Tetrahedron 65 (2009) 6941–6949

Contents lists available at ScienceDirect

Tetrahedron

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

Synthesis of novel benzoxazocino quinoliniums and quinolones under PTC conditions and their application in Suzuki cross coupling reaction for the construction of polynuclear heteroaromatics

Krishnendu B. Sahu [a], Abhijit Hazra [a], Priyankar Paira [a], Pritam Saha [a], Subhendu Naskar [a], Rupankar Paira [a], Sukdeb Banerjee [a], Niranjan P. Sahu [a], Nirup B. Mondal [a,*], Peter Luger [b,†], Manuela Weber [b]

[a] Indian Institute of Chemical Biology, Council of Scientific & Industrial Research, 4 Raja SC Mullick Road, Jadavpur, Kolkata 700 032, India
[b] Freie Universität Berlin, Institut für Chemie und Biochemie/Kristallographie, Fabeckstr. 36a, D-14195, Berlin, Germany

ARTICLE INFO

Article history:
Received 16 February 2009
Received in revised form 16 June 2009
Accepted 16 June 2009
Available online 21 June 2009

Keywords:
PTC
Benzoxazocinoquinolone
Biaryl quinolones
Suzuki coupling

ABSTRACT

A general and highly efficient synthetic protocol under phase transfer catalytic condition has been established for the synthesis of fused tetracyclic oxazocinoquinolone analogues which served as the precursors for novel biaryl quinolones using microwave assisted Suzuki cross coupling reaction.

1. Introduction

Important pharmaceuticals often possess heterocyclic moieties as their building blocks.[1] The extensive use of heterocyclic compounds may be attributed to the wide range of reaction types available that facilitate subtle structural modifications in the heterocyclic compounds.[2–4] Thus, investigations towards the understanding of reactivity of heterocyclic compounds are gaining significance, especially expedient syntheses leading to *N*-heteroaromatics which are potent inhibitors of lymphocyte apoptosis[5] and often form the framework of DNA intercalating agents.[6,7] Great efforts have, therefore, been made to discover and optimize new reactions/methodologies to facilitate the construction of heterocycles.[8,9] In this aspect phase transfer catalysis has long been recognized as a versatile methodology for organic synthesis in industry, academia and in process chemistry.[10] As a part of our continuing investigation on phase transfer catalysis for the construction of structurally unique *N*-heteroaromatics,[11,12] we report herein a one-pot reaction of 8-hydroxyquinolines leading to the formation of tetracyclic quinolinium cations and the corresponding quinolones having an benzoxazocino ring system like nefopam,[13–17] a widely used nonopioid analgesic. The synthesized molecules have further been utilized for the construction of structurally unique class of polycyclic heteroaromatics via Suzuki cross coupling reaction,[18,19] which has emerged as one of the most important carbon–carbon bond forming methods in the synthesis of pharmaceutical agents, organic materials, as well as natural products.[20–23]

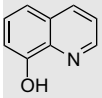
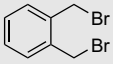
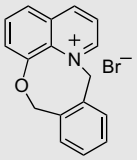
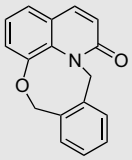
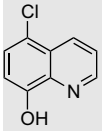
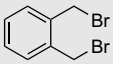
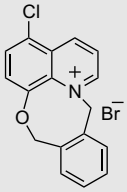
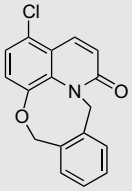
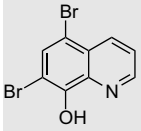
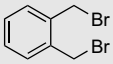
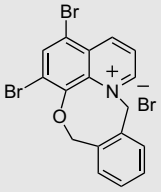
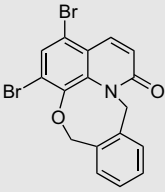
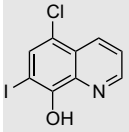
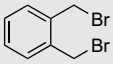
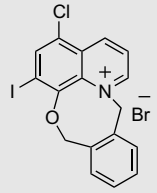
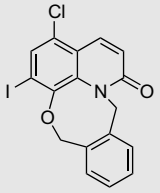
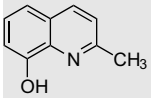
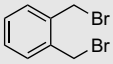
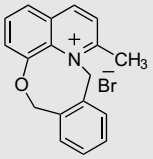
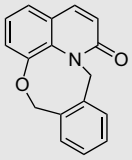
2. Result and discussion

Initially, the reaction of 8-hydroxyquinoline (**1a**) with α,α′-dibromo-ortho xylene (**2**) was studied under phase transfer catalytic condition and the progress of the reaction was monitored by TLC. The reaction was observed to be completed within 10 h. Usual workup followed by chromatographic separation afforded two products, characterized as benzoxazocino quinolinium (**3a**) and benzoxazocino quinolone (**4a**) from their MS, ^{1}H and ^{13}C NMR spectral analysis. This method was extended to differently substituted 8-hydroxyquinolines viz. 5-chloro (**1b**), 5,7-dibromo (**1c**), 5-chloro-7-iodo (**1d**), and 2-methyl (**1e**) derivatives. In all these cases quinolinium cations (**3a**–**e**) and their corresponding quinolones (**4a**–**d**) were isolated in excellent yields (Table 1). The

* Corresponding author. Tel.: +91 33 24733491; fax: +91 33 2473 5197.
E-mail addresses: nirup@iicb.res.in (N.B. Mondal), luger@chemie.fu-berlin.de (P. Luger).
† Tel.: +49 30 838 53411; fax: +49 30 838 53464.

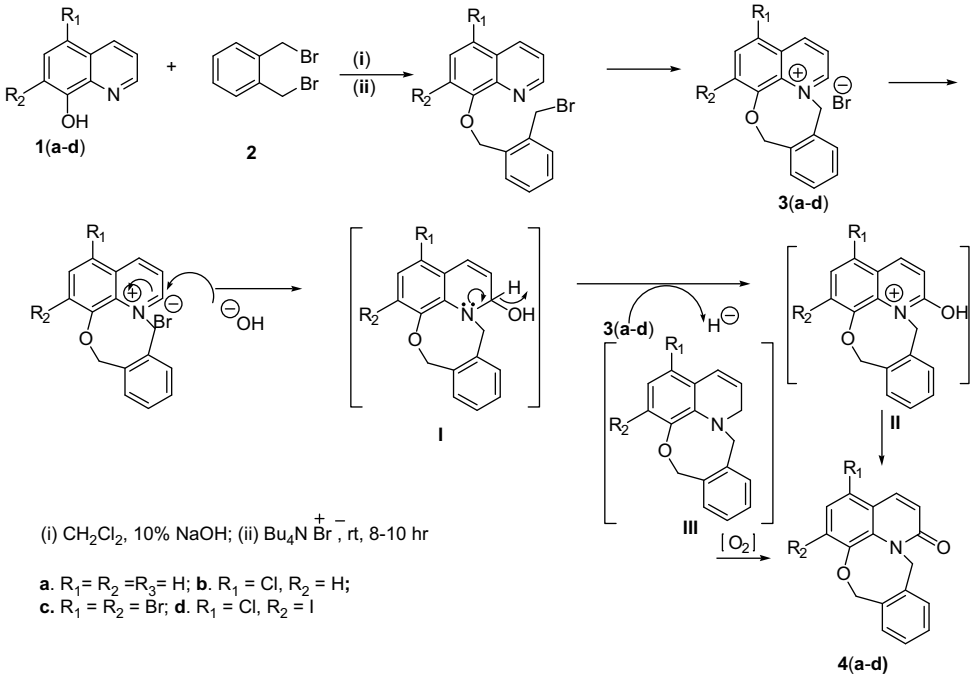
0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.06.061

Table 1
Construction of tetracyclic quinoliniums and quinolones using 8-hydroxy quinolines (**1a**–**e**) and α,α′-dibromo-*o*-xylene (**2**)[a]

