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Expeditious Synthesis of Imidazole- and Pyrrole-Fused Benzodiazocines§

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Abstract

A straightforward strategy for the synthesis of imidazole fused-benzodiazocine from 1-(2-nitrophenyl)-1*H*-imidazole-2-carbaldehyde via Morita-Baylis-Hillman reaction followed by reductive intramolecular cyclization is described. Alternatively the Horner-Wadsworth-Emmons reaction of this substrate with triethyl phosphonoacetate yielded (*E*)-ethyl 3-(1-(2-nitrophenyl)-1*H*-imidazol-2-yl) acrylate which upon sequential reduction, saponification and amide coupling furnished imidazole-fused- diazocinones. On the other hand 1-(2-nitrophenyl)-1*H*-pyrrole-2-carbaldehyde failed to undergo the Morita-Baylis-Hillman reaction but successfully yields (*E*)-ethyl 3-(1-(2-nitrophenyl)-1*H*-pyrrol-2-yl)acrylate via Horner-Wadsworth-Emmons reaction which through a similar series of reaction as for imidazole produced pyrrole-fused-diazocinone in good yields.

Keywords: Morita-Baylis-Hillman / Horner-Wadsworth-Emmons / fused-benzodiazocines / fused-benzodiazocinones / Reductive cyclization

Introduction

The nitrogen-containing eight-member benzo-fused ring system azocine and diazocine are structural elements of several pharmacologically active compounds.[1] But synthesis of these ring systems continues to be a challenging task because they cannot be readily prepared via traditional methods of heterocyclizations.[2] Therefore expeditious and general strategies towards generation of such heterocycles are required and as a consequence their synthesis remains an active area of research. Basavaiah et al. reported the synthesis of benzoazocine framework using Morita-Baylis-Hillman (MBH) chemistry.[3] In our continuing studies related to the exploitation of the MBH chemistry for the synthesis of scaffolds of pharmacological significance, we envisaged the synthesis of annulated benzodiazocines using this reaction as one of the key steps. Indeed the synthesis of 1,4-diazocine ring system which have been comprehensively reviewed by Varvounis and co-workers in their report related to pyrrolo[2,1-c][1,4]benzodiazocines indicates that the approach embarked by us is novel.[4] In principle, a C-N coupling between 2-fluoronitrobenzene and imidazole-2-carbaldehyde would afford a 1-(2-nitrophenyl)-1*H*-imidazole-2-carbaldehyde which upon MBH reaction followed by reductive cyclization would result in imidazole-annulated benzodiazocines. Alternating the protocol with 2-fluoronitrobenzene and pyrrole-2-carbaldehyde is expected to afford pyrrole-annulated benzodiazocine. Although, we have successfully accomplished the synthesis of tetrahydrobenzo[b]-imidazo[1,2-*d*][1,4]diazocines in good yields, we came across several interesting observations during the present study which prompts us to report our results herein.

Results and Discussion

Our protocol commenced by preparation of the required aldehydes **1** and **2** by coupling 2-fluoronitrobenzene or 2-fluoro-4-methyl-nitrobenzene and imidazole-2-carbaldehyde, respectively in the presence of K_2CO_3 in DMF at room temperature.[5c] Initial optimization studies were performed using **1** as the starting substrate. The reaction of **1** with methyl acrylate in the presence of DABCO under neat condition at room temperature was complete in 2 h to afford the required adduct **3a** in 70% yields. Reduction of the nitro-group in **3a** was investigated with Fe-AcOH and In-HCl mixture simultaneously. Treating **3a** with Fe-AcOH under heating at 90 ^{o}C for 20 min resulted in complete consumption of the starting material. Purification of the reaction mixture gave a product in 74% yields which was spectroscopically established to be 4,5,6,7-tetrahydrobenzo[b]imidazo[1,2-*d*][1,4]diazocine **5a**. On the other hand reduction in the presence of In-HCl at room temperature was complete within 15 min but the purification of crude yielded **5a** in 40% yields only. Formation of **5a** under both conditions implied that reduction of the aromatic nitro group leads to amino group which invariably induce regioselective Michael reaction onto the double bond. Interestingly, coupling constant for the C*H*OH proton indicated that the product to be the trans isomer exclusively. Structure of the product was unambiguously secured by carrying out the X-ray analysis of the crystal of **5a** (Fig. 1).[6] Subsequently the MBH reaction of **1** and **2** was carried out with different acrylates, acrylonitrile and methyl vinyl ketone (MVK) to obtain **3b-f** and **4a,e** in good yields. Notably reactions with n-butyl acrylate and *tert*-butyl acrylate were observed to be sluggish whereas the reaction of MVK was performed in a mixture of dioxane: water (1:1). In view of better results achieved with Fe-AcOH, substrates **3b-f** and **4a, e** were subjected to reductive cyclization in the presence of this reagent. Fortunately, all reactions were complete within 20 min resulting in the corresponding products **5b-f** and **6a,e** in 68-70 % yields, thereby establishing the generality of the protocol. The ^{1}H-NMR data for all compounds indicated that they had similar relative stereochemistry as **5a**.

