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Morita–Baylis–Hillman reaction of indole-2-carboxaldehyde: new vistas for indole-annulated systems☆

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ABSTRACT

DABCO-mediated Morita–Baylis–Hillman reactions of several 1-substituted-indole-2-carboxaldehydes are disclosed. It was discovered that carboethoxy or *tert*-butoxycarbonyl groups installed at N-1 undergo cleavage under the reaction conditions to afford 2-substituted indoles. Utility of the *N*-substituted adducts for preparing a variety of annulated indoles has been exemplified.

1. Introduction

The Morita–Baylis–Hillman (MBH) is a base-catalyzed carbon–carbon bond forming reaction between electrophiles generally aldehyde and electron-deficient alkenes.[1] It is a kind of domino process where the nucleophilic bases, such as amines and phosphines essentially initiate a conjugate addition to the activated alkene to afford an enolate, which reacts with aldehyde via an aldol type process followed by elimination of the base. Remarkable success in the ability of MBH products to afford diverse structural motifs has led to significant increase in the substrate base both with respect to aldehydes and alkenes.[2] In spite of great advancement, MBH reactions of indolecarboxaldehydes have not been reported till date.

The influence of indole-based compounds on innumerable biochemical processes in nature ensures that this heterocycle attracts the attention of synthetic and medicinal chemists alike. It is considered to be a privileged structure owing to its presence in large number of pharmaceutical agents, natural products and drug targets.[3] Development of new protocols leading to this core unit or strategies for introduction of substitution at different positions of indole remains an active area of research.[4]

Following our interest to greatly expand the synthetic applications of the MBH chemistry for affording annulated heterocyclic architecture,[5] we now report the results of our study on MBH reaction between indole-2-carboxaldehyde and activated alkenes under the influence of DABCO. Our results suggest an essential role of a substitution on the NH of indole to initiate MBH reaction. More importantly, we have demonstrated that the MBH adduct with naked NH can be even achieved in one-pot depending on the nature of the substitution on N-1. Further the MBH adducts are shown to be viable precursors to indole-annulated frameworks.

2. Results and discussions

The starting material, indole-2-carboxaldehyde **1** was efficiently prepared in a two-step process from commercially available ethyl indole-2-carboxylate.[6] Initially MBH reaction of **1** was attempted with methyl acrylate in the presence of DABCO. However even after 20 days of reaction time only a faint spot for the expected product appeared in the TLC analysis. Arresting the reaction at this stage followed by workup and purification yielded a trace amount of the adduct **2** (ca. <1%) (Scheme 1). Unsuccessful with this initial attempt, we decided to substitute the NH of indole and then investigate the MBH reaction.

As a consequence compounds **3**–**5** were prepared via reaction of **1** with benzyl bromide, ethyl chloroformate and *tert*-butoxycarbonyl anhydride, respectively, as outlined in Scheme 1.[7–9] The viability of the MBH reaction of protected indoles was initially tested by treating *N*-benzyl indole-2-carboxaldehyde **3** with methyl

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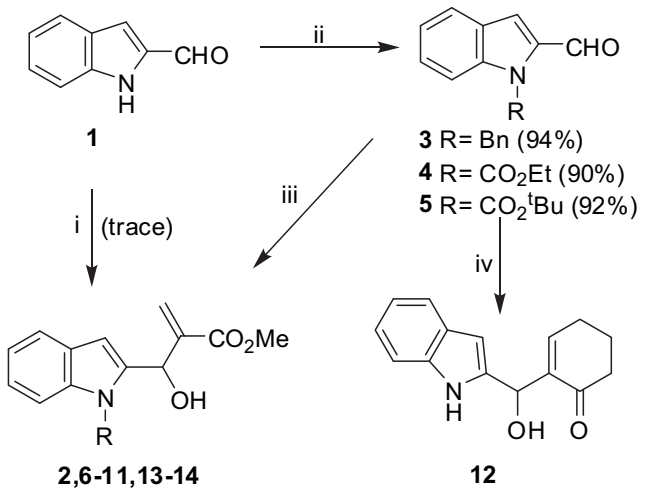
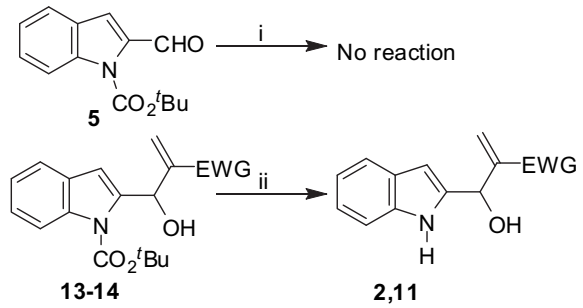