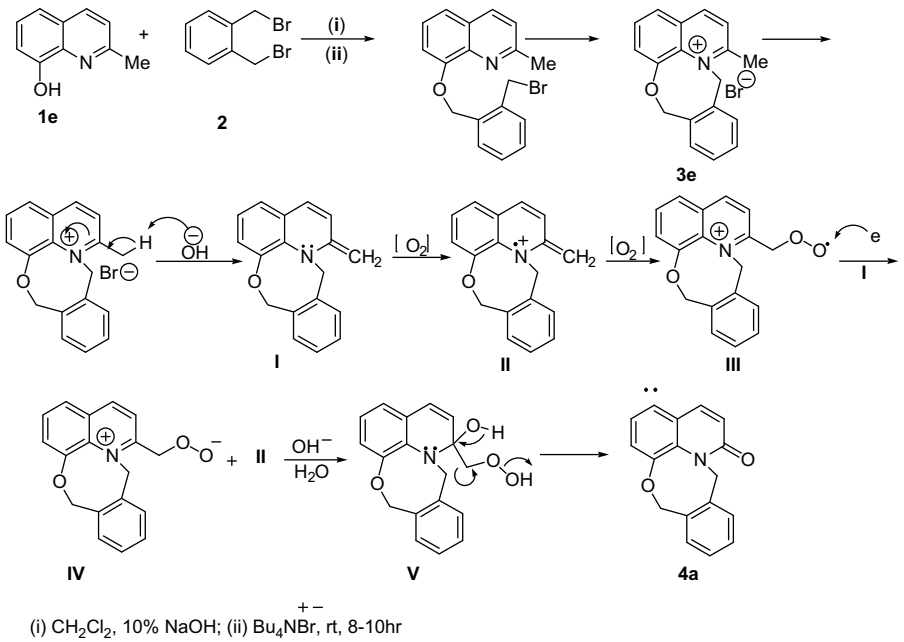
8 Hydroxy quinoline	Alkylating agents	Time (h)	Product[b] (%)[c]	
			Quinolinium	Quinolone
 **1a**	 **2**	8	 **3a** (30)	 **4a** (60)
 **1b**	 **2**	10	 **3b** (35)	 **4b** (45)
 **1c**	 **2**	9	 **3c** (25)	 **4c** (65)
 **1d**	 **2**	9	 **3d** (35)	 **4d** (40)
 **1e**	 **2**	6	 **3e** (40)	 **4a** (35)

[a] All the reactions were conducted with 8-hydroxy quinoline and dibromo-o-xylene under PTC condition.
[b] All the products are characterized by mass, ^{1}H, ^{13}C NMR.
[c] Isolated yield.

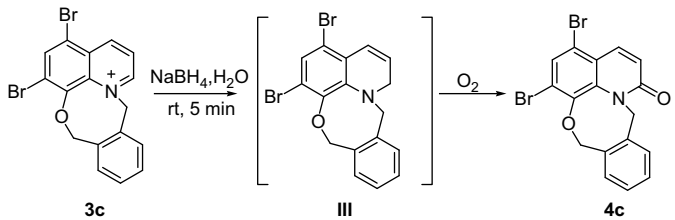
pathway for the formation of quinoliniums (**3a**–**e**) from 8-hydroxyquinolines (**1a**–**e**) might have occurred through initial ether formation followed by intramolecular cyclization. We believe that the conversion of these quinoliniums (**3a**–**e**) to quinolones (**4a**–**d**) has occurred via oxidative pathway (Schemes 1 and 2) as described for tricyclic quinolones.[12] However, for further confirmation of the reaction mechanism, we performed sodium borohydride reduction reaction on a model substrate **3c** and were able to isolate the key intermediate [**III**] and characterised by spectral analysis (^{1}H, ^{13}C NMR). The gradual transformion of intermediate **III** to quinolone (**4c**) as depicted in Scheme 3 strongly supports the porposed mechanism of quinolone formation from quinolinium via the proposed oxidative pathway. The spectral data (^{1}H, ^{13}C NMR and MS) of all the quinolones (**4a**–**d**) agreed well with the proposed structures but some ambiguity was observed in the ^{1}H NMR spectra of all the quinolinium cations (**3a**–**e**). The protons of N–CH_2 group gave rise to two doublets with one of the two protons resonating in aromatic region (δ 7.6–7.8). In the cases of quinolinium or isoquinolinium *N*-benzyl bromides the protons of the N–CH_2 group usually generate a singlet at δ 6.05–6.70.[24] The important correlations as revealed by 2D NMR analysis of quinolinium **3c** are shown in Figure 1. NOE results indicate that the more deshielded proton is not coplanar with the aromatic ring. The major contribution to its downfield shift is likely to be due to the near parallel orientation of the C–H bond with the p-orbitals of the aromatic ring(s), allowing greater overlap. For unambiguous determination of the structures, single crystal X-ray analysis of quinolinium **3c** and quinolone **4a** was carried out. Two molecules of **3c** formed the asymmetric unit, the unit cell consisting of two $[C_{17}H_{12}NOBr_2]^{+}$ cations, two Br^{-} anions



Scheme 1. Plausible reaction pathway leading to fused quinolone analogues (**4a**–**d**).



Scheme 2. Plausible reaction pathway leading to fused quinolone **4a** from **1e**.



Scheme 3. Sodium borohydride reduction of quinolinium **3c** for the isolation of intermedeate **III**.

and two water molecules. The ORTEP representations of the molecular structures of **3c** and **4a**, showing also the atomic numbering, is depicted in Figure 2. The molecular structures of **3c** and **4a** consist of a tetracyclic system of three planar six membered rings and one non-planar eight-membered ring. There are a number of short contacts between molecule 1 of **3c**, the counter ions and the water molecules as illustrated in Figure 3, while there are no intermolecular interactions of relevance seen in the crystal lattice of **4a**.

Afterwards, we attempted to arylate the dihalo-substituted quinolones (**4c**/**4d**) with differently substituted aryl boronic acids following the Suzuki coupling reaction under both traditional

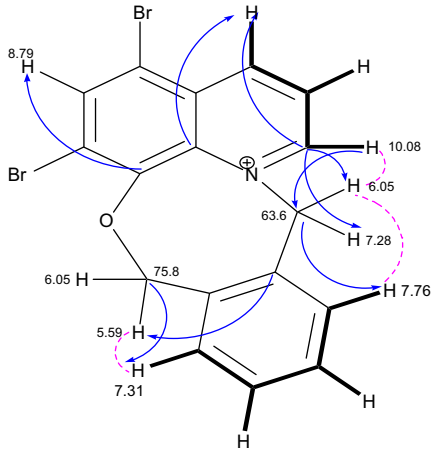


Figure 1. Important correlations COSY (—), HMBC (→), NOESY (- - -).

