unit using VG – 70 SEQ MASPEC II (scanning at RP 10 000). Combustion analyses (C, H, N) were carried out at the University of Cape Town. The synthesis and characterization of the 2-aryl-1,2,3,4-tetrahydro-1-methylsulfonyl-4-quinolones **1** are described elsewhere.[4]

General procedure for the preparation of oxime derivatives 2

A stirred mixture of the quinolone **1** (1 equiv.), hydroxylamine hydrochloride (1.5 equiv.) and sodium acetate trihydrate (1.5 equiv.) in ethanol (6 ml.mmol^{-1} of **1**) was refluxed for 4h. The mixture was filtered hot on a sintered funnel and the solvent was evaporated under reduced pressure. The residue was taken up in ether (50 ml), filtered, evaporated and recrystallised. The following products were prepared and characterized:

2a. Solid (67%); m.p. 168 – 170° C (EtOH); δ_H(200 MHz, $CDCl_3$) 2.99 (3H, s, SO_2Me), 3.13 (1H, dd, *J* 6.6 and 18.8 Hz, 3-H), 3.94 (1H, dd, *J* 1.4 and 18.8 Hz, 3-H), 5.86 (1H, d, *J* 6.4 Hz, 2-H), 7.07 – 7.35 (7H, m, 6-H, 7-H and C_6H_5), 7.64 (1H, d, *J* 8.4 Hz, 8-H), 7.86 (1H, dd, *J* 1.4 and 7.8 Hz, 5-H) and 9.18 (1H, s, OH); δ_C (50.0 MHz, $CDCl_3$) 26.9 (C-3), 40.1 (SO_2Me), 55.2 (C-2), 124.0 (C-8), 124.5 (C-4a), 125.5 (C-6), 125.9 (C-5), 126.8 (C-2′ and C-6′), 127.6 (C-4′), 128.5 (C-3′ and C-5′), 130.8 (C-7), 135.3 (C-1′), 138.2 (C-8a) and 149.7 (C-4); ν_{max}/ cm^{-1} 1140 (SO_2), 1320 (SO_2), 1610 (C=N) and 3250 (OH); m/z 316 (M^+, 41.6), 219 (100), 206 (17.9), 165 (10.1), 131 (25.8) and 77 (44.1). Anal. calc. for $C_{16}H_{16}N_2O_3S$ (316.38): C, 60.74, H, 5.10, N, 8.85%. Found: C, 60.78, H, 5.10, N, 8.89%.

2b. Solid (56%); m.p. 178 – 180°C (EtOH); δ_H(200 MHz, $CDCl_3$) 2.98 (3H, s, SO_2Me), 3.09 (1H, dd, *J* 6.6 and 19.0 Hz, 3-H), 3.89 (1H, d, *J* 18.8 Hz, 3-H), 5.82 (1H, d, *J* 6.2 Hz, 2-H), 6.89 (2H, t, *J* 8.7 Hz, 3-H′ and 5′-H), 7.12 (1H, dt, *J* 1.2 and 7.6 Hz, 6-H), 7.20–7.27 (2H, m, 2′-H and 6′-H), 7.30 (1H, dt, *J* 1.6 and 7.6 Hz, 7-H), 7.62 (1H, d, *J* 8.2 Hz, 8-H), 7.85 (1H, d, *J* 7.8 Hz, 5-H) and 8.79 (1H, br s, OH); δ_C (50.0 MHz, $CDCl_3$) 25.4 (C-3), 38.6 (SO_2Me), 53.2 (C-2), 114.0 (d, $^2J_{CF}$ 21.7 Hz, C-3′ and C-5′), 122.6 (C-8), 122.9 (C-4a), 124.1 (C-6), 124.6 (C-5), 127.2 (d, $^3J_{CF}$ 8.0 Hz, C-2′ and C-4′), 129.5 (C-7), 132.5 (d, $^4J_{CF}$ 3.1 Hz, C-1′), 133.5 (C-8a), 148.0 (C-4) and 158.1 (d, $^1J_{CF}$ 245.8 Hz, C-4′); ν_{max}/ cm^{-1} 1160 (SO_2), 1340 (SO_2), 1620 (C=N) and 3250 (OH); m/z 334 (M^+, 44.3), 237 (100), 224 (21.6), 131 (31.1) and 109 (38.6). Anal. calc. for $C_{16}H_{15}N_2FO_3S$ (334.37): C, 57.47, H, 4.52, N, 8.38%. Found: C, 57.48, H, 4.55, N, 8.36%.

