A Short and Convenient Synthesis and Evaluation of the Antiinfective Properties of Indoloquinoline Alkaloids: 10*H*-Indolo[3,2-*b*]quinoline and 7*H*-Indolo[2,3-*c*]quinolines

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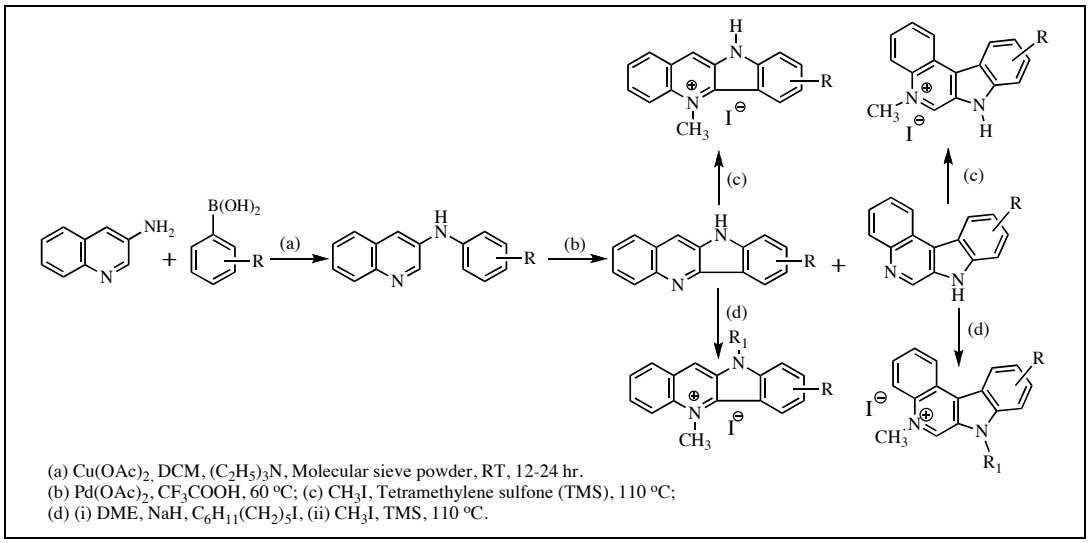

10*H*-Indolo[3,2-*b*]quinoline and 7*H*-indolo[2,3-*c*]quinoline have been synthesized in two steps using a modified approach to our previous reported method. Starting from commercially available 3-aminoquinoline and phenylboronic acid, the first step involved a copper acetate-catalyzed coupling reaction and the second utilized a palladium acetate-catalyzed intramolecular arylation reaction in the presence of trifluoroacetic acid as solvent. The anti-infective activity of a selected number of the compounds was also evaluated.

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INTRODUCTION

Several research publications in the last 30 years have demonstrated that cryptolepine and other indoloquinoline alkaloids isolated from *Cryptolepis sanguinolenta*, display interesting biological activities [1-4]. Cryptolepine (**1**), neocryptolepine (**2**) and isocryptolepine (**3**) are three of the thirteen alkaloids identified in extracts from the root of *C. sanguinolenta* (Fig 1) [5-8]. Isoneocryptolepine (**4**), also referred tp as 4-methyl-5,6-benz-4-ψ-carboline, was first synthesized by Kermack, et al. [Kermack, W. O.; Slater, R. H. *J. Chem Soc.,* **1928**, 789.] before its subsequent syntheses by others [5-8]. The biological activities associated with cryptolepine and a number of these alkaloids include, antibacterial, antifungal, antimalarial, anticancer, antiplatelet aggregation, analgesic, antihypertensive and several others [9]. The mechanism by which one structure could elicit such an array of activities has not been completely elucidated. However, several lines of evidence in the literature suggest that DNA intercalation and topoisomerase II inhibition are prime suspects [10]. Indeed, cryptolepine is reported to bind tightly to DNA and is cytotoxic toward B16 melanoma cells [11].