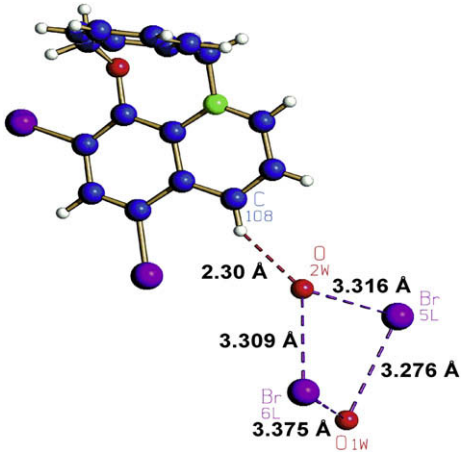
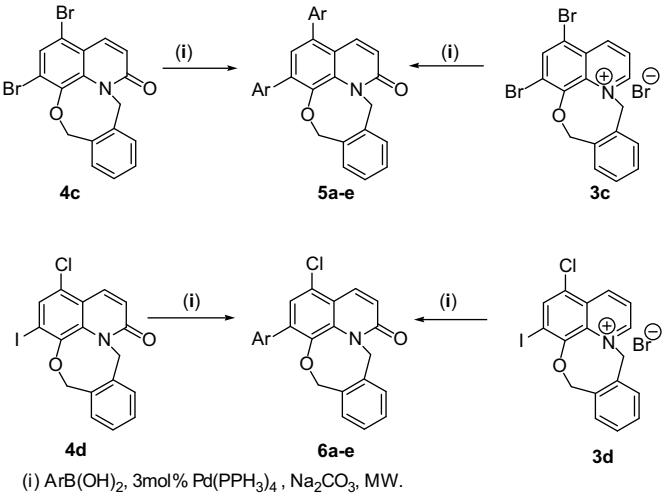


Figure 3. Short contacts in the crystal lattice of **3c** with contributions of molecule 1 of **3c**, the counter ions and the water molecules as illustrated here.

heating and microwave conditions[25] for the generation of polycyclic heteroaromatics (Scheme 4). Screening was done with various catalysts, bases, solvents and reaction conditions (microwave and heating) to optimize the reaction of dibromo-substituted quinolone (**4c**) with benzene boronic acid (Table 2). The microwave condition was found to be more effective than the traditional heating condition with respect to the yield of the products and the reaction time. $Pd(PPh_3)_4$ (3 mol %) proved to be the most effective catalyst when the reaction being carried out in DMF/H_2O (10:1) using Na_2CO_3 as a base (Table 2, entry 13). The reaction was also performed under aerobic conditions using $Pd(Cl)_2$ as catalyst without the presence of any ligand. The reaction proceeded smoothly but the yield of the biaryl products was slightly lower than with $Pd(PPh_3)_4$. It might have happened that under the reaction condition Pd nanoparticles are formed.

This coupling reaction was applied on a chloro-iodo substituted quinolone (**4d**). Under the reaction conditions **4c** yielded a diarylated quinolone (**5a**), **4d** yielded only a mono arylated one (**6a**). Similar diarylated and monoarylated quinolones (**5a** and **6a**) were also obtained from the dihalo substituted quinoliniums **3c** and **3d** (Scheme 4). By following TLC at short interval, it was observed that these quinoliniums (**3c**, **3d**) were first transformed to quinolones (**4c**, **4d**) in aerobic condition within 5 min and finally yielded the common Suzuki products (**5a** and **6a**). However, in inert atmosphere neither the quinolones nor the coupling products could be isolated. For the rationalization of this coupling reaction different boronic acids were used to synthesize both the mono and diarylated quinolones from **3c**, **4c** and **3d**, **4d** (Table 3).



Scheme 4. Suzuki reaction of quinoliniums (**3c**/**3d**) and quinolones (**4c**/**4d**) with aryl boronic acid.

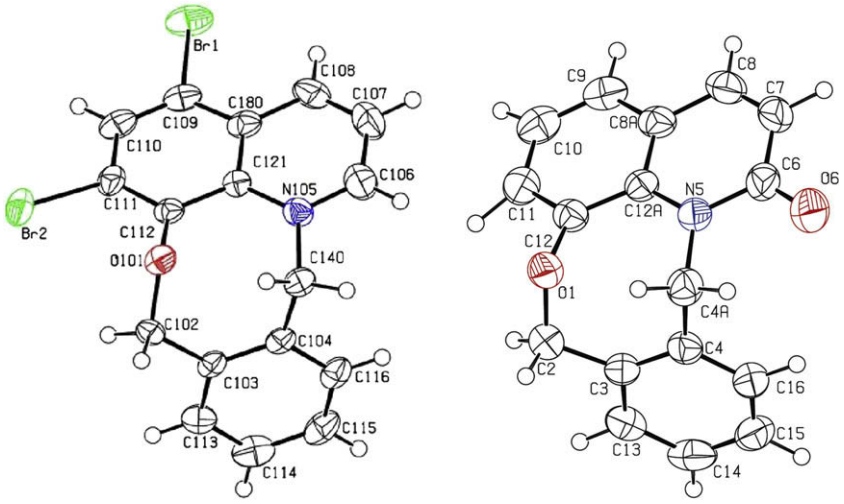


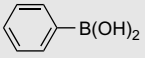
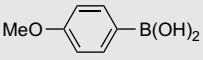
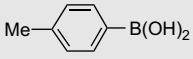
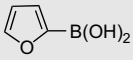
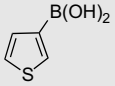
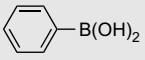
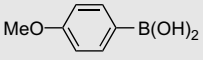
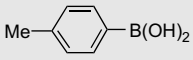
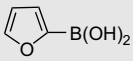
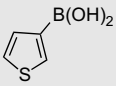
Figure 2. ORTEP representations[29,30] of the title compounds **3c** (cationic part, top) and **4a** (bottom), the displacement ellipsoids are drawn at a probability of 50%.

Table 2
Optimization of Suzuki coupling reaction conditions[a]

Entry	Catalyst	Conditions	Base	Solvent	Temp (°C)	Time	Yield (%)
1	$PdCl_2(PPh_3)_2$	Heat	K_2CO_3	Toluene	100	24 h	10
2	$Pd(PPh_3)_4$		K_2CO_3	Toluene	120	16 h	25
3	$Pd(OAc)_2$/PPh_3		Na_2CO_3	Toluene	145	18 h	20
4	$Pd(PPh_3)_4$		Cs_2CO_3	DMF	145	18 h	25
5	$Pd(PPh_3)_4$		Na_2CO_3	DMF/water	145	16 h	60
6	$Pd(PPh_3)_4$		K_3PO_4	DMF/water	140	24 h	20
7	$Pd(PPh_3)_4$		Na_2CO_3	THF/water	145	24 h	10
8	$PdCl_2$		Na_2CO_3	DMF/water	145	16 h	55
9	$PdCl_2(PPh_3)_2$	MW[b]	K_2CO_3	Toluene	120	10 min	20
10	$Pd(OAc)_2$/PPh_3		Na_2CO_3	Toluene	120	15 min	30
11	$Pd(PPh_3)_4$		Cs_2CO_3	DMF	120	10 min	52
12	$Pd(PPh_3)_4$		K_3PO_4	DMF/water	120	10 min	30
13	$Pd(PPh_3)_4$		Na_2CO_3	DMF/water	120	10 min	72
14	$Pd(Cl)_2$		Na_2CO_3	DMF/water	120	10 min	65

[a] Suzuki coupling reaction was optimised by choosing quinolone (**4c**) and benzene boronic acid as two model substrates.
[b] All the MW experiments were performed at 150 W maximum power in open vessel mode.

Table 3
Suzuki reaction of quinolinium/quinolone substrates with different aryl boronic acids

Quinolinium/quinolone	Boronic acid	Time (min)	Product	Isolated yield (%)	
				Heating[a]	MW[b]
3c/**4c**		15	**5a**	65	75
3c/**4c**		12	**5b**	70	82
3c/**4c**		13	**5c**	64	76
3c/**4c**		17	**5d**	55	65
3c/**4c**		17	**5e**	58	68
3d/**4d**		15	**6a**	50	62
3d/**4d**		16	**6b**	55	63
3d/**4d**		17	**6c**	63	74
3d/**4d**		20	**6d**	58	72
3d/**4d**		19	**6e**	60	75

[a] Suzuki coupling reaction under heating condition was carried out in DMF/H_2O using $Pd(PPh_3)_4$ catalyst and Na_2CO_3 at 140 °C.
[b] Suzuki coupling reaction under MW condition was carried out at 150 W, 120 °C in open vessal mode, other conditions were same as in heating mode.

3. Conclusion

In summary, we have demonstrated a facile one-pot synthesis of a novel class of fused tetracyclic heteroaromatics having a benzoxazocino ring system. We have also demonstrated the application of these molecules for the construction of novel polynuclear heteroaromatics utilizing the Suzuki reaction. The novelty of this versatile methodology lies in the operational simplicity, environment friendly mild reaction condition, and use of readily available starting materials. We presume that the structural similarities of these molecules with nefopam may show similar biological activities.