Scheme 1. Reagents and conditions: (i) CH_2=$CHCO_2Me$, DABCO, rt, 20 d; (ii) NaH, BnBr, DMF, rt, 1 h (for **3**), $ClCO_2Et$, NaH, THF, rt, 3 h (for **4**), $(Boc)_2O$, Et_3N, DMAP, CH_2Cl_2, rt, 10 h (for **5**); (iii) CH_2=CHEWG, DABCO, rt or 0 °C, 3 h to 4 days; (iv) 2-cyclohexen-1-one, DABCO, rt, 2 days.

acrylate in the presence of DABCO under neat conditions at room temperature. It was satisfying to observe that the reaction was completed in 3 days to yield the MBH adduct **6** in good yields (Table 1). Next **3** was treated with other alkenes to successfully afford the required adducts. As illustrated by the results in Table 1, acrylonitrile reacted faster as compared to acrylates. Following, aldehyde **4** was subjected to MBH reactions with various alkenes under similar conditions. Except acrylonitrile, all alkenes yielded the corresponding MBH adducts wherein the carboethoxy group on the nitrogen of indole was cleaved under the reaction condition (Table 1). Under basic conditions such deprotection of carboethoxy group in indole has been reported earlier.[10] Importantly for us, this in situ deprotection complimented our efforts to generate deprotected or protected MBH adduct depending on the substitution placed on the NH of the indole unit. For acrylonitrile it was discovered that the reaction has to be performed at 0 °C instead of the room temperature to obtain the MBH in 3 h.

adduct (entry 10 and 13, Table 1). Although deprotection of the *N*-Boc of indole is reported under the basic medium,[10] this is the first observation of DABCO-promoted Boc-deprotection of the indole nucleus. In order to examine whether this observation is general for *N*-Boc indoles, **5** was treated with DABCO under similar conditions. For this reaction, we did not observe cleavage of the Boc-group and the starting material was recovered unreacted even after 10 days. Unlike, when compounds **13** and **14** were treated with DABCO in THF they smoothly undergo cleavage of the Boc-group in 24 h to afford **2** and **11**, respectively (Scheme 2). Use of other bases instead of DABCO, including Et_3N or DMAP failed to effect this reaction. It is presumed that during the reaction DABCO act as nucleophile to attack at the carbonyl of the carbamate group leading to elimination of the Boc-group.[10a] Such an attack occurs only after the MBH adduct is formed and the hydroxy acrylate chain placed at 2-position of the indole may have a role in facilitating this event. In an effort to provide chemical evidence to this, reaction between **5** and acrylonitrile was performed at 0 °C with continuous monitoring to a stage when deprotected product **11** starts appearing (ca. 2.5 h). Reaction was arrested at this stage and subjected to purification to afford **14** in 79% (based on amount of reacted **5**) and unreacted **5** in 40% yields. Success with DABCO prompted us to examine DBU for similar deprotection of the Boc-group in **13** and **14**, which smoothly afforded the corresponding unprotected products **2** and **11**.



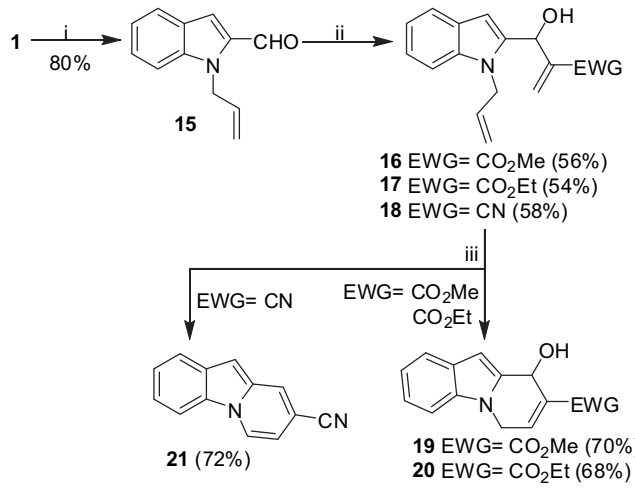
Scheme 2. Reagents and conditions: (i) DABCO, rt, 10 days; (ii) DABCO, THF, rt, 1 day.

