HETEROCYCLES, Vol. 104, No. 10, 2022, pp. 1745 - 1769. © 2022 The Japan Institute of Heterocyclic Chemistry
Received, 11th July, 2022, Accepted, 1st August, 2022, Published online, 10th August, 2022
DOI: 10.3987/COM-22-14718

MICROWAVE-INDUCED ONE STEP SYNTHESIS OF STRUCTURALLY DIVERSE LINEAR INDOLOQUINOLINES: CONCISE SYNTHESIS OF NORNEOCRYPTOLEPINE

Krisztián Biró, János Tatai, Bence Pollák, Márk Molnár, and Miklós Nyerges*

Servier Research Institute of Medicinal Chemistry, 7, Záhony utca, 1031, Budapest, Hungary; E-mail: miklos.nyerges@servier.com

Abstract – A general and efficient synthesis of diverse tetra- and pentacyclic indolo[2,3-*b*]quinoline derivatives was achieved through a microwave assisted, metal-free, base catalyzed domino Knoevenagel condensation, intramolecular cyclization process starting from simple oxindole and 2-amino-arylaldheydes. This approach provides a straightforward, atom-economical and concise route to access a diverse range of otherwise not easily available heterocycles in excellent yields with good tolerance of functional groups.

INTRODUCTION

Linear indoloquinoline alkaloids have received considerable attention due to their wide range of biological activities. In recent years, they have drawn much attention due to their remarkable antimalarial, cytotoxicity, antimuscarinic, antibacterial, antiviral, antimicotic, antihyperglycemic, antitumor and DNA intercalating properties.[1] For example, several tetracyclic indoloquinolines have been isolated from the dried roots of *Cryptolepis sanguinolenta*,[2] a shrub indigenous to West Africa, which are being used in folk medicine for the treatment of infectious diseases, such as malaria and amoebiasis. Major alkaloid isolated from *C. sanguinolenta* is cryptolepine (5-methylindolo[3,2-*b*]quinoline), accounts for most of the activity found in extracts from the plant (Figure 1). Beside that, a number of minor alkaloids have been isolated from this source, with the same heterocyclic ring *e.g.* 11-hydroxycryptolepine[3] or cryptolepionic acid[4] or with an isomeric scaffolds such as neocryptolepine (also known as cryptotackiene)[5] or isocryptolepine[6] containing indolo[2,3-*b*]quinoline and indolo[3,2-*c*]quinoline ring system, respectively. Some related natural products as cryptoheptine[3,7] or dimeric indoloquinoline alkaloids (*e.g.* quindolinocryptotackieine[8] or cryptospirolepine[9]) were also isolated from *C. sanguinolenta.* The 6*H*-indolo[2,3-*b*]quinoline itself named originally as quinindoline, is also a natural product – renamed as norneocryptolepine (or norcryptotackieine) after being isolated recently from the leaves of *Justicia betonica*.[10]

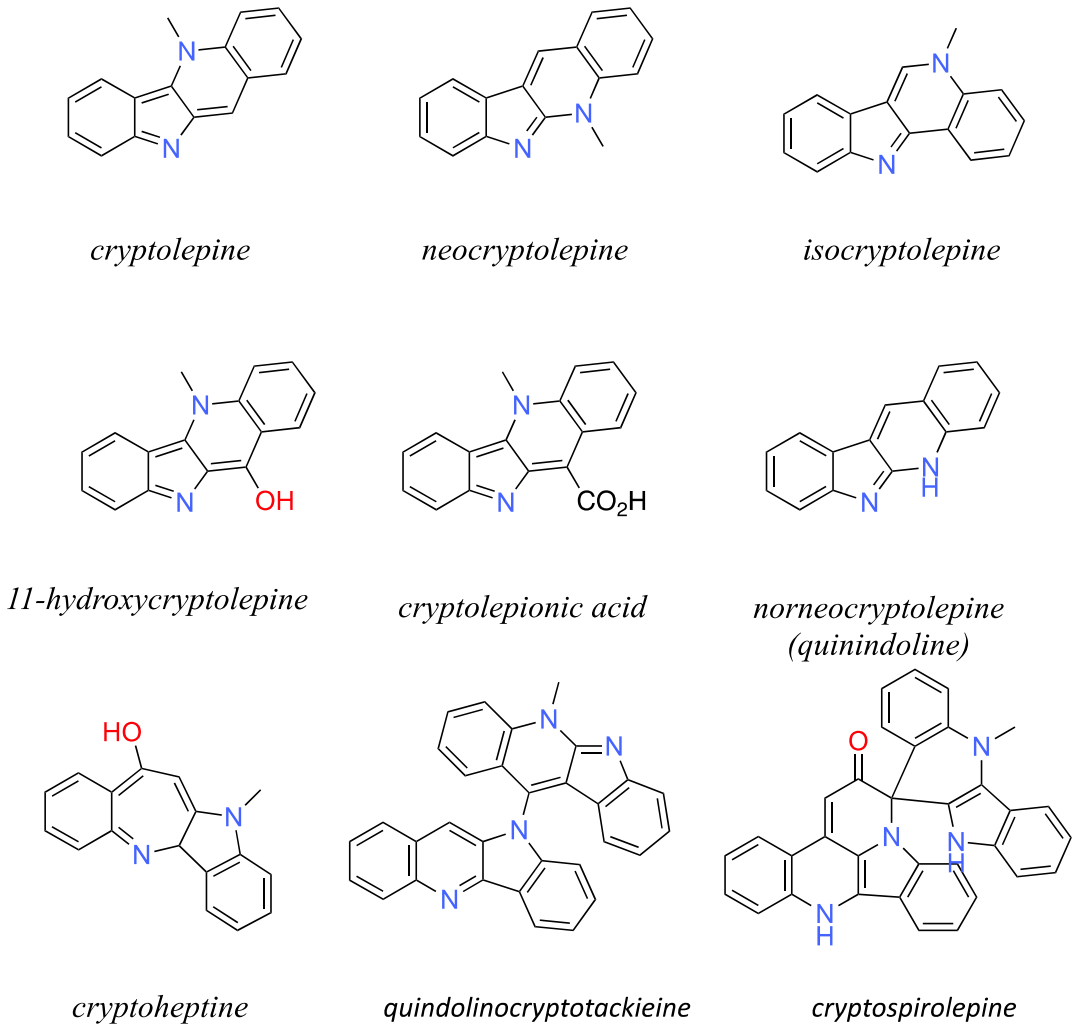


Figure 1. Alkaloids isolated from *Cryptolepis sanguinolenta*

Several methods for the synthesis of 6*H*-indolo[2,3-*b*]quinoline and its derivatives have been reported in the literature.[11] Most important among those are one-pot domino approaches some appear to be quite unique in their designs and, at the same time, usefulness of their strategies. The reaction between indole-3-carboxaldehyde and aniline resulting in directly the formation of norcryptotackieine has been described by various groups in refluxing Ph_2O,[12] employing RuY (Ru^{3+} ion-exchanged zeolite) in refluxing 1,4-dioxane,[13] or NBS under solvent-free condition,[14] and bismuth(III) salts in a microwave induced reaction.[15] Li *et al.* developed a Ru(III)-catalysed synthesis of indoloquinolines by the reaction between indoles and isoxazoles in the presence of $AgSbF_5$.[16] Facile one-pot synthesis of neocryptolepine was that published in 2011 by Seidel's group: these authors proposed the reaction between indole and 2-(methylamino)benzaldehyde in the presence of TFA under refluxing conditions in toluene.[17] An efficient and simple protocol for synthesis of indolo[2,3-*b*]quinolines by reactions of aminophenyl alcohols and indoles was described under the promotion of iron trichloride.[18] However, most of these methodologies

require higher temperature or much longer reaction times, sometimes with tedious product isolation procedures, toxicity of the catalyst or low product yields being additional impediments.

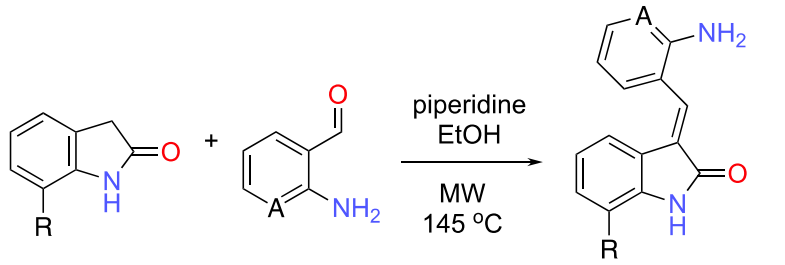
As highlighted indole itself, as well as several of its functionalized derivatives, including isatins[19] have been employed as starting materials for the preparation these indole-containing molecular frameworks, but surprisingly the easily available oxindoles have only rarely been considered as convenient starting materials.[20]

Recently we have shown that oxindoles can be used for the preparation of new chromeno[2,3-*b*]indole tetracycles by the reaction of 2'-hydroxyacetophenones or salicylaldehyde derivates. Under the harsh reaction conditions, the initially formed Knoevenagel adducts lost water, giving rise to the formation of ring closed tetracyclic products.[21]

We have envisaged the analogous reaction can be performed between oxindoles and various 2-aminobenzaldehydes. As a result of this study herein, we report a fast, efficient, clean and operationally highly simplified microwave-mediated one-pot method for the synthesis of 6*H*-indolo[2,3-*b*]quinolines and some new heterocycles with related structure.

RESULTS AND DISCUSSION

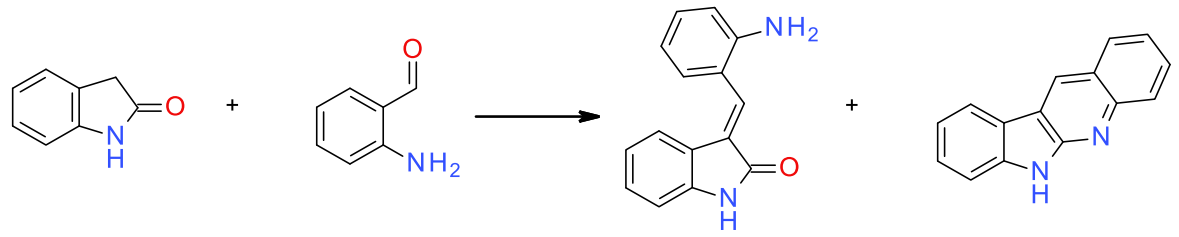
The reaction of 2-aminobenzaldehyde **2a** with oxindole **1a** is already known under classical Knoevenagel conditions (ethanol, catalytic piperidine, heating) and the formation of the expected 3-[(2-aminophenyl)methylene]indolin-2-one **3a** is described.[22] This and some closely analog reactions were easily reproduced under microwave conditions in our hand. Using the optimal conditions described earlier by us for such reactions[23] after a 30 min at 145 °C after cooling the expected products (**3a-c**) were filtered out from the reaction mixture with an acceptable yield in good purity (Scheme 1).



Scheme 1. The reaction of oxindole and 2-aminobenzaldehyde

To test our initial idea we selected the reaction of 2-aminobenzaldehyde **2a** with oxindole **1a** for optimization, with the hope to achieve the formation of the norneocryptolepine **4a** in a single step. Using our harsh conditions described for the synthesis of chromeno[2,3-*b*]indoles[21] (Table 1, Entry 1).

Table 1. *Screening of reaction conditions*



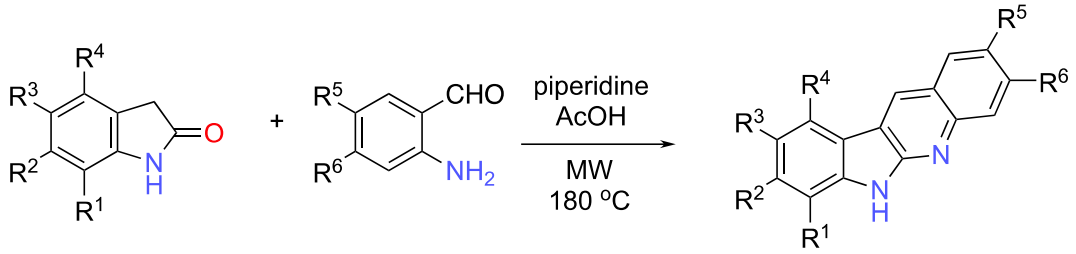
1a **2a** **3a** **4a**

Entry	**Solvent**	**Catalyst**	**Temp (°C)[a]**	**time**	**1a** (%)[b]	**2a** (%)	**3a** (%)	**4a** (%)
1	mesytilene	$BuNH_2$	reflux	1 day	60	0	5	11
2	EtOH	piperidine	145	30 min	20	13	38	4
			180	45 min	12	7	37	29
3	*n*BuOH	piperidine	145	30 min	33	22	33	2
			180	45 min	16	5	31	34
4	H_2O	piperidine	145	30 min	12	5	74	0
			180	45 min	13	8	9	53
5	CF_3Ph	piperidine	145	30 min	34	18	29	5
			180	45 min	19	0	22	46
6	DCE	piperidine	145	30 min	53	25	5	0
			180	45 min	19	0	0	42
7	DMF	piperidine	145	30 min	33	34	19	2
			180	45 min	12	19	34	7
8	AcOH	none	145	30 min	20	3	12	52
			180	45 min	26	0	11	41
9	**AcOH**	**piperidine**	145	30 min	23	4	17	43
			180	**45 min**	**12**	**0**	**8**	**76**
10	AcOH	$BuNH_2$	145	30 min	29	3	13	42
			180	45 min	20	0	7	62
11	AcOH	DBU	145	30 min	23	4	12	51
			180	45 min	13	0	5	54
12	AcOH	Et_3N	145	30 min	29	4	14	44
			180	45 min	19	0	6	66

a) Reactions conducted in an Anton-Paar MW reactor except of Entry 1; b) HPLC yields.

The formation of the expected product was observed in HPLC-MS, however, the fast decomposition of the heat sensitive 2-aminobenzaldehyde (**2a**) did not allow the further progress of the reaction. The switch from conventional heating to the microwave reactor significantly changed the possibilities, even at higher temperature in most cases some part of this reagent remained intact. Interestingly in alcohols (entries 2 and 3) we have observed only relatively low conversion in the ring closing step while in contrast in water a medium yield was observed at higher temperature (Entry 4).