4. Experimental section

4.1. General experimental

Melting points were determined with capillary melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO 410 FTIR spectrometer in KBr pellets. The NMR spectra were taken on a BRUKER 300/600 DPX spectrometer operating at 300/600 MHz for ^1H and 75/150 MHz for ^{13}C respectively, with tetramethylsilane (TMS) as an internal standard and the chemical shifts are reported in δ units. Mass spectra and HRMS (positive mode) were obtained using LC-ESI-Q-TOF micro mass spectrometer. All chromatographic purification was performed on silica gel (100–200 mesh) and was obtained from E. Merck India Ltd., Mumbai. Thin layer chromatography (TLC) was performed on precoated silica gel 60 F_{254} aluminium sheets (E. Merck, Germany) using the different solvent system and spots were visualized either under UV torch or on heating after spraying Liebermann–Burchard solution. A mono-mode microwave reactor, manufactured by CEM Corporation, USA was used for Suzuki reaction in open mode. Organic solvents used for the chemical synthesis and for chromatography acquired from E. Merck (India) were of analytical grade. 8-Hydroxyquinoline derivatives (**1a**–**e**), α,α′-dibromo-*o*-xylene (**2**), phase transfer catalyst (tetra butyl ammonium bromide) and boronic acids were purchased from Aldrich Chemical Ltd (USA).

4.2. General reaction procedure for the synthesis of fused tetra cyclic quinolinium (3a–e) and quinolones (4a–d)

Appropriate amount of 8-hydroxyquinoline analogue (**1a**–**e**) (3.3 mmol) was dissolved in 50 mL of dichloromethane in a 250 mL RB flask followed by the addition of 50 mL of 10% aqueous NaOH solution, and was stirred at room temperature for about 30 min. α,α′-Dibromo-*o*-xylene (**2**) (10 mmol, 1:3 ratio with respect to the substrate) was added successively to the stirred solution and stirring continued for 10 min. Finally, a catalytic amount of tetrabutylammonium bromide (Phase Transfer Catalyst) (0.3224 g, 1 mmol) was added to the solution and the reaction mixture was stirred at ambient temperature for 10 h. During the course of reaction, TLC was performed after every 2 h to monitor the progress of the reaction. After completion of the reaction, the contents of the reaction mixture were poured to a separating funnel; the organic layer was separated followed by extraction of the aqueous layer thrice with 25 mL of dichloromethane. The entire aqueous layer was further extracted with *n*-butanol for collecting the rest of the compounds. All the organic layers were mixed together, washed thoroughly with water until free from alkali, dried over sodium sulfate and evaporated to dryness in a rotary evaporator under reduced pressure. The residue was chromatographed over silica gel (60–120 mesh), eluting with a mixture of hexane–ethyl acetate and ethyl acetate–methanol in different ratios yielded the respective fused quinolinium cation (**3a**–**e**) and its quinolone (**4a**–**d**).

*4.2.1. Compound **3a***

Brown solid, 30% yield. Mp 236–238 °C; R_f (1% MeOH–$CHCl_3$) 0.25; IR (KBr, cm^{-1}) ν 3417, 3055, 2061, 1593, 1527, 1451; ^1H NMR (300 MHz, DMSO-d_6) δ 5.46 (1H, d, J=15.3 Hz), 6.01–6.09 (2H, m), 7.21–7.34 (4H, m), 7.74 (1H, d, J=7.5 Hz), 8.01 (1H, t, J=7.8 Hz), 8.18–

8.25 (3H, m), 9.25 (1H, d, J=8.4 Hz), 10.05 (1H, d, J=5.7 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 63.9 (CH_2), 79.2 (CH_2), 123.7 (CH), 128.0 (CH), 128.5 (CH), 129.4 (CH), 130.9 (CH), 131.0 (CH), 131.8 (CH), 132.1 (C), 132.8 (CH), 133.1 (C), 137.0 (2×C), 148.7 (CH), 149.9 (C), 151.6 (CH). HRMS [ESI] m/z calcd for $C_{17}H_{14}NO$: $[M-Br]^+$ 248.1075; found: 248.1055.

4.2.2. Compound ***4a***

White solid, 60% yield. Mp 186–188 °C; R_f (60% pet. ether–chloroform) 0.50; IR (KBr, cm^{-1}) ν 3446, 3011, 2908, 1647, 1580, 1454, 1244; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.11 (1H, d, J=15.0 Hz), 5.76–5.90 (2H, m), 6.31 (1H, d, J=13.5 Hz), 6.64 (1H, d, J=9.6 Hz), 6.97–6.99 (1H, m), 7.06–7.25 (4H, m), 7.34 (1H, d, J=7.5 Hz), 7.45 (1H, d, J=9.6 Hz), 7.52–7.55 (1H, m); ^{13}C NMR δ 44.7 (CH_2), 78.6 (CH_2), 121.7 (CH), 122.8 (CH), 122.9 (C), 125.3 (CH), 125.4 (CH), 125.6 (CH), 128.0 (2×CH), 132.5 (CH), 133.2 (C), 134.6 (C), 136.0 (C), 138.6 (CH), 146.6 (C), 162.1 (C). HRMS [ESI] m/z calcd for $C_{17}H_{13}NO_2Na$: $[M+Na]^+$ 286.0844; found: 286.0855.

4.2.3. Compound ***3b***

Brown solid, 35% yield. Mp 76–78 °C; R_f (1%MeOH–$CHCl_3$) 0.20; IR (KBr, cm^{-1}) ν 3432, 3073, 1585, 1527, 1153; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.49 (1H, d, J=15.0 Hz), 6.05–6.10 (2H, m), 7.22–7.38 (4H, m), 7.73 (1H, d, J=7.2 Hz), 8.23 (2H, dd, J=15.0, 8.4 Hz), 8.33 (1H, dd, J=8.7, 5.7 Hz), 9.32 (1H, d, J=8.7 Hz), 10.15 (1H, d, J=5.7 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 64.3 (CH_2), 79.2 (CH_2), 125.0 (CH), 127.9 (CH), 129.4 (CH), 129.5 (C), 129.7 (C), 131.03 (CH), 131.08 (CH), 131.8 (C), 132.0 (CH), 133.0 (CH), 134.4 (C), 136.9 (C), 144.9 (CH), 149.4 (C), 152.6 (CH). HRMS [ESI] m/z calcd for $C_{17}H_{13}ClNO$: $[M-Br]^+$ 282.0686; found: 282.0687.

4.2.4. Compound ***4b***

White crystal, 60% yield. Mp 176–177 °C; R_f (60% pet. ether–chloroform) 0.45; IR (KBr, cm^{-1}) ν 3430, 3087, 2906, 1658, 1574, 1448, 1243; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.10 (1H, d, J=15 Hz), 5.78–5.90 (2H, m), 6.32 (1H, d, J=13.5 Hz), 6.75 (1H, d, J=9.9 Hz), 6.99–7.02 (1H, m), 7.16–7.29 (4H, m), 7.50–7.53 (1H, m), 7.99 (1H, d, J=9.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 45.5 (CH_2), 79.1 (CH_2), 120.8 (C), 123.3 (CH), 124.0 (CH), 124.6 (C), 125.9 (CH), 126.2 (CH), 128.77 (CH), 128.83 (CH), 129.3 (C), 133.0 (CH), 134.9 (C), 135.3 (CH), 136.2 (C), 146.0 (C), 162.3 (C). HRMS [ESI] m/z calcd for $C_{17}H_{12}ClNO_2Na$: $[M+Na]^+$ 320.0454; found: 320.0459.