2c. Solid (60%); m.p. 208 –210° C (EtOH); δ_H(200 MHz, $CDCl_3$) 2.74 (3H, s, SO_2Me), 2.77 (1H, dd, *J* 6.4 and 18.8 Hz, 3-H), 3.63 (1H, dd, *J* 1.4 and 18.8 Hz, 3-H), 5.50 (1H, d, *J* 6.0 Hz, 2-H), 6.79 – 7.04 (6H, m, 6-H, 7-H and C_6H_4), 7.32 (1H, dd, *J* 1.0 and 8.4 Hz, 8-H), 7.68 (1H, dd, *J* 1.4

and 7.8 Hz, 5-H) and 9.18 (1H, s, OH); δ_C (50.0 MHz, $CDCl_3$) 25.7 (C-3), 39.3 (SO_2Me), 54.1 (C-2), 123.3 (C-8), 124.8 (C-4a), 124.9 (C-1′), 125.2 (C-6), 127.8 (C-3′ and C-5′), 127.9 (C-2′ and C-6′), 129.3 (C-5), 132.5 (C-8a), 133.8 (C-4′), 136.7 (C-7) and 146.5 (C-4); ν_{max}/ cm^{-1} 1160 (SO_2), 1340 (SO_2), 1620 (CO) and 3250 (NH); m/z 350 (M^+, 82.0), 253 (90.0), 218 (96.2) 190 (12.6), 131 (31.6) 102 (30.9) and 43 (100). Anal. calc. for $C_{16}H_{15}N_2O_3ClS$ (350.91): C, 54.76, H, 4.31, N, 8.02%. Found: C, 54.57, H, 4.29, N, 7.63%.

2d. Solid (70%); m.p 222° C (EtOH); δ_H (200 MHz, DMSO-d_6) 3.03 (1H, dd, *J* 6.2 and 18.6 Hz, 3-H), 3.23 (3H, s, SO_2Me), 3.78 (1H, d, *J* 18.2 Hz, 3-H), 6.16 (1H, d, *J*5.4 Hz, 2-H), 7.07 (1H, t, *J* 7.6 Hz, 6-H), 7.15 (2H, d, *J* 8.6 Hz, 3′-H and 5′-H), 7.28 (1H, dt, *J* 1.6 and 7.8 Hz, 7-H), 7.44 (2H, d, *J* 7.4 Hz, 2′-H and 6′-H), 7.54 (1H, d, *J* 7.4 Hz, 8-H), 7.82 (1H, dd, *J* 1.2 and 8.0 Hz, 5-H) and 11.7 (1H, s, OH); δ_C (50.0 MHz, DMSO-d_6) 26.1 (C-3), 40.0 (SO_2Me), 54.1 (C-2), 120.6 (C-8), 123.2 (C-1′), 124.9 (C-4a), 125.4 (C-6), 128.8 (C-2′, C-4′ and C-6′), 129.7 (C-5), 131.4 (C-3′ and C-5′), 134.6 (C-8a), 138.6 (C-7) and 146.9 (C-4); ν_{max}/ cm^{-1} 1160 (SO_2), 1345 (SO_2), 1610 (C=N) and 3250 (OH); m/z 379 (M^+ – 17, 10.8), 301 (32.0), 220 (29.7), 197 (33.9), 146 (6.2), 90 (14.9) and 43 (100). Anal. calc. for $C_{16}H_{15}N_2O_3BrS$ (395.28): C, 48.62, H, 3,82, N, 7.09%. Found: C, 48.48, H, 3.72, N, 7.19%.