Table 1
Results of the MBH reactions of **1**,**3**–**5** via Scheme 1

Entry	Aldehyde	R	Alkene	Conditions	*N*-Protected MBH adduct (Yield %)	*N*-Deprotected MBH adduct (Yield %)
1	**1**	H	Methyl acrylate	Neat, rt, 20 days	—	**2** (<1)
2	**3**	Bn	Methyl acrylate	Neat, rt, 3 days	**6** (70)	—
3[b]	**3**	Bn	Ethyl acrylate	Neat, rt, 4 days	**7** (65)	—
4	**3**	Bn	Acrylonitrile	Neat, rt, 2 days	**8** (72)	—
5	**4**	CO_2Et	Methyl acrylate	Neat, rt, 24 h	—	**2** (68)
6	**4**	CO_2Et	Ethyl acrylate	Neat, rt, 2 days	—	**9** (67)
7	**4**	CO_2Et	*tert*-Butyl acrylate	Neat, rt, 4 days	—	**10** (66)
8	**4**	CO_2Et	Acrylonitrile	Neat, 0 °C, 3 h	—	**11** (69)
9	**4**	CO_2Et	Cyclohex-1-ene-2-one	Neat, rt, 2 days	—	**12** (69)
10	**5**	$CO_2{}^tBu$	Methyl acrylate	Neat, rt, 24 h	**13** (24)	**2** (45)
11	**5**	$CO_2{}^tBu$	Ethyl acrylate	Neat, rt, 2 days	—	**9** (65)
12	**5**	$CO_2{}^tBu$	*tert*-Butyl acrylate	Neat, rt, 4 days	—	**10** (66)
13	**5**	$CO_2{}^tBu$	Acrylonitrile	Neat, 0 °C, 3 h	**14** (23)	**11** (47)
14	**5**	$CO_2{}^tBu$	Cyclohex-1-ene-2-one	Neat, rt, 2 days	—	**12** (68)

Subsequently MBH reactions of **5** with different activated alkenes were investigated. Interestingly similar to earlier results, reaction of **5** with higher acrylates and 2-cyclohexene-1-one afforded the *N*-deprotected MBH adducts in good yields (entry 11, 12 and 14, Table 1). But the MBH reaction of **5** with methyl acrylate and acrylonitrile afforded two products out of which the major product was identified as the *N*-deprotected adduct, whereas the minor product was spectrally characterized to be *N*-Boc protected

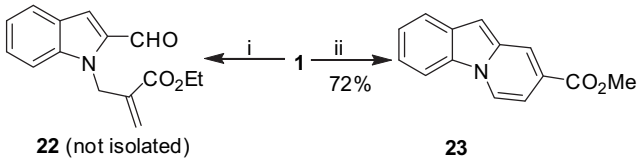
Having established the MBH reactions of indole-2-carboxaldehyde, we turned our attention to develop protocols for annulated indoles via use of *N*-substituted MBH adducts. Towards this objective, in one of the approaches *N*-allyl protected indole-2-carbaldehyde **15** was prepared[11] and subjected to MBH reaction with different alkenes. It was found that this substrate took longer times to react and yields of the afforded adducts **16**–**18** were moderate (54–58%) (Scheme 3). Compounds **16**–**18** were ideally suited for



Scheme 3. Reagents and conditions: (i) CH_2=$CHCH_2Br$, NaH, DMF, 0 °C- rt, 4 h; (ii) CH_2=CH–EWG, DABCO, rt, 2–4 days; (iii) Grubb's second Cat., CH_2Cl_2, reflux, 1.5 h.

