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Heteroatom directed photoannulation: synthesis of indoloquinoline alkaloids: cryptolepine, cryptotackieine, cryptosanguinolentine, and their methyl derivatives

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Abstract—A three-step synthesis of indoloquinoline alkaloids is described. The reaction of 2,3 and 4-substituted haloquinolines with anilines afforded the respective anilinoquinolines, which upon photocyclization gave the indoloquinolines. By regioselective methylation on quinoline nitrogen, furnished the alkaloids cryptotackieine, cryptosanguinolentine, cryptolepine, and the synthetic isomer isoneocryptolepine. Their methyl derivatives were also synthesized in search of new antiplasmodial drugs and DNA intercalating agents.

1. Introduction

Indoloquinoline alkaloids are receiving prominent attention in recent years as they are known to act as DNA intercalating agents[1] and exhibit antimalarial properties.[2,3] The World Health Organization placed malaria besides tuberculosis and AIDS as a major infectious disease. The roots of the West African plant *Cryptolepis sanguinolenta*,[4] a rich source of indoloquinoline alkaloids, have been used by Ghanaian healers to treat a variety of health disorders including malaria. Since 1974, a decoction of this plant has been used in the clinical therapy of rheumatism, urinary tract infections, malaria, and other diseases.[5,6] The linear indoloquinoline alkaloids cryptolepine (**1**) (5-methyl-5*H*-indolo[3,2-*b*]quinoline), cryptotackieine (**2**) (neocryptolepine, 5-methyl-5*H*-indolo[2,3-*b*]quinoline), and an angularly-fused alkaloid cryptosanguinolentine (**3**) (isocryptolepine, 5-methyl-5*H*-indolo[3,2-*c*]quinoline) are three of the characterized alkaloids, which behave as DNA intercalating agents, inhibiting DNA replication and transcription. These compounds also exhibit strong antiplasmodial activity. Cryptolepine binds 10-fold more tightly to DNA than other alkaloids and proves to be much more cytotoxic toward B16 melanoma cells.[7] It has been reported[8,9] that some methyl-substituted indoloquinolines act as cytotoxic agents, liposomally-formulated anticancer agents,[10] and DNA-Topoisomerase II inhibitors.[11]

Recent synthetic studies have detailed the preparation of indoloquinoline alkaloids by intramolecular reaction of iminophosphorane with isocyanate,[12,13] by the regioselective thermocyclization of the corresponding azide[14] or by *ortho*-metalation using a cross-coupling strategy.[15]

Recently, we have reported an efficient photochemical synthesis[16] and Fischer indole synthesis[17] toward a cryptosanguinolentine alkaloid. Here, we describe the synthesis of the titled alkaloids along with a synthetic indoloquinoline isomer, isoneocryptolepine (**4**), which also possesses promising in vitro antiplasmodial properties.[3] An approach based on a stepwise formation, starting from amination of the appropriate haloquinolines with anilines is discussed. The resultant intermediates on photochemical irradiation being treated in the presence of iodine catalyst for about 48–72 h undergo oxidative cyclization to afford the corresponding isomeric indoloquinolines.

In the last few decades, Schultz et al.[18,19,20] extensively investigated heteroatom directed-photoarylation[21,22] method to derive indoles,[23,24] benzothiophenes,[25] benzofurans,[25] and benzoselenophenes[22] by involving subsequent elimination of smaller molecules like H_2O, H_2, HCl, and MeOH. Several mechanisms have been considered for this diarylamine photocyclization.[26] The term 'heteroatom-directed photoarylation' characterizes photochemically-initiated electrocyclic reactions originating from the arrangements of an available electron pair in a heteroatom and those from at least one aromatic π-bond. An attractive feature of this technique is the regiospecificity of the aromatic substitution *ortho* to the heteroatom.