As a result of the interesting biological activities associated with the indoloquinoline alkaloids, several synthetic procedures have been reported in the literature. Mohan and colleagues [12,13] reported a photochemical synthetic procedure and a Fischer indole synthesis [14]

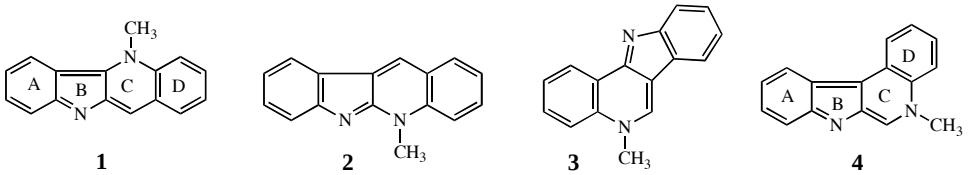


Figure 1

towards several angular quindolines. The former approach is based on a stepwise reaction of a haloquinoline with aniline and photochemical irradiation of the resultant intermediate in the presence of an iodine catalyst to afford isomeric indoloquinolines. Another synthetic methodology utilizing selective Buchwald–Hartwig amination with a regioselective Pd-catalyzed intramolecular arylation reaction has also been reported [15]. Zhang [16] also reported the synthesis of the N-demethylated precursor isoneocryptolepine via an intramolecular palladium-catalyzed Buchwald-Hartwig amination [17, 18] and Dutta [19] developed a method for the synthesis of quindolines using thermal cyclization of 3-arylamino-3-(2-nitrophenyl)propanal Schiff base. The cyclization was followed by triethyl phosphite mediated deoxygenation to produce the desired product.

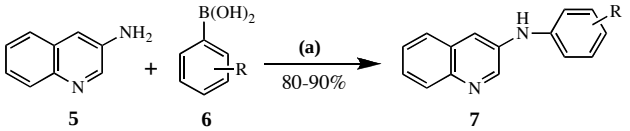
A cursory look at the methods stipulated above shows that several of the reported synthetic methods of indoloquinoline alkaloids suffer from poor yields, absence of readily available starting materials, or use reaction conditions that make it difficult to prepare substituted indoloquinoline alkaloids. Several years ago [20], we reported a method intended to alleviate the long delay in the synthetic approach of Holt and Petrow [21]. However, the palladium-catalyzed cyclization step resulted in very low yields. The low yields were attributed to the synthesis of non-linear indoloquinolines which were not of interest at the time. In continuation of our research program involving the design of cryptolepine analogs as novel anti-infective agents, we have explored a modification of the previous synthetic approach for the preparation of quindolines. In this paper, we report a short and convenient synthesis of substituted indoloquinolines using readily available starting materials and reagents which provides some advantages over several of the previous approaches. The biological evaluation of two sets of linear versus angular quindolines for their anti-infective activities is also reported.

RESULTS AND DISCUSSION

It was of interest to investigate A-ring substituted indoloquinolines as new anti-infective agents. The commercial availability of several substituted phenyl boronic acids makes the regio-selective $Pd(OAc)_2$-catalyzed intramolecular arylation approach a preferred tool to easily access these A-ring functionalized 10*H*-indolo[3,2-*b*]quinolines and 7*H*-indolo[2,3-*c*]quinolines. As a first step towards the synthesis of these scaffolds, we investigated the reaction of 3-aminoquinoline with substituted phenyl boronic acids in the presence of copper acetate and triethylamine. This reaction gave *N*-phenylquinoline-3-amines in good yields (80-90%). Next, a palladium acetate-catalyzed intramolecular C-C bond formation reaction in the presence of trifluoroacetic acid was carried out to give 10*H*-indolo[3,2-*b*]quinoline (**8c**) and 7*H*-indolo[2,3-*c*]quinoline (**9c**) in moderate to excellent yields (Scheme 2). Ortho substituted chlorophenyl-3-aminoquinoline gave selectively only one product (Table 1). For example, 2-chlorophenyl-3-aminoquinoline led to only 9-chloro-10*H*-indolo[3,2-*b*]quinoline (**8a** in Table 1) without loss of the halogen atom in 85% yield. On the other hand, *meta* and *para*-substituted phenyl 3-aminoquinolines led to a mixture of 10*H*-indolo[3,2-*b*]quinolines and 7*H*-indolo[2,3-*c*]quinolines (Table 1). Thus, this approach now places at our disposal a strategy of obtaining both compounds in high yields. For the linear indoloquinolines, we simply substitute at the *ortho*-position with a group that can easily be removed subsequently while the angular 7*H*-indolo[2,3-*c*]quinolines can be synthesized directly albeit with some linear indoloquinoline impurity which is easily removed by flash chromatography. Alkylation of the indoloquinolines was accomplished as previously reported [20, 22].