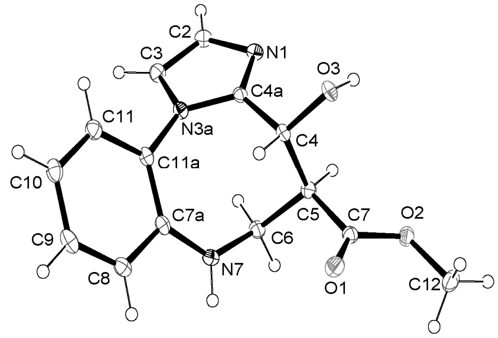
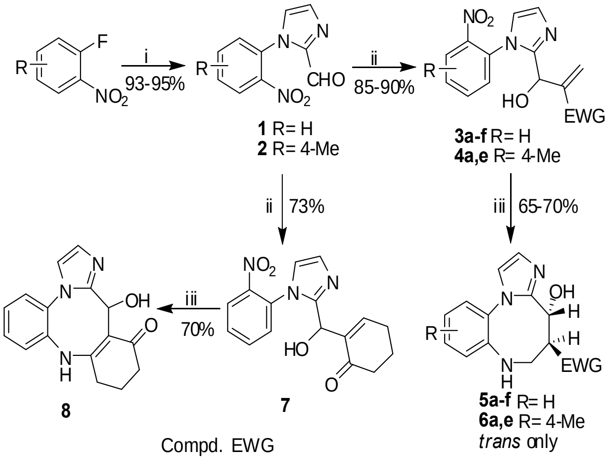


Figure 1. Crystal structure of **5a** at 35% probability level

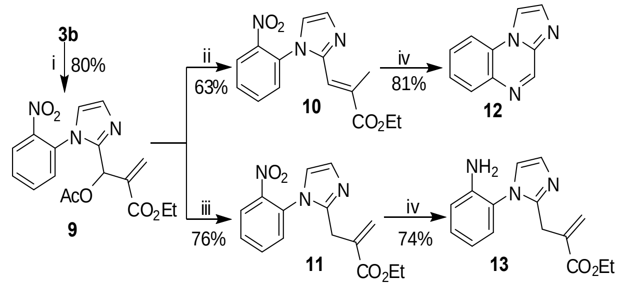


Compd.	EWG
a	CO_2Me
b	CO_2Et
c	$CO_2{}^nBu$
d	$CO_2{}^tBu$
e	CN
f	COMe

Scheme 1. Reagents and conditions- i) Imidazole-2-carbaldehyde, K_2CO_3, dry DMF, r.t., 2 h; ii) Acrylate, acrylonitrile, MVK or 2-cyclohexen-1-one, DABCO, neat or dioxane/H_2O, r.t., 2-48 h; iii) Fe-AcOH, 90 °C, 20 min.

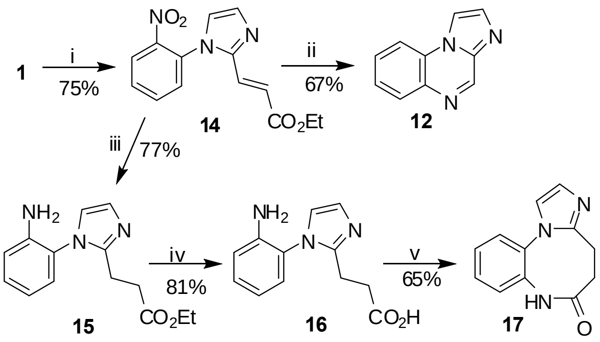
Nevertheless to assert it further, NOESY experiment with **5b** was performed. In this experiment no effect was observed between the C*H*OH and C*H*EWG proton, thereby, confirming the trans geometry of the product. The scope of the strategy was also evaluated with the MBH-adduct **7** furnished via reaction between **1** and 2-cyclohexen-1-one in the presence of DABCO in a mixture of dioxane: water. It was pleasing to find that the reduction of **7** in the presence of Fe-AcOH successfully furnished the desired product **8** in 70% yields.