Keywords: Indoloquinoline alkaloids; Photoannulation; Cryptolepine; Cryptotackieine; Cryptosanguinolentine.
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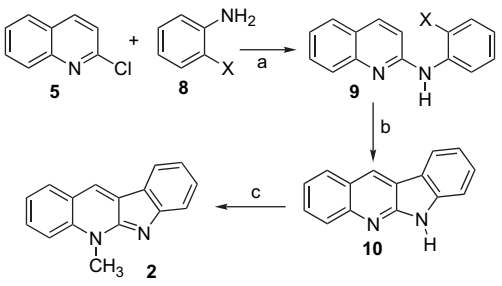
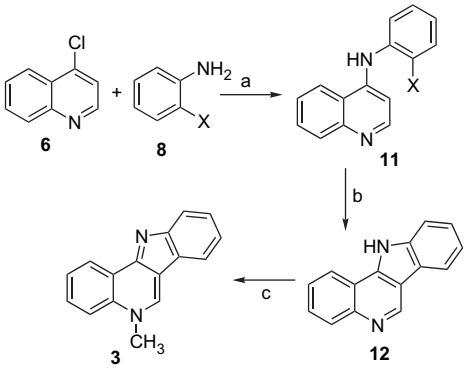
2. Results and discussion

To achieve our objective toward the synthesis of cryptotackieine (Scheme 1), cryptosanguinolentine (Scheme 2), and cryptolepine (Scheme 3), we have started from commercially available haloquinolines (**5**–**7**) and anilines (**8a**–**d**).



Where
8a) X = Cl, 8b) X = H, 8c) X = OH, 8d) X = OMe
a) 200 °C, 5h; b) hν, C_6H_6:CH_3OH:H_2SO_4 (60:30:1, v/v/v), I_2, rt.;
c) Me_2SO_4, CH_3CN, reflux, 6 h, K_2CO_3, 80%

Scheme 1.

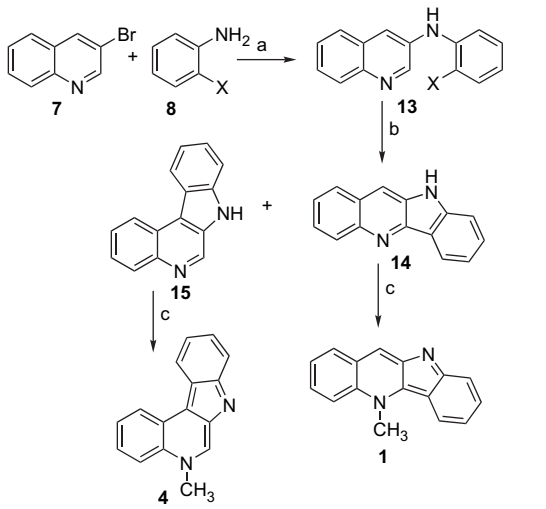


Where
8a) X = Cl, 8b) X = H, 8c) X = OH, 8d) X = OMe
a) 200 °C, 5h; b) hν, C_6H_6:CH_3OH:H_2SO_4 (60:30:1, v/v/v), I_2, rt.;
c) Me_2SO_4, CH_3CN, reflux, 6 h, K_2CO_3, 83%

Scheme 2.

It has been reported[27a–j] that aniline condenses with 2- and 4-chloroquinolines and many derivatives of haloquinolines on cautious heating at temperatures in the range of 100–200 °C. As a first step toward the synthesis of cryptotackieine (Scheme 1), regioselective amination of 2-chloroquinoline with 2-chloroaniline was carried out (**5**→**9a**). Several reports[28a–c] have appeared for such amination detailing the use of new catalysts. We have found the classical procedure[27a–h] more fruitful because the familiar procedure like Hartwig–Buchwald type amination requires expensive palladium catalysts.

In one approach, photochemical irradiation of anilinoquinolines in the absence of protic acid did not afford the desired products (**10** and **12**) when X=OH, and the yields were found to be ca. 55–60% when X=Cl, H, and OMe. Hence, we employed an acidic solvent system for the effective conversion to the desired photoproducts. Moreover, it should



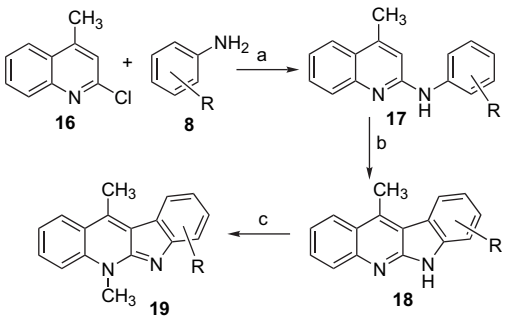
Where
8a) X = Cl, 8b) X = H;
a) 200 °C, 5h; b) hν, C_6H_6:CH_3OH:H_2SO_4 (60:30:1, v/v/v), I_2, rt.;
c) Me_2SO_4, CH_3CN, reflux, 6 h, K_2CO_3, 82-85%