Based on previous work in our laboratories, [22] 2 pairs of alkylated quindolines were evaluated for their antiinfective properties against AIDS related opportunistic pathogens. Results recorded in Table 2 show that N-methylated compound (**11**) shows no activity at 20 μg/ml, compound **10**, the salt form of compound **1** and compound **12**, have weak antifungal properties while compound **13** with ω-cyclohexylpentyl moiety on the indole N atom appears to have good antiinfective properties. Indeed, compound **13** is not only very potent and compares favorably with Amphotericin B, but has lower cytotoxicity towards Vero cells than Amphotericin B and thus warrant further Structure-Activity Relationship studies.

Scheme 1

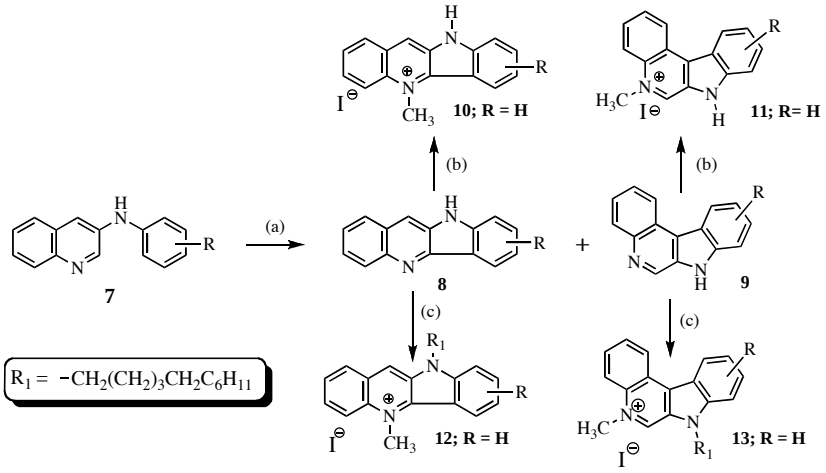


R= Cl, CF_3, OCF_3, OCH_3, $COOCH(CH_3)_2$

Reagents: (a) $Cu(OAc)_2$, DCM, $(C_2H_5)_3N$, Molecular sieve powder, RT, 12-24 hr.

In conclusion, the palladium catalyzed carbon-carbon bond formation is presented in this paper as a convenient method for the preparation of substituted 10*H*-indolo[3,2-*b*]quinoline and 7*H*-indolo[2,3-*c*]quinolines in high yields. However, this method has limitations as well. *Ortho* substituted phenyl boronic acids cannot produce angular indoloquinolines and thus other methods must be used to obtain such. Advantages such as product selectivity in case of *ortho* substitution, use of inexpensive catalyst, simple work up protocols and short

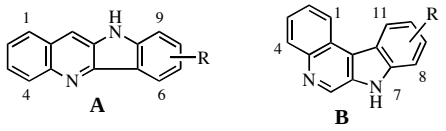
Scheme 2



Reagents: a) $Pd(OAc)_2$, CF_3COOH, 60 °C; b) CH_3I, Tetramethylene sulfone, 110 °C; c) (i) DME, NaH, $C_6H_{11}(CH_2)_5I$, (ii) CH_3I, Tetramethylene sulfone, 110 °C.

Table 1

Physicochemical data of 10*H*-indolo[3,2-*b*]quinoline and 7*H*-indolo[2,3-*c*]quinolines.



Entry	Product (**A**) (**8**)	M.P for (**8**) °C	Product (**B**) (**9**)	M.P for (**9**) °C	Product selectivity ratio (**A:B**)[a]	Yields (%)
a	9-Cl	272-274	No product	-	100:0	85
b	9-OCH_3	180-181	No product	-	100:0	74
c	H[b]	249-251	H	242-244	10:90	80
d	7-Cl	250-252	10-Cl	146-148	20:80	75
e	8-Cl	>270[c]	9-Cl	295-296	6:94	71
f	7-CF_3	252-254	10-CF_3	295-296	10:90	78
g	7-OCF_3	218-219	10-OCF_3	233-235	12:88	80
h	7-OCH_3	228-230	10-OMe	142-144	10:90	77
i	8-OCH_3	276-278	9-OMe	192-194	6:94	71
j	7-CO_2iPr	220-221	10-CO_2iPr	166-168	15:85	70

[a] the product ratio is based on isolated yields. [b] Previously reported in reference 20. [c] Decomposed.

