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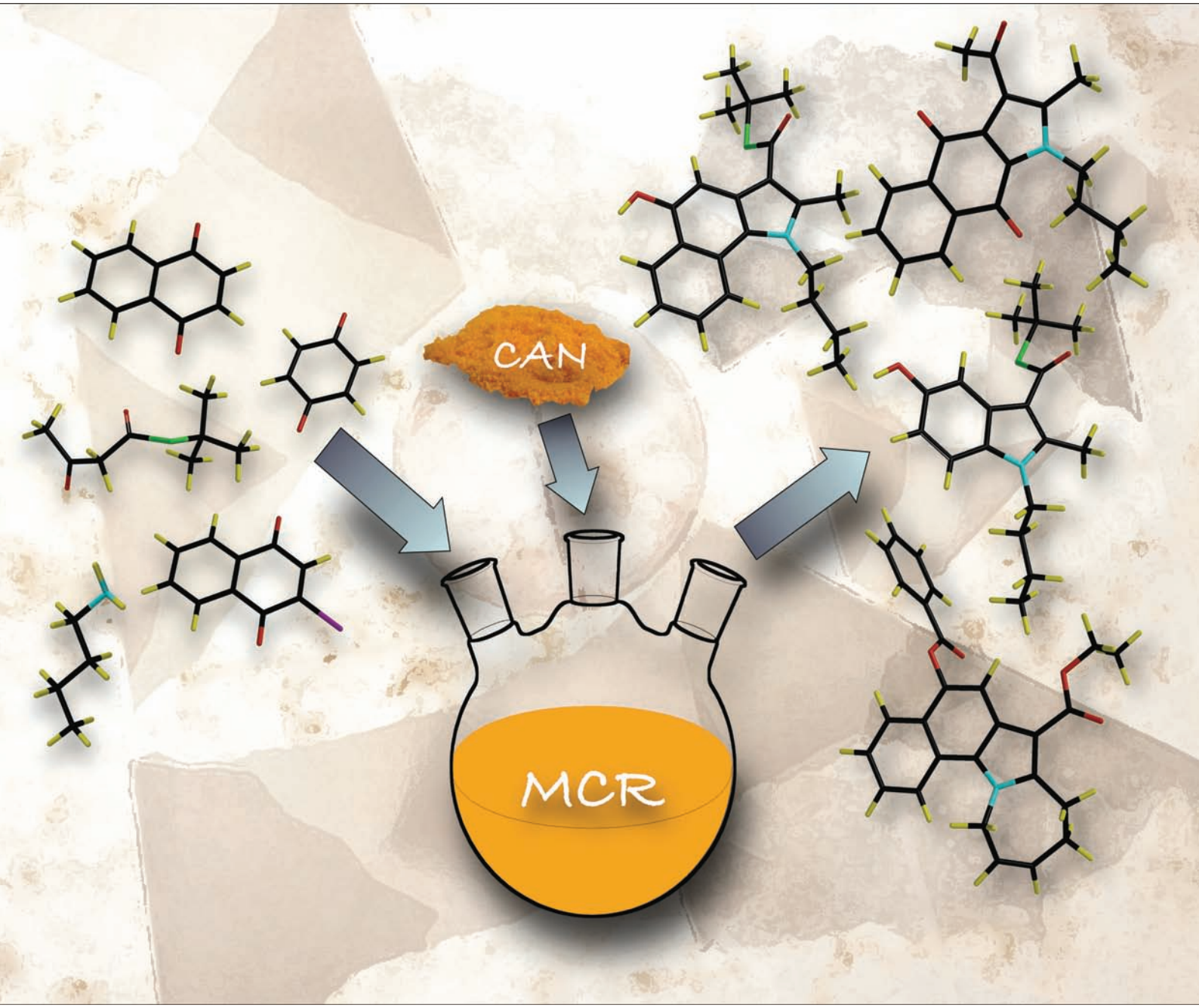

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Expedient, one-pot preparation of fused indoles *via* CAN-catalyzed three-component domino sequences and their transformation into polyheterocyclic compounds containing pyrrolo[1,2-*a*]azepine fragments†

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The CAN-catalyzed three-component between reaction between primary amines, β-dicarbonyl compounds and naphthoquinones or 2-bromonaphthoquinones afforded, respectively, 5-hydroxybenzo[*g*]indoles and benzo[*f*]indole-4,9-diones, the former of which were transformed into tetracyclic azepino[1,2-*a*]benzo[*g*]indole systems through a γ-alkylation/ring-closing metathesis sequence.

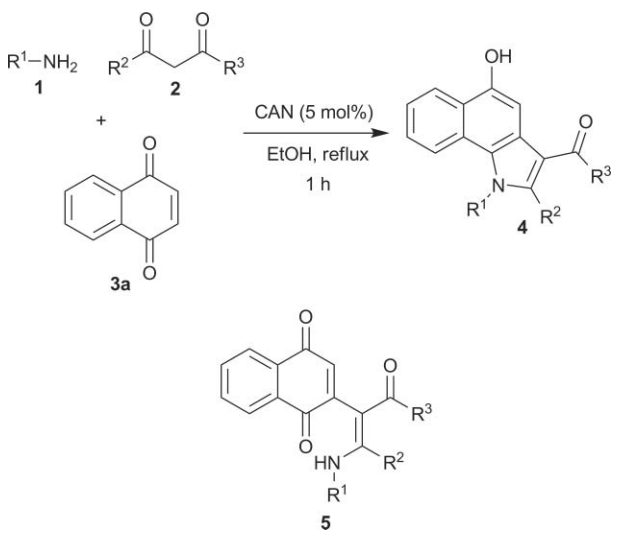
Introduction

The indole ring system is a widespread structural motif found in a large number of naturally occurring molecules and it can perhaps be considered as the most important single class of heterocyclic systems.[1] Indole derivatives possess a wide range of powerful and therapeutically interesting biological activities,[2] and indeed indole derivatives have been included in the "privileged scaffolds" category[3] because they comply with the definition proposed by Evans in that they constitute "a molecular framework able to provide ligands for diverse receptors".[4] Consequently, the development of new synthetic methodologies and the improvement of the existing synthetic routes for the construction of the indole scaffold is a very important topic in organic synthesis. The most common and traditional methods for the synthesis of indoles[5] include the Fischer, Bischler, Reissert, Madelung and Smith methodologies. In addition, organometallic reagents, particularly palladium compounds, have found widespread application in modern indole syntheses.[6] Among the available synthetic methodologies leading to indoles, the Nenitzescu reaction, *i.e.* the reaction between 1,4-benzoquinones and β-enaminones to afford 5-hydroxyindoles, has remained relatively unexplored despite its experimental simplicity and the pharmaceutical applications of some of the products derived from it.[7–9] The main drawbacks of this methodology include the problems associated with the purification of the acid-sensitive enaminones and the poor yields normally observed for the final products.

Results and discussion

The first purpose of our work was to overcome the problems associated with the Nenitzescu reaction and to extend its range of synthetic applications. As the main difficulty lies in the purification of the enaminones, we planned to carry out the reaction in a one-pot multicomponent fashion[10] using a Lewis acid with the two-fold mission of promoting the formation of enamines from 1,3-dicarbonyl compounds and primary amines and facilitating the subsequent Michael addition to quinones. Cerium(IV) ammonium nitrate (CAN) was our initial choice because of its low cost, non-toxicity, and moisture tolerance, together with its good Lewis acidity,[11] and also because there is literature precedent for the use of CAN as a catalyst in β-enaminone synthesis.[11e]

We started our study by conducting the reaction of n-butylamine **1a** and ethyl acetoacetate **2a** in ethanol in the presence of a catalytic amount of CAN (5 mol%) followed by the addition of 1,4-naphthoquinone **3a**, which was chosen because it has received relatively little attention as a Nenitzescu substrate. After stirring the reaction mixture at room temperature for 2 h, the fused indole **4a** was isolated in 27% yield together with quinone **5a** (63%) (see Scheme 1). An increase of the reaction time to 24 h furnished a complex mixture that contained only small amounts of **4a** and **5a**. Gratifyingly, we found subsequently that, under reflux conditions, the reaction afforded compound **4a** in 93% yield as a single product in only one hour. As mentioned below (see Scheme 3), we propose that the use of reflux conditions deviates the reaction



Scheme 1 CAN-catalyzed three-component reaction between primary amines, β-dicarbonyl compounds and 1,4-naphthoquinone.

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Table 1 Solvent optimization for the CAN-catalyzed reaction between butylamine, ethyl acetoacetate and 1,4-naphthoquinone

Entry	Solvent	Yield of **4a** (%)
1	Ethanol	93
2	CH_3CN	92
3	Methanol	57
4	THF	66
5	CH_2Cl_2	57
6	$(CH_2Cl)_2$	93
7	Toluene	67
8	1,4-Dioxane	90
9	$CHCl_3$	28

from the expected mechanistic pathway, explaining its very high efficiency and cleanliness. We next examined the model reaction in different solvents under the previously established time and temperature conditions. As shown in Table 1, ethanol, acetonitrile, 1,2-dichloroethane, and 1,4-dioxane were found to be excellent solvents for the reaction while methanol, THF, dichloromethane, toluene and (specially) chloroform were less effective. Ethanol was chosen as the optimal solvent for subsequent studies because of its low cost and toxicity.

The application of the optimized conditions (5 mol% CAN, 1 h reflux in ethanol) to a number of 1,3-dicarbonyl compounds allowing structural variation at R^1, R^2 and R^3 is summarized in Scheme 1 and Table 2. We initially sought to further optimize the model reaction, and found that an increase of the reflux time to 1.5 h led only to a slight improvement of the yield (entry 2), and also that the substitution of CAN by $InCl_3$ (10 mol%) as an alternative Lewis acid furnished the same product after a 2 h reflux without any significant change in the yield. We considered these improvements to have little significance and hence we retained for our subsequent reactions the 1 h reflux time and CAN as a catalyst because of its many previously mentioned advantages. The scope of the reaction included the use of β-keto esters and β-keto thioesters as the dicarbonyl component and aliphatic primary amines (n-butyl, allyl, propargyl, and benzyl amines, entries 3–10) or anilines having either electron-withdrawing or

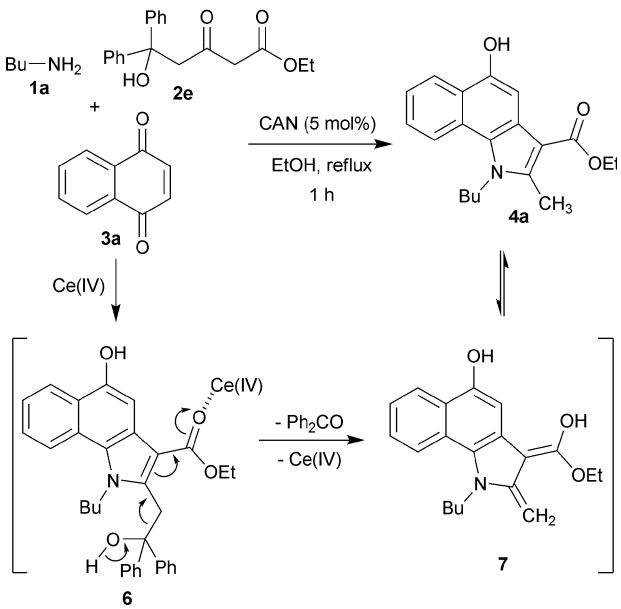
Table 2 Scope and yields of the three-component reaction between primary amines, β-dicarbonyl compounds and 1,4-naphthoquinone

Entry	Cmpd.	R^1	R^2	R^3	Yield (%)
1	**4a**	^{n}Bu	Me	OEt	93
2	**4a**	^{n}Bu	Me	OEt	96[a]
3	**4a**	^{n}Bu	Me	OEt	95[b]
4	**4b**	^{n}Bu	Me	OMe	96
5	**4c**	allyl	Me	OEt	90
6	**4d**	Bn	Me	OEt	90
7	**4e**	allyl	Me	OMe	89
8	**4f**	allyl	Me	S-^{t}Bu	87
9	**4g**	propargyl	Me	S-^{t}Bu	88
10	**4h**	propargyl	Me	OEt	75
11	**4i**	Ph	Me	OEt	65
12	**4j**	*p*-$OMeC_6H_4$	Me	OEt	55
13	**4j**	*p*-$OMeC_6H_4$	Me	OEt	73[c]
14	**4k**	*p*-ClC_6H_4	Me	OEt	50
15	**4k**	*p*-ClC_6H_4	Me	OEt	76[c]
16	**4l**	^{n}Bu	Me	S-^{t}Bu	70
17	**4m**	^{n}Bu	^{n}Pr	OEt	52

[a] Reaction time, 1.5 h. [b] $InCl_3$ (10 mol%) was used as a catalyst (2 h reaction time). [c] Isolated, crude enamines were used as starting materials.