Scheme 3.

be noted that the product yield for photocyclization in protic solvents was significantly higher than that in benzene alone. Consequently, all subsequent photoreactions were performed on **9**(**a**–**d**), **11**(**a**–**d**), **13**(**a**,**b**), **17**(**b**,**e**,**f**), and **21**(**b**,**e**,**f**) in benzene/methanol/sulfuric acid solution (60:30:1, v/v/v) in the presence of traces of iodine, which led via oxidative photocyclization to afford indoloquinolines **10**, **12**, **14**, **15**, **18**(**b**,**e**,**f**), and **22**(**b**,**e**,**f**). The cyclization of the resultant intermediates **9**(**a**–**d**) were found to occur at C-3 and not at C-1 position of the quinoline ring since the cyclization at the C-1 position requires carbon–nitrogen bond formation and would end with a net loss of aromaticity. In the final step, compound **4** was subjected to selective methylation on the quinoline nitrogen[8,12a,29] using $(CH_3)_2SO_4$ in CH_3CN or toluene refluxed for 6 h in the presence of K_2CO_3 to afford cryptotackieine (**2**). The same procedure was applied to compound **12** (Scheme 2), which afforded angularly-fused indoloquinoline alkaloid, cryptosanguinolentine (**3**).

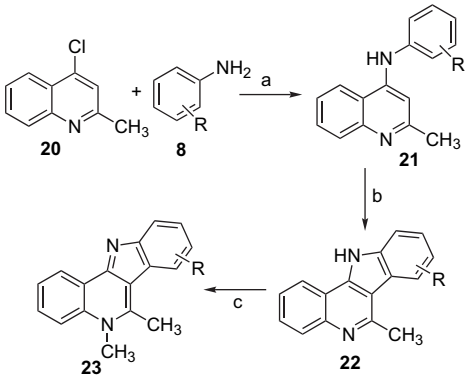
Interestingly, in the case of the reaction of 3-bromoquinoline with aniline (Scheme 3), the resulting intermediate **13** gave both linearly- and angularly-fused products. When irradiated, linear fusion provides quindoline as a minor product (16%), which on selective methylation on the quinoline nitrogen afforded the alkaloid, cryptolepine. On the other hand, the angularly-fused indoloquinoline (51%) **15** on methylation afforded isoneocryptolepine (**4**), which is a synthetic indoloquinoline alkaloid.[28a]

The methyl derivative of the alkaloids **2** and **3** was also prepared starting from 4-methyl-2-hydroxyquinoline and 2-methyl-4-hydroxyquinoline. On treatment with $POCl_3$ both compounds yielded their corresponding chloro-derivatives (**16** and **20**). Compounds **16** and **20**, on reaction with anilines (**8b**,**e**,**f**), followed by photochemical cyclization and regioselective methylation on the quinoline nitrogen, gave the newer derivatives **19**(**b**,**e**,**f**) and **23**(**b**,**e**,**f**), respectively (Schemes 4 and 5).



Where
8b) R = H, 8e) R = *o*-Me, 8f) R = *p*-Me,
a) Dry ethanol, reflux, 12h; b) hν, C_6H_6:CH_3OH:H_2SO_4 (60:30:1, v/v/v), I_2, rt.; c) Me_2SO_4, CH_3CN, reflux, 6 h, K_2CO_3, 81-82%

Scheme 4.



Where
8b) R = H, 8e) R = *o*-Me, 8f) R = *p*-Me,
a) Dry ethanol, reflux, 12h; b) hν, C_6H_6:CH_3OH:H_2SO_4 (60:30:1, v/v/v), I_2, rt.; c) Me_2SO_4, CH_3CN, reflux, 6 h, K_2CO_3, 80-83%

Scheme 5.