Table 2. *One-pot preparation of compounds* **4a-s**



1a-q **2a-d** **4a-s**

Entry	Oxindole	R^1	R^2	R^3	R^4	Aldehyde	R^5	R^6	Product	Yield (%)
1.	**1a**	H	H	H	H	**2a**	H	H	**4a**	76
2.	**1b**	**Cl**	H	H	H	**2a**	H	H	**4b**	89
3.	**1c**	H	**CF_3**	H	H	**2a**	H	H	**4c**	79
4.	**1d**	H	**F**	H	H	**2a**	H	H	**4d**	75
5.	**1e**	H	**Br**	H	H	**2a**	H	H	**4e**	81
6.	**1f**	H	H	H	**Br**	**2a**	H	H	**4f**	86
7.	**1g**	H	H	**Cl**	H	**2a**	H	H	**4g**	63
8.	**1h**	**OMe**	H	H	H	**2b**	H	**Br**	**4h**	92
9.	**1h**	**OMe**	H	H	H	**2c**	**OCH_2O**		**4i**	90
10.	**1i**	H	H	**OMe**	H	**2a**	H	H	**4j**	67
11.	**1j**	H	H	H	**Cl**	**2a**	H	H	**4k**	73
12.	**1k**	**OEt**	H	H	H	**2a**	H	H	**4l**	43
13.	**1l**	**OMe**	H	**Br**	H	**2a**	H	H	**4m**	72
14.	**1m**	H	**SO_2Me**	H	H	**2a**	H	H	**4n**	77
15.	**1n**	H	H	**NO_2**	H	**2a**	H	H	**4o**	88
16.	**1o**	**CF_3**	H	H	H	**2b**	H	**Br**	**4p**	72
17.	**1p**	H	H	H	**F**	**2d**	**Br**	H	**4q**	70
18.	**1g**	H	H	**Cl**	H	**2c**	**OCH_2O**		**4r**	69
19.	**1q**	**Br**	H	H	H	**2b**	H	**Br**	**4s**	85

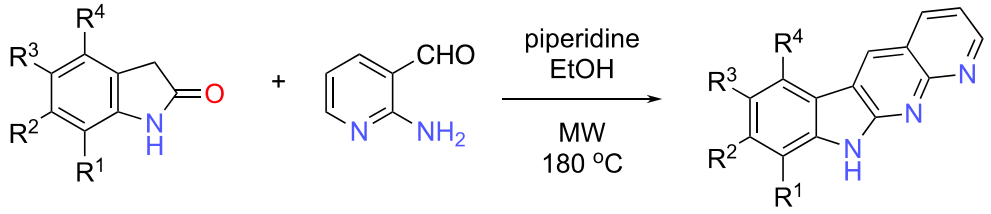
Switching to nonpolar or polar-aprotic solvents did not increase the yield of the expected product and finally in acetic acid in the presence of base the formation of the desired product become dominant.

Finally, we have selected to use the acetic acid/piperidine pair at 180 °C as in this case after dilution with water the expected product **4a** readily crystallized and it was isolated after a simple filtration in excellent purity and good yield.

Next, a series of oxindoles **1a-q** and 2-aminobenzaldehydes **2a-d** were examined for the tandem Knoevenagel condensation/cyclization reaction under these optimized conditions (Table 2). Most of the reactions were carried out smoothly to give the corresponding 6*H*-indolo[2,3-*b*]quinolines **4a-s** and moderate to satisfactory yields were obtained with various substituents on the reactants. Electron-donating or -withdrawing substituents at both the indole and aldehyde moieties were also tolerated to give the quinindolines **4** after a simple filtration from the reaction mixture.

On the basis of the above observations we have considered the synthesis of various aza-norcryptotackieine derivatives using different *N*-heterocycles as starting materials (Table 3). Several substituted derivatives of 10*H*-indolo[2,3-*b*][1,8]naphthyridine core have been already described earlier to show specific inhibition of benzodiazepine receptors[24] while other showed anticancer properties[25] when acetylamino moiety was placed at position 3, but their synthesis were rather complicated and not tolerant for many type of functional groups. To obtain this heterocyclic ring system we have used the 2-aminopyridine-3-carbaldehyde **5** in the

Table 3. *One-pot preparation of compounds* **6a-i**



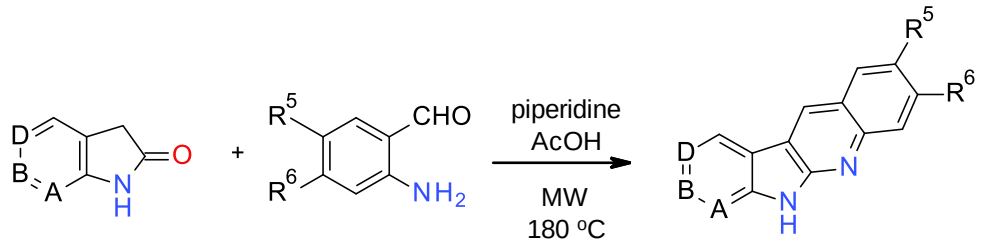
1 **5** **6**

Entry	Oxindole	R^1	R^2	R^3	R^4	Product	Yield (%)
1.	**1a**	H	H	H	H	**6a**	81
2.	**1b**	**Cl**	H	H	H	**6b**	80
3.	**1c**	H	**CF_3**	H	H	**6c**	89
4.	**1g**	H	H	**Cl**	H	**6d**	74
5.	**1p**	H	H	H	**F**	**6e**	60
6.	**1r**	**Cl**	H	H	**Cl**	**6f**	70
7.	**1s**	**Ph**	H	H	H	**6g**	38
8.	**1t**	H	H	**Me**	H	**6h**	48
9.	**1u**	**Cl**	H	H	**Br**	**6i**	70

reaction with several oxindoles (**1a-c, g, p-u**). As can be seen from the results summarized in Table 3 all the positions and substituents were well tolerated the compounds obtained in good yields again after simple filtration from the diluted reaction mixture.

Next, to expand the synthetic utility of this strategy, we have prepared a variety of new pyrido-pyrrolo[2,3-*b*]quinolines **8** starting from the commercially available azaoxindoles (Table 4). Gratifyingly, it was found that the 5,6 and 7-azaoxindoles **7a-c** with 2-aminobenzaldehydes **2a-e** under the optimized conditions rapidly converted into the desired tetracyclic products **8**, however, in the case of 6-azaoxindoles the yield was rather poor, as several unidentified polymeric by-product formed during the reaction (Entries 6-8).

Table 4. *One-pot preparation of compounds* **8a-k**

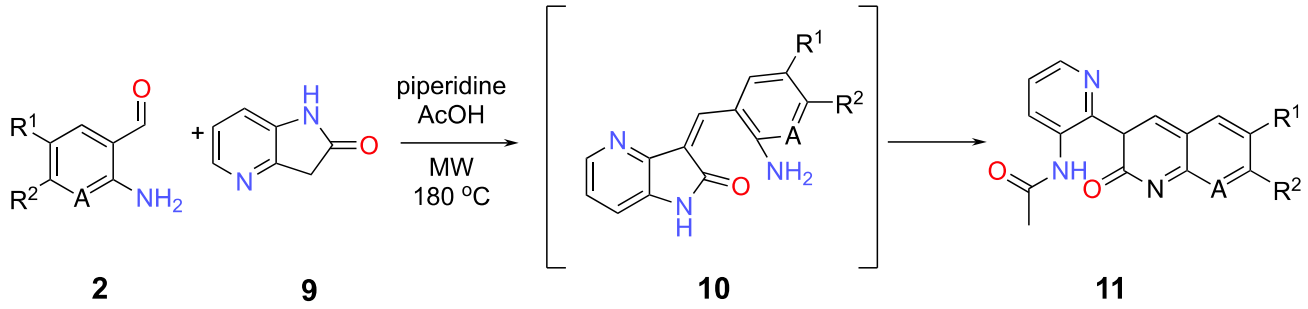


7 **2** **8**

Entry	Oxindole	A	B	D	Aldehyde	R^5	R^6	Product	Yield
1	**7a**	**N**	CH	CH	**2b**	H	**Br**	**8a**	70
2	**7a**	**N**	CH	CH	**2d**	**Br**	H	**8b**	67
3	**7a**	**N**	CH	CH	**2c**	**OCH_2O**		**8c**	63
4	**7a**	**N**	CH	CH	**2a**	H	H	**8d**	69
5	**7a**	**N**	CH	CH	**2e**	H	**OMe**	**8e**	60
6	**7b**	CH	**N**	CH	**2c**	**OCH_2O**		**8f**	28
7	**7b**	CH	**N**	CH	**2d**	**Br**	H	**8g**	31
8	**7b**	CH	**N**	CH	**2b**	H	**Br**	**8h**	34
9	**7c**	CH	CH	**N**	**2a**	H	H	**8i**	71
10	**7c**	CH	CH	**N**	**2b**	H	**Br**	**8j**	80
11	**7c**	CH	CH	**N**	**2c**	**OCH_2O**		**8k**	59

For our surprise in the reaction of 4-azaoxindole **9** with various 2-amino-arylaldehides **2** we could isolate in high yields the 3-pyridyl-quinoline derivatives (**11a-e**), instead of the formation of the expected tetracyclic products (Table 5). In spite of that the Knoevenagel reactions of **9** well described[26] to yield the adducts like **10** along with other reactions of **9**, but this type of ring opening of 4-azaoxindoles has never been observed before.

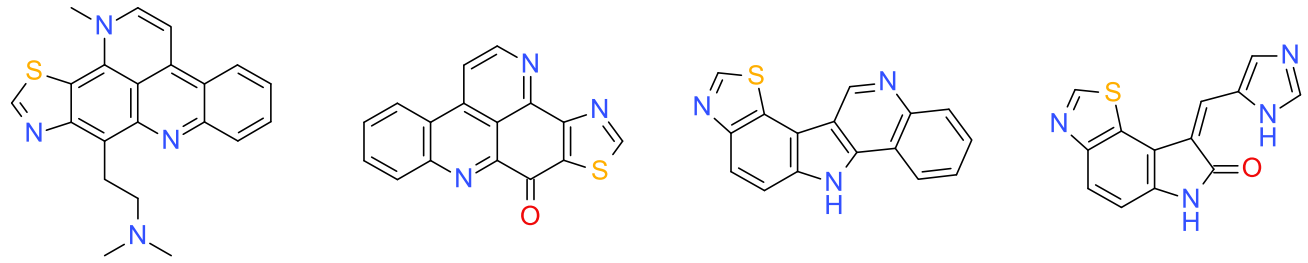
Table 5. *One-pot preparation of compounds* **11a-e**



2 **9** **10** **11**

Entry	Aldehyde	A	R^1	R^2	Product	Yield (%)
1	**2a**	CH	H	H	**11a**	70
2	**2b**	CH	H	**Br**	**11b**	60
3	**2c**	CH	**OCH_2O**		**11c**	51
4	**2d**	CH	**Br**	H	**11d**	67
5	**5**	**N**	H	H	**11e**	58

Numerous alkaloids known to have ring systems containing thiazoloheterocycles (mainly marine alkaloids *e.g.* dercitine[27] or kuanoamine[28]) and in addition in the recent years synthetic derivatives with thiazoloindolo[29] or thiazoloindolo[3,2-*c*]quinoline skeleton[30] has been described to show interesting biological activities.

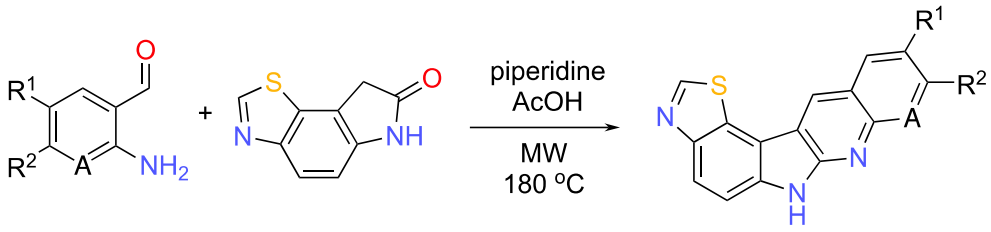


dercitine ***cytotoxic*** | ***kuanoamine A*** ***antiprotazoal*** | ***thiazoloindolo[3,2-c]quinoline*** ***topoisomerase inhibitor*** | ***imoxin*** ***kinase inhibitor***

Figure 2. Biologically active thiazolo-heterocycles

Based on that diversity, we have envisaged the use readily available 6,8-dihydropyrrolo[2,3-*g*][1,3]benzothiazol-7-one (**12**)[31] in the anellation reaction explored in this paper to generate hitherto unknown heterocycles potentially with a similar pharmacological properties. To our delight these reactions also run smoothly without exception in all cases the expected product **13** was isolated again with a simple filtration from the reaction mixture in high yields.

Table 6. *One-pot preparation of compounds* **13a-e**



2a-d, 5 **12** **13**

Entry	Aldehyde	A	R^1	R^2	Product	Yield (%)
1.	**2a**	CH	H	H	**13a**	78
2.	**2b**	CH	H	**Br**	**13b**	74
3.	**2c**	CH	**OCH_2O**		**13c**	71
4.	**2d**	CH	**Br**	H	**13d**	64
5.	**5**	**N**	H	H	**13e**	87

The mechanism of this kind of domino Knoevenagel condensation/intramolecular ring closure has been partly described by us.[21] On the basis of these and the new experimental results a tentative mechanism was delineated in Figure 3. The intermediate formed in the Knoevenagel condensation in its right isomeric form deprotonated at the applied high temperature by the effect of base present in the reaction mixture. Then the