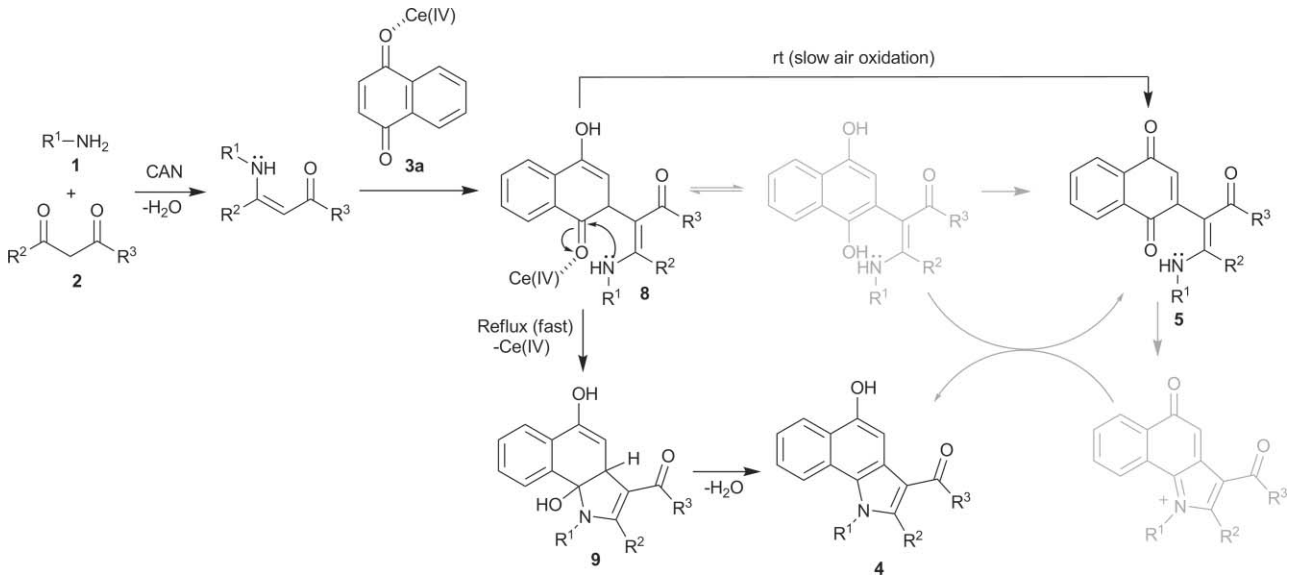
electron-releasing groups as the amine. All these substrates gave compounds **4** in good to excellent yields with the sole exception of arylamines (entries 11–15), for which yields were lower in the one-pot reaction due to the low reactivity of these amines with 1,3-dicarbonyls in the enamine formation step.[11e] However, the problem could be solved by use of isolated, crude enamines as starting materials. An attempt to use a α-branched primary amine, namely cyclohexylamine, afforded only the corresponding intermediate **5** (72% yield after 1 h reaction time in the presence of 5 mol% CAN), and all attempts to effect its cyclization were unsuccessful. Regarding the scope of the method in terms of the R^2 substituent, we verified that the reaction gave good results with alkyl substituents, but not when R^2 was aryl.

The reaction between n-butylamine, ethyl 5-hydroxy-3-oxo-5,5-diphenylpentanoate **2e** and 1,4-naphthoquinone did not afford the expected product, but gave instead the C_2-methyl derivative **4a** in 55% yield (Scheme 2). This reaction probably proceeded through the formation of the expected product **6**, which would be activated by CAN by coordination with the ester carbonyl to facilitate the elimination a molecule of benzophenone to give the observed indole **4a** *via* intermediate **7**.



Scheme 2 Loss of benzophenone in the reaction involving 5-hydroxy-3-oxo-5,5-diphenylpentanoate as the β-dicarbonyl component.

Regarding the mechanism of the three-component reaction, a detailed literature search on the mechanism of the Nenitzescu reaction showed that there are two possible routes to explain the observed product. The first one (mechanism *a*) is initiated by the formation of a carbon–carbon bond by a Michael addition of the enaminone to the quinone followed by a nucleophilic cyclization that generates a carbon–nitrogen bond. The second possibility involves the initial formation of a carbon–nitrogen bond by condensation of the enamine with the quinone carbonyl, and subsequent cyclization to form the carbon–carbon bond (mechanism *b*).[7] In our experimental conditions, we can rule out mechanism *b* in view of our isolation of compounds **5** on many occasions. The mechanism normally accepted for route *a* conventionally involves a redox process which, applied to our case, would



Scheme 3 Non-redox mechanistic proposal for the CAN-catalyzed three-component benzo[*g*]indole synthesis.

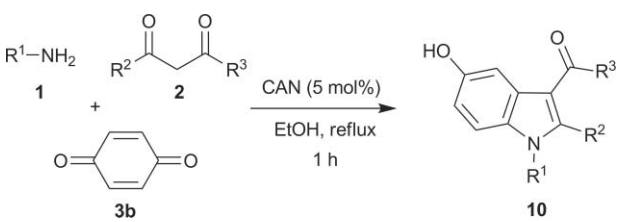
start by an initial Michael addition followed by tautomerism to the corresponding hydroquinone species. Its oxidation by air to quinone **5**, even in trace amounts, is enough to trigger a redox cycle in which **5** is cyclized to an iminium derivative, which is then reduced by the hydroquinone to give another molecule of **5** and the observed product **4**.[7,12] However, this mechanism seems not to be in operation in our case since treatment of isolated quinone **5a** with one equivalent of externally added hydroquinone under our standard reaction conditions (5 mol% of CAN in refluxing ethanol) did not afford compound **4a**. Based on these observations, we propose an alternative mechanism not involving any redox reaction, where the enamine formed by reaction between amines **1** and 1,3-dicarbonyl compounds **2** adds to the CAN-activated naphthoquinone to afford intermediate **8**, which at room temperature is slowly converted by air oxidation into the *p*-quinone derivative **5**. On the other hand, under our optimized conditions, which involve reflux temperature, intermediate **8** undergoes a fast intramolecular nucleophilic cyclization before tautomerism, prompted by coordination of Ce(IV) to its carbonyl group,[13] and this is followed by elimination of a molecule of water to furnish the observed fused indoles **4** (Scheme 3).

In order to further probe the generality of our three-component methodology, and also to facilitate its comparison with the standard Nenitzescu reaction, we studied its applicability to the reaction using *p*-benzoquinone **3b**, the most common substrate for the Nenitzescu reaction. Again, the expected 5-hydroxyindoles **10** were obtained in very good yields and the reaction had a similar scope to the one starting from naphthoquinone (Scheme 4, Table 3). The reaction between amines, ethyl 3-oxohexanoate and *p*-benzoquinone gave particularly good yields of the corresponding indoles having a propyl substituent at position 2, showing an enhanced reactivity for *p*-benzoquinone compared with 1,4-naphthoquinone (entries 7 and 8).

As an additional refinement of our study, we next briefly examined how the presence of a leaving group at the C-2 position of the starting quinone affected our three-component reaction, based on the hypothesis that this modification could change the

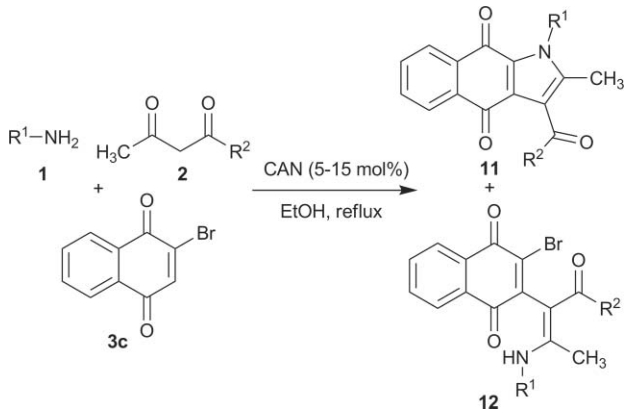
Table 3 Scope and yields of the three-component reaction between primary amines, β-dicarbonyl compounds and 1,4-benzoquinone

Entry	Compd	R^1	R^2	R^3	Yield (%)
1	**10a**	*n*Bu	Me	OEt	78
2	**10b**	allyl	Me	OEt	75
3	**10c**	Bn	Me	OEt	73
4	**10d**	propargyl	Me	OEt	69
5	**10e**	*n*Bu	Me	S-*t*Bu	86
6	**10f**	allyl	Me	S-*t*Bu	81
7	**10g**	*n*Bu	*n*Pr	OEt	82
8	**10h**	allyl	*n*Pr	OEt	78



Scheme 4 CAN-catalyzed three-component synthesis of 5-hydroxyindoles.

reaction mode to a Michael–Michael domino sequence, leading to a method for the preparation of linear tricyclic systems. Hence, we applied our three-component protocol to butylamine **1a**, ethyl acetoacetate **2a**, and 2-bromonaphthoquinone **3c**[14] as the Michael acceptor and observed the formation of indolequinone **11a** as the main product together with compound **12a**, which can be regarded as an intermediate of the pathway leading to **11a** (Scheme 5). Changes in the reflux time and catalyst load led to very similar results (Table 4), and indeed we found that the reaction could be performed at room temperature with little change in the final results (entry 4). When acetylacetone was used as the starting material, fused indolequinone **11b** was isolated as the only product in 67% yield (entry 7). It is noteworthy that literature precedent of a Nenitzescu reaction between 2-chloroanthracene-1,4,9,10-tetraone and a β-enaminone proceeded through the



Scheme 5 Three-component synthesis of benzo[*f*]indolequinones from primary amines, β-dicarbonyl compounds and 2-bromo-1, 4-naphthoquinone.