intramolecular ring-closure via metathesis reaction.[12,2h] Reacting **16**–**18** with Grubbs II generation catalyst in dichloromethane yielded the corresponding ring-closed products **19**–**21** in 68–72% yields. It was observed that for acrylates the dehydration did not occur and the isolated product (**19**,**20**) bear the hydroxyl group whereas for acrylonitrile derived substrate **18** the dehydration occurs to afford a fully aromatized product **21**. Such dehydration for acrylonitrile derived substrate during metathesis reaction has literature precedence.[13]

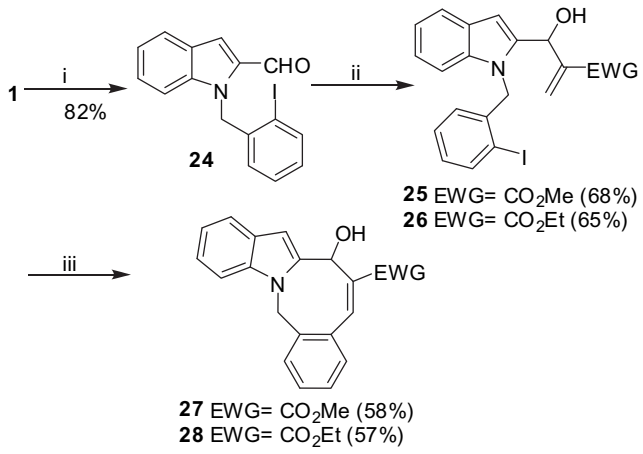
In an extension to the protocol it was envisaged that reaction between ethyl 2-(bromomethyl)acrylate (prepared from MBH adduct of formaldehyde) and **1** will lead to a new aldehyde **22**. Sequential MBH and metathesis reactions of **22** would result in another novel indole-annulated system. Unfortunately we discovered that reaction between ethyl 2-(bromomethyl)acrylate and **1** resulted in a mixture of products, which could not be characterized (Scheme 4). Alternatively, another substituted allyl bromide was screened for reaction with **1**. Interestingly the reaction of **1** with *trans* methyl 4-bromobut-2-enoate in the presence of NaH in DMF at room temperature resulted in a product in 72% yields, which was spectrally characterized to be methyl pyrido[1,2-*a*]indole-8-carboxylate **23**.[14]



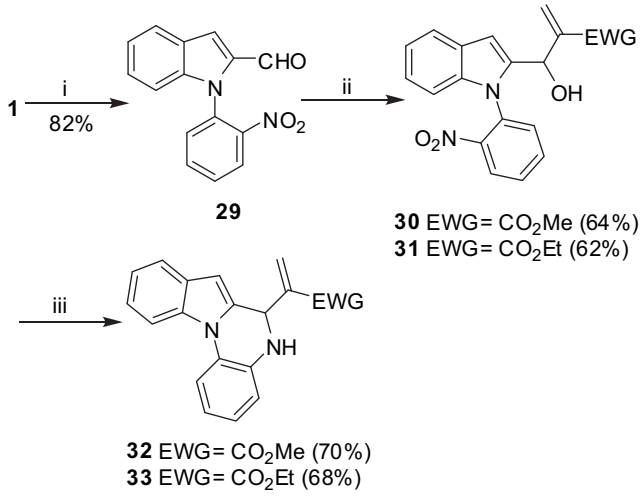
Scheme 4. Reagents and conditions: (i) $BrCH_2C(=CH_2)CO_2Et$, NaH, DMF, 0 °C to rt, 48 h; (ii) $BrCH_2CH$=$CHCO_2Me$, NaH, DMF, 0 °C to rt, 8 h.

In another strategy the NH of the indole-2-carboxaldehyde was protected with 2-iodobenzyl group and the resulting substrate **24** was subjected to MBH reaction with acrylates (Scheme 5).[15] This reaction yielded adducts **25** and **26**, which upon Heck coupling reaction in the presence of palladium complex under microwave condition afforded indole-fused benzoazocines (**27**–**28**) in moderate yields.[16]

Prompted by the success of the chemistry, we next embarked on protection of the NH of indole by 2-fluoronitrobenzene in the presence of K_2CO_3 to afford the aldehyde **29**.[17] MBH reaction of **29** with methyl and ethyl acrylate furnished adducts **30** and **31** in 64% and 62% yields, respectively (Scheme 6). It was assumed that reductive cyclization of the substrate would take place via attack of the aromatic amino group either on the double bond or the ester



Scheme 5. Reagents and conditions: (i) 2-Iodobenzyl chloride, NaH, DMF, 0 °C, 4.5 h; (ii) CH_2=CH–EWG, DABCO, rt, 2–4 days; (iii) $PdCl_2(PPh_3)_2$, Et_3N, DMF, MW, 150 °C, 30 min.