Table 2

Antifungal Activity of Indoloquinolines

Compound	Anti-infective Activity[b]: IC_{50}/MIC/MFC (μg/mL)[c]			Cytotoxicity, IC_{50} (μg/mL) in Vero Cells
	C. albicans	*C. neoformans*	*A. fumigatus*	
10[a]	2.0/>20/>20	15.6/>20/>20	>20/>20/>20	3.2
11	>20/>20/>20	>20/>20/>20	NT	NT
12	>20/>20/>20	15.0/>20/>20	NT/2.5/>20	NT
13	0.8/2.5/10.0	1.5/2.5/5.0	3.5/5.0/10.0	>10
Amph. B	0.3/0.6/1.3	1.5/2.5/2.5	1.5/2.5/2.5	6.5

a = Previously reported in references 22 and 23. NT: Not Tested. b = For the methods of determination of biological activities, refer to reference 22. IC_{50} = Concentration that inhibits 50% of fungal growth or produces cytotoxicity in 50% of Vero cells; MIC = Minimum inhibitory concentration; MFC = Minimum fungicidal concentration.

reaction times, make this method a useful and attractive procedure for the synthesis of indoloquinoline alkaloids.

Evaluation of alkylated indoloquinolines **10-13** indicates that 7*H*-indolo[2,3-*c*]quinolines display a favorable antifungal profile and thus, can serve as a new lead scaffold for further evaluation and development.

EXPERIMENTAL

General Procedure for the synthesis of phenyl-3-amino-quinoline (7a-i). A mixture of 3-aminoquinoline (1 g, 6.94 mmol), 4-chlorophenylboronic acid (1.63 g, 10.41 mmol, 1.5 eq), Et_3N (1.45 mL, 10.41 mmol, 1.6 eq), $Cu(OAc)_2$ (1.90 g, 10.41 mmol, 1.6 eq), molecular sieves, 4 Å (2 g) in CH_2Cl_2 (30 mL) was allowed to stir at room temperature and monitored by TLC for 12-24 hours. The reaction mixture was quenched by drop-wise addition of aqueous NH_3 (15 mL). The resulting mixture was extracted with CH_2Cl_2 (3 x 50 mL), washed with H_2O, brine solution and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure and the pure product was obtained by column chromatography using EtOAc and hexanes as eluent. ^{1}H NMR (DMSO-d_6): δ 7.24 (d, 2H, J = 8.7 Hz) , 7.34 (d, 2H, *J* = 9.0 Hz), 7.46-7.52 (m, 2H) , 7.78-7.82 (m, 1H), 7.84-7.90 (m, 2H), 8.68 (d, 1H, J = 3.0 Hz), 9.40 (s, 1H). Other substituted phenyl 3-aminoquinolines were similarly obtained.

General procedure for the synthesis of 10*H*-indolo[3,2-*b*]quinoline and 7*H*-indolo-[3,2-*c*]quinoline analogs (8 and 9). A mixture of 4-chlorophenylquinolin-3-yl-amine (200 mg, 0.78 mmol), CF_3COOH (8 mL) and $Pd(OAc)_2$ (176 mg, 0.78 mmol) was allowed to reflux at 60°C for 4-6 hour. The reaction mixture was allowed to cool to room temperature, poured on ice cold water (15 ml), neutralized with aqueous NH_3 and extracted with EtOAc (3 x 50 mL), washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified on chromatographic column using EtOAc and hexanes as eluent. The pure products were obtained as solids [(**8d**, 30 mg, 15%), (**9d**, 120 mg, 60%)].

9-Chloro-10*H*-indolo[3,2-*b*]quinoline (8a). ^{1}H nmr ($CDCl_3$): δ 7.40 (t, 1H, J = 7.8 Hz), 7.62 (d, 1H, J = 6.9 Hz), 7.80-7.68 (m, 2H, 8.32 (dd, 1H J = 1.2, 7.5 Hz), 8.48 (d, 1H, J = 8.1 Hz), 8.68 (dd, 1H, J = 1.2, 6.66 Hz), 8.92 (brs, 1H) 9.32 (s, 1H).