Table 4 Conditions and yields for the three-component reaction between primary amines, β-dicarbonyl compounds and 2-bromo-1,4-naphthoquinone

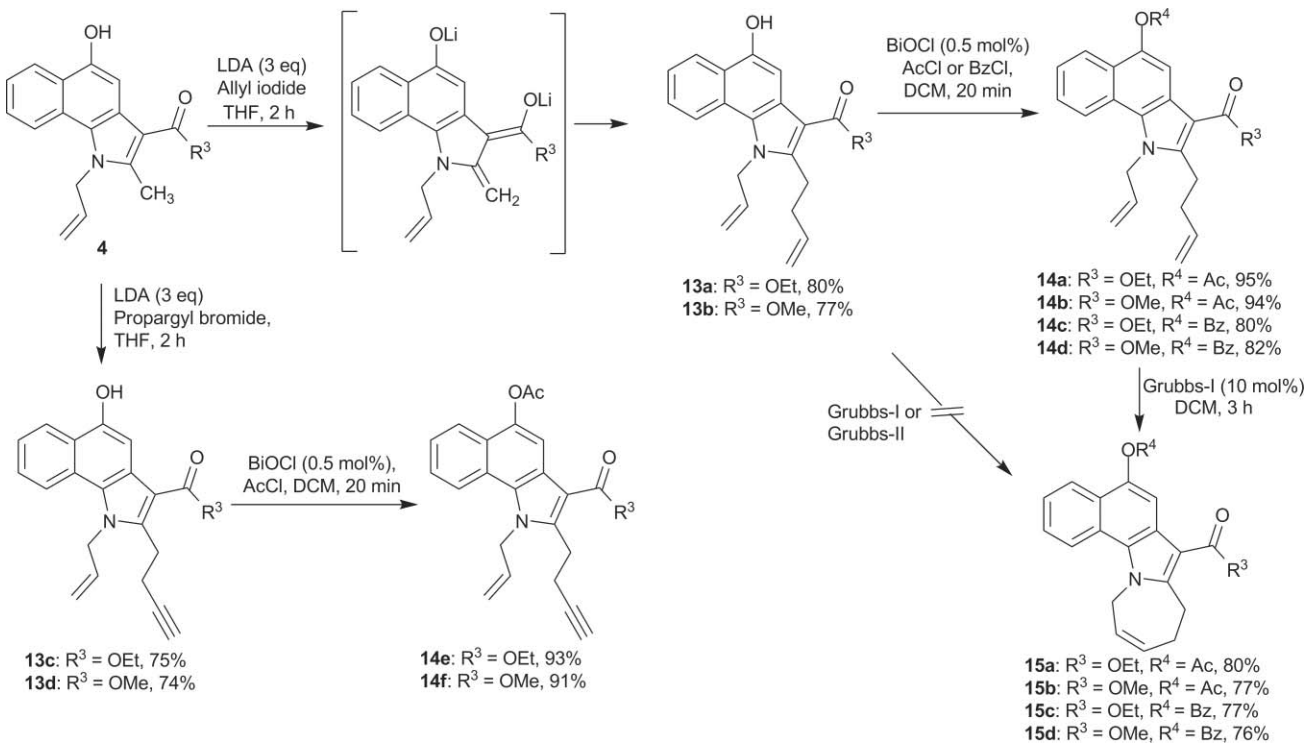
Entry		R^1	R^2	CAN (%)	Time/h	% **11**	% **12**
1	**a**	^{n}Bu	OEt	5	1	50	21
2	**a**	^{n}Bu	OEt	5	3	39	17
3	**a**	^{n}Bu	OEt	5	1	54[a]	18
4	**a**	^{n}Bu	OEt	5	1	51[b]	17
5	**a**	^{n}Bu	OEt	15	2.5	50	12
6	**a**	^{n}Bu	OEt	5	24	0[c]	0
7	**b**	^{n}Bu	Me	5	1	67	0
8	**c**	Bn	Me	5	1	51	0
9	**d**	allyl	Me	5	1	44	0
10	**e**	propargyl	Me	5	1	42	0

[a] Isolated, crude enamine was used. [b] Isolated enamine was used and the reaction was carried out at room temperature. [c] Decomposed.

standard pathway, affording an angular fused indole related to the anthracyclines.[15a] On the other hand, a few examples of two-component reactions between β-enaminones and bromoquinones that give linear products related to ours are known in the literature, but they required Ullman-type conditions (K_2CO_3, $CuBr_2$) and proceed only in 15–25% yields.[15b] Further studies on this transformation are in progress in our laboratory.

Finally, we reasoned that the functionality present in compounds **4** should allow their use as starting materials for novel routes to structurally complex nitrogen heterocycles. For instance, a ring-closing metathesis reaction between suitable substituents placed at the indole nitrogen and the adjacent methyl group should provide ready access to unusual tetracyclic compounds bearing a bridgehead nitrogen atom. In order to translate this idea into practice, we examined the possibility of using the acidity of the carbonyl-conjugated 2-methyl group of fused indoles **4** to introduce terminal alkenyl and alkynyl chains by a deprotonation–nucleophilic substitution sequence, although this type of deprotonation of 2-methylindoles has received little attention in the literature.[16] In the event, we discovered that treatment of N-allyl derivatives of compounds **4** with LDA in THF followed by addition of allyl iodide smoothly afforded the desired metathesis precursors **13** in high yields (Scheme 6). These alkylation reactions can be presumed to occur on dianion species generated by deprotonation of both the phenol and the C_2-methyl group and, interestingly, were completely regioselective in favour of the latter.

All efforts to achieve the ring-closing metathesis (RCM) and ring-closing enyne metathesis (RCEYM) reaction of **13** using Grubbs catalysts were unsuccessful. However, as shown in



Scheme 6 Synthesis of 9,12-dihydro-8*H*-azepino[1,2-*a*]benzo[*g*]indoles by ring-closing metathesis.

Scheme 6, the *O*-acetylated and benzoylated derivatives **14a–d** underwent smooth ring-closing reaction in the presence of 10 mol% of Grubbs 1st generation catalyst under mild experimental conditions in dichloromethane to give very good yields of compounds **15**, which are derivatives of the hitherto unknown 9,12-dihydro-8*H*-azepino[1,2-*a*]benzo[*g*]indole ring system and are of potential biological interest in view of the varied biological activities known for pyrrolo[1,2-*a*]azepine derivatives.[17] This efficient transformation is noteworthy in view of the difficulties often associated with the construction of medium-sized rings by RCM, specially from acyclic precursors, owing to entropic factors and transannular repulsions that develop as the ring is formed.[18] Indeed, to our knowledge, the synthesis of compounds **15** constitutes the first example of the preparation of a pyrrolo[1,2-*a*]azepine system by a metathesis strategy. On the other hand, the RCEYM reactions of **14e** and **14f** gave only traces of the desired products, even after assaying a variety of commercially available metathesis catalysts in different solvents including the highly effective fluorinated aromatic hydrocarbon metathesis solvents,[19] and also failed under an ethylene atmosphere, which is often used to promote ene-yne metathesis reactions.[20]

Conclusions

In summary, we have developed an efficient methodology for the synthesis of benzo[*g*]indoles and 5-hydroxyindoles based on a CAN-catalyzed, three-component enamine formation–Michael addition–intramolecular imine formation domino sequence starting from amines, β-dicarbonyl compounds and quinones, in a three-component variation of the Nenitzescu indole synthesis. The conventional oxidation–reduction mechanism normally accepted for the Nenitzescu reaction was ruled out under our conditions and the available experimental evidence led us to propose a non-redox mechanism different from the one commonly accepted for this reaction. The three-component protocol was also extended to the synthesis of linear benzo[*f*]indolequinones by using 2-bromoquinones as the starting materials. The benzo[*g*]indole derivatives were transformed into 9,12-dihydro-8*H*-azepino[1,2-*a*]benzo[*g*]-indoles, a new class of fused indole derivatives, using a C-alkylation/ring-closing metathesis strategy.

Experimental section

General experimental information

All reagents (Aldrich, Fluka, SDS, Probus) and solvents (SDS) were of commercial quality and were used as received. Reactions were monitored by thin layer chromatography, on aluminium plates coated with silica gel with fluorescent indicator (SDS CCM221254). Separations by flash chromatography were performed on silica gel (SDS 60 ACC 40–63 μm) or neutral alumina (Merck S22). Melting points were measured on a Reichert 723 hot stage microscope, and are uncorrected. Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrophotometer, with all compounds examined as KBr pellets or as thin films on NaCl disks. NMR spectra were obtained on a Bruker Avance 250 spectrometer operating at 250 MHz for ^{1}H and 63 MHz for ^{13}C (CAI de Resonancia Magnética Nuclear, Universidad Complutense). Elemental analyses were determined by the CAI de Microanálisis Elemental, Universidad Complutense, using a Leco 932 CHNS combustion microanalyzer.

General procedure for the synthesis of benzo[*g*]indoles 4 and *p*-quinone derivatives 5

To a stirred mixture of primary amines **1** (3 mmol) and 1,3-dicarbonyl compounds **2** (3 mmol) in ethanol (6 mL) was added CAN (5 mol%) and stirring was continued for 30 min at room temperature. 1,4-Naphthoquinone **3a** (3 mmol) was then added and the mixture was refluxed for further 30 min. After completion of the reaction, as indicated by tlc, dichloromethane (20 mL) was added to the mixture and the resulting solution was washed with water (5 mL), dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude reaction mixture was purified by silica column chromatography using petroleum ether–ethyl acetate mixture (80 : 20, v/v) as eluent. Characterization data for compounds **4** follow, and also for compound **5a**, which was isolated in 72% yield after 1 h reaction time at room temperature in the presence of 5 mol% CAN.

Ethyl 1-butyl-5-hydroxy-2-methyl-1*H*-benzo[*g*]indole-3-carboxylate (4a). Off-white solid; mp 191–192 °C; IR (KBr) 3266, 2963, 2933, 1646, 1599, 1521, 1415, 1334, 1247, 1123 cm^{-1}; ^{1}H NMR (DMSO-d$_6$, 250 MHz) δ 0.94 (t, J = 7.2 Hz, 3H), 1.37–1.48 (m, 5H), 1.73–1.84 (m, 2H), 2.77 (s, 3H), 4.28–4.36 (q, J = 7.1 Hz, 2H), 4.48–4.54 (t, J = 7.5 Hz, 2H), 7.43 (dd, J = 7.8, 7.1 Hz, 1H), 7.60 (dd, J = 8.3, 7.1 Hz, 1H), 7.72 (s, 1H), 8.26–8.31 (m, 2H), 9.76 (s, 1H); ^{13}C NMR (DMSO-d$_6$, 63 MHz) δ 12.0, 14.0, 14.9, 19.7, 31.8, 40.8, 59.3, 102.0, 104.0, 120.6, 122.5, 122.8, 123.2, 123.6, 123.8, 124.8, 126.7, 143.0, 148.6, 165.6; Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.53; H, 6.95; N, 4.19%.

Methyl 1-butyl-5-hydroxy-2-methyl-1*H*-benzo[*g*]indole-3-carboxylate (4b). Off-white solid; mp 221–222 °C; IR (KBr) 3281, 2954, 1654, 1598, 1522, 1441, 1333, 1248, 1199, 1121 cm^{-1}; ^{1}H NMR (DMSO-d$_6$, 250 MHz) δ 0.95 (t, J = 7.2 Hz, 3H), 1.38–1.50 (m, 2H), 1.74–1.83 (m, 2H), 2.78 (s, 3H), 3.86 (s, 3H), 4.53 (t, J = 7.6 Hz, 2H), 7.44 (dd, J = 7.8, 7.2 Hz, 1H), 7.62 (dd, J = 7.8, 7.6 Hz, 1H), 7.69 (s, 1H), 8.27–8.34 (m, 2H), 9.79 (s, 1H); ^{13}C NMR (DMSO-d$_6$, 63 MHz) δ 12.1, 14.0, 19.7, 31.8, 45.4, 50.9, 101.9, 103.9, 120.6, 122.5, 122.9, 123.2, 123.4, 123.8, 124.7, 126.8, 143.1, 148.6, 166.0; Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.08; H, 6.67; N, 4.23%.

Ethyl 1-allyl-5-hydroxy-2-methyl-1*H*-benzo[*g*]indole-3-carboxylate (4c). Off-white solid; mp 218–219 °C; IR (KBr) 3259, 2981, 1644, 1597, 1529, 1418, 1336, 1245, 1131 cm^{-1}; ^{1}H NMR (DMSO-d$_6$, 250 MHz) δ 1.41 (t, J = 7 Hz, 3H), 2.73 (s, 3H), 4.33 (q, J = 7.0 Hz, 2H), 4.65 (d, J = 17.2 Hz, 1H), 5.17–5.22 (m, 3H), 6.21–6.38 (m, 1H), 7.42 (dd, J = 7.8, 7.1 Hz, 1H), 7.54 (dd, J = 7.7, 6.8 Hz, 1H), 7.72 (s, 1H), 8.21–8.28 (m, 2H), 9.79 (s, 1H); ^{13}C NMR (DMSO-d$_6$, 63 MHz) δ 11.7, 14.9, 48.0, 59.4, 101.9, 104.3, 116.0, 120.9, 122.3, 122.9, 123.3, 123.6, 123.8, 124.4, 126.4, 133.9, 143.3, 148.6, 165.6; Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.48; H, 6.16; N, 4.54%.