Scheme 6. Reagents and conditions: (i) 2-Fluoronitrobenzene, K_2CO_3, DMF, 100 °C, 1.5 h; (ii) CH_2=CH–EWG, DABCO, rt, 2–4 days; (iii) Fe–AcOH, 100 °C, 2 h.

group. Unexpectedly, however, Fe–AcOH-promoted reductive cyclization in **30** and **31** resulted in the formation of a new indole-fused quinoxaline framework **32** and **33**, respectively.

3. Conclusions

In conclusion we have successfully achieved the MBH reaction of several *N*-substituted indole-2-carboxaldehydes. We have demonstrated that placing a suitable substitution at the NH makes the MBH adducts viable precursors to several new indole-annulated systems using robust reactions. The deprotection of the carboethoxy and *tert*-butoxycarbonyl protected indole-2-carboxaldehydes to afford the MBH adduct possessing no substitution on indole nucleus opens up new opportunities to make substitution at 3-position of indole and extend the chemistry further especially for indole-annulated architectures. Exploration of chemistry in this direction is underway.

4. Experimental

4.1. General

Melting points are uncorrected and were determined in capillary tubes on an apparatus containing silicon oil. IR spectra were

recorded using a Perkin–Elmer's RX I FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded either on a Bruker DPX-200 FT or Bruker Avance DRX-300 spectrometer, using TMS as an internal standard (chemical shifts in δ). The ESMS were recorded on MICROMASS Quadro-II LCMS system, respectively. Elemental analyses were performed on a Carlo Erba's 108 or an Elementar's Vario EL III microanalyzer. The reactions under microwave heating were carried out in a Biotage initiator 2.5 microwave system. All yields described herein are the isolated yields after column chromatography.

4.2. General procedure for the preparation of 2, 6–14, 16–18, 25, 26, 30,31 as exemplified for compound 2

To a well stirred solution of methyl acrylate (0.74 mL, 9.21 mmol) and DABCO (0.10 g, 0.92 mmol), compound **4** (0.2 g, 0.92 mmol) was added and the reaction was allowed to proceed for 24 h. On completion as monitored by the TLC the mixture was extracted with EtOAc (3×20 mL) and water (20 mL). The combined organic layer was washed with brine (2×20 mL), dried (Na_2SO_4) and concentrated to yield a crude residue. Purification by column chromatography over silica gel with EtOAc/hexane (30:70, v/v), R_f=0.15 (EtOAc/hexane 20:80, v/v) as eluent furnished the desired compound as a white solid in 68% yield (0.14 g). Following the similar procedure compound **5** afforded **2** in 45% yields (0.8 g from 0.2 g).

*4.2.1. Methyl 2-[hydroxy(1H-indol-2-yl)methyl]acrylate (**2**).* Mp 110–112 °C. IR (KBr) 1705 (CO_2Me), 3022 (=CH), 3459 (OH) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.41 (1H, d, J=6.3 Hz, CHO*H*), 3.79 (3H, s, CO_2CH_3), 5.72 (1H, d, J=6.4 Hz, C*H*OH), 5.93 (1H, s, =C*H*H), 6.34 (1H, s, =CH*H*), 6.37 (1H, s, ArH), 7.08 (1H, t, J=7.2 Hz, ArH), 7.17 (1H, t, J=7.2 Hz, ArH), 7.35 (1H, d, J=7.8 Hz, ArH), 7.55 (1H, d, J=7.7 Hz, ArH), 8.55 (1H, br s, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.4, 68.9, 100.1, 111.2, 120.0, 120.7, 122.2, 127.2, 128.3, 136.1, 138.4, 140.0, 167.2; MS (ESI) m/z 232.1 (M^++H). Anal. Calcd for $C_{13}H_{13}NO_3$ (231.0895) C 67.52, H 5.67, N 6.06; found C 67.78, H 5.85, N 5.84.