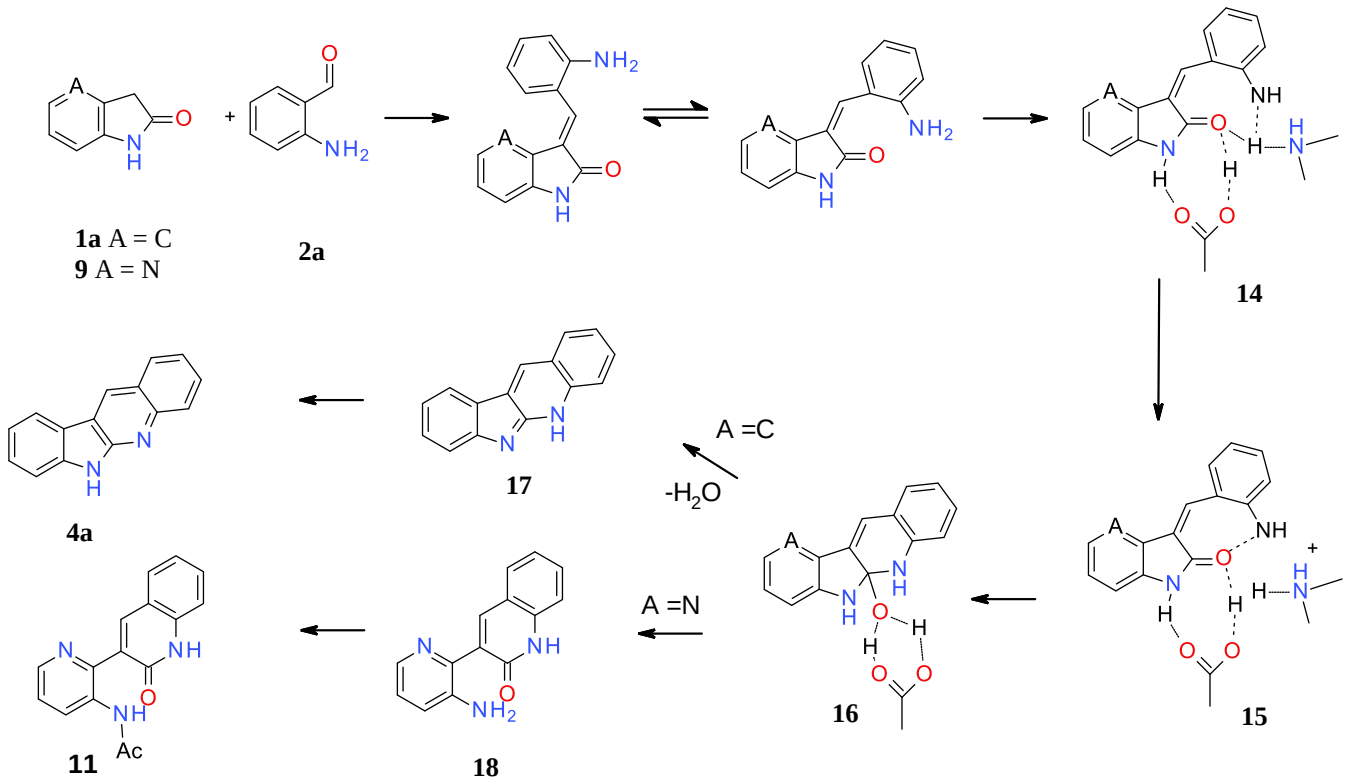


Figure 3. Proposed reaction mechanism

cyclization took place by the intramolecular nucleophilic attack on the indolinone carbonyl group. In almost all cases the water elimination from intermediate **16** occurs followed by the formation of the most stable fully aromatic heterocyclic system. This type of ring closure was described first, when the preformed 3-[(2-aminophenyl)methylidene]-1,3-dihydro-2*H*-indol-2-one **3a** was heated at 260 °C in a Kugelrohr apparatus at 0.005 Torr and the formed quinindoline **4a** was isolated by sublimation in low yield.[20a] Recently an improved procedure has been published by Kadam *et al.*,[20b] however, this two-steps approach still suffers by the use long reaction time (48 hours), strongly acidic conditions and problematic work-up.

In our hand, in one particular case instead of the water elimination from intermediate **16** the carbon-nitrogen bond of the original indolinone fragment was cleaved and the primarily formed amino-quinoline **18** is acetylated by the excess of acetic acid giving rise the formation of the isolated quinolinones **11**.

In conclusion, we have provided a one-pot preparation of structurally diverse linear (aza)indoloquinolines by sequential Knoevenagel condensation, intramolecular cyclization process starting from simple oxindole and 2-amino-arylaldheydes under microwave conditions. This method offers a practical and ideal strategy with high atom and step economy to the synthesis of wide range of the analogues of norneocryptolepine and its aza derivatives.

EXPERIMENTAL

General considerations

The starting materials were purchased from commercial sources. IR spectra were recorded with a Bruker Tensor 27 FT-IR spectrophotometer. ^{1}H, ^{13}C, NMR spectra were recorded in DMSO-d_6 with a Bruker Avance III. spectrometer operating at 500 MHz and 125 MHz respectively (^{1}H-, DEPTQ-, HSQC-, HMBC-NMR). High-resolution MS spectra were measured by Agilent 6230 TOF LC/MS spectrometer. All reagents and solvents were purchased and used without further purification.

General procedure for the synthesis of (3*E*)-3-[(2-aminoaryl)methylidene]-1,3-dihydro-2*H*-indol-2-ones: The corresponding oxindole (1 mmol) and 2-amino-arylaldehyde (1 mmol) was suspended in EtOH (4 mL) and piperidine (0.05 mL, 0.5 mmol) was added. The reaction mixture was irradiated in an *Anton-Paar* microwave reactor for 30 min at 145 ºC. After cooling the formed precipitate was collected by filtration, washed with EtOH and dried *in vacuo* to yield the title products.

(3*E*)-3-[(2-Aminophenyl)methylidene]-1,3-dihydro-2*H*-indol-2-one (3a): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 10.51 (s, 1H, NH), 7.55 (s, 1H, CH=), 7.46 (d, 1H, *J* = 7.6 Hz, H-4), 7.41 (d, 1H, *J* = 7.8 Hz, Ph-6'H), 7.18 (t, 1H, *J* = 7.6 Hz, H-6), 7.15 (t, 1H, *J* = 7.8 Hz, Ph-4'H), 6.85 (d, 1H, *J* = 7.6 Hz, H-7), 6.83 (t, 1H, *J* = 7.6 Hz, H-5), 6.78 (d, 1H, *J* = 7.8 Hz , Ph-3'H), 6.62 (t, 1H, *J* = 7.8 Hz, Ph-5'H), 5.52 (s, 2H, NH_2). ^{13}C-

NMR (125 MHz, DMSO-d_6): δ 169.4 (q, C-2), 148.4 (q, Ph-2'C), 142.8 (q, C-7*a*), 133.8 (CH=), 131.6 (CH, Ph-4'C), 129.8 (CH, C-6), 129.7 (CH, Ph-6'C), 126.4 (q, C-3), 122.0 (q, C-3*a*), 122.8 (CH, C-4), 121.3 (CH, C-5), 118.3 (q, Ph-1'C), 116.1 (CH, Ph-3'C), 115.9 (CH, Ph-5'C), 110.2 (CH, C-7). IR (KBr, cm^{-1}): 3122, 1697, 1599, 1458, 1334, 1230, 1203, 1155. HRMS $[M+H]^+$ found = 237.1024, $C_{15}H_{13}N_2O$ required 237.1028.

(3*E*)-3-[(2-Aminophenyl)methylidene]-7-chloro-1,3-dihydro-2*H*-indol-2-one (3b): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 10.93 (s, 1H, NH), 7.65 (s, 1H, CH=), 7.42 (d, 1H, *J* = 7.9 Hz, H-4), 7.40 (d, 1H, *J* = 7.8 Hz, Ph-6'H), 7.26 (d, 1H, *J* = 7.9 Hz, H-6), 7.17 (t, 1H, *J* = 7.8 Hz, Ph-4'H), 6.88 (t, 1H, *J* = 7.9 Hz, H-5), 6.78 (d, 1H, *J* = 7.8 Hz, Ph-3'H), 6.62 (t, 1H, *J* = 7.8 Hz, Ph-5'H), 5.61 (s, 2H, NH_2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 169.3 (q, C-2), 148.7 (q, Ph-2'C), 140.1 (q, C-7*a*), 135.8 (CH=), 132.0 (CH, Ph-4'C), 129.9 (CH, Ph-6'C), 129.3 (CH, C-6), 125.8 (q, C-3), 124.0 (q, C-7), 122.5 (CH, C-5), 121.3 (CH, C-4), 117.9 (q, Ph-1'C), 116.2 (CH, Ph-3'C), 116.0 (CH, Ph-5'C), 114.5 (q, C-3*a*). IR (KBr, cm^{-1}): 3130, 1699, 1633, 1610, 1438, 1323, 1228, 1213, 1195, 1132. HRMS $[M+H]^+$ found = 271.0634, $C_{15}H_{12}ClN_2O$ required 271.0638.

(3*E*)-3-[(2-Aminopyridin-3-yl)methylidene]-7-chloro-1,3-dihydro-2*H*-indol-2-one (3c): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 10.99 (s, 1H, NH), 8.08 (dd, 1H, *J* = 1.8 and 4.8 Hz, Py-6'H), 7.74 (dd, 1H, *J* = 1.8 and = 7.5 Hz, Py-4'H), 7.53 (s, 1H, CH=), 7.29 (d, 1H, *J* = 7.9 Hz, H-6), 7.29 (d, 1H, *J* = 7.9 Hz, H-4), 6.89 (t, 1H, *J* = 7.9 Hz, H-5), 6.66 (dd, 1H, *J* = 4.8 and 7.5 Hz, Py-5'H), 6.35 (s, 2H, NH_2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 169.0 (q, C-2), 158.0 (q, Py-2'C), 151.0 (CH, Py-6'C), 140.4 (q, C-7*a*), 138.0 (CH, Py-4'C), 134.1 (CH=), 129.6 (CH, C-6), 127.5 (q, C-3), 123.7 (q, C-7), 122.7 (CH, C-5), 121.4 (CH, C-4), 114.7 (q, Py-3'C), 112.9 (q, C-3*a*), 112.4 (CH, Py-5'C). IR (KBr, cm^{-1}): 3433, 1700, 1608, 1585, 1562, 1471, 1438, 1273, 1226, 1211, 1128. HRMS $[M+H]^+$ found = 272.0582, $C_{14}H_{11}ClN_3O$ required 272.0590.

General procedure the microwave mediated synthesis of indoloquinoline derivatives: The corresponding oxindole (1 mmol) and 2-amino-arylaldehyde (1 mmol) was suspended in acetic acid (4 mL) and piperidine (0.05 mL, 0.5 mmol) was added. The reaction mixture was irradiated in an *Anton-Paar* microwawe reactor for 60 min at 180 °C. After cooling the reaction mixture was diluted with water (30 mL) and the formed precipitate was collected by filtration, washed with excess of water and EtOH and dried *in vacuo* to yield the title products.

6*H*-Indolo[2,3-*b*]quinoline (4a): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.69 (s, 1H, NH), 9.05 (s, 1H, H-11), 8.26 (d, 1H, *J* = 7.7 Hz, H-10), 8.11 (d, 1H, *J* = 8.0, H-1), 7.98 (d, 1H, *J* = 8.0 Hz, H-4), 7.72 (t, 1H, *J* = 8.0 Hz, H-3), 7.53 (t, 1H, *J* = 7.7, H-8), 7.49 (d, 1H, *J* = 7.7 Hz, H-7), 7.48 (t, 1H, *J* = 8.0 Hz, H-2), 7.27 (t, 1H, *J* = 7.7 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.3 (q, C-5*a*), 146.7 (q, C-4*a*), 141.9 (q, C-6*a*), 129.1 (2 x CH, C-1 and C-3), 128.7 (CH, C-8), 128.0 (CH, C-11), 127.5 (CH, C-4), 124.1 (q, C-11*a*),

123.2 (CH, C-2), 122.3 (CH, C-10), 120.7 (q, C-10*a*), 120.1 (CH, C-9), 118.3 (q, C-10*b*), 111.4 (CH, C-7). IR (KBr, cm^{-1}): 3089, 1616, 1579, 1491, 1475, 1462, 1408, 1232. HRMS $[M+H]^+$ found = 219.0919, $C_{15}H_{11}N_2$ required 219.0922.

7-Chloro-6*H*-indolo[2,3-*b*]quinoline (4b): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.15 (s, 1H, NH), 9.12 (s, 1H, H-11), 8.24 (d, 1H, *J* = 7.8 Hz, H-10), 8.12 (d, 1H, *J* = 8.1 Hz, H-1), 8.02 (d, 1H, *J* = 8.1 Hz, H-4), 7.76 (t, 1H, *J* = 8.1 Hz, H-3), 7.60 (d, 1H, *J* = 7.8 Hz, H-8), 7.51 (t, 1H, *J* = 8.1 Hz, H-2), 7.27 (t, 1H, *J* = 7.8 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.4 (q, C-5*a*), 147.1 (q, C-4*a*), 139.0 (q, C-6*a*), 129.7 (CH, C-3), 129.3 (CH, C-1), 129.1 (CH, C-11), 128.1 (CH, C-8), 127.6 (CH, C-4), 124.3 (q, C-11*a*), 123.7 (CH, C-2), 122.9 (q, C-10*a*), 121.2 (CH, C-9), 121.0 (CH, C-10), 118.2 (q, C-10*b*), 115.8 (q, C-7). IR (KBr, cm^{-1}): 3120, 1612, 1579, 1489, 1404, 1226, 1178, 1130; HRMS $[M+H]^+$ found = 253.0529, $C_{15}H_{10}ClN_2$ required 253.0532.

8-Trifluoromethyl-6*H*-indolo[2,3-*b*]quinoline (4c):^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.05 (s, 1H, NH), 9.25 (s, 1H, H-11), 8.50 (d, 1H, *J* = 8.0 Hz, H-10), 8.16 (d, 1H, *J* = 8.1 Hz, H-1), 8.02 (d, 1H, *J* = 8.1 Hz, H-4), 7.79 (t, 1H, *J* = 8.1 Hz, H-3), 7.76 (br.s, 1H, H-7), 7.61 (d, 1H, *J* = 8.0 Hz, H-9), 7.53 (t, 1H, *J* = 8.1 Hz, H-2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.7 (q, C-5*a*), 147.5 (q, C-4*a*), 141.3 (q, C-6*a*), 130.1 (CH, C-11), 130.0 (CH, C-3), 129.4 (CH, C-1), 128.4 (q, C-8), 127.7 (CH, C-4), 125.2 (q, CF_3), 124.3 (q, C-11*a*), 124.1 (q, C-10*a*), 123.7 (CH, C-2), 123.2 (CH, C-10), 117.1 (q, C-10*b*), 116.5 (CH, C-9), 108.0 (CH, C-7). IR (KBr, cm^{-1}): 3080, 1620, 1581, 1498, 1483, 1448, 1322, 1234, 1113. HRMS $[M+H]^+$ found = 287.0792, $C_{16}H_{10}F_3N_2$ required 287.0796.

8-Fluoro-6*H*-indolo[2,3-*b*]quinoline (4d): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.84 (s, 1H, NH), 9.04 (s, 1H, H-11), 8.29 (dd, 1H, *J* = 9.0 Hz and 5.5 Hz, H-10), 8.10 (d, 1H, *J* = 8.3 Hz, H-1), 7.98 (d, 1H, *J* = 8.3 Hz, H-4), 7.73 (t, 1H, *J* = 8.3 Hz, H-3), 7.49 (t, 1H, *J* = 8.3 Hz, H-2), 7.25 (dd, 1H, *J* = 9.7 Hz and 2.4 Hz, H-7), 7.10 (td, 1H, *J* = 9.0 Hz and 2.4 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 162.9 (q, *J* = 245 Hz, C-8), 153.8 (q, C-5*a*), 146.4 (q, C-4*a*), 143.0 (q, C-6*a*), 129.2 (CH, C-3), 129.1 (CH, C-1), 127.8 (CH, C-11), 127.6 (CH, C-4), 124.3 (q, C-11*a*), 124.0 (CH, C-10), 123.5 (CH, C-2), 117.8 (q, C-10*b*), 117.5 (q, C-10*a*), 107.8 (CH, C-9), 98.4 (CH, C-7). IR (KBr, cm^{-1}): 3152, 1616, 1481, 1230, 1147. HRMS $[M+H]^+$ found = 237.0822, $C_{15}H_{10}FN_2$ required 237.0828.