9-Methoxy-10*H*-indolo[3,2-*b*]quinoline (8b). ^{1}H nmr (DMSO-d_6): δ 4.00 (s, 3H), 7.14 (d, 1H, J = 7.5 Hz), 7.30 (t, 1H, J = 8.1 Hz), 7.66-7.60 (m, 1H), 7.76 (m, 1H), 8.14 (dd, 1H, J = 1.2, 7.2 Hz), 8.18 (d, 1H, J = 8.1 Hz), 8.72 (dd, 1H, J = 0.9, 8.0 Hz), 12.30 (s, 1H), 9.22 (s, 1H).

10*H*-Indolo[3,2-*b*]quinoline (8c). ^{1}H nmr (DMSO-d_6): δ 7.30 (dd, 1H, J= 6.5, 7.1 Hz) , 7.64-7.58 (m, 4H), 7.98 (d, 1H, J=8.2Hz), 8.20 (d, 1H, J = 8.4Hz), 8.30 (s, 1H), 8.42 (d, 1H, J=8.4Hz), 11.40 (s, 1H, NH).

7-Chloro-10*H*-indolo[3,2-*b*]quinoline (8d). ^{1}H nmr (DMSO-d_6): δ 7.76-7.60 (m, 4H), 8.24-8.16 (m, 2H), 8.36 (d, 1H, *J* = 1.5 Hz), 8.54 (s, 1H), 11.80 (s, 1H).

8-Chloro-10*H*-indolo[3,2-*b*]quinoline (8e). ^{1}H nmr (CD_3OD): δ 7.44 (dd, 1H, J = 1.5, 6.9 Hz), 7.72 (d, 1H, J = 1.2 Hz), 7.80 (t, 1H, J = 8.1 Hz), 7.96 (t, 1H, J = 7.2 Hz), 8.26 (d, 1H, J = 8.4 Hz), 8.30 (d, 1H, J = 8.4 Hz), 8.44 (d, 1H, J = 8.7 Hz), 8.86 (s, 1H).

7-Trifluoromethyl-10*H*-indolo[3,2-*b*]quinoline (8f). ^{1}H nmr (CD_3OD): δ 7.62-7.56 (m, 1H), 7.74-7.66 (m, 2H), 7.86 (dd, 1H, J = 1.8, 6.9 Hz), 8.06 (d, 1H, J = 8.1 Hz), 8.21 (d, 1H, J = 8.4 Hz), 8.32 (s, 1H), 8.80 (s, 1H).

7-Trifluoromethoxy-10*H*-indolo[3,2-*b*]quinoline (8g). ^{1}H nmr ($CDCl_3$): δ 7.44 (d, 2H, J = 1.8 Hz), 7.60-7.54 (m, 1H), 7.70-7.66 (m, 1H), 7.94 (d, 1H, J = 8.1 Hz), 8.06 (s, 1H), 8.18 (brs, 1H), 8.32 (d, 1H, J = 8.4 Hz), 8.40 (d, 1H, J = 0.9 Hz).

7-Methoxy-10*H*-indolo[3,2-*b*]quinoline (8h). ^{1}H nmr ($CDCl_3$): δ 3.90 (s, 3H), 7.25 (s, 2H), 7.62 (t, 1H, J = 6.9 Hz), 7.74 (t, 1H, J = 6.9 Hz), 7.86 (d, 1H, J = 8.1 Hz), 8.06 (d, 1H, J = 8.4 Hz), 8.20 (brs, 1H), 8.76 (d, 1H, J = 2.1 Hz), 8.84 (d, 1H, J = 2.4 Hz).

8-Methoxy-10*H*-indolo[3,2-*b*]quinoline (8i). ^{1}H nmr (DMSO-d_6): δ 3.90 (s, 3H), 6.86 (dd, 1H, J = 2.1 , 6.6 Hz), 7.01 (d, 1H, J = 1.8 Hz), 7.50 (t, 1H, J = 7.2 Hz), 7.60 (t, 1H, J = 7.2 Hz), 8.04 (d, 1H, J = 2.8 Hz), 8.11 (d, 1H, J = 8.4 Hz), 8.15 (s, 1H), 8.18 (d, 1H, J = 8.7 Hz,) 11.24 (s, 1H).