3. Conclusion

We have developed an efficient three-step synthesis of the alkaloids cryptotackieine, cryptosanguinolentine, and cryptolepine. Due to the easy availability of the starting materials and high yields realized in the different steps, this approach proves to be more attractive. We have followed the synthetically-useful method of 'heteroatom-directed photoannulation technique' for the construction of linearly, as well as angularly-fused indoloquinoline alkaloids.

4. Experimental

4.1. General methods

^{1}H NMR and ^{13}C NMR (400 and 100 MHz) spectra were recorded in $CDCl_3$ and TMS was used as an internal reference. Melting points were determined and were uncorrected. Chromatographic purification was conducted by column chromatography using 60–120 mesh silica gel. Reagent grade aniline and ethyl acetoacetate were used after usual purification methods (for the preparation of the compounds **16** and **20**). Reaction progress was monitored by thin layer chromatography. Mass spectra were recorded on a JMS-D-300 mass spectrometer. Elemental analyses were recorded on EL III, Elementar Analysen Systeme. 2-Chloroquinoline, 4-chloroquinoline, 2-chloroaniline, and 3-bromoquinoline were purchased and used as received. 2-Methyl-4-hydroxyquinoline and 4-methylquinolin-2(1*H*)-one were prepared by using reported procedures.[30a,b] Photolysis was carried out in a RPR-100 Photochemical Reactor, fitted with 16 RPR UV lamps and using quartz tube.

4.2. Preparation of anilinoquinolines and their derivatives: 9(a–d), 11(a–d), 13(a,b), 17(b,e,f), and 21(b,e,f)

4.2.1. Preparation of anilinoquinolines: 9(a–d), 11(a–d), and 13(a,b). Equimolar mixture (10 mmol) of the compounds 2-chloroquinoline (1.63 g) (**5**) and 2-chloroaniline (1.24 g) (**8a**) were heated in flame, and then a violent reaction occurred at 200 °C. The reaction mixture was cooled; crystals of the product (**9a**) were crashed out. This was heated in NaOH (dilute), cooled down, and recrystallized with alcohol (yield: 72%, 1.83 g). Similarly, other anilinoquinolines were prepared using appropriate haloquinolines and anilines.

4.2.2. Preparation of anilinoquinoline derivatives: 17(b,e,f) and 21(b,e,f). To 2-chloro-4-methylquinoline (1.77 g, 10 mmol) (**16**) dissolved in dry ethanol was added aniline (0.91 g, 10 mmol) (**8b**) and then the mixture was refluxed for about 12 h. Then the excess of ethanol was distilled off and the residue was then subjected to silica gel-column chromatography using petroleum ether/ethyl acetate (85:15, v/v) as eluants, yielded the product (**17b**) in 74%. Similarly, its derivatives **17**(**e**,**f**) and **21**(**b**,**e**,**f**) were prepared by treating 2-chloro-4-methylquinoline and 4-chloro-2-methylquinolines (**20**) with their respective anilines (**8b**,**e**,**f**). Since these methyl derivatives **16** and **20** were aminated using this procedure we did not opt the other procedures.

4.3. Preparation of isomeric indoloquinoline moieties: 10, 12, 14, 15, 18(b,e,f), and 22(b,e,f)

4.3.1. Photochemical cyclization of the compound 9b: 6*H*-indolo[2,3-*b*]quinoline. Irradiation of a solution of **9b** (1.1 g, 5 mmol) in the solvent system benzene/methanol/sulfuric acid (60:30:1, v/v/v) with iodine (25 mg, 0.1 mmol) was carried out in a RPR-100 Photochemical Reactor, fitted with 16 RPR UV lamps. The solution placed in a quartz flask was irradiated for 48 h. When the reaction controlled by TLC showed complete disappearance of **9b** the solvent was removed in vacuo and then the residue was subjected to column chromatography on silica gel using petroleum ether/ethyl acetate (80:20, v/v) as eluants, which afforded the pure photoproduct **10** (0.76 g); 70%, mp >300 °C. Likewise, **12** (78%, 0.85 g) (from **11a**), **14** (16%, 0.17 g) and **15** (51%, 0.56 g) (from **13b**), **18b** (70%, 0.83 g), **18e** (67%, 0.82 g), **18f** (68%, 0.83 g), **22b** (65%, 0.75 g), **22e** (63%, 0.77 g), **22f** (69%, 0.85 g) were prepared from their appropriate anilinoquinolines on photochemical irradiation.