In order to diversify the range of products, next we employed the acetyl derivative **9** prepared from **3b** for similar intramolecular cyclization. Unfortunately this reaction resulted in a mixture of products which could not be separated and characterized. This outcome was attributed to highly unstable nature of **9**. Mechanistic considerations invoked us to investigate the reduction in compounds **10** and **11** which were readily afforded from **9**. It was anticipated that positioning the double bond in the side chain differently in these substrates may allow the intramolecular carbamate formation to precede the Michael reaction thereby resulting in fused-benzodiazocinone. Consequently **9** was subjected to reaction with $NaBH_4$ in S_N2Njand S_N2-fashion to afford compounds **10** and **11**, respectively following reported procedure (scheme 2).[7] Compound **10** was obtained as a mixture of E and Z isomers. Without separating these isomers, **10** was subjected to reduction in the presence of Fe-AcOH. This reaction yielded a product which was characterized to be **12** instead the expected fused-benzodiazocinone. The structure of **12** was in alignment with the reported melting point and spectroscopic data.[5] Perhaps due to aromaticity of the imidazole ring, the Michael reaction is favoured over the intramolecular amidation reaction leading to a 6-membered ring rather than a 8-membered ring (vide infra).



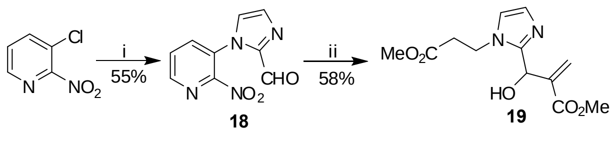
Scheme 2. Reagents and conditions- i) AcCl, Pyridine, CH_2Cl_2, 0 °C-r.t., 30 min; ii) $NaBH_4$, EtOH, r.t., 1 h; iii) $NaBH_4$, DABCO, THF/H_2O (1:1), r.t., 1 h; iv) Fe-AcOH, 90 °C, 20 min.

Simultaneously we investigated the substrate **11** for similar reaction. Reducing **11** in the presence of Fe-AcOH furnished a product in 74% yield which was established to be the aniline **13**. Several attempts to perform intramolecular cyclization in this substrate failed. Indeed it has been experienced by us earlier too that the nucleophilic attack of aniline in analogous MBH derivative is unsuccessful.[8] In a modified approach, therefore, we prepared **14** via Horner-Wadsworth-Emmons reaction of **1** with triethyl phosphonoacetate in the presence of NaH (scheme 3). Expectedly **14** was obtained as E-isomer exclusively. Reducing **14** in the presence of Fe-AcOH furnished a product which was identical to **12**. As an outcome of this result, we decided to reduce the double bond and examine whether intramolecular amidation is at all possible in this substrate. Henceforth, **14** was subjected to Raney-Ni promoted catalytic hydrogenation which smoothly afforded the product **15** in quantitative yields. Initial attempts to achieve intramolecular amidation in **15** employing NaH failed. Therefore, the ester group in **15** was first saponified in the presence of aq. LiOH to afford acid **16** which upon coupling reaction in the presence of EDCI yielded 4,5-dihydrobenzo[b]imidazo[1,2- *d*][1,4]diazocin-6(7*H*)-one **17**.



Scheme 3. Reagents and conditions-i) $(EtO)_3P{=}CHCO_2Et$, NaH, THF, 0 °C, 5 h; ii) Fe-AcOH, 90 °C, 20 min.; iii) H_2/Raney-Ni, EtOH, r.t., 1 h; iv) LiOH, THF/H_2O (3:1), r.t., 1 h; v) EDCI, NMM, dry CH_2Cl_2, -10°C, 45 min.