2e. Solid (69%); m.p. 162 – 163°C (EtOH); δ_H(200 MHz, $CDCl_3$) 2.98 (3H, s, SO_2Me), 3.08 (1H, dd, *J* 6.6 and 18.7 Hz, 3-H), 3.70 (3H, s, OMe), 3.88 (1H, dd, *J*1.5 and 18.7 Hz, 3-H), 5.80 (1H, d, *J* 6.2 Hz, 2-H), 6.73 (2H, d, *J* 8.8 Hz, 2′-H and 6′-H), 7.12 (1H, t, *J* 7.6 Hz, 6-H), 7.18 (2H, d, *J* 9.0 Hz, 3′-H and 5′-H), 7.29 (1H, dt, *J* 1.6 and 7.8 Hz, 7-H), 7.61 (1H, dd, *J* 1.1 and 8.3 Hz, 8-H), 7.87 (1H, dd, *J* 1.6 and 7.9 Hz, 5-H) and 8.17 (1H, s, OH); δ_C (50.0 MHz, $CDCl_3$) 27.0 (C-3), 40.1 (SO_2Me), 54.8 (OMe), 55.1 (C-2), 113.9 (C-3′ and C-5′), 124.1 (C-8), 124.6 (C-1′), 125.6 (C-7), 125.9 (C-5), 128.1 (C-2′ and C-6′), 130.3 (C-4a), 130.8 (C-6), 135.3 (C-8a), 149.9 (C-4) and 158.9 (C-4′); ν_{max}/ cm^{-1} 1180 (SO_2), 1260 (=C-O-CH_3), 1340 (SO_2), 1610 (C=N) and 3250 (OH); m/z 346 (M^+, 16.5), 249 (30.9), 207 (14.7), 193 (7.2), 134 (31.5), 103 (13.4) and 43 (100). Anal. calc. for $C_{17}H_{18}N_2O_4S$ (346.41): C, 58.94, H, 5.24, N, 8.09%. Found: C, 59.03, H, 5.25, 8.08%.

Preparation of O-mesyloxime derivatives 3. General procedure

A stirred solution of the oxime **2** (1 equiv.) in pyridine (3 ml.mmol^{-1} of **2**) was cooled to 0 - 5° C and then treated dropwise with methanesulfonyl chloride (1.3 equiv.). The mixture was stirred at 0 – 5° 0 for 30 minutes and allowed to warm to room temperature. After 2 hours at room temperature, ice-cold water was added and the precipitate was filtered and recrystallised to afford O-mesyloxime **3**. The following products were prepared and characterized:

3a. Solid (93%); m.p. 172 – 174°C (EtOH-EtOAc); δ_H (200 MHz, $CDCl_3$); 2.97 (3H, s, OSO_2CH_3), 3.07 (1H, dd, *J* 6.6 and 18.5 Hz, 3-H), 3.70 (3H, s, SO_2CH_3), 3.87 (1H, dd, *J* 1.6 and 18.7 Hz, 3-H), 5.84 (1H, d, *J* 6.2 Hz, 2-H), 7.15 – 7.28 (6H, m, 6-H and C_6H_5), 7.46 (1H, t, *J* 7.1 Hz, 7-H), 7.72 (1H, d, *J* 8.2 Hz, 8-H) and 8.02 (1H, d, *J* 7.0 Hz, 5-H); δ_C (50 MHz, $CDCl_3$) 29.1 (C-3), 36.5 (OSO_2CH_3), 40.5 (SO_2CH_3), 54.9 (C-2), 120.7 (C-4a), 124.2 (C-8), 125.3 (C-6 and C-4′), 126.4 (C-3′ and C-5′), 127.8 (C-5), 128.7 (C-2′ and C-6′), 133.0 (C-7), 136.9 (C-1′), 137.3 (C-8a) and 157.4 (C-4); m/z 394 (M^+, 51.6), 236 (20.8), 220 (38.1), 219 (100), 218 (34.7), 206 (40) and 77 (21.8) (Found: M^+, 394.0641. $C_{17}H_{18}O_5N_2S_2$ requires *M*, 394.0656).

3b. Solid (73%); m.p. 219 – 222°C (EtOH-EtOAc); δ_H (200 MHz, $CDCl_3$) 3.36 (3H, s, OSO_2CH_3), 3.42 (3H, s, SO_2CH_3), 3.52 (1H, d, *J* 6.6 Hz, 3-H), 3.86 (1H, dd, *J* 1.6 and 18.7 Hz, 3-H), 5.80 (1H, d, *J* 6.2 Hz, 2-H), 7.08 – 7.34 (5H, m, 2′-H, 3′-H, 5′-H, 6-H and 6′-H), 7.52 (1H, dt, *J* 1.6 and 7.9 Hz, 7-H), 7.71 (1H, d, *J* 7.6 Hz, 8-H) and 7.98 (1H, dd, *J* 1.4 and 8.1 Hz, 5-H); δ_C (50 MHz, $CDCl_3$) 28.5 (C-3), 36.6 (OSO_2CH_3), 40.5 (SO_2CH_3), 53.7 (C-2), 115.5 (d, $^2J_{CF}$ 21.2 Hz, C-3′ and C-5′), 120.9 (C-8), 124.9 (C-6), 125.1 (C-4a), 125.3 (C-5), 128.6 (d, $^3J_{CF}$8.4 Hz, C-2′ and C-6′), 132.9 (C-7), 134.4 (d, $^4J_{CF}$ 2.7 Hz, C-1′), 136.8 (C-8a), 157.5 (C-4), 161.4 (d, $^1J_{CF}$ 242.3 Hz, C-4′); m/z. 412 (M^+, 37.5), 237 (100), 224 (28.6), 223 (12.3) and 122 (12.8) (Found: M^+, 412.0564. $C_{17}H_{17}O_5N_2S_2F$ requires *M*, 412.0566).