Ethyl 1-benzyl-5-hydroxy-2-methyl-1*H*-benzo[*g*]indole-3-carboxylate (4d). Off-white solid; mp 240–241 °C; IR (KBr) 3264, 2928, 1641, 1599, 1523, 1416, 1336, 1293, 1247, 1124 cm^{-1}; ^{1}H

NMR (DMSO-d_6, 250 MHz): δ 1.43 (t, J = 7.0 Hz, 3H), 2.74 (s, 3H), 4.35 (q, J = 7.0 Hz, 2H), 5.90 (s, 2H), 7.05 (d, J = 7.4 Hz, 2H), 7.25–7.37 (m, 5H), 7.76 (s, 1H), 8.07–8.10 (m, 1H), 8.22–8.25 (m, 1H), 9.83 (s, 1H); ^{13}C NMR (DMSO-d_6, 63 MHz): δ 11.9, 14.9, 49.1, 59.5, 101.9, 104.6, 120.7, 122.3, 122.9, 123.4, 123.6, 123.8, 124.7, 125.9, 126.4, 127.6, 129.3, 137.4, 143.6, 148.8, 165.6; Anal. Calcd for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.90. Found: 76.50; H, 6.05; N, 3.78%.

Methyl 1-allyl-5-hydroxy-2-methyl-1*H*-benzo[*g*]indole-3-carboxylate (4e). Off-white solid; mp 220–221 °C; IR (KBr) 3256, 2980, 1644, 1623, 1597, 1530, 1415, 1335, 1245, 1130, 1071 cm^{-1}; ^{1}H NMR (DMSO-d_6, 250 MHz): δ 2.74 (s, 3H), 3.88 (s, 3H), 4.36 (d, J = 17.2 Hz, 1H), 5.19–5.24 (m, 3H), 6.25–6.36 (m, 1H), 7.44 (dd, J = 7.6, 7.1 Hz, 1H), 7.56 (dd, J = 7.5, 6.9 Hz, 1H), 7.71 (s, 1H), 8.23–8.30 (m, 2H), 9.81 (s, 1H); ^{13}C NMR (DMSO-d_6, 63 MHz): δ 11.7, 48.1, 50.9, 101.8, 104.1, 116.0, 120.9, 122.3, 123.0, 123.4, 123.6, 123.8, 124.3, 126.5, 133.9, 143.4, 148.7, 165.9; Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 72.96; H, 6.17; N, 4.52%.

***S*-*tert*-Butyl 1-allyl-5-hydroxy-2-methyl-1*H*-benzo[*g*]indole-3-carbothioate (4f).** Pale brown solid; mp 107–108 °C; IR (KBr) 3377.8, 2963, 1622, 1597, 1512, 1401, 1363, 1265, 1091, 982 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.68 (s, 9H), 2.72 (s, 3H), 4.90 (d, J = 17.5 Hz, 1H), 5.02 (s, 2H), 5.29 (d, J = 12.5 Hz, 1H), 6.13–6.25 (m, 1H), 7.43–7.55 (m, 2H), 7.90 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.36 (d, J = 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.9, 30.9, 48.5, 48.9, 103.2, 115.9, 117.9, 120.9, 122.5, 122.9, 123.4, 123.6, 123.7, 125.4, 126.6, 132.4, 141.0, 147.4, 189.3; Anal. Calcd for $C_{21}H_{23}NSO_2$: C, 71.36; H, 6.56; N, 3.96; S, 9.07. Found: C, 71.08; H, 6.36; N, 4.16; S, 8.73%.

***S*-*tert*-Butyl 5-hydroxy-2-methyl-1-(prop-2-ynyl)-1*H*-benzo[*g*]indole-3-carbothioate (4g).** Pale brown solid; mp 168–169 °C; IR (KBr) 3296, 2964, 2923, 1668, 1652, 1512, 1455, 1364, 1264, 1083, 989 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.66 (s, 9H), 2.20 (s, 1H), 2.86 (s, 3H), 5.16 (s, 2H), 7.28 (s, 1H), 7.51–7.64 (m, 2H), 7.83 (s, 1H), 8.38 (d, J = 7.5 Hz, 1H), 8.47 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.1, 30.8, 36.6, 48.9, 74.8, 76.6, 103.0, 116.3, 121.0, 122.5, 122.8, 123.4, 123.7, 123.8, 125.1, 126.9, 140.0, 147.6, 189.3; Anal. Calcd for $C_{21}H_{21}NSO_2$: C, 71.76; H, 6.02; N, 3.99; S, 9.12. Found: C, 71.48; H, 5.72; N, 4.17; S, 8.92%.

Ethyl 5-hydroxy-2-methyl-1-(prop-2-ynyl)-1*H*-benzo[*g*]indole-3-carboxylate (4h). Off-white solid; mp 235–236 °C; IR (KBr) 3305, 2976, 2924, 1635, 1598, 1525, 1457, 1418, 1336, 1244, 1133 cm^{-1}; ^{1}H NMR (DMSO-d_6, 250 MHz): δ 1.41 (t, J = 7.0 Hz, 3H), 2.81 (s, 3H), 3.53 (s, 1H), 4.33 (q, J = 7.0 Hz, 2H), 5.40 (s, 2H), 7.46 (dd, J = 7.8, 7.7 Hz, 1H), 7.62 (dd, J = 7.9, 7.8 Hz, 1H), 7.70 (s, 1H), 8.29 (d, J = 8.1 Hz, 1H), 8.50 (d, J = 8.6 Hz, 1H), 9.84 (s, 1H); ^{13}C NMR (DMSO-d_6, 63 MHz): δ 11.9, 14.8, 36.3, 59.5, 76.8, 79.2, 101.8, 104.7, 121.2, 122.4, 123.2, 123.4, 123.5, 123.6, 124.4, 126.5, 142.8, 148.8, 165.4; Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.01; H, 5.70; N, 4.34%.

Ethyl 5-hydroxy-2-methyl-1-phenyl-1*H*-benzo[*g*]indole-3-carboxylate (4i). Pale brown solid; mp 230–231 °C; IR (KBr) 3420, 2931, 1648, 1596, 1496, 1411, 1337, 1246, 1196, 1177, 1071 cm^{-1}; ^{1}H NMR (DMSO-d_6, 250 MHz): δ 1.42 (t, J = 7.0 Hz, 3H), 2.43 (s, 3H), 4.36 (q, J = 7.0 Hz, 2H), 6.81 (d, J = 8.5 Hz, 1H), 7.13 (dd, J = 8.3, 7.0 Hz, 1H), 7.31 (dd, J = 8.0, 7.2 Hz, 1H), 7.51–7.54 (m, 2H), 7.72–7.75 (m, 4H), 8.22 (d, J = 8.3 Hz, 1H), 9.87 (s, 1H); ^{13}C NMR (DMSO-d_6, 63 MHz): δ 13.0, 15.0, 59.5, 101.7, 105.1, 119.9, 122.3, 123.1, 123.4, 123.7, 124.2, 124.8, 125.9, 129.2, 130.2, 130.8, 139.3, 143.5, 148.9, 165.6; Anal. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.47; H, 5.56; N, 4.15%.

Ethyl 5-hydroxy-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*g*]-indole-3-carboxylate (4j). Pale brown solid; mp 216–217 °C; IR (KBr) 3273, 2928, 1652, 1514, 1384, 1298, 1249, 1176, 1136, 1033 cm^{-1}; ^{1}H NMR (DMSO-d_6, 250 MHz): δ 1.41 (t, J = 7.0 Hz, 3H), 2.43 (s, 3H), 3.93 (s, 3H), 4.35 (q, J = 7.0 Hz, 2H), 6.94 (d, J = 8.4 Hz, 1H), 7.15–7.46 (m, 6H), 7.74 (s, 1H), 8.22 (d, J = 8.3 Hz, 1H), 9.84 (s, 1H); ^{13}C NMR (DMSO-d_6, 63 MHz): δ 13.0, 14.9, 55.9, 59.4, 101.7, 104.9, 115.8, 119.9, 122.4, 123.0, 123.4, 123.6, 124.0, 125.0, 125.9, 130.2, 131.7, 143.9, 148.9, 160.1, 165.6; Anal. Calcd for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73. Found: C, 73.28; H, 5.77; N, 3.85%.

Ethyl 1-(4-chlorophenyl)-5-hydroxy-2-methyl-1*H*-benzo[*g*]indole-3-carboxylate (4k). Off-white solid; mp 250–251 °C; IR (KBr) 3282, 2927, 1649, 1493, 1386, 1339, 1259, 1137, 1090, 1015 cm^{-1}; ^{1}H NMR (DMSO-d_6, 250 MHz): δ 1.41 (t, J = 7.0 Hz, 3H), 2.42 (s, 3H), 4.36 (q, J = 7.0 Hz, 2H), 6.88 (d, J = 8.5 Hz, 1H), 7.21 (dd, J = 8.2, 7.0 Hz, 1H), 7.33 (dd, J = 8.1, 7.0 Hz, 1H), 7.57–7.61 (m, 2H), 7.74–7.81 (m, 3H), 8.23 (d, J = 8.2 Hz, 1H), 9.90 (s, 1H); ^{13}C NMR (DMSO-d_6, 63 MHz): δ 13.0, 14.8, 59.5, 101.6, 105.4, 119.7, 122.2, 123.2, 123.5, 123.8, 124.3, 124.9, 126.2, 130.8, 131.1, 134.9, 138.4, 143.5, 149.2, 165.3; Anal. Calcd for $C_{22}H_{18}ClNO_3$: C, 69.57; H, 4.78; N, 3.69. Found: C, 69.27; H, 4.94; N, 3.84%.

***S*-*tert*-Butyl 1-butyl-5-hydroxy-2-methyl-1*H*-benzo[*g*]indole-3-carbothioate (4l).** Dark brown viscous liquid; IR (neat) 2968, 2871, 1668, 1597, 1504, 1456, 1364, 1248, 1166, 1079 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.04 (t, J = 7.2 Hz, 3H), 1.52–1.61 (m, 2H), 1.67 (s, 9H), 1.89–1.95 (m, 2H), 2.80 (s, 3H), 4.43 (t, J = 7.3 Hz, 2H), 5.43 (s, 1H), 7.48–7.62 (m, 2H), 7.90 (s, 1H), 8.20 (d, J = 8.4 Hz, 1H), 8.39 (d, 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ (one aromatic carbon signal is merged with others) 13.3, 14.2, 20.5, 30.9, 32.2, 46.0, 48.9, 103.2, 115.8, 120.6, 122.9, 123.7, 123.4, 123.9, 124.8, 126.8, 140.5, 147.3, 189.4; Anal. Calcd. for $C_{22}H_{27}NO_2S$: C, 71.51; H, 7.36; N, 3.79; S, 8.68. Found: C, 71.25; H, 7.15; N, 3.58; S, 8.46%.