8-Bromo-6*H*-indolo[2,3-*b*]quinoline (4e): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.84 (s, 1H, NH), 9.10 (s, 1H, H-11), 8.22 (d, 1H, *J* = 8.3 Hz, H-10), 8.11 (d, 1H, *J* = 8.1 Hz, H-1), 7.99 (d, 1H, *J* = 8.1 Hz, H-4), 7.74 (t, 1H, *J* = 8.1 Hz, H-3), 7.64 (d, 1H, *J* = 1.7 Hz, H-7), 7.50 (t, 1H, *J* = 8.1 Hz, H-2), 7.43 (dd, 1H, *J* = 8.3 Hz and 1.7 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.3 (q, C-5*a*), 146.9 (q, C-4*a*), 143.0 (q, C-6*a*), 129.5 (CH, C-3), 129.2 (CH, C-1), 128.7 (CH, C-11), 127.6 (CH, C-4), 124.3 (q, C-11*a*), 124.1 (CH, C-10), 123.6 (CH, C-2), 123.0 (CH, C-9), 121.4 (q, C-8), 120.0 (q, C-10*a*), 117.6 (q, C-10*b*), 114.0 (CH, C-7). IR (KBr, cm^{-1}): 3109, 1608, 1471, 1444, 1406, 1321, 1226, 1057. HRMS $[M+H]^+$ found = 297.0021,

$C_{15}H_{10}BrN_2$ required 297.0027.

10-Bromo-6*H*-indolo[2,3-*b*]quinoline (4f): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.08 (s, 1H, NH), 9.41 (s, 1H, H-11), 8.24 (d, 1H, *J* = 8.1 Hz, H-1), 8.00 (d, 1H, *J* = 8.1 Hz, H-4), 7.78 (t, 1H, *J* = 8.1 Hz, H-3), 7.55-7.50 (m, 2H, H-2 and H-7), 7.50-7.46 (m, 2H, H-8 and H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 152.8 (q, C-5*a*), 146.8 (q, C-4*a*), 143.3 (q, C-6*a*), 129.9 (2 x CH, C-3 and C-11), 129.8 (CH, C-8), 129.7 (CH, C-1), 127.4 (CH, C-4), 123.8 (CH, C-9), 123.8 (q, C-11*a*), 123.6 (CH, C-2), 119.5 (q, C-10*a*), 117.7 (q, C-10*b*) 117.4 (q, C-10), 110.7 (CH, C-7). IR (KBr, cm^{-1}): 3057, 1606, 1485, 1437, 1400, 1303, 1255, 1161, 1126. HRMS $[M+H]^+$ found = 297.0021, $C_{15}H_{10}BrN_2$ required 297.0027.

9-Chloro-6*H*-indolo[2,3-*b*]quinoline (4g): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.85 (s, 1H, NH), 9.13 (s, 1H, H-11), 8.39 (d, 1H, *J* = 2.2 Hz, H-10), 8.10 (d, 1H, *J* = 8.1 Hz, H-1), 7.99 (d, 1H, *J* = 8.1 Hz, H-4), 7.75 (t, 1H, *J* = 8.1 Hz, H-3), 7.55 (dd, 1H, *J* = 8.5 and 2.2 Hz, H-8), 7.52-7.48 (m, 2H, H-2 and H-7). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.4 (q, C-5*a*), 147.1 (q, C-4*a*), 140.4 (q, C-6*a*), 129.6 (CH, C-3), 129.3 (CH, C-1), 129.2 (CH, C-11), 128.4 (CH, C-8), 127.6 (CH, C-4), 124.3 (q, C-11*a*), 124.1 (q, C-9), 123.5 (CH, C-2), 122.3 (q, C-10a), 122.1 (CH, C-10), 117.5 (q, C-10*b*), 112.9 (CH, C-7). IR (KBr, cm^{-1}): 3087, 1614, 1583, 1483, 1460, 1450, 1394, 1278, 1253, 1230, 1066. HRMS $[M+H]^+$ found = 253.0528, $C_{15}H_{10}ClN_2$ required 253.0532.

3-Bromo-7-methoxy-6*H*-indolo[2,3-*b*]quinoline (4h): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.97 (s, 1H, NH), 9.08 (s, 1H, H-11), 8.16 (d, 1H, *J* = 2.0 Hz, H-4), 8.07 (d, 1H, *J* = 8.7 Hz, H-1), 7.85 (d, 1H, *J* = 7.7 Hz, H-10), 7.61 (dd, 1H, *J* = 8.7 and 2.0 Hz, H-2), 7.24 (t, 1H, *J* = 7.7 Hz, H-9), 7.19 (d, 1H, *J* = 7.7 Hz, H-8), 3.99 (s, 3H, *O*CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.6 (q, C-5*a*), 147.4 (q, C-4*a*), 145.9 (q, C-7), 131.7 (q, C-6*a*), 131.0 (CH, C-1), 129.2 (CH, C-4), 128.4 (CH, C-11), 126.2 (CH, C-2), 122.8 (q, C-11*a*), 122.4 (q, C-3), 121.6 (q, C-10*a*), 121.2 (CH, C-9), 119.1 (q, C-10*b*), 114.6 (CH, C-10), 110.3 (CH, C-8), 56.2 (CH_3). IR (KBr, cm^{-1}): 3124, 1581, 1506, 1460, 1396, 1273, 1259, 1220, 1093, 1064, 1010. HRMS $[M+H]^+$ found = 327.0128, $C_{16}H_{12}BrN_2O$ required 327.0133.

7-Methoxy-2*H*,6*H*-[1,3]dioxolo[4,5-*g*]indolo[2,3-*b*]quinoline (4i): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.63 (s, 1H, NH), 8.81 (s, 1H, H-11), 7.75 (d, 1H, *J* = 7.9 Hz, H-10), 7.45 (s, 1H, H-12), 7.32 (s, 1H, H-4), 7.17 (t, 1H, *J* = 7.9 Hz, H-9), 7.10 (d, 1H, *J* = 7.9 Hz, H-8), 6.18 (s, 2H, H-2), 3.98 (s, 3H, *O*CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 152.1 (q, C-5*a*), 150.6 (q, C-3*a*), 145.8 (q, C-7), 145.4 (q, C-12*a*), 145.0 (q, C-4*a*), 130.7 (q, C-6*a*), 127.2 (CH, C-11), 121.7 (q, C-10*a*), 120.5 (CH, C-9), 120.2 (q, C-11*a*), 116.2 (q, C-10*b*), 114.0 (CH, C-10), 109.1 (CH, C-8), 104.0 (CH, C-4), 103.8 (CH, C-12), 102.1 (CH_2, C-2), 56.0 (CH_3). IR (KBr, cm^{-1}): 3270, 1587, 1496, 1462, 1388, 1278, 1255, 1230, 1193, 1033. HRMS $[M+H]^+$ found = 293.0923, $C_{17}H_{13}N_2O_3$ required 293.0926.

9-Methoxy-6*H*-indolo[2,3-*b*]quinoline (4j): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.49 (s, 1H, NH), 9.04 (s, 1H, H-11), 8.08 (d, 1H, *J* = 8.0 Hz, H-1), 7.95 (d, 1H, *J* = 8.0 Hz, H-4), 7.88 (d, 1H, *J* = 2.5 Hz, H-10),

7.70 (t, 1H, *J* = 8.0 Hz, H-3), 7.46 (t, 1H, *J* = 8.0 Hz, H-2), 7.40 (d, 1H, *J* = 8.6 Hz, H-7), 7.16 (dd, 1H, *J* = 8.6 and 2.5 Hz, H-8), 3.88 (s, 3H, *O*CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.0 (q, C-5*a*), 153.7 (q, C-9), 146.8 (q, C-4*a*), 136.3 (q, C-6*a*), 129.1 (2 x CH, C-1 and C-3), 128.1 (CH, C-11), 127.4 (CH, C-4), 123.8 (q, C-11*a*), 123.0 (CH, C-2), 121.2 (q, C-10*a*), 118.6 (q, C-10*b*), 117.1 (CH, C-8), 112.1 (CH, C-7), 105.9 (CH, C-10), 56.1 (CH_3). IR (KBr, cm^{-1}): 3091, 1489, 1460, 1390, 1213, 1159. HRMS $[M+H]^+$ found = 249.1023, $C_{16}H_{13}N_2O$ required 249.1028.

10-Chloro-6*H*-indolo[2,3-*b*]quinoline (4k): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.16 (s, 1H, NH), 9.32 (s, 1H, H-11), 8.26 (d, 1H, *J* = 8.0 Hz, H-1), 8.01 (d, 1H, *J* = 8.0 Hz, H-4), 7.79 (t, 1H, *J* = 8.0 Hz, H-3), 7.56 (t, 1H, *J* = 7.9 Hz, H-8), 7.54 (t, 1H, *J* = 8.0 Hz, H-2), 7.50 (d, 1H, *J* = 7.9 Hz, H-7), 7.34 (d, 1H, *J* = 7.9 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 152.4 (q, C-5*a*), 146.1 (q, C-4*a*), 143.1 (q, C-6*a*), 130.8 (CH, C-11), 130.1 (CH, C-3), 129.7 (2 x CH, C-1 and C-8), 129.0 (q, C-10), 126.9 (CH, C-4), 124.1 (q, C-11*a*), 123.7 (CH, C-2), 120.8 (CH, C-9), 117.9 (q, C-10*a*), 117.1 (q, C-10*b*), 110.4 (CH, C-7). IR (KBr, cm^{-1}): 3061, 1610, 1573, 1489, 1440, 1402, 1305, 1255, 1166, 1128. HRMS $[M+H]^+$ found = 253.0524, $C_{15}H_{10}ClN_2$ required 253.0532.

7-Ethoxy-6*H*-indolo[2,3-*b*]quinoline (4l): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.75 (s, 1H, NH), 9.09 (s, 1H, H-11), 8.10 (d, 1H, *J* = 7.9 Hz, H-1), 7.98 (d, 1H, *J* = 7.9 Hz, H-4), 7.84 (d, 1H, *J* = 7.6 Hz, H-10), 7.71 (t, 1H, *J* = 7.9 Hz, H-3), 7.47 (t, 1H, *J* = 7.9 Hz, H-2), 7.19 (t, 1H, *J* = 7.6 Hz, H-9), 7.15 (d, 1H, *J* = 7.6 Hz, H-8), 4.27 (q, 2H, *J* = 7.0 Hz, *O*CH_2), 1.46 (t, 3H, *J* = 7.0 Hz, CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.2 (q, C-5*a*), 146.8 (q, C-7), 144.9 (q, C-4*a*), 131.9 (q, C-6*a*), 129.1 (2 x CH, C-1 and C-3), 128.1 (CH, C-11), 127.5 (CH, C-4), 124.1 (q, C-11*a*), 123.2 (CH, C-2), 121.8 (q, C-10*a*), 120.8 (CH, C-9), 118.6 (q, C-10*b*), 114.5 (CH, C-10), 111.3 (CH, C-8), 64.4 (CH_2), 15.3 (CH_3). IR (KBr, cm^{-1}): 3267, 2970, 1618, 1587, 1504, 1402, 1379, 1296, 1255, 1215, 1095. HRMS $[M+H]^+$ found = 263.1179, $C_{17}H_{15}N_2O$ required 263.1184.

9-Bromo-7-methoxy-6*H*-indolo[2,3-*b*]quinoline (4m): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.00 (s, 1H, NH), 9.11 (s, 1H, H-11), 8.12 (d, 1H, *J* = 1.7 Hz, H-10), 8.09 (d, 1H, *J* = 7.8 Hz, H-1), 7.99 (d, 1H, *J* = 7.8 Hz, H-4), 7.74 (t, 1H, *J* = 7.8 Hz, H-3), 7.50 (t, 1H, *J* = 7.8 Hz, H-2), 7.31 (d, 1H, *J* = 1.7 Hz, H-8), 4.02 (s, 3H, *O*CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.0 (q, C-5*a*), 147.2 (q, C-4*a*), 146.5 (q, C-7), 130.6 (q, C-6*a*), 129.5 (CH, C-3), 129.2 (2 x CH, C-1 and C-11), 127.6 (CH, C-4), 124.1 (q, C-11*a*), 123.5 (CH, C-2), 122.9 (q, C-10*a*), 117.5 (q, C-10*b*), 117.2 (CH, C-10), 112.9 (CH, C-8), 112.1 (q, C-9), 56.7 (CH_3). IR (KBr, cm^{-1}): 3257, 1703, 1643,1618, 1577, 1489, 1437, 1390, 1342, 1292, 1207, 1107, 1010. HRMS $[M+H]^+$ found = 327.0128, $C_{16}H_{12}BrN_2O$ required 327.0133.

8-(Methanesulfonyl)-6*H*-indolo[2,3-*b*]quinoline (4n): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.17 (s, 1H, NH), 9.28 (s, 1H, H-11), 8.55 (d, 1H, *J* = 7.9 Hz, H-10), 7.99 (s, 1H, H-7), 8.17 (d, 1H, *J* = 7.9 Hz, H-1), 8.03 (d, 1H, *J* = 7.9 Hz, H-4), 7.82 (d, 1H, *J* = 7.9 Hz, H-9), 7.81 (t, 1H, *J* = 7.9 Hz, H-3), 7.54 (t, 1H, *J* =

7.9 Hz, H-2), 3.30 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.8 (q, C-5*a*), 147.6 (q, C-4*a*), 141.2 (q, C-6*a*), 140.2 (q, C-8), 130.5 (CH, C-11), 130.2 (CH, C-3), 129.5 (CH, C-1), 127.7 (CH, C-4), 124.9 (q, C-10*a*), 124.3 (q, C-11*a*), 123.8 (CH, C-2), 123.1 (CH, C-10), 118.4 (CH, C-9) , 117.0 (q, C-10*b*), 110.1 (CH, C-7), 44.5 (CH_3). IR (KBr, cm^{-1}): 3012, 1641, 1612, 1583, 1485, 1494, 1404, 1292, 1230, 1136. HRMS $[M+H]^+$ found = 297.0696, $C_{16}H_{13}N_2O_2S$ required 297.0697.