4.2.5. Compound ***3c***

Brown crystalline solid, 25% yield. Mp 151–152 °C; R_f (1% MeOH–$CHCl_3$) 0.30; IR (KBr, cm^{-1}) ν 3417, 3056, 2021, 1584, 1384, 1082; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.60 (1H, d, J=15.3 Hz), 6.03–6.1 (2H, m), 7.27–7.41 (4H, m), 7.78 (1H, d, J=7.5 Hz), 8.33 (1H, dd, J=6.0, 8.7 Hz), 8.78 (1H, s), 9.27 (1H, d, J=8.7 Hz), 10.12 (1H, d, J=5.7 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 64.5 (CH_2), 76.7 (CH_2), 121.0 (C), 125.4 (CH), 126.8 (C), 127.9 (CH), 129.5 (CH), 130.5 (C), 131.1 (CH), 131.8 (C), 132.8 (CH), 135.4 (C), 136.3 (C), 138.5 (CH), 146.8 (C), 147.9 (CH), 153.2 (CH). HRMS [ESI] m/z calcd for $C_{17}H_{12}Br_2NO$: $[M-Br]^+$ 403.9286; found: 403.9345.

4.2.6. Compound ***4c***

White crystal, 65% yield, Mp 190–191 °C; R_f (60% pet. ether–chloroform) 0.50; IR (KBr, cm^{-1}) ν 3431, 3071, 2927, 1658, 1556, 1422; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (1H, d, J=15.3 Hz), 5.73 (1H, d, J=14.7 Hz), 5.85 (1H, d, J=13.5 Hz), 6.28 (1H, d, J=13.5 Hz), 6.75 (1H, d, J=9.9 Hz), 7.04–7.07 (1H, m), 7.20–7.26 (2H, m), 7.53–7.56 (1H, m), 7.63 (1H, s), 7.91 (1H, d, J=9.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.0 (CH_2), 76.9 (CH_2), 119.4 (C), 121.4 (C), 121.6 (C), 123.6 (CH), 126.3 (CH), 128.9 (CH), 129.0 (CH), 130.6 (CH), 132.8 (CH), 134.8 (C), 135.8 (C), 136.4 (C), 137.8 (CH), 143.4 (C), 162.3 (C). HRMS [ESI], m/z calcd for $C_{17}H_{11}Br_2NO_2Na$: $[M+Na]^+$ 441.9054; found: 441.9088.

4.2.7. Compound ***3d***

White solid, 35% yield. Mp 77–79 °C; R_f (1% MeOH–$CHCl_3$) 0.30; IR (KBr, cm^{-1}) ν 3428, 3056, 1584, 1503, 1385, 1363, 750; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.58 (1H, d, J=15.3 Hz), 6.00 (2H, m), 7.33 (4H, m), 7.77 (1H, d, J=7.2 Hz), 8.32 (1H, dd, J=6.0, 8.4 Hz), 8.71 (1H, s), 9.31 (1H, d, J=8.4 Hz), 10.04 (1H, d, J=5.7 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 63.5 (CH_2), 76.2 (CH_2), 104.7 (C), 124.1 (CH), 127.0 (CH), 128.5 (CH), 128.9 (C), 129.1 (C), 130.1 (CH), 131.7 (CH), 133.3 (C), 135.3 (2×C), 139.5 (CH), 144.3 (CH), 148.3 (C), 151.8 (CH). HRMS [ESI] m/z calcd for $C_{17}H_{12}ClNO$: $[M-Br]^+$ 407.9652; found: 407.9662.

4.2.8. Compound ***4d***

White solid, 65% yield, Mp 162–164 °C; R_f (60% pet. ether–chloroform) 0.50; IR (KBr, cm^{-1}) ν 3446, 1660, 1558, 1443, 1418, 1233, 1143, 743; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.29 (1H, d, J=15.3 Hz), 5.72 (1H, d, J=15.3 Hz), 5.87 (1H, d, J=13.5 Hz), 6.15 (1H, d, J=13.8 Hz), 6.76 (1H, d, J=9.6 Hz), 7.05 (1H, m), 7.24 (2H, m), 7.59 (1H, m), 7.68 (1H, s), 7.96 (1H, d, J=9.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.4 (CH_2), 77.7 (CH_2), 95.9 (C), 120.9 (C), 123.7 (CH), 126.1 (CH), 128.80 (CH), 128.82 (CH), 129.7 (C), 132.9 (CH), 133.0 (CH), 134.8 (2×C), 135.2 (CH), 135.6 (C), 145.7 (C), 162.2 (C). HRMS [ESI], m/z calcd for $C_{17}H_{11}ClNO_2Na$: $[M+Na]^+$ 445.9421; found: 445.9438.

4.2.9. Compound ***3e***

Gray crystalline solid, 40% yield. Mp 210–212 °C; R_f (1% MeOH–$CHCl_3$) 0.20; IR (KBr, cm^{-1}) ν 3424, 3038, 1601, 1516, 1437, 1122; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.42 (1H, d, J=14.7 Hz), 5.97 (2H, m), 6.92 (1H, d, J=14.4 Hz), 7.32 (3H, m), 7.60 (1H, d, J=7.2 Hz), 7.92 (1H, t, J=8.1 Hz), 8.14 (3H, m), 9.06 (1H, d, J=8.4 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) δ 24.7 (CH_3), 57.2 (CH_2), 78.7 (CH_2), 127.3 (CH), 128.0 (2×CH), 129.4 (CH), 130.2 (CH), 130.8 (CH), 131.0 (CH), 131.0 (C), 131.9 (C), 133.4 (CH), 134.6 (C), 137.4 (C), 146.8 (CH), 150.1 (C), 163.2 (C). HRMS [ESI] m/z calcd for $C_{18}H_{16}NO$: $[M-Br]^+$ 262.1232; found: 262.1185.

4.2.9.1. Isolation and characterization of intermediate ***III*** *from* ***3c***. Quinolinium bromide **3c** (0.5 mmol) was dissolved in 50 mL of water in a 100 mL RB flask under argon atmosphere with continuous stirring. A small amount of sodium borohydride was added and stirring continued for about 5 min. The product **III** was obtained by simple filtration of the reaction mixture followed by washing with distilled water cautiously avoiding aerial oxidation and kept under vacuum.

Intermediate **III** was obtained as white powdered solid in 40%yield. Mp 140–141 °C; R_f (60% pet. ether–chloroform) 0.50; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91 (2H, s), 4.60 (2H, s), 5.24 (2H, s), 7.05 (7H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.8 (CH_2), 58.2 (CH_2), 77.7 (CH_2), 116.6 (C), 116.9 (C), 123.7 (C), 124.4 (CH), 124.8 (CH), 126.4 (CH), 127.6 (CH), 127.7 (CH), 130.1 (CH), 135.3 (C), 135.7 (C), 140.0 (C), 144.5 (C). MS [ESI] m/z for $C_{17}H_{13}Br_2NONa$: $[M+Na]^+$ 430.09.

4.3. General reaction procedure for the synthesis of diarylated (5a–e) and mono arylated (6a–e) quinolones by Suzuki cross coupling reaction

The Suzuki coupling reaction of dibromo quinolone (**4c**) with benzene boronic acid, representative of the general reaction protocol, was carried out both in traditional heating and microwave irradiation condition, RB flask was used for the former and microwave vessel was used for the latter one.

Thus, for the standardization of the reaction in MW 0.1 g of (**4c**) (0.23 mmol) was taken in a mortar followed by addition of benzene

boronic acid 0.0765 mg, (0.59 mmol), catalyst [$Pd(PPh_3)_4$] (0.007 mmol), and base (Na_2CO_3) (1.8 mmol) and mixed well using a pestle. The mixture was placed in microwave vessel with the solvent DMF/H_2O (10:1) and irradiated (150 W) for 10 min. The reaction mixture transformed to brown-black and the bulk temperature was found to be 120 °C. After completion of the reaction, the contents were cooled to room temperature. Water was added to the mixture, the content was transferred to a separating funnel and extracted with ethyl acetate. The organic layer was washed thoroughly with water until free from alkali, dried over anhydrous sodium sulfate, and evaporated to dryness in a rotary evaporator under reduced pressure. The residue was chromatographed over silica gel (60–120, mesh), eluting with a mixture of hexane–ethyl acetate in different ratios.