Ethyl 1-butyl-5-hydroxy-2-propyl-1*H*-benzo[*g*]indole-3-carboxylate (4m). Brown solid; mp 166–167 °C; IR (KBr) 2959, 2870, 1654, 1600, 1513, 1450, 1332, 1245, 1124, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.03–1.14 (m, 6H), 1.48–1.58 (m, 5H), 1.67–1.77 (m, 2H), 1.91–1.98 (m, 2H), 3.22 (t, J = 7.5 Hz, 2H), 4.46–4.55 (m, 4H), 6.59 (br-s, 1H), 7.46–7.64 (m, 2H), 8.02 (s, 1H), 8.25 (dd, J = 8.5 Hz, 1H), 8.46 (d, J = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 14.2, 14.7, 14.9, 20.5, 24.0, 28.3, 32.8, 46.0, 60.2, 102.9, 104.5, 120.5, 123.0, 123.2, 123.6, 124.1, 124.6, 125.5, 126.7, 147.3, 148.0, 166.9; Anal. Calcd. for $C_{22}H_{27}NO_3$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.37; H, 7.43; N, 4.29%.

(*E*)-Ethyl 3-(butylamino)-2-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)but-2-enoate (5a). Brownish viscous liquid; IR (neat, NaCl): 2960, 2931, 1706, 1652, 1594 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): 0.99 (t, J = 7.2 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H), 1.40–1.54

(m, 2H), 1.60–1.71 (m, 2H), 1.97 (s, 3H), 3.31 (q, $J = 6.8$ Hz, 2H), 4.06 (q, $J = 7.1$ Hz, 2H), 6.76 (s, 1H), 7.71–7.78 (m, 2H), 8.07–8.15 (m, 2H), 9.77 (s, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): 14.2, 14.7, 17.6, 20.5, 32.4, 43.8, 59.7, 89.7, 126.2, 127.2, 132.8, 133.3, 133.7, 133.8, 137.5, 149.4, 162.0, 169.2, 185.9, 186.0; Anal. Calcd. For $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10; Found: C, 70.10; H, 6.41; N, 4.01%.

Synthesis of 5-hydroxyindole derivatives 10

The general procedure for the synthesis of compounds **4** was employed for the reaction between primary amines **1**, 1,3-dicarbonyl compounds **2** and *p*-benzoquinone **3b** for the synthesis of 5-hydroxyindole derivatives **10**.

Ethyl 1-butyl-5-hydroxy-2-methyl-1*H*-indole-3-carboxylate (10a). Off-white solid; mp 145–146 °C; IR (KBr) 2965, 2927, 2863, 1652, 1621, 1520, 1469, 1440, 1379, 1283, 1245, 1185, 1157, 1116 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.98 (t, $J = 7.2$ Hz, 3H), 1.33–1.49 (m, 5H), 1.75 (m, 2H), 2.76 (s, 3H), 4.09 (t, $J = 7.4$ Hz, 2H), 4.41 (q, $J = 7.1$ Hz, 2H), 4.98 (s, 1H), 6.81 (dd, $J = 2.3$, 8.7 Hz, 1H), 7.18 (d, $J = 8.7$ Hz, 1H), 7.63 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.6, 14.2, 14.9, 20.6, 32.3, 43.6, 60.0, 103.6, 106.7, 110.4, 111.7, 128.3, 131.3, 145.5, 152.1, 167.0; Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.51; H, 7.52; N, 5.30%.

Ethyl 1-allyl-5-hydroxy-2-methyl-1*H*-indole-3-carboxylate (10b). Pale brown solid; mp 132–133 °C; IR (KBr) 3288, 2986, 1655, 1620, 1522, 1471, 1433, 1379, 1292, 1249, 1185, 1155, 1120, 1034 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.35 (t, $J = 7.1$ Hz, 3H), 2.62 (s, 3H), 4.31 (q, $J = 7.1$ Hz, 2H), 4.58–4.61 (m, 2H), 4.74 (dq, $J = 0.85$, 17.1 Hz, 1H), 5.07 (dq, $J = 0.85$, 10.3 Hz, 1H), 5.75–5.92 (m, 2H), 6.72 (dd, $J = 2.5$, 8.7 Hz, 1H), 7.02 (d, $J = 8.7$, 1H), 7.62 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.3, 15.0, 45.8, 60.0, 104.0, 106.8, 110.5, 111.9, 117.2, 128.2, 131.4, 132.3, 145.7, 152.1, 166.9; Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.20; H, 6.63; N, 5.49%.

Ethyl 1-benzyl-5-hydroxy-2-methyl-1*H*-indole-3-carboxylate (10c). Off-white solid; mp 191–192 °C; IR (KBr) 3291, 2971, 2926, 1644, 1623, 1520, 1475, 1438, 1358, 1293, 1249, 1180, 1142, 1120, 1032 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.48 (t, $J = 7.1$ Hz, 3H), 2.74 (s, 3H), 4.42 (q, $J = 7.1$ Hz, 2H), 5.34 (s, 2H), 6.78 (dd, $J = 2.5$, 8.7 Hz, 1H), 7.00 (dd, $J = 2.4$, 7.8 Hz, 1H), 7.12 (d, $J = 8.7$ Hz, 1H), 7.29–7.35 (m, 5H), 7.66 (d, $J = 2.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 12.5, 15.0, 47.0, 60.0, 104.4, 106.9, 110.7, 111.9, 126.3, 128.0, 128.2, 129.4, 131.9, 136.7, 146.0, 151.9, 166.7. Anal. Calcd. for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.42; H, 6.37; N, 4.47%.

Ethyl 5-hydroxy-2-methyl-1-(prop-2-ynyl)-1*H*-indole-3-carboxylate (10d). Off-white solid; mp 201–202 °C; IR (KBr) 3285, 2985, 1654, 1622, 1528, 1486, 1434, 1378, 1348, 1292, 1249, 1184, 1151, 1126, 1034 cm^{-1}; ^{1}H NMR (DMSO-d_6, 250 MHz): δ 1.41 (t, $J = 6.9$ Hz, 3H), 2.14 (s, 1H), 2.78 (s, 3H), 3.42 (s, 2H), 5.15 (q, $J = 7$ Hz, 2H), 6.75 (d, $J = 7.6$ Hz, 1H), 7.44 (s, 2H), 9.08 (s, 1H); ^{13}C NMR (DMSO-d_6, 63 MHz): δ 12.4, 15.3, 33.1, 59.7, 75.9, 79.5, 103.8, 106.4, 111.4, 112.5, 127.9, 130.5, 145.4, 153.7, 165.9; Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.20; H, 5.88; N, 5.44; found: C, 69.90; H, 5.55; N, 5.20%.

***S*-*tert*-Butyl 1-butyl-5-hydroxy-2-methyl-1*H*-indole-3-carbothioate (10e).** Off-white solid; mp 133–134 °C; IR (KBr) 3438, 2959, 2870, 1627, 1596, 1587, 1495, 1459, 1412, 1362, 1321, 1197, 1163, 1067 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.97 (t, $J = 7.1$ Hz, 3H), 1.32–1.47 (m, 2H), 1.64 (s, 9H), 1.69–1.74 (m, 2H), 2.74 (s, 3H), 4.06 (t, $J = 7.4$ Hz, 2H), 5.05 (s, 1H), 6.83 (dd, $J = 2.3$, 8.6 Hz, 1H), 7.16 (d, $J = 8.7$ Hz, 1H), 7.80 (d, $J = 2.1$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.4, 14.2, 20.6, 30.9, 32.2, 43.5, 48.5, 107.4, 110.6, 111.6, 114.0, 126.5, 131.4, 143.7, 151.7, 188.6; Anal. Calcd for $C_{18}H_{25}NO_2S$: C, 67.67; H, 7.89; N, 4,38; S, 10.04. Found: C, 67.48; H, 7.72; N, 4,65; S, 9.90%.

***S*-*tert*-Butyl 1-allyl-5-hydroxy-2-methyl-1*H*-indole-3-carbothioate (10f).** Pale brownish viscous liquid; IR (neat) 2962, 2922, 1622, 1597, 1501, 1473, 1409, 1362, 1219, 1164, 1085, 1065, 1021 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.64 (s, 9H), 2.70 (s, 3H), 4.65–4.67 (m, 2H), 4.84 (d, $J = 17.1$ Hz, 1H), 5.16 (d, $J = 10.3$ Hz, 1H), 5.57 (s, 1H), 5.82–5.97 (m, 1H), 6.82 (dd, $J = 2.3$, 8.7 Hz, 1H), 7.09 (d, $J = 8.7$ Hz, 1H), 7.82 (d, $J = 2.3$ Hz. 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.1, 30.8, 45.6, 48.6, 107.4, 110.6, 111.9, 114.3, 117.3, 126.5, 131.4, 132.1, 143.9, 152.0, 188.9; Anal. Calcd for $C_{17}H_{21}NO_2S$: C, 67.29; H, 6.98; N, 4.62; S, 10.57. Found: C, 67.03; H, 6.96; N, 4.63; S, 10.36%.

Ethyl 1-butyl-5-hydroxy-2-propyl-1*H*-indole-3-carboxylate (10g). Off-white solid; mp 124–125 °C; IR (KBr) 3336, 2961, 2872, 1688, 1651, 1521, 1470, 1444, 1379, 1296, 1245, 1180, 1147, 1111, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.99 (t, $J = 7.5$ Hz, 3H), 1.07 (t, $J = 7.3$ Hz, 3H), 1.35–1.50 (m, 2H), 1.45 (t, $J = 7.1$ Hz, 3H), 1.65–1.83 (m, 4H), 3.09–3.15 (m, 2H), 4.08 (t, $J = 7.3$ Hz, 2H), 4.41 (q, $J = 7.1$ Hz, 2H), 5.79 (s, 1H), 6.84 (dd, $J = 2.4$, 8.7 Hz, 1H), 7.18 (d, $J = 8.7$ Hz, 1H), 7.74 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 14.2, 14.7, 14.9, 20.7, 23.7, 28.4, 32.6, 43.7, 60.0, 103.0, 106.8, 110.7, 111.8, 128.5, 131.2, 149.7, 152.3, 166.8; Anal. Calcd $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 71.00; H, 8.11; N, 4.66%.

Ethyl 1-allyl-5-hydroxy-2-propyl-1*H*-indole-3-carboxylate (10h). Pale brown solid; mp 116–117 °C; IR (KBr) 3362, 2964, 2870, 1691, 1659, 1525, 1470, 1378, 1247, 1182, 1148, 1115, 1031 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.06 (t, $J = 7.2$ Hz, 3H), 1.46 (t, $J = 7.0$ Hz, 3H), 1.62–1.72 (m, 2H), 3.10 (t, $J = 7.6$ Hz, 2H), 4.41 (q, $J = 7.0$ Hz, 2H), 4.73 (s, 2H), 4.88 (d, $J = 17.4$ Hz, 1H), 5.19 (d, $J = 10.0$ Hz, 1H), 5.65 (s, 1H), 5.89–6.00 (m, 1H), 6.82 (d, $J = 8.6$ Hz, 1H), 7.13 (d, $J = 8.6$ Hz, 1H), 7.72 (s, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 14.6, 14.9, 23.5, 28.2, 45.9, 60.0, 103.6, 106.8, 110.9, 111.9, 117.3, 128.4, 131.4, 132.8, 149.9, 152.3, 166.6; Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4,87. Found: C, 70.86; H, 7.13; N, 5.11%.

Synthesis of indolequinones 11 and the bromoquinone intermediates 12

The general procedure for the synthesis of compounds **4** was employed for the reaction between butylamine **1a**, 1,3-dicarbonyl compounds **2** and 2-bromo-1,4-naphthoquinone **3c** for the synthesis of compounds **11** and **12**. See Table 4 for reaction times and catalyst load.

Ethyl 1-butyl-2-methyl-4,9-dioxo-4,9-dihydro-1*H*-benzo[*f*]indole-3-carboxylate (11a). Dark brown viscous liquid; IR (neat)

2960, 2931, 2865, 1706, 1652, 1273 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.01 (t, J = 4.2 Hz, 3H), 1.39–1.54 (m, 5H), 1.70–1.82 (m, 2H), 2.51 (s, 3H), 4.41–4.50 (m, 4H), 7.65–7.72 (m, 2H), 8.11–8.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ (two carbons are merged with others) 11.2, 14.1, 14.6, 20.4, 32.9, 46.2, 61.6, 114.5, 126.2, 126.6, 127.1, 130.4, 133.3, 133.6, 134.2, 165.2, 176.4, 179.9. Anal. Calcd. for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.53; H, 5.98; N, 3.81%.