9-Nitro-6*H*-indolo[2,3-*b*]quinoline (4o): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.48 (s, 1H, NH), 9.37 (s, 1H, H-11), 9.29 (d, 1H, *J* = 2.4 Hz, H-10), 8.44 (dd, 1H, *J* = 8.9 Hz and 2.4 Hz, H-8), 8.14 (d, 1H, *J* = 8.0 Hz, H-1), 8.04 (d, 1H, *J* = 8.0 Hz, H-4), 7.80 (t, 1H, *J* = 8.0 Hz, H-3), 7.64 (d, 1H, *J* = 8.9 Hz, H-7), 7.57 (t, 1H, *J* = 8.0 Hz, H-2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.0 (q, C-5*a*), 147.3 (q, C-4*a*), 146.1 (q, C-9), 140.9 (q, C-6*a*), 130.5 (CH, C-3), 130.4 (CH, C-11), 129.5 (CH, C-1), 127.8 (CH, C-4), 124.5 (q, C-11*a*), 124.4 (CH, C-8), 124.2 (CH, C-2), 120.9 (q, C-10*a*), 119.1 (CH, C-10), 117.7 (q, C-10*b*), 111.5 (CH, C-7). IR (KBr, cm^{-1}): 3089, 1614, 1585, 1515, 1481, 1460, 1334, 1298, 1265, 1230, 1182, 1124, 1080. HRMS $[M+H]^+$ found = 264.0770, $C_{15}H_{10}N_3O_2$ required 264.0773.

3-Bromo-7-(trifluoromethyl)-6*H*-indolo[2,3-*b*]quinoline (4p): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.40 (s, 1H, NH), 9.25 (s, 1H, H-11), 8.59 (d, 1H, *J* = 7.8 Hz, H-10), 8.22 (d, 1H, *J* = 2.0 Hz, H-4), 8.13 (d, 1H, *J* = 8.7 Hz, H-1), 7.87 (d, 1H, *J* = 7.8 Hz, H-8), 7.68 (dd, 1H, *J* = 8.7 and 2.0 Hz, H-2), 7.46 (t, 1H, *J* = 7.8 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.3 (q, C-5*a*), 147.8 (q, C-4*a*), 137.7 (q, C-6*a*), 131.3 (CH, C-1), 129.4 (2 x CH, C-4 and C-11), 127.0 (CH, C-2), 126.6 (CH, C-10), 125.5 (CH, C-8), 124.6 (q, CF_3), 123.2 (2 x q, C-3 and C-11*a*), 122.8 (q, C-10*a*), 120.3 (CH, C-9), 117.5 (q, C-10*b*), 112.5 (q, C-7). IR (KBr, cm^{-1}): 3439, 1614, 1442, 1340, 1305, 1224, 1176, 1049. HRMS $[M+H]^+$ found = 364.9897, $C_{16}H_9BrF_3N_2$ required 364.9901.

2-Bromo-10-fluoro-6*H*-indolo[2,3-*b*]quinoline (4q): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.12 (s, 1H, NH), 8.99 (s, 1H, H-11), 8.49 (d, 1H, *J* = 2.3 Hz, H-1), 7.94 (d, 1H, *J* = 9.0 Hz, H-4), 7.84 (dd, 1H, *J* = 9.0 and 2.3 Hz, H-3), 7.58 (td, 1H, *J* = 8.1 and 5.6 Hz, H-8), 7.35 (d, 1H, *J* = 8.1 Hz, H-7), 7.10 (dd, 1H, *J* = 10.0 and 8.1 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 158.7 (q, *J* = 249 Hz, C-10), 153.0 (q, C-5*a*), 145.2 (q, C-4*a*), 144.1 (q, C-6*a*), 132.4 (CH, C-3), 131.0 (CH, C-1), 130.5 (CH, C-8), 129.7 (CH, C-4), 129.2 (CH, C-11), 125.7 (q, C-11*a*), 115.9 (q, C-10*b*), 115.8 (q, C-2), 108.5 (q, C-10*a*), 108.0 (CH, C-7), 106.4 (CH, C-9). IR (KBr, cm^{-1}): 3078, 1624, 1583, 1512, 1492, 1450, 1398, 1350, 1288, 1269, 1238, 1043. HRMS $[M+H]^+$ found = 314.9929, $C_{15}H_9BrFN_2$ required 314.9933.

9-Chloro-2*H*,6*H*-[1,3]dioxolo[4,5-*g*]indolo[2,3-*b*]quinoline (4r): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.69 (s, 1H, NH), 8.89 (s, 1H, H-11), 8.27 (d, 1H, *J* = 2.0 Hz, H-10), 7.48 (dd, 1H, *J* = 8.5 and 2.0 Hz, H-8), 7.46 (d, 1H, *J* = 8.5 Hz, H-7), 7.44 (s, 1H, H-12), 7.34 (s, 1H, H-4), 6.20 (s, 2H, H-2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 152.4 (q, C-5*a*), 151.0 (q, C-3*a*), 145.7 (q, C-12*a*), 145.4 (q, C-4*a*), 139.5 (q, C-6*a*), 128.0 (CH, C-11), 127.5 (CH, C-8), 124.0 (q, C-9), 122.2 (q, C-10*a*), 121.4 (CH, C-10), 120.3 (q, C-11*a*),

115.1 (q, C-10*b*), 112.8 (CH, C-7), 104.1 (CH, C-4), 103.9 (CH, C-12), 102.2 (CH_2). IR (KBr, cm^{-1}): 2902, 1492, 1464, 1280, 1226, 1066, 1033. HRMS $[M+H]^+$ found = 297.0427, $C_{16}H_{10}ClN_2O_2$ required 297.0431.

3,7-Dibromo-6*H*-indolo[2,3-*b*]quinoline (4s): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.20 (s, 1H, NH), 9.17 (s, 1H, H-11), 8.30 (d, 1H, *J* = 7.8 Hz, H-10), 8.20 (d, 1H, *J* = 2.0 Hz, H-4), 8.11 (d, 1H, *J* = 8.7 Hz, H-1), 7.76 (d, 1H, *J* = 7.8 Hz, H-8), 7.66 (dd, 1H, *J* = 8.7 and 2.0 Hz, H-2), 7.24 (t, 1H, *J* = 7.8 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.7 (q, C-5*a*), 147.6 (q, C-4*a*), 140.7 (q, C-6*a*), 131.5 (CH, C-8), 131.3 (CH, C-1), 129.4 (2 x CH, C-4 and C-11), 126.7 (CH, C-2), 123.1 (q, C-11*a*), 123.0 (q, C-3), 122.5 (q, C-10*a*), 122.0 (CH, C-9), 121.6 (CH, C-10), 118.9 (q, C-10*b*), 104.0 (q, C-7). IR (KBr, cm^{-1}): 3396, 1614, 1564, 1495, 1437, 1409, 1388, 1352, 1301, 1253, 1224, 1176, 1124. HRMS $[M+H]^+$ found = 374.9126, $C_{15}H_9Br_2N_2$ required 374.9132.

10*H*-Indolo[2,3-*b*][1,8]naphthyridine (6a): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.91 (br.s., 1H, NH), 9.11 (s, 1H, H-5), 9.00 (dd, 1H, *J* = 4.3 and 2.0 Hz, H-2), 8.56 (dd, 1H, *J* = 8.0 and 2.0 Hz, H-4), 8.28 (d, 1H, *J* = 7.7 Hz, H-6), 7.56 (t, 1H, *J* = 7.7 Hz, H-8), 7.53 (d, 1H, *J* = 7.7 Hz, H-9), 7.51 (dd, 1H, *J* = 8.0 and 4.3 Hz, H-3), 7.29 (t, 1H, *J* = 7.7 Hz, H-7). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 155.5 (q, C-10*a*), 154.7 (q, C-11*a*), 152.6 (CH, C-2), 142.6 (q, C-9*a*), 138.4 (CH, C-4), 129.0 (2 x CH, C-5 and C-8), 122.5 (CH, C-6), 120.5 (q, C-5*b*), 120.4 (CH, C-7), 119.1 (CH, C-3), 119.1 (q, C-5*a*), 118.3 (q, C-4*a*), 111.8 (CH, C-9). IR (KBr, cm^{-1}): 3055, 1614, 1579, 1487, 1460, 1402, 1246, 1220. HRMS $[M+H]^+$ found = 220.0871, $C_{14}H_{10}N_3$ required 220.0874.

9-Chloro-10*H*-indolo[2,3-*b*][1,8]naphthyridine (6b): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.43 (s, 1H, NH), 9.22 (s, 1H, H-5), 9.06 (dd, 1H, *J* = 4.3 and 2.0 Hz, H-2), 8.61 (dd, 1H, *J* = 8.1 and 2.0 Hz, H-4), 8.28 (d, 1H, *J* = 7.8 Hz, H-6), 7.65 (d, 1H, *J* = 7.8 Hz, H-8), 7.57 (dd, 1H, *J* = 8.1 and 4.3 Hz, H-3), 7.33 (t, 1H, *J* = 7.8 Hz, H-7). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 155.3 (q, C-10*a*), 154.7 (q, C-11*a*), 153.2 (CH, C-2), 139.2 (q, C-9*a*), 138.7 (CH, C-4), 130.4 (CH, C-5), 128.5 (CH, C-8), 122.5 (q, C-5*b*), 121.7 (CH, C-7), 121.3 (CH, C-6), 119.7 (CH, C-3), 118.9 (q, C-5*a*), 118.6 (q, C-4*a*), 116.0 (q, C-9). IR (KBr, cm^{-1}): 3280, 1614, 1568, 1487, 1437, 1406, 1382, 1338, 1246, 1209, 1180, 1138, 1120. HRMS $[M+H]^+$ found = 254.0482, $C_{14}H_{10}ClN_3$ required 254.0485.

8-(Trifluoromethyl)-10*H*-indolo[2,3-*b*][1,8]naphthyridine (6c): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.31 (s, 1H, NH), 9.33 (s, 1H, H-5), 9.08 (dd, 1H, *J* = 4.2 and 2.0 Hz, H-2), 8.62 (dd, 1H, *J* = 8.1 and 2.0 Hz, H-4), 8.53 (d, 1H, *J* = 8.0 Hz, H-6), 7.80 (s, 1H, H-9), 7.65 (d, 1H, *J* = 8.0 Hz, H-7), 7.58 (dd, 1H, *J* = 8.1 and 4.2 Hz, H-3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 155.5 (q, C-10*a*), 155.1 (q, C-11*a*), 153.6 (CH, C-2), 141.2 (q, C-9*a*), 138.8 (CH, C-4), 131.4 (CH, C-5), 123.8 (q, C-5*b*), 123.6 (CH, C-6), 128.5 (q, C-8), 125.1 (q, CF_3), 119.7 (CH, C-3), 118.6 (q, C-4*a*), 117.0 (CH, C-7), 116.9 (q, C-5*a*), 108.3 (CH, C-9). IR (KBr, cm^{-1}): 3022, 1579, 1489, 1450, 1317, 1265, 1228, 1153, 1111, 1055. HRMS $[M+H]^+$ found = 288.0743, $C_{15}H_9F_3N_3$ required 288.0748.

7-Chloro-10*H*-indolo[2,3-*b*][1,8]naphthyridine (6d): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.11 (s, 1H, NH), 9.19 (s, 1H, H-5), 9.04 (dd, 1H, *J* = 4.2 and 2.0 Hz, H-2), 8.57 (dd, 1H, *J* = 8.1 and 2.0 Hz, H-4), 8.42 (d, 1H, *J* = 2.1 Hz, H-6), 7.59 (dd, 1H, *J* = 8.4 and 2.1 Hz, H-8), 7.54 (d, 1H, *J* = 8.4 Hz, H-9), 7.54 (dd, 1H, *J* = 8.1 and 4.2 Hz, H-3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 155.3 (q, C-10*a*), 154.8 (q, C-11*a*), 153.2 (CH, C-2), 140.6 (q, C-9*a*), 138.6 (CH, C-4), 130.4 (CH, C-5), 128.8 (CH, C-8), 124.9 (q, C-7), 122.3 (CH, C-6), 122.0 (q, C-5*b*), 119.5 (CH, C-3), 118.4 (q, C-4*a*), 118.1 (q, C-5*a*), 113.1 (CH, C-9). IR (KBr, cm^{-1}): 3032, 1610, 1597, 1573, 1485, 1450, 1382, 1276, 1246, 1217, 1064. HRMS $[M+H]^+$ found = 254.0481, $C_{14}H_9ClN_3$ required 254.0485.

6-Fluoro-10*H*-indolo[2,3-*b*][1,8]naphthyridine (6e): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.29 (s, 1H, NH), 9.09 (s, 1H, H-5), 9.05 (dd, 1H, *J* = 4.2 and 2.0 Hz, H-2), 8.71 (dd, 1H, *J* = 8.1 and 2.0 Hz, H-4), 7.60 (td, 1H, *J* = 8.1 and 5.7 Hz, H-8), 7.57 (dd, 1H, *J* = 8.1 and 4.2 Hz, H-3), 7.38 (d, 1H, *J* = 8.1 Hz, H-9), 7.13 (dd, 1H, *J* = 10.0 and 8.1 Hz, H-7). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 158.7 (q, *J* = 250 Hz, C-6), 154.7 (q, C-10*a*), 154.2 (q, C-11*a*), 152.9 (CH, C-2), 144.1 (q, C-9*a*), 139.0 (CH, C-4), 131.1 (CH, C-5), 130.6 (CH, C-8), 119.5 (CH, C-3), 118.8 (q, C-4*a*), 115.9 (q, C-5*a*), 108.4 (q, C-5*b*), 108.2 (CH, C-9), 106.7 (CH, C-7). IR (KBr, cm^{-1}): 1626, 1584, 1492, 1454, 1402, 1315, 1282, 1271, 1244. HRMS $[M+H]^+$ found = 238.0775, $C_{14}H_9FN_3$ required 238.0780.

6,9-Dichloro-10*H*-indolo[2,3-*b*][1,8]naphthyridine (6f): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.77 (s, 1H, NH), 9.42 (s, 1H, H-5), 9.10 (dd, 1H, *J* = 4.2 and 2.1 Hz, H-2), 8.74 (dd, 1H, *J* = 8.1 and 2.1 Hz, H-4), 7.67 (d, 1H, *J* = 8.4 Hz, H-8), 7.60 (dd, 1H, *J* = 8.1 and 4.2 Hz, H-3), 7.38 (d, 1H, *J* = 8.4 Hz, H-7). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.8 (q, C-10*a*), 154.7 (q, C-11*a*), 153.9 (CH, C-2), 140.2 (q, C-9*a*), 139.1 (CH, C-4), 132.3 (CH, C-5), 129.2 (CH, C-8), 127.8 (q, C-6), 121.8 (CH, C-7), 120.0 (CH, C-3), 119.3 (q, C-5*b*), 118.7 (q, C-4*a*), 117.5 (q, C-5*a*) 114.9 (q, C-9). IR (KBr, cm^{-1}): 3020, 1608, 1572, 1473, 1390, 1377, 1340, 1319, 1305, 1269, 1251, 1139. HRMS $[M+H]^+$ found = 288.0090, $C_{14}H_8Cl_2N_3$ required 288.0095.