10*H*-Indolo[3,2-*b*]quinoline-7-carboxylic acid isopropyl ester (8j). ^{1}H nmr ($CDCl_3$): δ 1.41 (s, 3H), 1.43 (s, 3H), 5.40-5.30 (m, 1H), 7.48 (dd, 1H, J = 0.6, 8.1 Hz), 7.60-7.56 (m, 1H), 7.72-7.68 (m, 1H), 7.96 (dd, 1H, J = 1.5, 6.6 Hz), 8.08 (s, 1H), 8.24 (brs, 1H), 8.38-8.32 (m, 2H), 9.26 (d, 1H, J = 1.8 Hz).

7*H*-indolo[2,3-*c*]quinoline (9c). ^{1}H nmr (DMSO-d_6): δ 12.20 (s, 1H), 9.26 (s, 1H), 8.80 (dd., 1H, J = 0.9, 7.2 Hz), 8.66 (d, 1H, J = 8.4 Hz), 8.17 (d, 1H, J = 7.8 Hz), 7.76-7.72 (m, 2H), 7.66-7.54 (m, 2H), 7.40 (t, 1H, J = 8.4 Hz).

10-Chloro-7*H*-indolo[2,3-*c*]quinoline (9d). ^{1}H nmr (DMSO-d_6): δ 7.58-7.56 (dd, 1H, J = 2.1, 6.6 Hz), 7.74-7.62 (m, 3H), 8.16 (d, 1H, J = 8.1 Hz), 8.72 (d, 1H, J = 1.5 Hz), 8.80 (d, 1H, *J* = 8.1 Hz), 9.26 (s, 1H), 12.34 (s, 1H).

9-Chloro-7*H*-indolo[2,3-*c*]quinoline (9e). ^{1}H nmr (CD_3OD): δ 7.38 (dd, 1H, J = 1.5, 6.9 Hz), 7.68 (t, 2H, J = 6.9 Hz), 7.77 (t, 1H, J = 7.2 Hz), 8.16 (d, 1H, J = 8.4 Hz), 8.56 (d, 1H, J = 8.4 Hz), 8.72 (d, 1H, J = 8.1 Hz), 9.13 (s, 1H).

10-Trifluoromethyl-7*H*-indolo[2,3-*c*]quinoline (9f). ^{1}H nmr (CD_3OD): δ 7.70 (t, 1H, J = 8.1 Hz), 7.84-7.78 (m, 3H), 8.18 (d, 1H, J = 8.4 Hz), 8.72 (d, 1H, J = 2.4 Hz), 8.83 (s, 1H), 9.18 (s, 1H).

10-Trifluoromethoxy-7*H*-indolo[2,3-*c*]quinoline (9g). ^{1}H nmr (DMSO-d_6): δ 7.56 (dd, 1H, J = 1.2, 7.8 Hz), 7.70-7.64 (m, 1H), 7.84 (d, 1H, J = 8.7 Hz), 8.16 (d, 1H, J = 7.2 Hz), 8.68 (s, 1H), 8.78-7.73 (m, 1H), 8.80 (d, 1H, J = 8.1 Hz), 9.31 (s, 1H), 12.40 (s, 1H).

10-Methoxy-7*H*-indolo[2,3-*c*]quinoline (9h). ^{1}H nmr (DMSO-d_6): δ 4.00 (s, 3H), 7.22 (dd, 1H, J = 2.4, 6.3 Hz), 7.68-7.60 (m, 2H), 7.74 (t, 1H, J = 6.9 Hz), 8.04 (d, 1H, J = 2.1 Hz), 8.14 (d, 1H, J = 7.8 Hz), 8.76 (d, 1H, J = 8.1 Hz), 9.22 (s, 1H), 12.00 (s, 1H).

9-Methoxy-7*H*-indolo[2,3-*c*]quinoline (9i). ^{1}H nmr (DMSO-d_6): δ 4.10 (s, 3H), 6.86 (d, 1H, J = 7.8 Hz), 7.30 (d, 1H, J = 7.5 Hz), 7.50 (t, 1H, J = 8.1 Hz), 7.64-7.58 (m, 2H), 8.10 (dd, 1H, J = 1.2, 6.3 Hz), 9.20 (s, 1H), 9.52 (dd, 1H, J = 1.8, 6.6 Hz), 12.20 (s, 1H).