4.4. Preparation of isomeric indoloquinoline alkaloids 2, 3, 1, and 4 and their derivatives 19(b,e,f) and 23(b,e,f)

4.4.1. Regioselective methylation of indoloquinolines. Regioselective methylation was done using the reported

procedure.[8] The methylated products **2** (80%, 0.37 g), **3** (83%, 0.38 g), **1** (82%, 0.094 g), **4** (84%, 0.19 g), **19b** (82%, 0.40 g), **19e** (81%, 0.42 g), **19f** (82%, 0.425 g), and **23b** (82%, 0.40 g), **23e** (80%, 0.42 g), **23f** (83%, 0.43 g) were obtained from **10** (2 mmol), **12** (2 mmol), **14** (0.5 mmol), **15** (1 mmol), **18**(**b**,**e**,**f**), and **22**(**b**,**e**,**f**) (2 mmol), respectively.

Compound **9a**. Yield: 72% (1.83 g); mp 137 °C; IR (KBr): 1046, 3215, 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.75 (1H, d, J=7.2 Hz, Quin–C_3–H), 7.05–7.42 (m, 4H, Ph–H), 7.66 (1H, t, J=7.8 Hz, C_6–H), 7.89 (1H, t, J=7.8 Hz, C_7–H), 7.99 (1H, d, J=7.2 Hz, C_5–H), 8.08 (1H, d, J=7.2 Hz, C_4–H), 8.19 (1H, d, J=8.2 Hz, C_8–H), 10.81 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): C_3-118.23, C_4'-119.37, C_2'-119.52, C_3''-121.54, C_6-121.92, C_5-125.25, C_3'-125.32, C_7-126.45, C_4-127.43, C_8-128.05, C_{4a}-129.11, C_2''–Cl-135.71, C_1'-148.23, C_{8a}-148.61, C_2-159.24. EIMS (70 eV, *m/e*): 254 (M^+), 256 (M+2). Anal. Calcd for $C_{15}H_{11}N_2Cl$: C 70.73, H 4.35, N 11.00. Found: C 70.56, H 4.37, N 10.96.

Compound **10**. Yield: 70%, 0.761 g (from **9b**); mp >300 °C; IR (KBr): 1615, 3156 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.05–7.95 (m, 5H, Ar–H), 7.98 (1H, d, J=7.4 Hz, C_4–H), 8.11 (1H, d, J=7.8 Hz, C_1–H), 8.25 (1H, d, J=8.0 Hz, C_{10}–H), 9.05 (1H, s, C_{11}−H), 11.61 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): C_7-111.13, C_4-118.97, C_9-119.94, C_{11a}-120.51, C_{10}-122.03, C_2-122.91, C_{10a}-123.92, C_1-127.33, C_{11}-127.74, C_{10b}-128.17, C_3-128.41, C_8-128.83, C_{4a}-141.53, C_{6a}-146.72, C_{5a}-154.40. EIMS (70 eV, *m/e*): 218 (M^+); Anal. Calcd for $C_{15}H_{10}N_2$: C 82.55, H 4.62, N 12.84. Found: C 82.41, H 4.63, N 12.80.

Compound **11a**. Yield: 74% (1.88 g); mp 142 °C; IR (KBr): 1045, 3220, 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.77 (1H, d, J=7.2 Hz, Quin–C_3–H), 7.04–7.43 (4H, m, Ph–H), 7.66 (1H, t, J=7.6 Hz, C_6–H), 7.90 (1H, t, J=8.0 Hz, C_7–H), 7.98 (1H, d, J=7.2 Hz, C_5–H), 8.09 (1H, d, J=7.6 Hz, C_8–H), 8.63 (1H, d, J=8.2 Hz, C_2–H), 10.71 (1H, br s, NH); ^{13}C NMR: C_3-107.11, C_3''-115.37, C_3'-119.71, C_5-120.33, C_1'-121.07, C_6-124.78, C_7-127.52, C_4'-127.76, C_2'-129.63, C_8-130.82, C_{4a}-132.13, C_2''–Cl-145.39, C_4-145.79, C_{8a}-149.01, C_2-151.32. EIMS (70 eV, *m/e*): 254 (M^+), 256 (M+2); Anal. Calcd for $C_{15}H_{11}N_2Cl$: C 70.73, H 4.35, N 11.00. Found: C 70.56, H 4.31, N 10.96.