3c. Solid (78%); m.p. 191 – 193°C (EtOH-EtOAc); δ_H (200 MHz, $CDCl_3$) 3.06 (3H, s, OSO_2CH_3), 3.23 (1H, dd, *J* 6.4 and 18.8 Hz, 3-H), 3.24 (3H, s, SO_2CH_3), 3.89 (1H, dd, *J* 1.8 and 18.7 Hz, 3-H), 5.83 (1H, d, *J* 5.2 Hz, 2-H), 7.13 (5H, s, 3′-H and 5′-H), 7.20 (2H, s, 2′-H and 6′-H), 7.22 (1H, dt, *J* 1.4 and 8.0 Hz, 6-H), 7.45 (1H, dt, *J* 1.4 and 7.7 Hz, 7-H), 7.72 (1H, d, *J* 8.4 Hz, 8-H) and 8.01 (1H, dd, *J* 1.4 and 8.0 Hz, 5-H); δ_C

(50 MHz, $CDCl_3$) 29.1 (C-3), 36.7 (OSO_2CH_3), 40.6 (SO_2CH_3), 54.5 (C-2), 121.1 (C-1′), 124.6 (C-8), 125.6 (C-6), 128.0 (C-3′ and C-5′), 129.0 (C-2′ and C-6′), 132.5 (C-5), 133.4 (C-7), 134.0 (C-4a), 135.9 (C-8a), 136.8 (C-4′) and 157.3 (C-4); m/z 428 (M^+, 53.5), 349 (11.1), 268 (61.2), 254 (80.5), 253 (100) and 218 (78.5) (Found: M^+, 428.0260. $C_{17}H_{17}O_5N_2S_2{}^{35}Cl$ requires *M*, 428.0267).

3d. Solid (94%); m.p. 191 – 193°C (EtOH-EtOAc); δ_H (200 MHz, DMSO-d_6) 3.36 (3H, s, OSO_2CH_3), 3.43 (3H, s, SO_2CH_3), 3.52 (1H, dd, *J* 6.4 and 18.8 Hz, 3-H), 3.86 (1H, dd, *J* 1.8 and 18.8 Hz, 3-H), 5.78 (1H, d, *J* 6.4 Hz, 2-H), 7.16 – 7.24 (3H, m, 3′-H, 5′-H and 6-H), 7.46 – 7.56 (3H, m, 2′-H, 6′-H and 7-H), 7.70 (1H, d, *J* 8.4 Hz, 8-H) and 7.97 (1H, d, 8.0 Hz, 5-H); δ_C (50 MHz, DMSO-d_6) 28.3 (C-3), 36.6 (OSO_2CH_3), 40.3 (SO_2CH_3), 53.8 (C-2), 120.9 (C-8), 121.0 (C-4′), 124.9 (C-6), 125.0 (C-1′), 125.4 (C-7), 128.7 (C-3′ and C-5′), 131.6 (C-2′ and C-6′), 132.9 (C-5), 136.8 (C-4a), 137.7 (C-8a) and 157.3 (C-4); m/z 472 (M^+, 35.9), 316 (27.4), 301 (41.1), 297 (56.2), 296 (44.3), 286 (321.9), 219 (33.9), 218 (100) and 182 (21.5) (Found: M^+, 471.9771. $C_{17}H_{17}O_5N_2S_2{}^{79}Br$ requires *M*, 471.9762).