9-Phenyl-10*H*-indolo[2,3-*b*][1,8]naphthyridine (6g): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.90 (s, 1H, NH), 9.18 (s, 1H, H-5), 9.03 (dd, 1H, *J* = 4.2 and 2.0 Hz, H-2), 8.59 (dd, 1H, *J* = 8.1 and 2.0 Hz, H-4), 8.32 (d, 1H, *J* = 7.6 Hz, H-6), 7.74 (d, 2H, *J* = 7.7 Hz, Ph-2'H and Ph-6'H), 7.59 (d, 1H, *J* = 7.6 Hz, H-8), 7.57 (t, 2H, *J* = 7.7 Hz, Ph-3'H and Ph-5'H), 7.54 (dd, 1H, *J* = 8.1 and 4.2 Hz, H-3), 7.46 (t, 1H, *J* = 7.7 Hz, Ph-4'H), 7.42 (t, 1H, *J* = 7.6 Hz, H-7). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 155.9 (q, C-10*a*), 154.8 (q, C-11*a*), 152.8 (CH, C-2), 139.4 (q, C-9*a*), 138.4 (CH, C-4), 138.1 (q, Ph-1'C), 129.5 (2 x CH, Ph-3'C and Ph-5'C), 129.4 (CH, C-8), 129.2 (CH, C-5), 129.1 (2 x CH, Ph-2'C and Ph-6'C), 128.0 (CH, Ph-4'H), 125.8 (q, C-9), 121.6 (CH, C-6), 121.5 (q, C-5*b*), 121.3 (CH, C-7), 119.3 (CH, C-3), 119.1 (q, C-5*a*), 118.5 (q, C-4*a*). IR (KBr, cm^{-1}): 3056, 1602, 1573, 1489, 1408, 1392, 1247, 1215. HRMS $[M+H]^+$ found = 296.1182, $C_{20}H_{14}N_3$ required 296.1187.

7-Methyl-10*H*-indolo[2,3-*b*][1,8]naphthyridine (6h): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.95 (s, 1H,

NH), 9.06 (s, 1H, H-5), 8.99 (dd, 1H, *J* = 4.2 and 2.0 Hz, H-2), 8.55 (dd, 1H, *J* = 8.1 and 2.0 Hz, H-4), 8.08 (s, 1H, H-6), 7.50 (dd, 1H, *J* = 8.1 and 4.2 Hz, H-3), 7.43 (d, 1H, *J* = 8.1 Hz, H-9), 7.39 (d, 1H, *J* = 8.1 Hz, H-8), 2.49 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 155.4 (q, C-10*a*), 154.6 (q, C-11*a*), 152.5 (CH, C-2), 140.3 (q, C-9*a*), 138.4 (CH, C-4), 130.2 (CH, C-8), 129.4 (q, C-7), 128.8 (CH, C-5), 122.4 (CH, C-6), 120.6 (q, C-5*b*), 119.0 (CH, C-3), 119.0 (q, C-5*a*), 118.3 (q, C-4*a*), 111.4 (CH, C-9), 21.5 (CH_3). IR (KBr, cm^{-1}): 2970, 1616, 1579, 1489, 1442, 1390, 1247, 1219. HRMS $[M+H]^+$ found = 234.1026, $C_{15}H_{12}N_3$ required 234.1031.

6-Bromo-9-chloro-10*H*-indolo[2,3-*b*][1,8]naphthyridine (6i): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 13.13 (s, 1H, NH), 9.69 (s, 1H, H-5), 9.21 (dd, 1H, *J* = 4.6 and 1.9 Hz, H-2), 9.10 (d, 1H, *J* = 8.0 Hz, H-4), 7.81 (dd, 1H, *J* = 8.0 and 4.6 Hz, H-3), 7.67 (d, 1H, *J* = 8.4 Hz, H-8), 7.60 (d, 1H, *J* = 8.4 Hz, H-7). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 155.3 (q, C-10*a*), 151.2 (q, C-11*a*), 151.1 (CH, C-2), 143.6 (CH, C-4), 140.6 (q, C-9*a*), 132.1 (CH, C-5), 130.1 (CH, C-8), 125.8 (CH, C-7), 120.8 (q, C-5*b*), 119.8 (CH, C-3), 119.3 (q, C-4*a*), 116.2 (2 x q, C-5*a* and C-6), 116.0 (q, C-9). IR (KBr, cm^{-1}): 3048, 1697, 1606, 1583, 1379, 1321, 1247, 1198, 1159. HRMS $[M+H]^+$ found = 331.9584, $C_{14}H_8BrClN_3$ required 331.9590.

8-Bromo-11*H*-pyrido[3',2':4,5]pyrrolo[2,3-*b*]quinoline (8a): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.44 (s, 1H, NH), 9.16 (s, 1H, H-5), 8.63 (dd, 1H, *J* = 7.6 and 1.7 Hz, H-4), 8.52 (dd, 1H, *J* = 5.0 and 1.7 Hz, H-2), 8.20 (d, 1H, *J* = 2.0 Hz, H-9), 8.10 (d, 1H, *J* = 8.6 Hz, H-6), 7.65 (dd, 1H, *J* = 8.6 and 2.0 Hz, H-7), 7.33 (dd, 1H, *J* = 7.6 and 5.0 Hz, H-3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.7 (q, C-11*a*), 153.0 (q, C-10*a*), 148.7 (CH, C-2), 147.6 (q, C-9*a*), 131.1 (CH, C-6), 130.7 (CH, C-4), 129.8 (CH, C-5), 129.5 (CH, C-9), 126.8 (CH, C-7), 123.2 (q, C-5*a*), 123.0 (q, C-8), 117.1 (q, C-4*a*), 116.8 (CH, C-3), 114.2 (q, C-4*b*). IR (KBr, cm^{-1}): 3047, 1600, 1579, 1483, 1427, 1411, 1390, 1354, 1271, 1232. HRMS $[M+H]^+$ found = 297.9974, $C_{14}H_9BrN_3$ required 297.9980.

7-Bromo-11*H*-pyrido[3',2':4,5]pyrrolo[2,3-*b*]quinoline (8b): ^{1}H-NMR(500 MHz, DMSO-d_6): δ 12.42 (s, 1H, NH), 9.09 (s, 1H, H-5), 8.63 (dd, 1H, *J* = 7.6 and 1.7 Hz, H-4), 8.53 (dd, 1H, *J* = 5.0 and 1.7 Hz, H-2), 8.38 (d, 1H, *J* = 2.3 Hz, H-6), 7.95 (d, 1H, *J* = 9.0 Hz, H-9), 7.86 (dd, 1H, *J* = 9.0 and 2.3 Hz, H-8), 7.33 (dd, 1H, *J* = 7.6 and 5.0 Hz, H-3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.8 (q, C-11*a*), 152.8 (q, C-10*a*), 148.8 (CH, C-2), 145.5 (q, C-9*a*), 132.5 (CH, C-8), 130.9 (CH, C-6), 130.8 (CH, C-4), 129.8 (CH, C-9), 128.7 (CH, C-5), 125.8 (q, C-5*a*), 117.3 (q, C-4*b*), 116.8 (CH, C-3), 115.9 (q, C-7), 114.0 (q, C-4*a*). IR (KBr, cm^{-1}): 3014, 1599, 1577, 1431, 1390, 1348, 1273, 1226, 1139, 1062. HRMS $[M+H]^+$ found = 297.9975, $C_{14}H_9BrN_3$ required 297.9980.

2*H*,6*H*-[1,3]Dioxolo[4,5-*g*]pyrido[3',2':4,5]pyrrolo[2,3-*b*]quinoline (8c): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.14 (s, 1H, NH), 8.89 (s, 1H, H-11), 8.53 (dd, 1H, *J* = 7.6 and 1.6 Hz, H-10), 8.45 (dd, 1H, *J* = 5.0 and 1.6 Hz, H-8), 7.48 (s, 1H, H-12), 7.36 (s, 1H, H-4), 7.26 (dd, 1H, *J* = 7.6 and 5.0 Hz, H-9), 6.21 (s, 2H, H-2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.7 (q, C-6*a*), 151.4 (q, C-5*a*), 151.0 (q, C-3*a*), 147.6 (CH, C-

8), 145.8 (q, C-12*a*), 145.3 (q, C-4*a*), 129.7 (CH, C-10), 128.5 (CH, C-11), 120.7 (q, C-11*a*), 116.2 (CH, C-9), 114.3 (q, C-10*a*), 114.1 (q, C-10*b*), 104.2 (CH, C-4), 103.9 (CH, C-12), 102.3 (CH_2). IR (KBr, cm^{-1}): 3037, 1602, 1492, 1462, 1431, 1384, 1230, 1157, 1037. HRMS $[M+H]^+$ found = 264.0768, $C_{15}H_{10}N_3O_2$ required 264.0773.

11*H*-Pyrido[3',2':4,5]pyrrolo[2,3-*b*]quinoline (8d): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.30 (s, 1H, NH), 9.12 (s, 1H, H-5), 8.63 (dd, 1H, *J* = 7.7 and 1.6 Hz, H-4), 8.50 (dd, 1H, *J* = 5.0 and 1.6 Hz, H-2), 8.13 (d, 1H, *J* = 7.9 Hz, H-6), 8.01 (d, 1H, *J* = 7.9 Hz, H-9), 7.76 (t, 1H, *J* = 7.9 Hz, H-8), 7.52 (t, 1H, *J* = 7.9 Hz, H-7), 7.31 (dd, 1H, *J* = 7.7 and 5.0 Hz, H-3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.6 (q, C-11*a*), 152.6 (q, C-10*a*), 148.3 (CH, C-2), 147.0 (q, C-9*a*), 130.4 (CH, C-4), 129.7 (CH, C-8), 129.6 (CH, C-5), 129.2 (CH, C-6), 127.7 (CH, C-9), 124.5 (q, C-5*a*), 123.7 (CH, C-7), 116.6 (q, C-4*b*), 116.5 (CH, C-3), 114.3 (q, C-4*a*). IR (KBr, cm^{-1}): 3055, 1599, 1579, 1489, 1427, 1400, 1332, 1274, 1234, 1132. HRMS $[M+H]^+$ found = 220.0870, $C_{14}H_{10}N_3$ required 220.0874.

8-Methoxy-11*H*-pyrido[3',2':4,5]pyrrolo[2,3-*b*]quinoline (8e): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.93 (br.s, 1H, NH), 8.96 (dd, 1H, *J* = 4.3 and 2.0 Hz, H-2), 8.93 (s, 1H, H-5), 8.51 (dd, 1H, *J* = 8.1 and 2.0 Hz, H-4), 8.15 (d, 1H, *J* = 8.5 Hz, H-6), 7.49 (dd, 1H, *J* = 8.1 and 4.3 Hz, H-3), 7.03 (d, 1H, *J* = 2.3 Hz, H-9), 6.89 (dd, 1H, *J* = 8.5 Hz and 2.3 Hz, H-7), 3.89 (s, 3H, *O*CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 161.0 (q, C-8), 155.7 (q, C-10*a*), 154.0 (q, C-11*a*), 151.9 (CH, C-2), 144.0 (q, C-9*a*), 138.0 (CH, C-4), 127.0 (CH, C-5), 123.6 (CH, C-6), 119.3 (q, C-4*b*), 119.1 (CH, C-3), 118.6 (q, C-4*a*), 113.6 (q, C-5*a*), 108.9 (CH, C-7), 95.9 (CH, C-9), 55.9 (CH_3). IR (KBr, cm^{-1}): 3053, 1618, 1573, 1408, 1319, 1273, 1197, 1157, 1101. HRMS $[M+H]^+$ found = 250.0975, $C_{15}H_{12}N_3O$ required 250.0980.

2*H*,6*H*-[1,3]Dioxolo[4,5-*g*]pyrido[4',3':4,5]pyrrolo[2,3-*b*]quinoline (8f): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 11.84 (br.s, 1H, NH), 9.03 (s, 1H, H-11), 8.85 (s, 1H, H-7), 8.44 (d, 1H, *J* = 5.1 Hz, H-9), 8.15 (d, 1H, *J* = 5.1 Hz, H-10), 7.50 (s, 1H, H-12), 7.37 (s, 1H, H-4), 6.22 (s, 2H, CH_2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 152.2 (q, C-5*a*), 151.7 (q, C-3*a*), 146.9 (q, C-4*a*), 145.9 (q, C-12*a*), 140.0 (CH, C-9), 137.0 (q, C-6*a*), 133.9 (CH, C-7), 129.9 (CH, C-11), 126.6 (q, C-10*a*), 120.5 (q, C-11*a*), 115.9 (CH, C-10), 113.9 (q, C-10*b*), 104.0 (2 x CH, C-4 and C-12), 102.4 (CH_2). IR (KBr, cm^{-1}): 3066, 1631, 1464, 1390, 1255, 1205, 1161, 1033. HRMS $[M+H]^+$ found = 264.0768, $C_{15}H_{10}N_3O_2$ required 264.0773.

7-Bromo-11*H*-pyrido[4',3':4,5]pyrrolo[2,3-*b*]quinoline (8g): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.15 (br.s, 1H, NH), 9.26 (s, 1H, H-5), 8.92 (s, 1H, H-1), 8.52 (d, 1H, *J* = 5.1 Hz, H-3), 8.42 (d, 1H, *J* = 2.3 Hz, H-6), 8.24 (d, 1H, *J* = 5.1 Hz, H-4), 7.97 (d, 1H, *J* = 9.0 Hz, H-9), 7.89 (dd, 1H, *J* = 9.0 and 2.3 Hz, H-8). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.4 (q, C-10*a*), 146.8 (q, C-9*a*), 140.5 (CH, C-3), 138.0 (q, C-11*a*), 134.2 (CH, C-1), 133.2 (CH, C-8), 131.2 (CH, C-6), 130.6 (CH, C-5), 129.8 (CH, C-9), 126.4 (q, C-4*a*), 125.4 (q, C-5*a*), 117.2 (q, C-4*b*), 116.6 (CH, C-4), 115.9 (q, C-7). IR (KBr, cm^{-1}): 3053, 1641, 1606, 1566, 1464, 1398, 1357, 1236. HRMS $[M+H]^+$ found = 297.9974, $C_{14}H_9BrN_3$ required 297.9980.

8-Bromo-11*H*-pyrido[4',3':4,5]pyrrolo[2,3-*b*]quinoline (8h): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.52 (br.s, 1H, NH), 9.31 (s, 1H, H-5), 8.93 (s, 1H, H-1), 8.50 (d, 1H, *J* = 5.1 Hz, H-3), 8.24 (d, 1H, *J* = 5.1 Hz, H-4), 8.22 (d, 1H, *J* = 2.0 Hz, H-9), 8.13 (d, 1H, *J* = 8.7 Hz, H-6), 7.65 (dd, 1H, *J* = 8.7 and 2.0 Hz, H-7). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.0 (q, C-10*a*), 148.8 (q, C-9*a*), 140.4 (CH, C-3), 138.4 (q, C-11*a*), 134.4 (CH, C-1), 131.5 (2 x CH, C-5 and C-6), 129.4 (CH, C-9), 126.6 (CH, C-7), 126.5 (q, C-4*a*), 123.7 (q, C-8), 122.7 (q, C-5*a*), 117.1 (q, C-4*b*), 116.5 (CH, C-4). IR (KBr, cm^{-1}): 3053, 1635, 1562, 1481, 1392, 1255, 1238. HRMS [M+H]$^+$ found = 297.9974, $C_{14}H_9BrN_3$ required 297.9980.