Compound **12**. Yield: 78%, 0.85 g (from **11a**); mp >220 °C (decomp.). Spectral and analytical data of this compound coincide with our earlier reported one.[16]

Compound **13**. Yield: 70% (1.54 g); mp 116 °C; IR (KBr): 3276, 1611 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.94–7.48 (5H, m, Ph–H), 7.66 (1H, t, J=7.8 Hz, C_6–H), 7.89 (1H, t, J=7.8 Hz, C_7–H), 7.99 (1H, d, J=8.0 Hz, C_5–H), 8.09 (1H, s, C_4–H), 8.23 (1H, d, J=8.2 Hz, C_8–H), 8.42 (1H, s, C_2–H), 10.44 (1H, br s, NH); ^{13}C NMR: C_4'-104.26, C_3'- and C_3''-114.27, C_2'- and C_2''-119.46 and 120.34, C_5-123.19, C_6-124.44, C_7-127.06, C_8-128.13, C_4-129.77, C_{4a}-131.31, C_1'-142.87, C_3-150.02, C_{8a}-150.98, C_2-151.51. EIMS (70 eV, *m/e*): 220 (M^+); Anal. Calcd for $C_{15}H_{12}N_2$: C 81.79, H 5.49, N 12.72. Found: C 81.61, H 5.51, N 12.69.

Compound **17b**. Yield: 74%, (1.73 g); mp 145 °C; IR (KBr): 3256, 2925, 2857, 1605 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.49 (3H, s, Ar–CH_3), 6.75 (1H, s, Quin–C_3–H), 7.05–7.38 (5H, m, Ph–H), 7.66 (1H, t, J=7.4 Hz, C_6–H), 7.89 (1H, t, J=8.0 Hz, C_7–H), 7.97 (1H, d, J=8.2 Hz, C_5–H), 8.08 (1H, d, J=8.2 Hz, C_8–H), 10.51 (1H, br s, NH); ^{13}C NMR: C_4–CH_3-20.01, C_3-10.38, C_4-119.60, C_4'-121.70, C_2'- and C_2''-124.70, C_3'- and C_3''-125.33, C_6-125.52, C_5-127.94, C_7-130.02, C_8-134.08, C_{4a}-135.00, C_1'-135.78, C_{8a}-152.15, C_2-153.94. EIMS (70 eV, *m/e*): 234 (M^+); Anal. Calcd for $C_{16}H_{14}N_2$: C 82.02, H 6.02, N 11.96. Found: C 82.07, H 6.03, N 11.95.

Compound **18b**. Yield: 72% (0.83 g); mp 206 °C; IR (KBr): 3196, 2921, 2845 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.50 (3H, s, C_{11}–CH_3), 7.25–8.00 (6H, m, Ar–H), 8.11 (1H, d, J=8.12 Hz, C_4–H), 8.36 (1H, d, J=8.10 Hz, C_{10}–H), 10.75 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): C_{11}–CH_3-20.35, C_{10a}-103.65, C_9-121.67, C_8-122.48, C_{10b}-122.62, C_{10}-124.03, C_1-124.34, C_2-126.63, C_3-127.86, C_7-128.11, C_4-129.88, C_{11a}-130.07, C_{6a}-132.79, C_{11}-143.55, C_{4a}-149.47, C_{5a}-161.56. EIMS (70 eV, *m/e*): 232 (M^+). Anal. Calcd for $C_{16}H_{12}N_2$: C 82.73, H 5.21, N 12.06. Found: C 82.60, H 5.23, N 12.01.