3e. Solid (94%), m.p. 159 – 161°C (EtOH-EtOAc); δ_H (200 MHz, $CDCl_3$) 3.04 (3H, s, OSO_2CH_3), 3.21 (1H, dd, *J* 6.2 and 18.4 Hz, 3-H), 3.23 (3H, s, OSO_2CH_3), 3.70 (3H, s, OCH_3), 3.87 (1H, d, *J* 18.4 Hz, 3-H), 5.79 (1H, d, *J* 5.4 Hz, 2-H), 6.75 (2H, d, *J* 8.6 Hz, 3′-H and 5′-H), 7.12 (2H, d, *J* 8.4 Hz, 2′-H and 6′-H), 7.15 (1H, t, *J* 7.6 Hz, 6-H), 7.42 (1H, dt, *J* 1.2 and 7.9 Hz, 7-H), 7.67 (1H, d, *J* 8.4 Hz, 8-H) and 8.00 (1H, d, *J* 8.0 Hz, 5-H); δ_C (50 MHz, $CDCl_3$) 29.3 (C-3), 36.6 (OSO_2CH_3), 40.6 (SO_2CH_3), 54.6 (C-2), 55.1 (OCH_3), 114.1 (C-3′ and C-5′), 121.2 (C-1′), 124.5 (C-8), 125.4 (C-6), 127.8 (C-2′ and C-6′), 128.1 (C-4a), 129.3 (C-5), 133.1 (C-7), 137.0 (C-8a), 157.8 (C-4) and 159.1 (C-4′); m/z 424 (M^+, 8.7), 346 (88.7), 329 (24.0), 266 (77.9), 249 (100), 236 (39.7), 192 (13.0), 134 (57.7) and 121 (49.9) (Found: M^+, 424.0756. $C_{18}H_{20}O_6N_2S_2$ requires *M*, 424.0763).

Synthesis of 4-amino-2-arylquinolines 5. General procedure

O-Mesyloxime **3** (1 equiv.) was added slowly and in small portions to a stirred solution of sodium ethoxide (21% in ethanol, 1.3 equiv.) in ethanol (3 ml.mmol^{-3}of **3**). The mixture was stirred at room temperature for 3 hours and then boiled under reflux for 18 hours. The cooled mixture was poured into ice-cold water and the resulting precipitate was filtered and purified by column chromatography (methanol as eluent) to afford (i) starting material and (ii) **5**.

4-Amino-2-phenylquinoline 5a

Solid (86%); m.p. 166 – 168°C; δ_H (200 MHz, DMSO-d_6) 6.91 (2H, br S, NH$_2$), 7.14 (1H, s, 3-H), 7.35 – 7.55 (4H, m, 3′-H, 4′-H, 5′-H and 7-H), 7.63 (1H, t, *J* 8.5 Hz, 6-H), 7.86 (1H, d, *J* 8.6 Hz, 8-H), 8.09 (2H, d, *J* 6.8 Hz, 2′-H and 6′-H) and 8.18 (1H, d, *J* 8.2 Hz, 5-H); δ_C (50 MHz, DMSO-d_6) 99.1 (C-3), 117.8 (C-4a), 122.2 (C-8), 123.6 (C-6), 126.8 (C-3′ and C-5′), 128.5 (C-2′ and C-6′), 128.9 (C-4′), 129.0 (C-5), 129.3 (C-7), 139.8 (C-1′), 148.5 (C-8a), 152.6 (C-4) and 156.1 (C-2); ν_{max}/ cm^{-1} 3100 (NH$_2$); m/z 220 (M^+, 100) and 219 (54.3), 204 (Found: M^+, 220.0998. $C_{13}H_{12}N_2$ requires *M*, 221.001).

4-Amino-2-(4′-fluorophenyl)quinoline 5b

Solid (81%), m.p. 179 – 182° C; δ_H (200 MHz, DMSO-d_6) 8.99(2H, br s, NH$_2$), 7.09 (1H, s, 3-H), 7.28 – 7.40 (3H, m, 3′-H, 5′-H and 7-H), 7.60 (1H, t, J 7.6 Hz, 6-H), 8.84 (1H, d, J 8.6 Hz, 8-H), 8.08 – 8.21 (3H, m, 2′-H, 5-H and 6′-H); δ_C (50 MHz, DMSO-d_6) 98.8 (C-3), 115.4 (d, $^2J_{CF}$ 21.6 Hz, C-3′ and C-5′), 117.6 (C-4a), 122.3 (C-8), 123.7 (C-6), 128.6 (C-5), 128.9 (d, $^3J_{CF}$ 8.7 Hz, C-2′ and C-6′), 129.6 (C-7), 136.0 (d, $^4J_{CF}$ 2.7 Hz, C-1′), 148.2 (C-8a), 152.8 (C-4), 154.9 (C-2) and 162.8 (d, $^1J_{CF}$ 244.3 Hz, C-4′); ν_{max}/ cm^{-1} 3150 (NH$_2$); m/z 238 (M^+, 100) and 237 (50.5) (Found: M^+, 238.0894. $C_{13}H_{11}N_2F$ requires *M*, 238.0906).