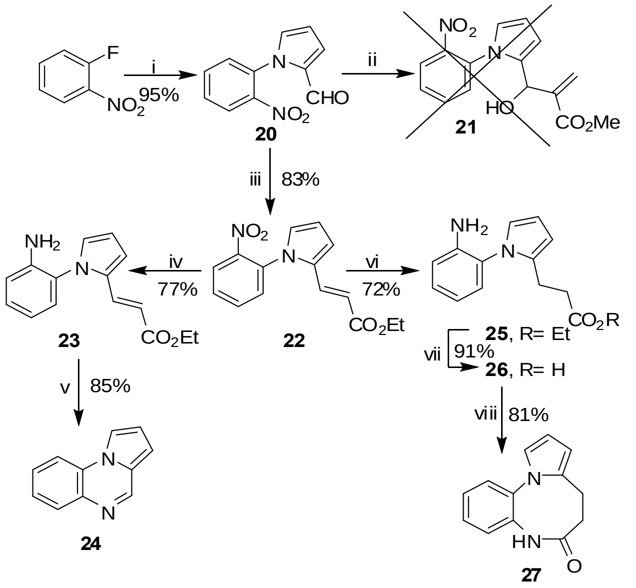
Success of the strategy with 1-(2-nitrophenyl)-1*H*-imidazole-2-carbaldehyde invoked us to examine our protocol with 1-(2-nitropyridin-3-yl)-1*H*-imidazole-2-carbaldehyde. Accordingly **18** was prepared by reaction between 2-chloro-3-nitropyridine and imidazole-2-carbaldehyde in the presence of K_2CO_3 in DMF at room temperature. Reaction of **18** with methyl acrylate in the presence of DABCO was complete in 2 h at room temperature to afford a product in 58% yields. Based on the spectral evidence, this compound was established to be **19** instead of the expected MBH adduct (scheme 4). It is likely that in the presence of DABCO, simultaneous to the MBH reaction dealkylation of the imidazole takes place making NH free which undergoes Michael addition with the acrylate to afford the unexpected product **19**.



Scheme 4. Reagents and conditions- i) Imidazole-2-carbaldehyde, K_2CO_3, dry DMF, r.t., 3.5 h; ii) Methyl acrylate, DABCO, r.t., 2 h.

To investigate the potential of this strategy for the synthesis of pyrrole-fused bezodiazocine, we then prepared 1-(2-nitrophenyl)-1*H*-pyrrole-2-carbaldehyde **(20)** by reacting 2-fluoronitrobenzene with pyrrole-2-carbaldehyde in the presence of K_2CO_3 in DMF.[9] Unfortunately all attempts to perform the MBH reaction with **20** failed to produce the required product **21** (scheme 5). Undeterred by the failure, we proceeded to investigate the Horner-Wadsworth-Emmons-mediated strategy for generating pyrrole-fused-diazocinone.

Therefore reaction of **20** with triethyl phosphonoacetate in the presence of NaH in THF was performed to yield the desired product **22** in 83% yields as E-isomer exclusively. In order to examine the probability of intramolecular amidation in **22**, it was subjected to reduction in the presence of Fe-AcOH. Unlike **14**, reduction here resulted in a product which was delineated to be **23**. Attempts to induce intramolecular cyclization by treating **23** with NaH in THF yielded **24** in 85% yields.[9] Hence **22** was first reduced catalytically via Raney-Ni under hydrogenation conditions to afford the amino derivative **25**. Saponification of **25** by aq. LiOH smoothly afforded the required acid **26** in 91% yields. An intramolecular coupling reaction in **26** in the presence of EDCI furnished the desired 7,8-dihydrobenzo[b]pyrrolo[1,2-*d*][1,4]diazocin-6(5*H*)-one **27** in 81% yields.



Scheme 5. Reagents and conditions- i) Pyrrole-2-carbaldehyde, K_2CO_3, dry DMF, r.t., 2 h; ii) methyl acrylate, DABCO, r.t., 3 weeks; iii) $(EtO)_3P{=}CHCO_2Et$, NaH, THF, 0 °C, 5 h; iv) Fe-AcOH, 90 °C, 20 min; v) NaH, THF, 80 °C, 1 h; vi) H_2/Raney-Ni, EtOH, r.t., 1 h; vii) LiOH, THF/H_2O (3:1), r.t., 1 h; viii) EDCI, NMM, dry CH_2Cl_2, -10°C, 45 min.

From the results achieved so far a plausible mechanism for the formation of **12** or **24** is delineated in Fig. 2. It is speculated that he Michael reaction of the amino group onto the double bond leads to intermediate **III**, which rearranges to **IV**. Participation of N-1 through two double bonds of imidazole or pyrrole ring eliminates the ethyl acetate from the molecule resulting in the observed products. In principle, if the aromatic subunit (imidazole or pyrrole) is replaced by a non-aromatic unit where no double bond is present the elimination of ethyl acetate would be prevented. In order to assess this hypothesis we embarked on investigation with **31** which was readily obtained from proline ester as outlined in scheme 6. Coupling of proline ester 2-fluoronitrobenzene yielded **28** whose reduction with DIBAL-H smoothly furnished the alcohol **29**. Swern oxidation of **29** afforded the aldehyde **30** which upon Horner-Wadsworth-Emmons reaction with triethyl