Compound **19b**. Yield: 82% (0.40 g); mp >250 °C; IR (KBr): 2916, 2874, 1612 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.44 (3H, s, C_{11}–CH_3), 3.66 (3H, s, C_5–CH_3), 7.25–7.87 (7H, m, Ar–H), 8.41 (1H, d, J=8.24 Hz, C_{10}–H); ^{13}C NMR ($CDCl_3$): C_{11}–CH_3-21.63, C_5–CH_3-46.65, C_{10a}-105.39, C_9-121.07, C_{10b}-122.57, C_{10}-123.53, C_8-123.55, C_1-124.03, C_2-125.36, C_7-129.25, C_4-129.60, C_3-127.94, C_{11a}-130.14, C_{6a}-131.30, C_{11}-141.22, C_{4a}-147.23, C_{5a}-158.83. EIMS (70 eV, *m/e*): 278 (M^+); Anal. Calcd for $C_{19}H_{22}N_2$: C 81.97, H 7.97, N 10.06. Found: C 81.73, H 7.99, N 10.02.

Compound **21b**. Yield: 70% (1.64 g); mp 162 °C; IR (KBr): 3234, 2941, 2886 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.41 (3H, s, Ar–CH_3), 6.49 (1H, s, Quin–C_3–H), 7.08–7.48 (5H, m, Ph–H), 7.67 (1H, t, J=7.6 Hz, C_6–H), 7.89 (1H, t, J=7.6 Hz, C_7–H), 8.02 (1H, d, J=8.0 Hz, C_5–H), 8.12 (1H, d, J=8.2 Hz, C_8–H), 10.18 (1H, br s, NH); ^{13}C NMR: C_2–CH_3-27.34, C_3-110.78, C_3'- and C_3''-115.71, C_2'- and C_2''-119.42, C_4'-120.11, C_5-120.45, C_6-124.33, C_7-127.62, C_8-129.15, C_{4a}-131.77, C_1'-144.79, C_{8a}-149.34, C_2-155.13, C_4-157.50. EIMS (70 eV, *m/e*): 234 (M^+); Anal. Calcd for $C_{16}H_{14}N_2$: C 82.02, H 6.02, N 11.96. Found: C 81.95, H 6.03, N 11.89.

Compound **22b**. Yield: 65% (0.75 g); mp 235 °C; IR (KBr): 3207, 2936, 2885 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.43 (3H, s, C_6–CH_3), 7.33–7.88 (7H, m, Ar–H), 8.07 (1H, d, J=8.04 Hz, C_4–H), 10.51 (1H, br s, NH); ^{13}C NMR ($CDCl_3$): C_6–CH_3-23.14, C_{10}-118.64, C_9-119.54, C_7-120.29, C_{6a}-122.57, C_8-124.43, C_2-124.69, C_3-126.73, C_{6b}-126.78, C_1-127.41, C_4-129.44, C_{11b}-130.11, C_{10a}-135.67, C_{11a}-136.73, C_{4a}-150.17, C_6-154.75. EIMS (70 eV, *m/e*): 232 (M^+); Anal. Calcd for $C_{16}H_{12}N_2$: C 82.73, H 5.21, N 12.06. Found: C 82.66, H 5.22, N 12.10.

Compound **23b**. Yield: 82% (0.40 g); mp 197 °C; IR (KBr): 2922, 2857, 1606 cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.43 (3H, s, C_6–CH_3), 3.75 (3H, s, C_5–CH_3), 7.36–7.92 (7H, m, Ar–H),

8.26 (1H, d, J=7.86 Hz, C_4–H); ^{13}C NMR ($CDCl_3$): C_6–CH_3-22.14, C_5–CH_3-41.12, C_{10}-117.23, C_9-118.49, C_7-121.34, C_8-123.45, C_{6a}-123.54, C_2-124.55, C_3-126.30, C_1-127.81, C_4-129.66, C_{11b}-130.05, C_{10a}-135.03, C_{11a}-135.41, C_{6b}-136.07, C_{4a}-149.69, C_6-157.61. EIMS (70 eV, *m*/*e*): 246 (M^+); Anal. Calcd for $C_{17}H_{14}N_2$: C 82.90, H 5.73, N 11.37. Found: C 82.67, H 5.74, N 11.41.

The spectral data for the compounds **2** (Yield 80%, 0.37 g), **3** (Yield 83%, 0.38 g), and **1** are identical with those reported[4d,4e,4a–c] for the natural products, respectively. The spectral data of **15** and **4** coincide with the earlier reported compound.[28a]

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