The reaction that carried out under traditional heating condition was performed in a 100 mL two-necked RB flask fitted with a guard tube. The well-mixed mixture of the substrate, catalyst, reagent and base was taken in the reaction flask followed by addition of the solvent. The flask was placed on an oil bath with constant stirring for 12 h at 140–145 °C. After completion of the reaction, usual workup followed by chromatographic separation yielded the product. It was observed that the MW condition yielded higher (76%, within 10 min) compared to the heating condition (55%, 12 h with constant stirring) (Table 2).

4.3.1. Compound **5a**

White solid, Mp 194–195 °C; R_f (60% pet. ether–$CHCl_3$) 0.60; IR (KBr, cm^{-1}) ν 3434, 1656, 1586, 1446, 1421, 701; ^1H NMR (600 MHz, $CDCl_3$) δ 4.58 (1H, d, J=15.0 Hz), 5.33 (1H, d, J=15.0 Hz), 5.98 (1H, d, J=13.8 Hz), 6.34 (1H, d, J=13.8 Hz), 6.61 (1H, d, J=10.2 Hz), 6.85 (1H, d, J=7.8 Hz), 7.13 (1H, s), 7.18 (1H, dt, J=1.2, 7.8 Hz), 7.23 (1H, t, J=7.2 Hz), 7.32 (2H, m), 7.39 (1H, m), 7.43 (3H, m), 7.49 (2H, m), 7.57 (1H, d, J=7.2 Hz), 7.61 (1H, d, J=9.6 Hz), 7.66 (2H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 46.1 (CH_2), 76.2 (CH_2), 120.2 (C), 121.4 (CH), 125.7 (CH), 126.6 (CH), 127.7 (CH), 127.8 (CH), 128.09 (CH), 128.14 (CH), 128.4 (CH), 128.45 (CH), 129.3 (2×CH), 129.86 (2×CH), 129.90 (2×CH), 132.5 (CH), 134.5 (C), 135.0 (C), 136.3 (C), 136.8 (CH), 137.4 (C), 137.7 (C), 137.9 (C), 139.0 (C), 143.0 (C), 162.8 (C). HRMS [ESI] m/z calcd for $C_{29}H_{21}NO_2Na$: $[M+Na]^+$ 438.1470; found: 438.1484.

4.3.2. Compound **5b**

White solid, Mp 194–195 °C; R_f (60% pet. ether–chloroform) 0.45; IR (KBr, cm^{-1}) ν 3453, 1660, 1607, 1585, 1512, 1246, 836; ^1H NMR (300 MHz, $CDCl_3$) δ 3.84 (3H, s), 3.89 (3H, s), 4.59 (1H, d, J=15.0 Hz), 5.33 (1H, d, J=15.0 Hz), 5.99 (1H, d, J=13.5 Hz), 6.33 (1H, d, J=13.5 Hz), 6.62 (1H, d, J=9.9 Hz), 6.84 (1H, d, J=7.2 Hz), 6.96 (2H, m), 7.02 (2H, m), 7.10 (1H, s), 7.20 (4H, m), 7.60 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.1 (CH_2), 55.3 (CH_3), 55.3 (CH_3), 76.0 (CH_2), 113.8 (2×CH), 113.9 (2×CH), 120.07 (C), 120.9 (CH), 125.7 (CH), 126.5 (CH), 128.05 (CH), 128.07 (CH), 129.9 (C), 130.5 (2×CH), 131.0 (2×CH), 131.3 (C), 132.5 (CH), 134.6 (C), 135.0 (C), 136.4 (C), 136.9 (C), 137.0 (CH), 137.5 (C), 142.7 (C), 159.2 (C), 159.3 (C), 162.8 (C). HRMS [ESI], m/z calcd for $C_{31}H_{25}NO_4Na$: $[M+Na]^+$ 498.1681; found: 498.1682.

4.3.3. Compound **5c**

White solid. Mp 104–105°C; R_f (60% pet. ether–$CHCl_3$) 0.75; IR (KBr, cm^{-1}) ν 3445, 1659, 1586, 1426, 825; ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (3H, s), 2.45 (3H, s), 4.60 (1H, d, J=15 Hz), 5.32 (1H, d, J=14.7 Hz), 6.0 (1H, d, J=13.8 Hz), 6.33 (1H, d, J=13.5 Hz), 6.60 (1H, d, J=9.9 Hz), 6.84 (1H, d, J=7.2 Hz), 7.11 (1H, s), 7.27 (9H, m), 7.52 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2 (CH_3), 21.4 (CH_3), 46.2 (CH_2), 76.2 (CH_2), 120.2 (C), 121.2 (CH), 125.8 (CH), 125.9 (C), 126.7 (CH), 126.9 (CH), 128.1 (CH), 128.2 (CH), 129.2 (CH), 129.3 (2×CH), 129.5 (2×CH), 129.7 (CH), 129.9 (CH), 132.6 (CH), 134.62 (C), 134.85 (C), 135.1 (C), 136.2 (C), 136.5 (C), 137.0 (CH), 137.5 (C), 137.6 (C), 138.0 (C), 143.0 (C), 162.9 (C). HRMS [ESI] m/z calcd for $C_{31}H_{25}NO_2Na$: $[M+Na]^+$ 466.1783; found: 466.1767.

4.3.4. Compound **5d**

White solid, Mp 195–196 °C; R_f (60% pet. ether–chloroform) 0.45; IR (KBr, cm^{-1}) ν 3442, 1657, 1589, 1455, 1425, 743; ^1H NMR (300 MHz, $CDCl_3$) δ 4.96 (1H, d, J=15 Hz), 5.68 (1H, d, J=15.3 Hz), 5.98 (2H, m), 6.61 (4H, m), 6.97 (1H, d, J=6.9 Hz), 7.25 (3H, m), 7.57 (2H, s), 7.66 (1H, d, J=6.9 Hz), 7.87 (1H, s), 8.07 (1H, d, J=9.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 47.2 (CH_2), 76.8 (CH_2), 109.8 (CH), 111.2 (CH), 111.5 (CH), 112.1 (CH), 118.9 (C), 120.5 (CH), 121.4 (CH), 125.2 (CH), 125.8 (C), 126.0 (C), 127.8 (2×CH), 132.2 (CH), 134.5 (C), 135.1 (C), 135.2 (C), 136.1 (CH), 142.4 (CH), 142.7 (CH), 143.0 (C), 148.8 (C), 151.5 (C), 162.5 (C). HRMS [ESI], m/z calcd for $C_{25}H_{17}NO_4Na$: $[M+Na]^+$ 418.1055; found: 418.1010.

4.3.5. Compound **5e**

White solid. Mp 225–226 °C; R_f (60% pet. ether–chloroform) 0.50; IR (KBr, cm^{-1}) ν 3452, 1651, 1589, 1470, 1427, 790; ^1H NMR (600 MHz, $CDCl_3$) δ 4.70 (1H, d, J=15.0 Hz), 5.46 (1H, d, J=15.0 Hz), 5.99 (1H, d, J=13.2 Hz), 6.30 (1H, d, J=13.8 Hz), 6.62 (1H, d, J=10.2 Hz), 6.89 (1H, d, J=7.2 Hz), 7.12 (1H, dd, J=1.2, 5.4 Hz), 7.19 (1H, dt, J=1.2, 7.8 Hz), 7.23 (1H, m), 7.28 (1H, s), 7.42 (1H, dd, J=3.0, 5.4 Hz), 7.47 (1H, dd, J=3.0, 4.8 Hz), 7.55 (1H, dd, J=1.2, 4.8 Hz), 7.59 (1H, d, J=7.2 Hz), 7.69 (1H, s), 7.70 (1H, s), 7.72 (1H, dd, J=1.2, 3.0 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 46.2 (CH_2), 76.2 (CH_2), 120.4 (C), 121.4 (CH), 124.1 (CH), 124.3 (CH), 125.61 (CH), 125.68 (CH), 125.72 (CH), 125.97 (CH), 128.1 (CH), 128.15 (CH), 128.4 (CH), 129.2 (CH), 132.0 (C), 132.5 (CH), 132.6 (C), 134.9 (C), 135.0 (C), 136.2 (C), 136.6 (CH), 137.5 (C), 139.3 (C), 143.2 (C), 162.8 (C). HRMS [ESI] m/z calcd for $C_{25}H_{17}NO_2S_2Na$: $[M+Na]^+$ 450.0598; found: 450.0594.