3-Acetyl-1-butyl-2-methyl-1*H*-benzo[*f*]indole-4,9-dione (11b). Pale yellow solid; mp 115–116 °C; IR (KBr) 2960.8, 2930, 2870, 1652, 1592, 1495, 1469, 1433, 1354, 1269, 1210, 1096, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.86 (t, J = 7.3 Hz, 3H), 1.25–1.40 (m, 2H), 1.55–1.67 (m, 2H), 2.29 (s, 3H), 2.58 (s, 3H), 4.32 (t, J = 7.5 Hz, 2H), 7.55 (dd, J = 3.3, 5.7 Hz, 2H), 7.98 (dd, J = 3.2, 5.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 11.2, 14.2, 20.5, 30.1, 32.1, 32.8, 46.1, 123.2, 125.6, 126.7, 127.0, 129.9, 133.6, 133.7, 133.9, 141.6, 176.4, 181.1, 199.8; Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.57; H, 6.32; N, 4.15%.

3-Acetyl-1-benzyl-2-methyl-1*H*-benzo[*f*]indole-4,9-dione (11c). Yellow solid; mp 163–164 °C; IR (neat) 1651, 1591, 1496, 1269 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.39 (s, 3H), 2.76 (s, 3H), 5.86 (s, 3H), 7.11 (d, J = 8.0 Hz, 2H), 7.29–7.38 (m, 3H), 7.70–7.74 (m, 2H), 8.12–8.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 11.3, 32.1, 49.2, 123.5, 125.7, 126.6, 126.8, 127.1, 128.2, 129.4, 130.2, 133.6, 133.7, 133.8, 133.9, 135.9, 142.4, 176.6, 181.1, 199.6; Anal. Calcd. for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08. Found: C, 76.72; H, 4.82; N, 4.01%.

3-Acetyl-1-allyl-2-methyl-1*H*-benzo[*f*]indole-4,9-dione (11d). Yellow solid; mp 117–118 °C; IR (neat) 1652, 1591, 1496, 1430, 1270, 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.42 (s, 3H), 2.74 (s, 3H), 4.97 (d, J = 17.1 Hz, 1H), 5.21 (t, J = 12.3 Hz, 3H), 5.94–6.09 (m, 1H), 7.69 (m, 2H), 8.10–8.16 (m, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 10.9, 32.1, 48.0, 117.6, 123.2, 125.5, 126.7, 127.0, 129.9, 132.2, 133.5, 133.6, 133.7, 133.9, 142.1, 176.4, 181.0, 199.6; Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.45; H, 5.06; N, 4. 68%.

3-Acetyl-2-methyl-1-(prop-2-ynyl)-1*H*-benzo[*f*]indole-4,9-dione (11e). Yellow solid; mp 194–195 °C; IR (neat) 1668, 1653, 1592, 1494, 1267, 1210, 1104 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.40 (t, J = 2.3 Hz, 1H), 2.55 (s, 3H), 2.75 (s, 3H), 5.44 (d, J = 2.3 Hz, 2H), 7.71–7.77 (m, 2H), 8.15–8.20 (m, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 10.6, 31.6, 34.8, 73.5, 121.1, 122.8, 125.1, 126.2, 126.6, 128.8, 132.8, 133.2, 133.4, 141.6, 176.1, 180.4, 198.8; Anal. Calcd. for $C_{18}H_{13}NO_3$: C, 74.22; H, 4.50; N, 4.81. Found: C, 73.92; H, 4.39; N, 4.78%.

(*E*)-Ethyl 2-(3-bromo-1,4-dioxo-1,4-dihydronaphthalen-2-yl)-3-(butylamino)but-2-enoate (12a). Pale brown solid; mp 98–99 °C; IR (KBr) 2962, 2929, 1682, 1599, 1464, 1382, 1278, 1242, 1160, 1067 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.99 (t, J = 7.2 Hz, 3H), 1.10 (t, J = 7.1 Hz, 3H), 1.40–1.55 (m, 2H), 1.61–1,72 (m, 2H), 1.87 (s, 3H), 3.32 (q, J = 6.7 Hz, 2H), 4.07 (q, J = 7.1 Hz, 2H), 7.73–7.81 (m, 2H), 8.13–8.23 (m, 2H), 9.67 (s, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 14.2, 14.8, 17.4, 20.5, 32.4, 43.7, 59.6, 90.9, 124.6, 127.7, 127.8, 131.9, 132.5, 134.0, 134.4, 150.1, 161.6, 168.1, 179.1, 182.8. Anal. Calcd. for $C_{20}H_{22}BrNO_4$: C, 57.15; H, 5.28; N, 3.33. Found: C, 57.07; H, 5.20; N, 3.52%.

General procedure for the introduction of substituents on the C-2 methyl group of 4: synthesis of compounds 13

A solution of compounds **4** (1 mmol) in dry THF (4 mL) was added to LDA (3 mmol), prepared from BuLi (3.3 mmol) and diisopropylamine (3 mmol) in dry THF (4 mL), slowly at −20 °C and the reaction mixture was stirred for 30 min at the same temperature. Allyl iodide or propargyl bromide (2.2 mmol) was then added and stirring was continued for further 2 h. The reaction was quenched by adding saturated NH_4Cl solution and extracted with dichloromethane (2 × 10 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and the solvent was evaporated. The crude mixture was purified by silica column chromatography eluting with petroleum ether-ethyl acetate mixture (80 : 20, v/v).

Ethyl 1-allyl-2-(but-3-enyl)-5-hydroxy-1*H*-benzo[*g*]indole-3-carboxylate (13a). Off-white solid; mp 181–182 °C; IR (KBr) 3288, 2984, 1635, 1622, 1599, 1512, 1450, 1128, 1072, 987 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.50 (t, J = 7.1 Hz, 3H), 2.46 (q, J = 6.7 Hz, 2H), 3.29 (t, J = 6.8 Hz, 2H), 4.49 (q, J = 7.1 Hz, 2H), 4.90 (d, J = 17.1 Hz, 1H), 5.09 (d, J = 14.2 Hz, 2H), 5.20 (s, 3H), 5.32 (d, J = 9.4 Hz, 1H), 5.89–6.05 (m, 1H), 6.21–6.32 (m, 1H), 7.46–7.60 (m, 2H), 7.96 (s, 1H), 8.21 (d, J = 8.2 Hz, 1H), 8.42 (d, J = 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 15.0, 25.7, 34.4, 48.3, 60.2, 102.8, 105.1, 115.8, 117.9, 120.9, 122.7, 123.5, 123.6, 123.9, 124.9, 125.2, 126.6, 133.0, 137.8, 146.7, 147.9, 166.6; Anal. Calcd for $C_{22}H_{23}NO_3$: C, 75.62; H, 6.63; N, 4.01. Found: C, 75.36; H, 6.53; N, 3.74%.

Methyl 1-allyl-2-(but-3-enyl)-5-hydroxy-1*H*-benzo[*g*]indole-3-carboxylate (13b). Off-white solid; mp 181–182 °C; IR (KBr) 3311, 2985, 1638, 1598, 1450, 1334, 1243, 1126, 999 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.46 (q, J = 6.7 Hz, 2H), 3.28 (t, J = 5.4 Hz, 2H), 4.03 (s, 3H), 4.90 (d, J = 17.1 Hz, 1H), 5.09 (d, J = 10.1 Hz, 1H), 5.19 (s, 3H), 5.33 (d, J = 10.5 Hz, 1H), 5.89–6.05 (m, 1H), 6.19–6.33 (m, 1H), 6.58 (s, 1H), 7.47–7.60 (m, 2H), 8.02 (s, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.45 (d, J = 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 25.7, 34.4, 48.3, 51.5, 102.8, 104.9, 115.9, 117.9, 121.0, 122.8, 123.4, 123.6, 123.9, 124.9, 125.2, 126.6, 133.0, 137.8, 146.9, 148.1, 167.0; Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 74.84; H, 6.28; N, 4.02%.

Ethyl 1-allyl-2-(but-3-ynyl)-5-hydroxy-1*H*-benzo[*g*]indole-3-carboxylate (13c). Off-white solid; mp 201–202 °C; IR (KBr) 3302, 2982, 1646, 1624, 1600, 1518, 1450, 1334, 1244, 1128, 1074 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.50 (t, J = 7.1 Hz, 3H), 2.03 (q, J = 2.6 Hz, 1H), 2.67 (t, J = 7.7 Hz, 2H), 3.43 (t, J = 7.5 Hz, 2H), 4.50 (q, J = 7.0 Hz, 2H), 4.85 (d, J = 17.8 Hz, 1H), 5.32 (s, 3H), 6.22–6.34 (m, 1H), 7.47–7.61 (m, 2H), 7.99 (s, 1H), 8.21 (d, J = 8.2 Hz, 1H), 8.43 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 14.9, 19.5, 25.3, 48.5, 60.5, 69.9, 83.6, 102.6, 105.4, 117.9, 120.9, 122.8, 123.6, 123.8, 123.9, 124.9, 125.3, 126.7, 133.0, 144.9, 148.3, 166.5; Anal. Calcd for $C_{22}H_{21}NO_3$: C, 76.06; H, 6.09; N, 4.03. Found: C, 75.86, H, 5.85; N, 4.05%.

Methyl 1-allyl-2-(but-3-ynyl)-5-hydroxy-1*H*-benzo[*g*]indole-3-carboxylate (13d). Pale brown solid; mp 160–161 °C; IR (KBr) 3299, 2984, 1648, 1624, 1600, 1522, 1449, 1407, 1335, 1244, 1124, 1072 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.02 (s, 1H), 2.66

(t, J = 7.1 Hz, 2H), 3.43 (t, J = 7.3 Hz, 2H), 4.02 (s, 3H), 4.88 (d, J = 17.2 Hz, 1H), 5.16–5.33 (m, 3H), 6.23–6.34 (m, 1H), 7.47–7.60 (m, 2H), 7.90 (s, 1H), 8.21 (d, J = 8.2 Hz, 1H), 8.42 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 19.3, 25.0, 48.6, 51.5, 69.9, 83.6, 102.8, 105.4, 117.9, 121.0, 122.8, 123.6, 123.7, 123.9, 124.6, 125.4, 126.8, 132.9, 145.3, 148.0, 166.7; Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.34; H, 5.92; N, 4.21%.

General procedure for the acetylation and benzoylation of compounds 13: synthesis of compounds 14

To a stirred suspension of compound **13** (1 mmol) and BiOCl (5–10 mol%) in dichloromethane (3 mL) under argon was added acetyl or benzoyl chloride (2 mmol) at room temperature. The reaction was completed in 20 min as indicated by tlc. The mixture was diluted with dichloromethane (10 mL), washed with saturated $NaHCO_3$ solution, water and brine. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated. Purification of the crude mixture by Al_2O_3 (neutral, activity grade II-III) column chromatography eluting with petroleum ether–ethyl acetate mixture (85 : 15, v/v) gave the compounds **14**.