5*H*-Pyrido[3',4':4,5]pyrrolo[2,3-*b*]quinoline (8i): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 9.35 (s, 1H, H-1), 9.10 (s, 1H, H-11), 8.47 (d, 1H, *J* = 5.5 Hz, H-3), 8.11 (d, 1H, *J* = 8.0 Hz, H-10), 7.99 (d, 1H, *J* = 8.0 Hz, H-7), 7.72 (t, 1H, *J* = 8.0 Hz, H-8), 7.52 (d, 1H, *J* = 5.5 Hz, H-4), 7.48 (t, 1H, *J* = 8.0 Hz, H-9). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 147.3 (CH, C-3), 147.1 (3 x q, C-4*a*, C-5*a* and C-6*a*) 143.8 (CH, C-1), 129.6 (CH, C-10), 129.1 (CH, C-8), 128.6 (CH, C-7), 127.7 (CH, C-11), 124.3 (q, C-10*a*), 123.4 (CH, C-9), 118.1 (q, C-11*b*), 116.8 (q, C-11*a*). 107.6 (CH, C-4). IR (KBr, cm^{-1}): 1650, 1575, 1483, 1400, 1236, 1008. HRMS [M+H]$^+$ found = 220.0870, $C_{14}H_{10}N_3$ required 220.0869.

8-Bromo-5*H*-pyrido[3',4':4,5]pyrrolo[2,3-*b*]quinoline (8j): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.32 (br.s, 1H, NH), 9.43 (d, 1H, *J* = 1.0 Hz, H-1), 9.22 (s, 1H, H-11), 8.58 (d, 1H, *J* = 5.6 Hz, H-3), 8.22 (d, 1H, *J* = 2.0 Hz, H-7), 8.12 (d, 1H, *J* = 8.7 Hz, H-10), 7.67 (dd, 1H, *J* = 8.7 and 2.0 Hz, H-9), 7.49 (dd, 1H, *J* = 5.6 and 1.0 Hz, H-4). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.5 (q, C-5*a*), 148.1 (CH, C-3), 147.6 (q, C-6*a*), 146.7 (q, C-4*a*), 144.3 (CH, C-1), 131.2 (CH, C-10), 129.6 (CH, C-7), 129.4 (CH, C-11), 127.0 (CH, C-9), 123.4 (q, C-10*a*), 123.1 (q, C-8), 117.7 (q, C-11*b*), 116.8 (q, C-11*a*), 107.0 (CH, C-4). IR (KBr, cm^{-1}): 2990, 1610, 1468, 1385, 1234, 1166, 1057. HRMS [M+H]$^+$ found = 297.9974, $C_{14}H_9BrN_3$ required 297.9974.

2*H*,6*H*-[1,3]Dioxolo[4,5-*g*]pyrido[3',4':4,5]pyrrolo[2,3-*b*]quinoline (8k): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 9.30 (s, 1H, H-10), 8.92 (s, 1H, H-11), 8.45 (d, 1H, *J* = 5.6 Hz, H-8), 7.48 (s, 1H, H-12), 7.43 (d, 1H, *J* = 5.6 Hz, H-7), 7.36 (s, 1H, H-4), 6.20 (s, 2H, CH_2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.4 (q, C-4*a*), 153.3 (q, C-5*a*), 150.9 (q, C-3*a*), 147.0 (q, C-6*a*), 146.6 (CH, C-8), 145.7 (q, C-12*a*), 143.4 (CH, C-10), 143.3 (q, C-10*a*), 127.6 (CH, C-11), 120.6 (q, C-11*a*), 118.2 (q, C-10*b*), 107.2 (CH, C-7), 104.2 (CH, C-4), 103.9 (CH, C-12), 102.2 (CH_2). IR (KBr, cm^{-1}): 1607, 1574, 1464, 1402, 1254, 1232, 1035. HRMS [M+H]$^+$ found = 264.0768, $C_{15}H_{10}N_3O_2$ required 264.0768.

***N*-[2-(2-Oxo-1,2-dihydroquinolin-3-yl)pyridin-3-yl]acetamide (11a):** ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.30 (s, 1H, Q-NH), 9.64 (s, 1H, NH), 8.43 (dd, 1H, *J* = 4.6 and 1.4 Hz, Py-6'H), 8.26 (s, 1H, Q-4'H), 8.18 (dd, 1H, *J* = 8.3 and 1.4 Hz, Py-4'H), 7.84 (d, 1H, *J* = 8.0 Hz, Q-5'H), 7.60 (t, 1H, *J* = 8.0 Hz, Q-7'H), 7.43 (d, 1H, *J* = 8.0 Hz, Q-8'H), 7.43 (dd, 1H, *J* = 8.3 and 4.6 Hz, Py-5'H), 7.27 (t, 1H, *J* = 8.0 Hz, Q-6'H), 1.97 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 168.9 (q, C=O), 161.6 (q, Q-2'C), 147.6 (q, Py-2'C),

145.5 (CH, Py-6'C), 143.1 (CH, Q-4'C), 139.3 (q, Q-8*a*'C), 134.1 (q, Py-3'C), 131.9 (CH, Py-4'C), 131.7 (q, Q-3'C), 131.6 (CH, Q-7'C), 129.1 (CH, Q-5'C), 123.5 (CH, Py-5'C), 122.8 (CH, Q-6'C), 119.9 (q, Q-4*a*'C), 115.6 (CH, Q-8'C), 24.2 (CH_3). IR (KBr, cm^{-1}): 3038, 1693, 1546, 1487, 1419, 1361, 1303. HRMS $[M+H]^+$ found = 280.1081, $C_{16}H_{14}N_3O_2$ required 280.1086.

***N*-[2-(7-Bromo-2-oxo-1,2-dihydroquinolin-3-yl)pyridin-3-yl]acetamide (11b):** ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.28 (br.s, 1H, Q-NH), 9.50 (br.s, 1H, NH), 8.42 (dd, 1H, *J* = 4.6 and 1.4 Hz, Py-6'H), 8.21 (s, 1H, Q-4'H), 8.19 (d, 1H, *J* = 8.2 and 1.4 Hz, Py-4'H), 7.80 (d, 1H, *J* = 8.4 Hz, Q-5'H), 7.58 (d, 1H, *J* = 2.0 Hz, Q-8'H), 7.43 (dd, 1H, *J* = 8.4 and 2.0 Hz, Q-6'H), 7.43 (dd, 1H, *J* = 8.2 and 4.6 Hz, Py-5'H), 1.97 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 169.0 (q, C=O), 161.3 (q, Q-2'C), 147.3 (q, Py-2'C), 145.4 (CH, Py-6'C), 142.0 (CH, Q-4'C), 140.4 (q, Q-8*a*'C), 134.2 (q, Py-3'C), 132.3 (q, Q-3'C), 131.9 (CH, Py-4'C), 131.0 (CH, Q-5'C), 125.6 (CH, Q-6'C), 124.5 (q, Q-7'C), 123.6 (CH, Py-5'C), 119.0 (q, Q-4*a*'C), 117.7 (CH, Q-8'C), 24.2 (CH_3). IR (KBr, cm^{-1}): 2988, 1666, 1637, 1597, 1570, 1539, 1487, 1454, 1421, 1365, 1307, 1224, 1070. HRMS $[M+H]^+$ found = 358.0187, $C_{16}H_{13}BrN_3O_2$ required 358.0191.

***N*-[2-(6-Oxo-5,6-dihydro-2*H*-[1,3]dioxolo[4,5-*g*]quinolin-7-yl)pyridin-3-yl]acetamide (11c):** ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.39 (s, 1H, Q-NH), 9.99 (s, 1H, NH), 8.42 (dd, 1H, *J* = 4.6 and 1.5 Hz, Py-6'H), 8.26 (s, 1H, Q-8'H), 8.16 (dd, 1H, *J* = 8.3 and 1.5 Hz, Py-4'H), 7.41 (dd, 1H, *J* = 8.3 and 4.6 Hz, Py-5'H), 7.39 (s, 1H, Q-9'H), 6.94 (s, 1H, Q-4'H), 6.15 (s, 2H, CH_2), 1.98 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 168.8 (q, C=O), 161.6 (q, Q-6'C), 151.6 (q, Q-3*a*'C), 147.5 (q, Py-2'C), 145.5 (CH, Py-6'C), 144.4 (q, Q-9*a*'C), 143.6 (CH, Q-8'C), 136.8 (q, Q-4*a*'C), 134.0 (q, Py-3'C), 132.0 (CH, Py-4'C), 128.2 (q, Q-7'C), 123.2 (CH, Py-5'C), 114.6 (q, Q-8*a*'C), 106.0 (CH, Q-9'C), 102.6 (CH_2), 95.3 (CH, Q-4'C), 24.4 (CH_3). IR (KBr, cm^{-1}): 3030, 1666, 1641, 1583, 1541, 1487, 1456, 1408, 1309, 1242. HRMS $[M+H]^+$ found = 324.0981, $C_{17}H_{14}N_3O_4$ required 324.0984.

***N*-[2-(6-Bromo-2-oxo-1,2-dihydroquinolin-3-yl)pyridin-3-yl]acetamide (11d):** ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.34 (br.s, 1H, Q-NH), 9.50 (br.s, 1H, NH), 8.42 (dd, 1H, *J* = 4.6 and 1.4 Hz, Py-6'H), 8.19 (d, 1H, *J* = 8.2 and 1.4 Hz, Py-4'H), 8.19 (s, 1H, Q-4'H), 8.10 (d, 1H, *J* = 2.2 Hz, Q-5'H), 7.74 (dd, 1H, *J* = 8.8 and 2.2 Hz, Q-7'H), 7.44 (dd, 1H, *J* = 8.2 and 4.6 Hz, Py-5'H), 7.36 (d, 1H, *J* = 8.8 Hz, Q-8'H), 1.97 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 169.0 (q, C=O), 161.4 (q, Q-2'C), 147.2 (q, Py-2'C), 145.4 (CH, Py-6'C), 141.4 (CH, Q-4'C), 138.4 (q, Q-8*a*'C), 134.2 (q, Py-3'C), 133.9 (CH, Q-7'C), 133.0 (q, Q-3'C), 131.9 (CH, Py-4'C), 130.9 (CH, Q-5'C), 123.6 (CH, Py-5'C), 121.7 (q, Q-4*a*'C), 117.7 (CH, Q-8'C), 114.4 (q, C-6'C), 24.2 (CH_3). IR (KBr, cm^{-1}): 2989, 1666, 1640, 1599, 1575, 1539, 1454, 1398, 1369, 1305, 1249, 1222, 1203, 1072. HRMS $[M+H]^+$ found = 358.0186, $C_{16}H_{13}BrN_3O_2$ required 358.0191.

***N*-[2-(2-Oxo-1,2-dihydro-1,8-naphthyridin-3-yl)pyridin-3-yl]acetamide (11e):** ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.53 (s, 1H, N-NH), 9.41 (s, 1H, NH), 8.59 (dd, 1H, *J* = 4.7 and 1.8 Hz, N-7'H), 8.41 (dd,

1H, *J* = 4.6 and 1.4 Hz, Py-6'H), 8.26 (dd, 1H, *J* = 7.8 and 1.8 Hz, N-5'H), 8.20 (dd, 1H, *J* = 8.2 and 1.4 Hz, Py-4'H), 8.18 (s, 1H, N-4'H), 7.43 (dd, 1H, *J* = 8.2 and 4.6 Hz, Py-5'H), 7.32 (dd, 1H, *J* = 7.8 and 4.7 Hz, N-6'H), 1.97 (s, 3H, CH_3). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 169.1 (q, C=O), 162.3 (q, N-2'C), 151.5 (CH, N-7'C), 150.2 (q, N-8*a*'C), 147.2 (q, Py-2'C), 145.4 (CH, Py-6'C), 141.2 (CH, N-4'C), 137.5 (CH, N-5'C), 134.2 (q, Py-3'C), 133.1 (q, N-3'C), 131.8 (CH, Py-4'C), 123.6 (CH, Py-5'C), 119.2 (CH, N-6'C), 115.1 (q, N-4*a*'C), 24.2 (CH_3). IR (KBr, cm^{-1}): 3252, 1693, 1593, 1537, 1454, 1415, 1365, 1298, 1220. HRMS $[M+H]^+$ found = 281.1031, $C_{15}H_{13}N_4O_2$ required 281.1038.

6*H*-[1,3]Thiazolo[5',4':4,5]indolo[2,3-*b*]quinoline (13a): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.18 (s, 1H, NH), 9.45 (s, 1H, H-2), 9.03 (s, 1H, H-12), 8.32 (d, 1H, *J* = 7.9 Hz, H-11), 8.30 (d, 1H, *J* = 8.7 Hz, H-4), 8.05 (d, 1H, *J* = 7.9 Hz, H-8), 7.78 (t, 1H, *J* = 7.9 Hz, H-9), 7.74 (d, 1H, *J* = 8.7 Hz, H-5), 7.55 (t, 1H, *J* = 7.9 Hz, H-10). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 152.9 (q, C-6*a*), 152.7 (CH, C-2), 148.8 (q, C-3*a*), 146.6 (q, C-7*a*), 140.2 (q, C-5*a*), 129.5 (CH, C-9), 129.4 (CH, C-11), 128.4 (CH, C-12), 127.6 (q, C-12*c*), 127.6 (CH, C-8), 124.3 (q, C-11*a*), 123.7 (CH, C-4), 123.6 (CH, C-10), 116.9 (q, C-12*a*), 113.1 (q, C-12*b*), 111.1 (CH, C-5). IR (KBr, cm^{-1}): 3136, 1599, 1488, 1388, 1276, 1253. HRMS $[M+H]^+$ found = 276.0591, $C_{16}H_{10}N_3S$ required 276.0595.