4.3.6. Compound **6a**

White solid. Mp 85–86 °C; R_f (60% pet. ether–chloroform) 0.75; IR (KBr, cm^{-1}) ν 3434, 1660, 1584, 1419; ^1H NMR (300 MHz, $CDCl_3$) δ 4.47 (1H, d, J=15 Hz), 5.27 (1H, d, J=14.7 Hz), 5.91 (1H, d, J=13.5 Hz), 6.29 (1H, d, J=13.5 Hz), 6.77 (2H, m), 7.18 (3H, m), 7.48 (4H, m), 7.60 (2H, m), 8.01 (1H, d, J=9.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.0 (CH_2), 76.0 (CH_2), 119.5 (C), 122.6 (CH), 125.4 (CH), 125.7 (CH), 128.19 (CH), 128.21 (CH), 128.27 (CH), 128.4 (C), 128.55 (2×CH), 129.1 (2×CH), 132.3 (CH), 134.5 (C), 134.8 (CH), 135.4 (C), 135.9 (C), 136.6 (C), 138.4 (C), 142.4 (C), 162.5 (C). HRMS [ESI], m/z calcd for $C_{23}H_{16}ClNO_2Na$: $[M+Na]^+$ 396.0767; found: 396.0777.

4.3.7. Compound **6b**

White solid. Mp 84–85 °C; R_f (60% pet. ether–chloroform) 0.45; IR (KBr, cm^{-1}) ν 3428, 1658, 1583, 1514, 1452, 1426, 1249; ^1H NMR (300 MHz, $CDCl_3$) δ 3.90 (3H, s), 4.51 (1H, d, J=15.0 Hz), 5.29 (1H, d, J=14.7 Hz), 5.92 (1H, d, J=13.5 Hz), 6.29 (1H, d, J=13.2 Hz), 6.78 (2H, m), 7.04 (2H, m), 7.19 (3H, m), 7.54 (3H, m), 8.0 (1H, d, J=9.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.0 (CH_2), 55.3 (CH_3), 75.9 (CH_2), 114.1 (2×CH), 119.2 (C), 122.4 (CH), 125.4 (CH), 125.7 (CH), 128.2 (CH), 128.3 (CH), 128.4 (C), 128.8 (C), 130.4 (2×CH), 132.4 (CH), 134.7 (C), 134.8 (CH), 135.5 (C), 136.0 (C), 138.1 (C), 142.4 (C), 159.6 (C), 162.6 (C). HRMS [ESI], m/z calcd for $C_{24}H_{18}ClNO_3Na$: $[M+Na]^+$ 426.0873; found: 426.0910.

4.3.8. Compound **6c**

White solid. Mp 64–65 °C; R_f (60% pet. ether–chloroform) 0.65; IR (KBr, cm^{-1}) ν 3434, 2922, 1660, 1583, 1450, 1421; ^1H NMR (300 MHz, $CDCl_3$) δ 2.46 (3H, s), 4.50 (1H, d, J=15.0 Hz), 5.29 (1H, d, J=15.0 Hz), 5.92 (1H, m), 6.29 (1H, d, J=13.2 Hz), 6.78 (2H, m), 7.23 (5H, m), 7.51 (3H, m), 8.01 (1H, d, J=9.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3 (CH_3), 46.0 (CH_2), 75.9 (CH_2), 119.3 (C), 122.4 (CH), 122.8 (C), 125.4 (CH), 125.7 (CH), 128.18 (CH), 128.21 (CH), 128.95 (2×CH), 129.3 (2×CH), 132.3 (CH), 132.6 (C), 133.6 (C), 134.6 (C),

134.8 (CH), 136.0 (C), 138.1 (C), 138.4 (C), 142.4 (C), 162.5 (C). HRMS [ESI], m/z calcd for $C_{24}H_{18}ClNO_2Na$: $[M+Na]^+$ 410.0924; found: 410.0929.

4.3.9. Compound **6d**

White solid. Mp 165–166 °C; R_f (60% pet. ether–chloroform) 0.55; IR (KBr, cm^{-1}) ν 3428, 1660, 1586, 1443, 741; ^1H NMR (300 MHz, $CDCl_3$) δ 4.96 (1H, d, J=15 Hz), 5.70 (1H, d, J=15.3 Hz), 6.00 (2H, m), 6.62 (1H, d, J=1.5 Hz), 6.73 (1H, d, J=9.6 Hz), 6.97 (1H, d, J=6.9 Hz), 7.23 (3H, m), 7.59 (1H, s), 7.65 (1H, d, J=6.9 Hz), 7.76 (1H, s), 8.01 (1H, d, J=9.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.9 (CH_2), 77.0 (CH_2), 112.3 (CH), 112.5 (CH), 119.0 (C), 120.7 (CH), 122.3 (CH), 125.4 (CH), 126.8 (C), 128.0 (CH), 128.2 (CH), 128.8 (C), 132.5 (CH), 134.5 (C), 134.9 (CH), 135.4 (C), 135.7 (C), 142.0 (C), 142.9 (CH), 148.2 (C), 162.5 (C). HRMS [ESI], m/z calcd for $C_{21}H_{14}ClNO_3Na$: $[M+Na]^+$ 386.0560; found: 386.0550.

4.3.10. Compound **6e**

White solid. Mp 124–126 °C; R_f (60% pet. ether–chloroform) 0.60; IR (KBr, cm^{-1}) ν 3433, 1660, 1583, 1445, 1421; ^1H NMR (600 MHz, $CDCl_3$) δ 4.63 (1H, d, J=15.0 Hz), 5.43 (1H, d, J=15.0 Hz), 5.94 (1H, d, J=13.2 Hz), 6.25 (1H, d, J=13.8 Hz), 6.75 (1H, d, J=9.6 Hz), 6.86 (1H, d, J=7.2 Hz), 7.17 (1H, dt, J=1.2, 7.8 Hz), 7.22 (1H, t, J=7.2 Hz), 7.36 (1H, s), 7.47 (1H, dd, J=3.0, 4.8 Hz), 7.51 (1H, dd, J=1.2, 4.8 Hz), 7.55 (1H, d, J=7.8 Hz), 7.71 (1H, m), 8.00 (1H, d, J=9.6 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 46.2 (CH_2), 76.3 (CH_2), 119.4 (C), 122.5 (CH), 124.6 (CH), 124.8 (CH), 125.7 (CH), 125.9 (CH), 128.2 (CH), 128.24 (CH), 128.3 (CH), 128.5 (C), 132.4 (CH), 133.0 (C), 134.6 (C), 134.8 (CH), 135.7 (C), 135.8 (C), 136.6 (C), 142.6 (C), 162.5 (C). HRMS [ESI], m/z calcd for $C_{21}H_{14}ClNO_2SNa$: $[M+Na]^+$ 402.0331; found: 402.0330.