Ethyl 5-acetoxy-1-allyl-2-(but-3-enyl)-1*H*-benzo[*g*]indole-3-carboxylate (14a). Off-white solid; mp 101–102 °C; IR (KBr) 2982, 1761, 1693, 1527, 1418, 1365, 1206, 1149 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.49 (t, J = 7.1 Hz, 3H), 2.41–2.53 (m, 5H), 3.31 (t, J = 7.6 Hz, 2H), 4.46 (q, J = 7.1 Hz, 2H), 4.91 (d, J = 17.1 Hz, 1H), 5.05 (d, J = 10.8 Hz, 1H), 5.19 (d, J = 10.6 Hz, 3H), 5.33 (d, J = 10.5 Hz, 1H), 5.88–6.04 (m, 1H), 6.22–6.33 (m, 1H), 7.47–7.60 (m, 2H), 7.96 (d, J = 7.9 Hz, 1H), 8.18 (s, 1H), 8.27 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 15.0, 21.5, 25.5, 34.3, 48.3, 60.1, 106.3, 113.7, 115.9, 118.2, 121.6, 122.6, 122.9, 123.8, 124.5, 125.0, 126.6, 128.2, 132.8, 137.7, 142.6, 147.7, 165.8, 170.6; Anal. Calcd for $C_{24}H_{25}NO_4$: C, 73.64; H, 6.44; N, 3.58. Found: C, 73.39; H, 6.40; N, 3.71%.

Methyl 5-acetoxy-1-allyl-2-(but-3-enyl)-1*H*-benzo[*g*]indole-3-carboxylate (14b). Off-white solid; mp 115–116 °C; IR (KBr) 2949, 1760, 1698, 1528, 1435, 1397, 1365, 1207, 1113, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.41–2.53 (m, 5H), 3.32 (t, J = 7.7 Hz, 2H), 3.99 (s, 3H), 4.91 (d, J = 17.0 Hz, 1H), 5.06 (d, J = 10.4 Hz, 1H), 5.20 (d, J = 10.9 Hz, 3H), 5.34 (d, J = 10.7 Hz, 1H), 5.88–6.01 (m, 1H), 6.22–6.33 (m, 1H), 7.47–7.60 (m, 2H), 7.97 (d, J = 7.9 Hz, 1H), 8.15 (s, 1H), 8.26 (d, J = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ (one aromatic carbon is merged with others) 22.2, 26.2, 34.9, 49.0, 52.0, 114.4, 116.7, 118.9, 122.4, 123.4, 123.6, 124.2, 125.2, 125.7, 127.3, 128.9, 133.4, 138.3, 143.3, 148.7, 166.9, 171.3; Anal. Calcd for $C_{23}H_{23}NO_4$: C, 73.19; H, 6.14; N, 3.71. Found: C, 72.90; H, 6.20; N, 3.83%.

Ethyl 1-allyl-5-(benzoyloxy)-2-(but-3-enyl)-1*H*-benzo[*g*]indole-3-carboxylate (14c). Off-white solid; mp 115–116 °C; IR (KBr) 3073, 2981, 1738, 1694, 1527, 1451, 1418, 1247, 1192, 1112, 1087, 1021 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.49 (t, J = 7.1 Hz, 3H), 2.48 (q, J = 6.7 Hz, 2H), 3.30–3.36 (m, 2H), 4.45 (q, J = 7.1 Hz, 2H), 4.90–5.37 (m, 6H), 5.90–6.05 (m, 1H), 6.22–6.35 (m, 1H), 7.43–7.64 (m, 4H), 7.75 (tt, J = 1.3, 8.6 Hz, 1H), 8.03 (dd, J = 1.1, 8.2 Hz, 1H), 8.28 (d, J = 8.0 Hz, 2H), 8.42 (dd, J = 1.5, 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 15.0, 25.6, 34.3, 48.3, 60.1, 106.4, 113.9, 115.9, 118.1, 121.6, 122.7, 123.0, 123.8, 124.5, 125.2, 126.7, 128.2, 129.1, 130.0, 130.8, 132.9, 134.0, 137.7, 142.8, 147.7, 165.9, 166.2; Anal. Calcd for $C_{29}H_{27}NO_4$: C, 76.80; H, 6.00; N, 3.09. Found: C, 76.64; H, 5.97; N, 3.26%.

Methyl 1-allyl-5-(benzoyloxy)-2-(but-3-enyl)-1*H*-benzo[*g*]indole-3-carboxylate (14d). Off-white solid; mp 118–119 °C; IR (KBr) 2930, 1734, 1697, 1623, 1526, 1246, 1192, 1115, 1088, 1068 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.47 (q, J = 6.9 Hz, 2H), 3.34 (t, J = 7.8 Hz, 2H), 3.98 (s, 3H), 4.94 (d, J = 17.2 Hz, 1H), 5.10 (d, J = 15.6 Hz, 1H), 5.21 (d, J = 15.7 Hz, 3H), 5.35 (d, J = 10.6 Hz, 1H), 5.90–6.06 (m, 1H), 6.22–6.36 (m, 1H), 7.44–7.76 (m, 5H), 8.03 (d, J = 8.1 Hz, 1H), 8.23–8.31 (m, 2H), 8.40 (d, J = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 25.5, 34.3, 48.4, 51.4, 106.2, 113.9, 116.0, 118.2, 121.7, 122.7, 123.0, 123.6, 124.6, 125.2, 126.7, 128.2, 129.1, 130.0, 130.8, 132.8, 134.1, 137.7, 142.9, 148.1, 166.2, 166.3; Anal. Calcd for $C_{28}H_{25}NO_4$: C, 76.52; H, 5.73; N, 3.19. Found: C, 76.31; H, 5.91; N, 3.32%.

Ethyl 5-acetoxy-1-allyl-2-(but-3-ynyl)-1*H*-benzo[*g*]indole-3-carboxylate (14e). Pale brown viscous liquid; IR (neat) 2984, 1760, 1694, 1625, 1527, 1418, 1366, 1208, 1112, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.52 (t, J = 7.1 Hz, 3H), 2.03 (d, J = 2.5 Hz, 1H), 2.55 (s, 3H), 2.70 (t, J = 7.2 Hz, 2H), 3.45 (t, J = 6.9 Hz, 2H), 4.49 (q, J = 7.1 Hz, 2H), 4.90 (d, J = 16.7 Hz, 1H), 5.33 (s, 3H), 6.24–6.36 (m, 1H), 7.49–7.59 (m, 2H), 7.98 (d, J = 7.8 Hz, 1H), 8.18 (s, 1H), 8.27 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 13.5, 17.9, 20.0, 23.5, 47.1, 58.8, 68.6, 82.0, 105.2, 112.2, 116.6, 120.2, 121.2, 121.5, 122.1, 123.2, 123.7, 125.3, 126.8, 131.3, 141.3, 144.7, 164.2, 169.1; Anal. Calcd for $C_{24}H_{23}NO_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 73.85; H, 5.88; N, 3.47%.

Methyl 5-acetoxy-1-allyl-2-(but-3-ynyl)-1*H*-benzo[*g*]indole-3-carboxylate (14f). Off-white solid; mp 95–96 °C; IR (KBr) 3294, 2950, 1760, 1698, 1624, 1528, 1435, 1397, 1365, 1268, 1207, 1150, 1115, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.01 (t, J = 2.6 Hz, 1H), 2.52 (s, 3H), 2.68 (t, J = 7.2 Hz, 2H), 3.45 (t, J = 7.3 Hz, 2H), 4.00 (s, 3H), 4.90 (d, J = 17 Hz, 1H), 5.32–5.35 (m, 3H), 6.22–6.36 (m, 1H), 7.48–7.61 (m, 2H), 7.97 (d, J = 8.0 Hz, 1H), 8.13 (s, 1H), 8.27 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 19.2, 21.5, 24.8, 48.6, 51.5, 70.1, 83.5, 106.5, 113.7, 118.1, 121.7, 122.7, 122.9, 123.4, 124.7, 125.2, 126.8, 128.3, 132.8, 142.8, 146.5, 166.2, 170.6; Anal. Calcd for $C_{23}H_{21}NO_4$: C, 73.58; H, 5.64; N, 3.73. Found: C, 73.24; H, 5.65; N, 3.98%.

General procedure for the ring-closing metathesis reaction of compounds 14: synthesis of 9,12-dihydro-8*H*-azepino[1,2-*a*]benzo[*g*]indole derivatives 15

To a stirred solution of compounds **14** (0.5 mmol) in dry dichloromethane (2 mL) was added Grubbs 1st generation catalyst (10 mol%) and stirring was continued for 3 h at room temperature under argon atmosphere. After completion of the reaction the solvent was evaporated and the crude mixture was purified by Al_2O_3 (neutral, activity grade II–III) column chromatography using petroleum ether–ethyl acetate mixture (80 : 20, v/v) as eluent.

Ethyl 5-acetoxy-9,12-dihydro-8*H*-azepino[1,2-*a*]benzo[*g*]indole-7-carboxylate (15a). Off-white solid; mp 138–139 °C; IR (KBr) 3436, 3023, 2901, 1762, 1619, 1623, 1542, 1450, 1364, 1204, 1107,

1058 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): δ 1.44 (t, $J = 7.1$ Hz, 3H), 2.52 (s, 5H), 3.76 (s, 2H), 4.45 (q, $J = 7.1$ Hz, 2H), 5.30 (s, 2H), 5.87 (d, $J = 11.3$ Hz, 1H), 6.01 (s, 1H), 7.46–7.60 (m, 2H), 7.96 (d, $J = 8.0$ Hz, 1H), 8.11 (s, 1H), 8.32 (d, $J = 8.3$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 15.0, 21.5, 23.0, 28.8, 44.3, 60.1, 105.4, 113.9, 121.0, 122.5, 122.8, 123.1, 123.2, 124.4, 125.0, 126.4, 128.2, 134.9, 142.3, 149.9, 166.2, 170.6; Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82, N, 3.85. Found: C, 72.52; H, 5.90; N, 3.89%.

Methyl 5-acetoxy-9,12-dihydro-8*H*-azepino[1,2-*a*]benzo[*g*]indole-7-carboxylate (15b). Off-white solid; mp 167–168 °C; IR (KBr) 3430, 3028, 2944, 1753, 1693, 1622, 1543, 1430, 1396, 1365, 1205, 1111, 1059 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): δ 2.53 (s, 5H), 3.77 (q, $J = 5.6$ Hz, 2H), 3.99 (s, 3H), 5.31 (d, $J = 7.3$ Hz, 2H), 5.89 (d, $J = 11.3$ Hz, 1H), 6.01 (s, 1H), 7.47–7.61 (m, 2H), 7.97 (d, $J = 8.1$ Hz, 1H), 8.10 (s, 1H), 8.33 (s, 1H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ (one aromatic carbon is merged with others) 21.5, 23.0, 28.8, 44.3, 51.4, 105.2, 113.9, 121.0, 122.5, 122.8, 123.1, 124.5, 125.0, 126.4, 128.2, 134.8, 142.3, 150.0, 166.6, 170.7; Anal. Calcd for $C_{21}H_{19}NO_4$: C, 72.19; H, 5.48; N, 4.01. Found: C, 71.84; H, 5.55; N, 4.01%.

Ethyl 5-(benzoyloxy)-9,12-dihydro-8*H*-azepino[1,2-*a*]benzo[*g*]indole-7-carboxylate (15c). Off-white solid; mp 168–169 °C; IR (KBr) 2978, 2926, 1737, 1694, 1623, 1540, 1450, 1402, 1301, 1247, 1179, 1111, 1088 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): δ 1.46 (t, $J = 7.0$ Hz, 3H), 2.58 (m, 2H), 3.81 (t, $J = 6.0$ Hz, 2H), 4.44 (q, $J = 7.0$ Hz, 2H), 5.36 (m, 2H), 5.88–5.94 (m, 1H), 6.02–6.09 (m, 1H), 7.43–7.76 (m, 5H), 8.02 (d, $J = 8.2$ Hz, 1H), 8.22 (s, 1H), 8.36–8.42 (m, 3H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ (four aromatic carbons are merged with others) 15.0, 23.0, 28.8, 44.3, 60.1, 105.5, 114.0, 121.0, 122.6, 122.9, 123.3, 124.5, 125.2, 126.4, 128.2, 129.1, 130.0, 130.8, 134.0, 134.9, 142.5, 149.9, 166.2; Anal. Calcd for $C_{27}H_{23}NO_4$: C, 76.22; H, 5.45; N, 3.29; found: C, 75.97; H, 5.48; N, 3.30%.