9-Bromo-6*H*-[1,3]thiazolo[5',4':4,5]indolo[2,3-*b*]quinoline (13b): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.32 (s, 1H, NH), 9.45 (s, 1H, H-2), 9.07 (s, 1H, H-12), 8.31 (d, 1H, *J* = 8.7 Hz, H-4), 8.28 (d, 1H, *J* = 8.8 Hz, H-11), 8.23 (d, 1H, *J* = 2.1 Hz, H-8), 7.74 (d, 1H, *J* = 8.7 Hz, H-5), 7.67 (dd, 1H, *J* = 8.8 and 2.1 Hz, H-10). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.2 (q, C-6*a*), 152.9 (CH, C-2), 148.9 (q, C-3*a*), 147.2 (q, C-7*a*), 140.4 (q, C-5*a*), 131.3 (CH, C-11), 129.4 (CH, C-8), 128.6 (CH, C-12), 127.8 (q, C-12*c*), 126.6 (CH, C-10), 124.0 (CH, C-4), 123.1 (q, C-11*a*), 122.8 (q, C-9), 117.4 (q, C-12*a*), 113.1 (q, C-12*b*), 111.3 (CH, C-5). IR (KBr, cm^{-1}): 3042, 1597, 1475, 1444, 1409, 1381, 1350, 1253, 1172, 1055. HRMS $[M+H]^+$ found = 353.9696, $C_{16}H_9BrN_3S$ required 353.9700.

6*H*,10*H*-[1,3]Dioxolo[4,5-*g*][1,3]thiazolo[5',4':4,5]indolo[2,3-*b*]quinoline (13c): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.02 (s, 1H, NH), 9.41 (s, 1H, H-2), 8.83 (s, 1H, H-13), 8.23 (d, 1H, *J* = 8.7 Hz, H-4), 7.70 (d, 1H, *J* = 8.7 Hz, H-5), 7.67 (s, 1H, H-12), 7.39 (s, 1H, H-8), 6.22 (s, 2H, CH_2). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 152.3 (CH, C-2), 151.8 (q, C-6*a*), 150.9 (q, C-8*a*), 148.6 (q, C-3*a*), 145.8 (q, C-11*a*), 144.9 (q, C-7*a*), 139.1 (q, C-13*c*), 127.3 (CH, C-13), 127.1 (q, C-5*a*), 122.8 (CH, C-4), 120.7 (q, C-12*a*), 114.6 (q, C-13*a*), 113.1 (q, C-13*b*), 111.1 (CH, C-5), 104.0 (2 x CH, C-8 and C-12), 102.3 (CH_2). IR (KBr, cm^{-1}): 3082, 1597, 1471, 1377, 1276, 1253, 1232, 1161, 1058, 1033. HRMS $[M+H]^+$ found = 320.0490, $C_{17}H_{10}N_3O_2S$ required 320.0493.

10-Bromo-6*H*-[1,3]thiazolo[5',4':4,5]indolo[2,3-*b*]quinoline (13d): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.29 (br.s, 1H, NH), 9.45 (s, 1H, H-2), 9.05 (s, 1H, H-12), 8.60 (d, 1H, *J* = 2.3 Hz, H-11), 8.31 (d, 1H, *J* = 8.7 Hz, H-4), 7.99 (d, 1H, *J* = 9.0 Hz, H-8), 7.86 (dd, 1H, *J* = 9.0 and 2.3 Hz, H-9), 7.75 (d, 1H, *J* = 8.7

Hz, H-5). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 153.0 (q, C-6*a*), 152.9 (CH, C-2), 148.8 (q, C-3*a*), 145.0 (q, C-7*a*), 140.4 (q, C-12*c*), 132.2 (CH, C-9), 131.1 (CH, C-11), 129.8 (CH, C-8), 127.8 (q, C-5*a*), 127.6 (CH, C-12), 125.6 (q, C-11*a*), 124.1 (CH, C-4), 117.5 (q, C-10), 115.8 (q, C-12*a*), 112.9 (q, C-12*b*), 111.3 (CH, C-5). IR (KBr, cm^{-1}): 3070, 1595, 1481, 1448, 1396, 1350, 1249, 1176, 1138, 1055. HRMS $[M+H]^+$ found = 353.9697, $C_{16}H_9BrN_4S$ required 353.9700.

6*H*-[1,3]Thiazolo[5',4':4,5]indolo[2,3-*b*][1,8]naphthyridine (13e): ^{1}H-NMR (500 MHz, DMSO-d_6): δ 12.43 (s, 1H, NH), 9.47 (s, 1H, H-2), 9.14 (s, 1H, H-12), 9.08 (dd, 1H, *J* = 4.2 and 2.0 Hz, H-9), 8.79 (dd, 1H, *J* = 8.2 and 2.0 Hz, H-11), 8.33 (d, 1H, *J* = 8.7 Hz, H-4), 7.77 (d, 1H, *J* = 8.7 Hz, H-5), 7.59 (dd, 1H, *J* = 8.2 and 4.2 Hz, H-10). ^{13}C-NMR (125 MHz, DMSO-d_6): δ 154.6 (q, C-6*a*), 154.3 (q, C-7*a*), 153.1 (CH, C-9), 153.0 (CH, C-2), 149.0 (q, C-3*a*), 140.5 (q, C-5*a*), 138.7 (CH, C-11), 129.6 (CH, C-12), 127.9 (q, C-12*c*), 124.1 (CH, C-4), 119.6 (CH, C-10), 118.7 (q, C-11*a*), 117.5 (q, C-12*a*), 112.9 (q, C-12*b*), 111.4 (CH, C-5). IR (KBr, cm^{-1}): 3043, 1579, 1479, 1408, 1390, 1271, 1255, 1170, 1122, 1055. HRMS $[M+H]^+$ found = 277.0544, $C_{15}H_9N_4S$ required 277.0548.

ACKNOWLEDGEMENTS

The authors acknowledge Barbara Balázs and Tamás Gáti for NMR spectroscopy measurements.

REFERENCES

1. S. D. Shnyder and C. W. Wright, 'Recent Advances in the Chemistry and Pharmacology of Cryptolepine,' in *Progress in the Chemistry of Organic Natural Products*, 2021, **115**, pp. 177-203 and references cited therein.
2. (a) O. A. Olajide, A. M. Ajayi, and C. W. Wright, *Phytother. Res.*, 2009, **23**, 1421; (b) V. Y. A. Barku, Y. Opoku-Boahen, and E. Y. Dzotsi, *Int. Res. J. Biochem. Bioinforma.*, 2012, **2**, 58; (c) K. Cimanga, T. De Bruyne, A. Lasure, B. Van Poel, L. Pieters, M. Claeys, D. V. Berghe, K. Kambu, L. Tona, and A. J. Vlietinck, *Planta Med.*, 1996, **62**, 22; (d) P. Grellier, L. Ramiaramanana, V. Millerioux, E. Deharo, J. Schrével, F. Frappier, F. Trigalo, B. Bodo, and J. L. Pousset, *Phytother. Res.*, 1996, **10**, 317.
3. A. Paulo, E. T. Gomes, and P. J. Houghton, *J. Nat. Prod.*, 1995, **58**, 1485.
4. A. Paulo, E. T. Gomes, J. Steele, D. C. Warhurst, and P. J. Houghton, *Planta Med.*, 2000, **66**, 30.
5. (a) K. Cimanga, T. De Bruyne, L. Pieters, M. Claeys, and A. Vlietinck, *Tetrahedron Lett.*, 1996, **37**, 1703; (b) M. H. M. Sharaf, P. L. Schiff Jr., A. N. Tackie, C. H. Phoebe Jr., and G. E. Martin, *J. Heteterocycl. Chem.*, 1996, **33**, 239.
6. J. L. Pousset, M. T. Martin, A. Jossang, and B. Bodo, *Phytochemistry*, 1995, **39**, 735.
7. P. Zhang and D. E. Bierer, *J. Nat. Prod.*, 2000, **63**, 643.
8. K. Blinov, M. Elyashberg, E. R. Martirosian, S. G. Molodtsov, A. J. Williams, A. N. Tackie, M. M.

H. Sharaf, P. L. Schiff Jr., R. C. Crouch, G. E. Martin, C. E. Hadden, J. E. Guido, and K. A. Mills, *Magn. Reson. Chem.*, 2003, **41**, 577.

9. (a) A. N. Tackie, G. L. Boye, M. H. M. Sharaf, P. L. Schiff Jr., R. C. Crouch, T. D. Spitzer, R. L. Johnson, J. Dunn, D. Minick, and G. E. Martin, *J. Nat. Prod.*, 1993, **56**, 653; (b) J. Saurí, W. Bermel, A. V. Buevich, E. C. Sherer, L. A. Joyce, M. H. M. Sharaf, P. L. Schiff Jr., T. Parella, R. T. Williamson, and G. E. Martin, *Angew. Chem. Int. Ed.*, 2015, **54**, 10160.
10. G. V. Subbaraju, J. Kavitha, D. Rajasekhar, and J. I. Jimenez, *J. Nat. Prod.*, 2004, **67**, 461.
11. (a) A. B. J. Bracca, D. A. Heredia, E. L. Larghi, and T. S. Kaufman, *Eur. J. Org. Chem.*, 2014, 7979; (b) P. T. Parvatkar and P. S. Parameswaran, *Curr. Org. Synth.*, 2016, **13**, 58; (c) D. A. Aksenov, N. A. Arutyunov, A. Z. Gasanova, N. A. Aksenov, A. V. Aksenov, C. Lower, and M. Rubin, *Tetrahedron Lett.*, 2021, **82**, 153395; (d) M. Uyanik, H. Tanaka, and K. Ishihara, *Asian J. Org. Chem.*, 2021, **10**, 164; (e) L.-H. Yeh, H.-K.Wang, G. Pallikonda, Y.-L. Ciou, and J.-C. Hsieh, *Org. Lett.*, 2019, **21**, 1730; (f) B.-S. Li, Y. Wang, R. S. J. Proctor, Y. Zhang, R. D. Webster, S. Yang, B. Song, and Y. R. Chi, *Nat. Commun.*, 2016, **7**, 12933.
12. (a) P. T. Parvatkar, P. S. Parameswaran, and S. G. Tilve, *J. Org. Chem.*, 2009, **74**, 8369; (b) H. K. Kadam and S. G. Tilve, *J. Heterocycl. Chem.*, 2016, **53**, 2066.
13. A. Khorshidi and K. J. Tabatabaeian, *Mol. Catal. A: Chem.*, 2011, **344**, 128.
14. R. Ghorbani-Vaghei and S. M. Malaekehpoor, *Tetrahedron Lett.*, 2012, **53**, 4751.
15. P. T. Parvatkar, P. S. Parameswaran, D. Bandyopadhyay, S. Mukherjee, and B. K. Banik, *Tetrahedron Lett.*, 2017, **58**, 2948.
16. S. Yu, Y. Li, X. Zhou, H. Wang, L. Kong, and X. Li, *Org. Lett.*, 2016, **18**, 2812.
17. M. K. Vecchione, A. X. Sun, and D. Seidel, *Chem. Sci.*, 2011, **2**, 2178.
18. Z. Yan, C. Wan, J. Wan, and Z. Wang, *Org. Biomol. Chem.*, 2016, **14**, 4405.
19. (a) J. Yang, H. Song, X. Xiao, J. Wang, and Y. Qin, *Org. Lett.*, 2006, **8**, 2187; (b) J. H. Hall and E. Patterson, *J. Am. Chem. Soc.*, 1967, **89**, 5856; (c) H. R. Snyder, C. B. Thompson, and R. L. Hinman, *J. Am. Chem. Soc.*, 1952, **74**, 2009.
20. (a) M. Pailer, A. Schleppnik, and A. Meller, *Monatsh. Chem.*, 1965, **96**, 1695; (b) H. K. Kadam, D. D. Malik, L. Salgaonkar, K. Mandrekar, and S. G. Tilve, *Synth. Commun.*, 2017, **47**, 1980.
21. E. Gráczol-Fördős, T. Novák, G. Blaskó, I. Fejes, F. Perron-Sierra, and M. Nyerges, *Heterocycles*, 2013, **87**, 2053.
22. (a) L. Zhang, W. Ren, X. Wang, J. Zhang, J. Liu, L. Zhao, and X. Zhang, *Eur. J. Med. Chem.*, 2017, **126**, 1071; (b) W. Ren, X.-Y. Wang, J.-J. Li, M. Tian, J. Liu, L. Ouyang, and J.-H. Wang, *RSC Adv.*, 2017, **7**, 1863.
23. K. E. Treuerné Balázs, M. Molnár, Z. Madarász, and M. Nyerges, *Synth. Commun.*, 2020, **50**, 3245.

24. (a) A. Da Settimo, G. Primofiore, P. L. Ferrarini, C. Mori, C. Martini, E. Pennacchi, and A. Lucacchini, *Il Farmaco*, 1986, **41**, 577; (b) A. Da Settimo, G. Primofiore, G. Biagi, C. Martini, M. Zoppi, and A. Lucacchini, *Il Farmaco*, 1982, **37**, 740; (c) A. Da Settimo, G. Primofiore, V. Santerini, G. Biagi, and L. D'Amico, *J. Org. Chem.*, 1977, **42**, 1725.
25. H. Mastalarz, R. Jasztold-Howorko, F. Rulko, A. Croisy, and D. Carrez, *Arch. Pharm.*, 2004, **337**, 434.
26. (a) H. Zou, L. Zhang, J. Ouyang, M. A. Giulianotti, and Y. Yu, *Eur. J. Med. Chem.*, 2011, **46**, 5970; (b) V. Bernard-Gauthier, A. Aliaga, An. Aliaga, M. Boudjemeline, R. Hopewell, A. Kostikov, P. Rosa-Neto, A. Thiel, and R. Schirrmacher, *ACS Chem. Neurosci.*, 2015, **6**, 260.
27. G. P. Gunawardana, S. Kohmoto, S. P. Gunasekera, O. J. McConnell, and F. E. Koehn, *J. Am. Chem. Soc.*, 1988, **110**, 4856.
28. A. R. Carroll and P. J. Scheuer, *J. Org. Chem.*, 1990, **55**, 4426.
29. (a) H. Eo, C. H. Reed, and R. J. Valentine, *Biomed. Pharmacother.*, 2020, **128**, 110238; (b) N. V. Jammi, L. R. Whitby, and P. A. Beal, *Biochem. Biophys. Res. Commun.*, 2003, **308**, 50.
30. (a) A. Beauchard, A. Jaunet, L. Murillo, B. Baldeyrou, A. Lansiaux, J.-R. Chérouvrier, L. Domon, L. Picot, C. Bailly, T. Besson, and V. Thiéry, *Eur. J. Med. Chem.*, 2009, **44**, 3858; (b) A. Beauchard, H. Chabane, S. Sinbandhit, P. Guenot, V. Thiéry, and T. Besson, *Tetrahedron*, 2006, **62**, 1895.
31. H. N. Bramson, J. Corona, S. T. Davis, S. H. Dickerson, M. Edelstein, S. V. Frye, R. T. Gampe, P. A. Harris, A. Hassell, W. D. Holmes, R. N. Hunter, K. E. Lackey, B. Lovejoy, M. J. Luzzio, V. Montana, W. J. Rocque, D. Rusnak, L. Shewchuk, J. M. Veal, D. H. Walker, and L. F. Kuyper, *J. Med. Chem.*, 2001, **44**, 4339.