4.4. X-ray experiments, structure determination and refinements

X-ray data collection for **3c** was carried out on a Huber four circle diffractometer (Mo Kα radiation, λ=0.7107 Å, graphite monochromator) equipped with a Bruker APEX CCD area detector. A total of 47,419 reflections ($2\theta \leq 61.6°$) were measured in six runs, each with 600 frames in φ increments of 0.3°. Integration and merging with SAINT and XPREP, absorption correction with SADABS.[26] Structure solution (program SIR 2002[27]) and refinement (SHELXL[28]) ran routinely. C, N, O and Br atoms were refined anisotropically, isotropic displacement parameters were assigned to the hydrogens, which were put into calculated positions according to steric considerations. The asymmetric unit consist of two $[C_{17}H_{12}NO_1Br_2]^+$ cations, two Br^- anions and two water molecules. The water hydrogens were not determined.

X-ray data collection for **4a** was carried out on a Stoe four circle diffractometer (Ni-filtered Cu Kα radiation, λ=1.5418 Å) equipped with point detector within a hemisphere of reciprocal space ($2\theta \leq 130°$) in the ω-2θ-scan modus with variable scan range and variable scan speed. 2 Standard reflections measured every 90 min showed no significant variations during the data collection.

Structure solution and refinement (programs SIR 2002[27] and SHELXL[28]) ran routinely. C, N and O atoms were refined anisotropically, isotropic displacement parameters were assigned to the hydrogens, which could all be located from a difference synthesis.

4.4.1. Crystal data for **3c**

$[C_{17}H_{12}N_1O_1Br_2]^+ \times Br^- \times H_2O$, M_r=504.01, brown block shaped crystals were grown from CH_3OH/MeCN. Dimensions of the specimen used for X-ray experiments 0.70×0.55×0.30 mm. Space group monoclinic $P2_1/c$. Lattice constants (Å) a=16.356(3), b=26.542(5), c=7.774(2), β=93.12(3)°, cell volume V=3369.9(12) $Å^3$, formula units/cell Z=8, X-ray density ρ_x=1.979 g cm^{-3}, $2\theta_{max}$=61.58°. Number of independent reflections 9386, unobserved ($F_o<4\sigma(F_o)$) 4300, linear absorption coeff. μ=71.9 cm^{-1}, R_{int}=0.081, R_σ=0.083. After convergence of refinements R_1=0.068, Rw=0.164, GoF=1.03.

4.4.2. Crystal data for **4a**

$C_{17}H_{13}NO_2$, M_r=263.28, light yellow block shaped crystals were grown from $CHCl_3$/Hexane. Dimensions of the specimen used for X-ray experiments 0.62×0.60×0.20 mm. Space group triclinic P1bar. Lattice constants (Å) a=7.140(1), b=8.596(1), c=10.976(1), α=76.52(1)°, β=79.99(1)°, γ=71.60(1)°, cell volume V=617.9(1) $Å^3$, formula units/cell Z=2, X-ray density ρ_x=1.415 g cm^{-3}, $2\theta_{max}$=129.94°. Total/independent number of reflections 2282/2099, R_{int}=0.011, R_σ=0.011, unobserved ($F_o<4\sigma(F_o)$) 183, linear absorption coeff. μ=7.5 cm^{-1}. After convergence of refinements R_1=0.051, Rw=0.152, GoF=1.15.

Acknowledgements

We thank to the Council of Scientific and Industrial Research for fellowships to K.B.S., A.H., P.P., P.S., S.N., R.P.. We are also thankful to Dr. B. Achari, Emeritus Scientist, CSIR, for his valuable suggestions.

Supplementry data

^1H and ^{13}C NMR spectra of all new compounds associated with this article can be found in the online version. Crystallographic data in CIF format are available free of charge via the Internate at CCDC 704566/704567 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk). Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.06.061.

References and notes

1. Czarnik, A. W. *Acc. Chem. Res.* **1996**, *29*, 112–113.
2. Fagnoni, M. *Heterocycles* **2003**, *60*, 1921–1958.
3. Hajos, G.; Riedl, Z.; Kollenz, G. *Eur. J. Org. Chem.* **2001**, 3405–3414.
4. Majumdar, K. C.; Basu, P. K.; Mukhopadhyay, P. P. *Tetrahedron* **2004**, *60*, 6239–6278.
5. Barchechath, S. D.; Tawatao, R. I.; Corr, M.; Carson, D. A.; Cottam, H. B. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1785–1788.
6. Brana, M. F.; Cacho, M.; Gradillas, A.; Pascual-teresa, B.; Ramos, A. *Curr. Pharm. Des.* **2001**, *7*, 1745–1780.
7. Martinez, R.; Chacon-Garcia, L. *Curr. Med. Chem.* **2005**, *12*, 127–151.
8. Nicolaou, K. C.; Huang, X.; Giuseppone, N.; Rao, P. B.; Bella, M.; Reddy, M. V.; Snyder, S. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 4705–4709.
9. Ollis, W. D.; Stanforthand, S. P.; Ramsden, C. A. *Tetrahedron* **1985**, *41*, 2239–2329.
10. Maruoka, K. *Org. Process Res. Dev.* **2008**, *12*, 679–697.
11. Dutta, R.; Mandal, D.; Panda, N.; Mondal, N. B.; Banerjee, S.; Kumer, S.; Weber, M.; Lugar, P.; Sahu, N. P. *Tetrahedron Lett.* **2004**, *45*, 9361–9364.
12. Paira, P.; Hazra, H.; Sahu, K. B.; Banerjee, S.; Mondal, N. B.; Sahu, N. P.; Weber, M.; Lugar, P. *Tetrahedron* **2008**, *64*, 4026–4036.
13. Alfonsi, P.; Adam, F.; Passarel, A.; Guiqnard, B.; Sessler, D. I.; Chauvin, M. *Anesthesiology* **2004**, *100*, 37–43.
14. Rosamilia, A. E.; Mayes, P. A.; Papadopoulos, R.; Campi, E. M.; Roy Jackson, W.; Rash, L.; Jarrott, B. *Aust. J. Chem.* **2002**, *55*, 577–585.
15. Heel, R. C.; Broqden, R. N.; Pakes, G. E.; Speight, T. M.; Avery, G. S. *Drugs* **1980**, *19*, 249–267.
16. Wang, R. I.; Waite, E. M. *J. Chin. Pharmacol.* **1979**, *19*, 395–402.
17. Cohen, A.; Hernandez, C. M. *J. Int. Med. Res.* **1976**, *4*, 138–143.
18. For recent reviews, see: (a) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1470.
19. Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147–168.
20. Kertesz, M.; Choi, C. H.; Yang, S. *Chem. Rev.* **2005**, *105*, 3448–3481.
21. Capdeville, R.; Buchdunger, E.; Zimmermann, J.; Matter, A. *Nat. Rev. Drug Discovery* **2002**, *1*, 493–502.
22. Tomori, H.; Fox, J. M.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 5334–5341.
23. Lightowler, S.; Hirz, M. *Chem. Mater.* **2005**, *17*, 5538–5549.
24. Jean-Gérard, L.; Pauvert, M.; Collet, S.; Guingan, A.; Evain, M. *Tetrahedron* **2007**, *63*, 11250–11259.
25. Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225–9283.

26. Siemens (2004). SMART, SAINT, XPREP and SADABS. Area Detector Control and Integration Software. Bruker Analytical X-ray Instruments Inc., Madison, wisconsin, USA.
27. SIR 2002: Burla, M. C.; Camalli, M.; Carrozzini, B.; Cascarano, G. L.; Giacovazzo, C.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **2003**, *36*, 1103.
28. Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112–122.
29. Burnett, M. N.; Johnson, C. K. *ORTEP III, Oak Ridge Thermal Ellipsoid Plot Program for Crystal Structure Illustration*; Oak Ridge National Laboratory Report ORNL-6895: Oak Ridge, Tennessee, TN, USA, 1996.
30. Keller, E.; Pierrard, J. S. *Schakal99. A Fortran Program for the Graphical Representation of Molecular and Crystallographic Models*; Univ. Freiburg: Germany, 1999.