4.3. General procedure for the preparation of 19–21 as exemplified for compound 19

To a well stirred suspension of Grubbs second Generation catalyst (0.016 g, 0.018 mmol) in dry CH_2Cl_2 (10 ml) at room temperature, compound **16** (0.05 g, 0.18 mmol) was added. The reaction mixture was heated at 40 °C for 1.5 h under nitrogen atmosphere. Thereafter, the solvent was evaporated to obtain the crude residue, whose purification by column chromatography over silica gel with EtOAc/hexane (12:88, v/v), R_f=0.23 (EtOAc/hexane 20:80, v/v) as eluent furnished the desired compound **19** as a yellow solid in 70% yield (0.03 g).

*4.3.1. Methyl 9-hydroxy-6,9-dihydropyrido[1,2-a]indole-8-carboxylate (**19**).* Mp 110–112 °C. IR (KBr) 1703 (CO_2Me), 3505 (OH) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.19 (1H, d, J=3.5 Hz, CHO*H*), 3.90 (3H, s, CO_2CH_3), 4.74–4.94 (2H, m, NCH_2), 5.85 (1H, s, C*H*OH), 6.71 (1H, s, =CH), 7.14–7.21 (1H, m, ArH), 7.24–7.26 (1H, m, ArH), 7.31–7.36 (2H, m, ArH), 7.65 (1H, d, J=7.7 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 42.6, 52.5, 60.1, 100.5, 109.2, 120.6, 121.2, 122.0, 128.5, 129.9, 134.5, 134.8, 135.5, 166.4; Mass (ESI) m/z 244.1 (M^++H). Anal. Calcd for $C_{14}H_{13}NO_3$ (243.0895) C 69.12, H 5.39, N 5.76; found C 69.28, H 5.62, N 5.51.

*4.3.2. Ethyl 9-hydroxy-6,9-dihydropyrido[1,2-a]indole-8-carboxylate (**20**).* The title compound was prepared from **17** following the general procedure described above and after purification by column chromatography over silica gel with EtOAc/hexane(20:80, v/v), R_f=0.24 (EtOAc/hexane 20:80, v/v) as eluent was obtained as yellow solid in 65% yield (0.029 g from 0.05 g); mp 118–120 °C. IR (KBr) 1701 (CO_2Et), 3509 (OH) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.40 (3H, t, J=7.1 Hz, $CO_2CH_2CH_3$), 3.30 (1H, d, J=3.6 Hz, CHO*H*), 4.36 (2H, q, J=7.1 Hz, $CO_2CH_2CH_3$), 4.82–4.88 (2H, m, NCH_2), 5.86 (1H, s, C*H*OH), 6.71 (1H, s, =CH), 7.12–7.21 (1H, m, ArH), 7.24–7.28 (1H, m, ArH), 7.31–7.38 (2H, m, ArH), 7.66 (1H, d, J=7.2 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 42.4, 60.0, 61.6, 100.4, 109.2, 120.5, 121.1, 121.9, 128.4, 129.9, 134.2, 134.8, 135.4, 165.9; MS (ESI) m/z 258.2 (M^++H). Anal. Calcd for $C_{15}H_{15}NO_3$ (257.1052) C 70.02, H 5.88, N 5.44; found C 70.31, H 5.97, N 5.23.

*4.3.3. Pyrido[1,2-a]indole-8-carbonitrile (**21**).* The title compound was prepared from **18** following the above described procedure and after purification by column chromatography over silica gel with EtOAc/hexane(20:80, v/v), R_f=0.55 (EtOAc/hexane 10:90, v/v) as eluent was obtained as yellow solid in 72% yield (0.031 g from 0.05 g); mp 105–107 °C. IR (neat) 2227 (CN) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.53 (1H, dd, J_1=1.6 Hz, J_2=7.3 Hz, ArH), 6.94 (1H, s, ArH), 7.39–7.46 (2H, m, ArH), 7.85–7.91 (3H, m, ArH), 8.33 (1H, d, J=7.3 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 97.1, 104.6, 106.5, 110.7, 118.7, 121.8, 122.6, 124.0, 125.1, 127.6, 129.5, 130.5, 133.4; MS (ESI) m/z 193.4 (M^++H). Anal. Calcd for $C_{13}H_8N_2$ (192.0687) C 81.23, H 4.20, N 14.57; found C 81.42, H 4.46, N 14.30.