4-Amino-2-(4′-chlorophenyl)quinoline 5c

Solid (89%), m.p. 210 – 212° C; δ_H (200 MHz, DMSO-d_6) 7.06 (1H, s, 3-H), 7.55 (1H, t, *J* 7.6 Hz, 6-H), 7.75 (2H, d, *J* 8.2 Hz, 2′-H and 6′-H), 7.81 (1H, t, *J* 7.6 Hz, 7-H), 7.95 (1H, d, *J* 8.6 Hz, 8-H), 8.01 (2H, d, *J* 8.4 Hz, 3′-H and 5′-H), 8.07 (2H, br s, NH$_2$) and 8.32 (1H, d, *J* 8.4 Hz, 5-H); δ_C (50 MHz, DMSO-d_6) 99.9 (C-3), 116.5 (C-4a), 122.9 (C-8), 124.4 (C-6), 125.2 (C-5), 129.0 (C-3′ and C-5′), 129.3 (C-2′ and C-6′), 132.0 (C-7), 134.0 (C-1′), 135.3 (C-4′), 143.5 (C-8a), 152.5 (C-4) and 155.7 (C-2); ν_{max}/ cm^{-1} 3100 (NH$_2$); m/z 254 (M^+, 100), 253 (36.8) and 149 (22.1) (Found: M^+, 254.0608. $C_{13}H_{11}N_2{}^{35}Cl$ requires *M*, 254.0611).

4-Amino-2-(4′-bromophenyl)quinoline 5d

Solid (86%); m.p. 167 – 169° C; δ_H (200 MHz, DMSO-d_6) 6.93 (2H, br s, NH_2), 7.14 (1H, s, 3-H), 7.63 (1H, t, *J* 8.0 Hz, 6-H), 7.69 (1H, t, *J* 8.2 Hz, 7-H), 7.69 (2H, d, *J* 8.6 Hz, 2′-H and 6′-H), 7.86 (1H, d, *J* 8.0 Hz, 8-H), 8.06 (2H, d, *J* 8.4 Hz, 3′-H and 5′-H) and 8.19 (1H, d, *J* 82 Hz, 5-H); δ_C(50 MHz, DMSO-d_6) 98.8 (C-3), 117.9 (C-4a), 122.3 (C-8), 122.4 (C-6), 123.7 (C-4′), 128.8 (C-2′ and C-6′), 129.2 (C-5), 129.4 (C-7), 131.5 (C-3′ and C-5′), 139.1 (C-1′), 148.7 (C-8a), 152.6 (C-4) and 154.9 (C-2); ν_{max}/ cm^{-1} 3100 (NH_2); m/z 298 (M^+, 100), 219 (33.2) and 109 (29.5) (Found: M^+, 298.0101. $C_{13}H_{11}N_2{}^{79}Br$ requires *M*, 298.0106).

4-Amino-2-(4′-methoxyphenyl)quinoline 5e

Solid (88%), m.p. 187 – 191°C; δ_H (200 MHz, DMSO-d_6) 3.82 (3H, s, OCH_3), 7.06 (2H, d, *J* 8.6 Hz, 2′-H and 6′-H), 7.07 (2H, br s, NH_2), 7.37 (1H, t, *J* 7.6 Hz, 6-H), 7.62 (1H, t, *J* 7.6 Hz, 7-H), 7.84 (1H, d, *J* 8.6 Hz, 8-H), 8.03 (2H, d, *J* 8.6 Hz, 3′-H and 5′-H) and 8.17 (1H, d, *J* 8.4 Hz, 5-H); δ_C (50 MHz, DMSO-d_6) 55.3 (OCH_3), 98.6 (C-3), 114.0 (C-3′ and C-5′), 117.4 (C-4a), 122.4 (C-8), 123.5 (C-6), 128.0 (C-5), 128.3 (C-2′ and C-6′), 129.7 (C-7), 131.4 (C-1′), 147.7 (C-8a), 152.9 (C-4), 155.3 (C-2) and 160.3 (C-4′); ν_{max}/ cm^{-1} 3150 (NH_2); m/z 250 (M^+, 100) and 235 (20.4) (Found: M^+, 250.1096. $C_{14}H_{14}N_2O$ requires *M*, 250.1106).

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