Methyl 5-(benzoyloxy)-9,12-dihydro-8*H*-azepino[1,2-*a*]benzo[*g*]indole-7-carboxylate (15d). Off-white solid; mp 199–200 °C; IR (KBr) 2926, 1734, 1698, 1623, 1601, 1542, 1450, 1396, 1248, 1190, 1114, 1087, 1068, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz): δ 2.58–2.60 (m, 2H), 3.82 (t, $J = 6.0$ Hz, 2H), 3.96 (s, 3H), 5.36 (d, $J = 5.0$ Hz, 2H), 5.88–5.96 (m, 1H), 6.03–6.11 (m, 1H), 7.43–7.76 (m, 5H), 8.01 (d, $J = 8.4$ Hz, 1H), 8.19 (s, 1H), 8.37–8.42 (m, 3H); ^{13}C NMR ($CDCl_3$, 63 MHz): δ 23.0, 28.8, 44.3, 51.3, 105.3, 114.1, 121.0, 122.5, 122.9, 123.2, 123.3, 124.5, 125.3, 126.5, 128.2, 129.1, 130.0, 130.8, 134.0, 134.9, 142.6, 150.1, 166.3, 166.6; Anal. Calcd for $C_{26}H_{21}NO_4$: C, 75.90; H, 5.14; N, 3.40. Found: C, 75.64; H, 5.38; N, 3.35%.

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References

1 For selected reviews and monographs of indole related compounds, see: (*a*) M. Ishikura and K. Yamada, *Nat. Prod. Rep.*, 2009, **26**, 803–852; (*b*) K. Higuchi and T. Kawasaki, *Nat. Prod. Rep.*, 2007, **24**, 843–868; (*c*) T. Kawasaki and K. Higuchi, *Nat. Prod. Rep.*, 2005, **22**, 761–793 and the previous reports of the series cited therein; (*d*) *Indoles*, ed. R. J. Sundberg Academic Press: London, 1996; (*e*) R. J. Sundberg, in *Comprehensive Heterocyclic Chemistry II*, ed. A. R. Katritzky, C. W. Ress, E. F. V. Scriven and C. W. Bird, Pergamon Press, Oxford, 1996, Vol. 2, p 119; (*f*) M. d'Ischia, A. Napolitano and A. Pezzella, in *Comprehensive Heterocyclic Chemistry*, ed. A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor, Elsevier, Oxford, 2008, Vol. 3, Chapter 3.04; (*g*) S. R. Walker, E. J. Carter, B. C. Huff and J. C. Morris, *Chem. Rev.*, 2009, **109**, 3080–3098.

2 For representative recent reviews and accounts that describe the biological importance of indoles, see: (*a*) S. A. Patil, R. Patil and D. D. Miller, *Curr. Med. Chem.*, 2009, **16**, 2531–2565; (*b*) F. R. de Sa Alves, E. J. Barreiro and C. A. M. Fraga, *Mini-Rev. Med. Chem.*, 2009, **9**, 782–793; (*c*) H. Xu and M. Lu, *Curr. Pharm. Des.*, 2009, **15**, 2120–2148; (*d*) F. H. Sarkar and Y. Li, *Cancer Treat. Rev.*, 2009, **35**, 597–607; (*e*) P. Kutschy and R. Mezencev, *Targets Heterocyclic Sys.*, 2008, **12**, 120–148; (*f*) C. Manera, T. Tuccinardi and A. Martinelli, *Mini-Rev. Med. Chem.*, 2008, **8**, 370–387; (*g*) J.-R. Weng, C.-H. Tsai, S. K. Kulp and C.-S. Chen, *Cancer Lett.*, 2008, **262**, 153–163; (*h*) S. Suzen, *Top. Heterocycl. Chem.*, 2007, **11**, 145–178; (*i*) N. Steffan, A. Grundmann, W.-B. Yin, A. Kremer and S.-M. Li, *Curr. Med. Chem.*, 2009, **16**, 218–231; (*j*) C. V. Galliford and K. A. Scheidt, *Angew. Chem., Int. Ed.*, 2007, **46**, 8748–8758; (*k*) U. Pindur and T. Lemster, *Curr. Med. Chem.*, 2001, **8**, 1681–1698.

3 For some applications of the "privileged scaffold" concept in drug design, see: (*a*) G. Muller, *Drug Discovery Today*, 2003, **8**, 681–691; (*b*) R. W. DeSimone, K. S. Currie, S. A. Mitchell, J. W. Darrow and D. A. Pippin, *Comb. Chem. High Throughput Screen.*, 2004, **7**, 473–493; (*c*) L. Costantino and D. Barlocco, *Curr. Med. Chem.*, 2006, **13**, 65–85; (*d*) A. A. Shelat and R. Kiplin Guy, *Nat. Chem. Biol.*, 2007, **3**, 442–446.

4 B. E. Evans, K. E. Rittle, M. G. Bock, R. M. DiPardo, R. M. Freidinger, W. L. Whitter, G. F. Lundell, D. F. Verber, P. S. Anderson, R. S. L. Chang, V. J. Lotti, D. H. Cerino, T. B. Chen, P. J. Kling, K. A. Kunkel, J. P. Springer and J. Hirshfield, *J. Med. Chem.*, 1988, **31**, 2235–2246.

5 For selected reviews on indole synthesis, see: (*a*) G. W. Gribble, *J. Chem. Soc., Perkin Trans. 1*, 2000, 1045–1075; (*b*) G. R. Humphrey and J. T. Kuethe, *Chem. Rev.*, 2006, **106**, 2875–2911; For a recent review on more sustainable approaches for the synthesis of N-based heterocycles including indoles, see: (*c*) N. R. Candeias, L. C. Branco, P. M. P. Gois, C. A. M. Afonso and A. F. Trindade, *Chem. Rev.*, 2009, **109**, 2703–2802.

6 For a comprehensive review on the synthesis and functionalization of indoles through palladium-catalyzed reactions, see: S. Cacchi and G. Fabrizi, *Chem. Rev.*, 2005, **105**, 2873–2920.

7 For a review of Nenitzescu reaction, see: S. A. Patil, R. Ratil and D. D. Miller, *Curr. Org. Chem.*, 2008, **12**, 691–717.

8 For selected examples of the Nenitzescu reaction, see: (*a*) J. M. Pawlak, V. V. Khau, D. R. Hutchison and M. J. Martinelli, *J. Org. Chem.*, 1996, **61**, 9055–9059; (*b*) D. M. Ketcha, L. J. Wilson and D. E. Portlock, *Tetrahedron Lett.*, 2000, **41**, 6253–6257.

9 For some medicinal applications of 5-hydroxyindole derivatives, see: (*a*) Shefali, S. K. Srivastava, S. M. Husbands and J. W. Lewis, *J. Med. Chem.*, 2005, **48**, 635–638; (*b*) J. Landwehr, S. George, E.-M. Karg, D. Poeckel, D. Steinhilber, R. Troschütz and O. Werz, *J. Med. Chem.*, 2006, **49**, 4327–4332; (*c*) E.-M. Karg, S. Luderer, C. Pergola, U. Bühring, A. Rossi, H. Northoff, L. Sautebin, R. Troschütz and O. Werz, *J. Med. Chem.*, 2009, **52**, 3474–3483.

10 For selected reviews and monographs on multicomponent reactions, see: (*a*) A. Dömling and I. Ugi, *Angew. Chem. Int. Ed.*, 2000, **39**, 3168–3210; (*b*) D. J. Ramón and M. Yus, *Angew. Chem., Int. Ed.*, 2005, **44**, 1602–1634; (*c*) *Multicomponent Reactions*, ed. J. Zhu and H. Bienaymé, Wiley-VCH: Weinheim, 2005; (*d*) A. Dömling, *Chem. Rev.*, 2006, **106**, 17–89.

11 For recent selected examples of CAN-catalyzed reactions, see: (*a*) V. Sridharan, S. Maiti and J. C. Menéndez, *J. Org. Chem.*, 2009, **74**, 9365–9371; (*b*) V. Sridharan, P. Ribelles, M. T. Ramos and J. C. Menéndez, *J. Org. Chem.*, 2009, **74**, 5715–5718; (*c*) V. Sridharan, S. Maiti and J. C. Menéndez, *Chem.–Eur. J.*, 2009, **15**, 4565–4572; (*d*) V. Sridharan and J. C. Menéndez, *Org. Lett.*, 2008, **10**, 4303–4306; (*e*) V. Sridharan, C. Avendaño and J. C. Menéndez, *Synlett*, 2007, 881–884; For a review, see: (*f*) V. Sridharan and J. C. Menéndez, *Chem. Rev.*, 2010, **110**, DOI: 10.1021/cr100004p.

12 For mechanistic discussions of the Nenitzescu reaction involving redox processes, see: (*a*) U. Kuckländer, *Tetrahedron*, 1972, **28**, 5251–5259; (*b*) J. B. Patrick and E. K. Saunders, *Tetrahedron Lett.*, 1979, **20**,

4009–4012; (*c*) J.-L. Bernier and J.-P. Hénichart, *J. Org. Chem.*, 1981, **46**, 4197–4198.
13 For an example of a Lewis acid-catalyzed Nenitzescu reaction, see: V. S. Velezheva, A. G. Kornienko, S. V. Topilin, A. D. Turashev, A. S. Peregudov and P. Brennan, *J. Heterocycl. Chem.*, 2006, **43**, 873–879.
14 For the synthesis of 2-bromonaphthoquinone, see: P. Bachu, J. Sperry and M. A. Brimble, *Tetrahedron*, 2008, **64**, 4827–4834.
15 (*a*) L. W. Schenck, K. Kuna, W. Frank, A. Albert, C. Asche and U. Kucklaender, *Bioorg. Med. Chem.*, 2006, **14**, 3599–3614; (*b*) P. J. O'Sullivan, *Tetrahedron Lett.*, 1992, **33**, 535–538.
16 For selected examples, see: (*a*) M. V. Rao, S. Basaveswara, J. Satyanarayana, H. Ila and H. Junjappa, *Tetrahedron Lett.*, 1995, **36**, 3385–3388; (*b*) B. Joseph, O. Cornec and J.-Y. Merour, *Tetrahedron*, 1998, **54**, 7765–7776; (*c*) A. Mouaddib, B. Joseph, A. Aissa, J.-Y. Merour and S. Leonce, *Heterocycles*, 1999, **51**, 2127–2137.
17 M. Bonanni, M. Marradi, F. Cardona, S. Cicchi and A. Goti, *Beilstein J. Org. Chem.*, 2007, **3**, 44 and references therein.
18 For a review of the synthesis of oxygen and nitrogen heterocycles using ring-closing metathesis reactions, see: A. Deiters and S. F. Martin, *Chem. Rev.*, 2004, **104**, 2199.
19 For the influence of fluorinated aromatic hydrocarbon solvents on metathesis reactions, see: C. Samojowicz, M. Bieniek, A. Zarecki, R. Kadyrov and K. Grela, *Chem. Commun.*, 2008, 6282–6284.
20 For selected examples of the acceleration of RCEYM reactions in the presence of ethylene, see references 11a,c and: (*a*) A. Núñez, A. M. Cuadro, J. Álvarez-Builla and J. J. Vaquero, *Chem. Commun.*, 2006, 2690–2692; (*b*) N. Saito, Y. Sato and M. Mori, *Org. Lett.*, 2002, **4**, 803–805; (*c*) M. Mori, N. Sakakibara and A. Kinoshita, *J. Org. Chem.*, 1998, **63**, 6082–6083.