4.4. General procedure for the preparation of 27,28 as exemplified for compound 27

An oven dried microwave vial charged with **25** (0.05 g, 0.11 mmol), Et_3N (0.03 ml, 0.22 mmol), $PdCl_2(PPh_3)_2$ (0.001 g, 0.001 mmol) in dry DMF (2 mL) was heated at 150 °C with stirring under microwave for 0.5 h. The reaction was diluted with a 5 mL of ether and washed with saturated aqueous NH_4Cl solution (2×2 ml). The aqueous part was extracted with ether (2×5 ml). The combined organic part was washed with brine and dried over Na_2SO_4. The solvent was evaporated to yield a crude residue, which upon purification via silica gel column chromatography using EtOAc/hexane (18:82, v/v), R_f=0.35 (EtOAc/hexane 20:80, v/v) as eluent yielded **25** as a pink solid in 58% (0.021 g) yield.

*4.4.1. Methyl 7-hydroxy-7,14-dihydroindolo[1,2-b][2]benzazocine-6-carboxylate (**27**).* Mp 119–121 °C. IR (KBr) 1682 (CO_2Me), 3499 (OH) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (3H, s, CO_2CH_3), 4.40 (1H, d, J=9.9 Hz, CHO*H*), 4.86 (1H, d, J=14.0 Hz, NC*H*H), 5.30 (1H, d, J=14.0 Hz, NCH*H*), 5.39 (1H, d, J=9.0 Hz, C*H*OH), 6.66 (1H, s, ArH), 7.11 (1H, t, J=7.1 Hz, ArH), 7.23–7.27 (1H, m, ArH), 7.37–7.41 (3H, m, ArH), 7.53 (2H, d, J=8.0 Hz, ArH), 7.61 (1H, d, J=8.0 Hz, ArH), 8.08 (1H, s, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 47.4, 52.5, 66.8, 100.5, 109.2, 119.9, 121.2, 121.7, 128.4, 128.6, 128.7, 130.0, 131.3, 132.9, 134.5, 136.1, 138.3, 139.2, 140.3, 166.9; MS (ESI) m/z 320.2 (M^++H). Anal. Calcd for $C_{20}H_{17}NO_3$ (319.1208) C 75.22, H 5.37, N 4.39; found C 75.36, H, 5.53, N 4.15.

*4.4.2. Ethyl 7-hydroxy-7,14-dihydroindolo[1,2-b][2]benzazocine-6-carboxylate (**28**).* The title compound was prepared from **26** following the above described general procedure and after purification by column chromatography over silica gel with EtOAc/hexane (15:85, v/v), R_f=0.40 (EtOAc/hexane 20:80, v/v) as eluent was obtained as a pink solid in 57% yield (0.02 g from 0.05 g); mp 139–141 °C. IR (KBr) 1709 (CO_2Et), 3462 (OH) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.36 (3H, t, J=7.1 Hz, $CO_2CH_2CH_3$), 4.24–4.35 (2H, m, $CO_2CH_2CH_3$), 4.46 (1H, d, J=9.7 Hz, CHO*H*), 4.85 (1H, d, J=14.0 Hz, NC*H*H), 5.29 (1H, d, J=14.0 Hz, NCH*H*). 5.39 (1H, d, J=9.6 Hz, C*H*OH), 6.65 (1H, s, ArH), 7.06–7.28 (1H, m, ArH), 7.20–7.28 (1H, m, ArH), 7.35–7.40 (3H, m, ArH), 7.49–7.54 (2H, m, ArH), 7.60 (1H, d, J=7.7 Hz, ArH), 8.07 (1H, s, =CH); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 14.3, 47.4, 61.7, 66.9, 100.4, 109.2, 119.9, 121.1, 121.7, 128.4, 128.5, 128.7, 129.9, 131.3, 133.1, 134.5, 136.2, 140.0, 166.4; MS (ESI) m/z 334.2 (M^++H). Anal. Calcd for $C_{21}H_{19}NO_3$ (333.1365) C 75.66, H 5.74, N 4.20; found C 75.82, H 5.91, N 4.03.