7*H*-Indolo[2,3-*c*]quinoline-10-carboxylic acid isopropyl ester (9j). ^{1}H nmr (DMSO-d_6): δ 1.39 (s, 3H), 1.41 (s, 3H), 5.26-5.20 (m, 1H), 7.70 (t, 1H, J = 6.9 Hz), 7.82 (t, 2H, J = 6.9 Hz), 8.16 (dd, 1H, J = 1.5, 7.5 Hz), 8.20 (d, 1H, J = 8.4 Hz), 8.70 (d, 1H, J = 8.1 Hz), 9.16 (s, 1H), 9.30 (s, 1H), 12.50 (s, 1H).

5-Methyl-10*H*-indolo[3,2-*b*]quinolinium iodide (10). Mp 280–283 °C; ^{1}H nmr (DMSO-d_6) δ 5.04 (s, 3 H), 7.52 (ddd, 1H, J = 7.7, 7.7, 1.0 Hz), 7.86 (d, 1H, J = 8.3 Hz), 7.93 (dd, 1H, J = 7.2, 7.2 Hz), 7.96 (dd, 1H, J = 8.1, 8.1 Hz), 8.17 (ddd, 1H, J = 8.0, 8.0, 1.4 Hz), 8.58 (dd, 1H, J = 7.4, 1.0 Hz), 8.77 (d, 1H, J =

9.1 Hz), 8.81 (d, 1H, J = 8.5 Hz), 9.30 (s, 1H), 12.87 (s, 1H); *Anal.* Calcd. for $C_{16}H_{13}N_2I$, C, 53.35; H, 3.64; N, 7.78. Found: C, 53.33;, H, 3.66; N, 7.69.

5-Methyl-7*H*-indolo[2,3-*c*]quinolinium iodide (11). Mp 281-283°C; ^{1}H nmr (DMSO-d_6) δ 4.80 (s, 3H), 7.56 (t, 1H, J = 6.9 Hz), 7.85 (t, 1H, J = 6.3 Hz), 7.94 (d, 1H, J = 8.1 Hz), 8.12-8.09 (m, 2H), 8.56 (d, 1H, J = 9.9 Hz), 8.94 (d, 1H, J = 8.4 Hz), 9.20 (d, 1H, J = 9.6 Hz), 9.92 (s, 1H), 13.20 (s, 1H). *Anal.* Calcd. for $C_{16}H_{13}IN_2$: C, 53.35; H, 3.64; N, 7.78, Found: C, 53.18; H, 3.84; N, 7.71.

10-(5-Cyclohexyl-pentyl)-5-methyl-10*H*-indolo[3,2-*b*]quinolinium iodide (12). M.p 215–217 °C; ^{1}H nmr (DMSO-d_6) δ 1.38 (m, 2H), 1.59 (m, 2H), 1.87 (m, 2H), 2.49 (t, 2H, J = 3.0 Hz), 4.70 (t, 2H, J = 7.1 Hz), 5.05 (s, 6H), 7.12 (m, 5H), 7.57 (t, 1H, J = 8.0 Hz), 8.02 (m, 3H), 8.19 (t, 1H, J = 7.5 Hz), 8.52 (d, 1H, J = 7.6 Hz), 8.75 (d, 1H, J = 9.0 Hz), 8.85 (d, 1H, J = 8.4 Hz), 9.60 (s, 1H). *Anal.* Calcd for $C_{27}H_{27}IN_2$: C, 64.04; H, 5.37; N, 5.53. Found: C, 63.77; H, 5.40; N, 5.56.

7-(5-Cyclohexylpentyl)-5-methyl-7*H*-indolo[2,3-*b*]quinolinium iodide (13). M.p 249-251 °C; ^{1}H nmr (DMSO-d_6): δ 0.80-0.60 (m, 2H), 1.20-1.00 (m, 6H), 1.40-1.20 (m, 4H), 1.60-1.42 (m, 5H), 2.00-1.80 (m, 2H), 4.60-4.80 (m, 5H), 7.60 (t, 1H, J = 7.5 Hz), 7.90 (t, 1H, J = 8.4 Hz), 8.16-8.06 (m, 3H), 8.58 (m, 1h), 8.96 (d, 1H, J = 8.1 Hz), 9.20 (m, 1H),10.20 (s, 1H). *Anal.* Calcd. for $C_{27}H_{33}IN_2$. 1.8 H_2O: C, 59.44; H, 5.96; N, 5.06. Found: C, 59.52; H, 6.10; N, 5.14.

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