4.5. General procedure for preparation of 32,33 as exemplified for 33

Iron powder (0.08 g, 1.56 mmol) was added to a solution of **30** (0.10 g, 0.30 mmol) in glacial AcOH (2 mL) and the reaction was heated at 100 °C with stirring under nitrogen for 1.5 h. On completion, the reaction mixture was poured into 10% aqueous $NaHCO_3$ solution with stirring by a glass rod. EtOAc (30 ml) was added to this mixture and the contents were passed through a bed of Celite. The organic layer was separated and the aqueous layer was extracted with EtOAc (3×10 ml). The organic layers were pooled, dried (Na_2SO_4) and evaporated in vacuo to afford a residue that was purified by column chromatography over silica gel with EtOAc/hexane (5:95, v/v), R_f=0.80 (EtOAc/hexane 20:80, v/v) as eluent to obtain **32** as brown oil in 70% (0.07 g) yield.

*4.5.1. Methyl 2-(5,6-dihydroindolo[1,2-a]quinoxalin-6-yl)acrylate (**32**).* IR (neat) 1721 (CO_2Me), 3376 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.82 (3H, s, CO_2CH_3), 4.77 (1H, br s, NH), 5.31 (1H, s, =C*H*H), 5.60 (1H, s, C*H*NH), 6.21 (1H, s, =CH*H*), 6.41 (1H, s, ArH), 6.81 (1H, dd, J_1=2.4 Hz, J_2=7.5 Hz, ArH), 6.94–7.03 (2H, m, ArH), 7.17–7.31 (2H, m, ArH), 7.64 (1H, d, J=7.6 Hz, ArH), 7.88 (1H, d, J=6.7 Hz, ArH), 8.01 (1H, d, J=8.4 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.9, 52.3, 100.3, 111.9, 116.7, 116.8, 120.1, 121.1, 121.3, 122.7, 124.4, 127.0, 128.0, 129.7, 134.0, 134.5, 135.5, 138.8, 166.9; MS (ESI) m/z 305.1 (M^++H). Anal. Calcd for $C_{19}H_{16}N_2O_2$ (304.1212) C 74.98, H 5.30, N 9.20; found C 75.21, H 5.56, N 8.97.

*4.5.2. Ethyl 2-(5,6-dihydroindolo[1,2-a]quinoxalin-6-yl)acrylate (**33**).* The title compound was prepared from **31** following the general procedure described above and after purification by column chromatography over silica gel with EtOAc/hexane(5:95, v/v), R_f=0.82 (EtOAc/hexane 20:80, v/v) as eluent was obtained as red oil in 68% yield (0.06 g from 0.10 g). IR (neat) 1716 (CO_2Et), 3415 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (3H, t, J=7.1 Hz, $CO_2CH_2CH_3$), 4.21–4.33 (2H, m, $CO_2CH_2CH_3$), 4.79 (1H, br s, NH), 5.28 (1H, s, =C*H*H), 5.59 (1H, s, C*H*NH), 6.21 (1H, s, =CH*H*), 6.41 (1H, s, ArH), 6.78–6.83 (1H, m, ArH), 6.92–7.04 (2H, m, ArH), 7.15–7.33 (2H, m, ArH), 7.67 (1H, m, ArH), 7.85–7.90 (1H, m, ArH), 8.01 (1H, d, J=8.0 Hz, ArH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.3, 52.0, 61.3, 100.3, 111.9, 116.7, 120.1, 121.1, 121.2, 122.7, 124.4, 127.0, 127.8, 129.7, 134.0, 134.6, 135.5, 139.0, 166.4; MS (ESI) m/z 319.2 (M^++H). Anal. Calcd for $C_{20}H_{18}N_2O_2$ (318.1368) C 75.45, H 5.70, N 8.80; found C 75.71, H 5.43, N 9.03.

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Supplementary data

Remaining experimental procedures and spectroscopic data and copies of NMR spectra of all compounds are included. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.07.078. These data include MOL files and InChIKeys of the most important compounds described in this article.

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