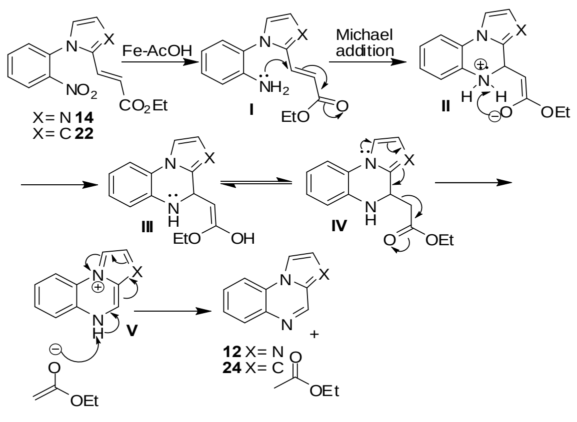
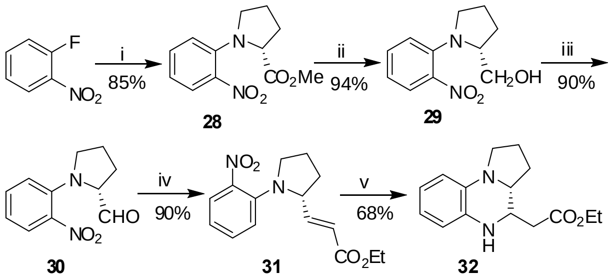


Figure 2. Plausible mechanism for the formation of **14** and **24**.



Scheme 6. Reagents and conditions- i) *l*-Proline ester, K_2CO_3, dry DMF, r.t., 3.5 h; ii) DIBAL-H, PhMe, 0 °C, 30 min.; iii) $(CO_2Cl)_2$, dry DMSO, Et_3N, dry CH_2Cl_2, -78 °C-r.t., 2 h; iv) $(EtO)_3P{=}CHCO_2Et$, NaH, THF, 0 °C, 5 h; v) Fe-AcOH, 90 °C, 20 min.

phosphonoacetate provided the required ester **31**. Reducing **31** in the presence of Fe-AcOH furnished a product which was spectrally characterised to be **32**. Isolation of **32** confirmed that once the aromatic unit comprising of double bonds is replaced by a non-aromatic unit having saturated system, the elimination of ethyl acetate does not occur.

Conclusions

In conclusion we have developed a facile, efficient and general protocol for the synthesis of fused-benzodiazocine framework either via MBH or Horner-Wadsworth-Emmons chemistry. Though we have exemplified this approach with imidazole and pyrrole, we are trying to generate new substrates for evaluating the scope of this approach.

Experimental Section

Melting points are uncorrected and were determined in capillary tubes on a Precision melting point apparatus containing silicon oil. IR spectra were recorded using a Perkin Elmerôs 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. The HRMS spectra were recorded as EI-HRMS on a JEOL system or as DART-HRMS (recorded as ES+) on a JEOL-AccuTOF JMS-T100LC Mass spectrometer having DART (Direct Analysis in Real Time) source. Elemental analyses were performed on a Carlo Erbaôs 108 or an Elementarôs Vario EL *III* microanalyzer. The room temperature varied between 20°C and 35°C. All column chromatographic purifications were performed on silica-gel (100-200 mesh). Compound **9** was found to be unstable and was therefore immediately utilized for next reaction.

General procedure for the synthesis of compounds 1, 2, 20, 28 as exemplified for compound 1- To a stirred solution of imidazole-2-carbaldehyde (1.17 g, 12.2 mmol) in dry DMF (15 mL), K_2CO_3 (3.05 g, 22.1 mmol) was added and the reaction was continued at room temperature for 30 min. Thereafter 2-fluoronitrobenzene (1.2 mL, 11.1 mmol) was added and the reaction was stirred for additional 1.5 h at room temperature. On completion of the reaction as monitored by TLC, the contents were poured into water (150 mL) under stirring with glass rod. Thereafter the aqueous layer was extracted with EtOAc (4 × 60 mL). The organic layers were combined and washed with water (80 mL), subsequently with brine (80 mL), dried over anhydrous Na_2SO_4 and concentrated to yield the crude product. Purification of the crude via column chromatography using EtOAc/hexanes (1:1, v/v) as the eluent furnished **1** as a white solid (2.32 g, 97%).

Methyl 2-[(2*S*)-1-(2-nitrophenyl)pyrrolidin-2-yl]acetate (28): This compound was isolated in 85% yield (2.26 g from 1.50 g) as a yellow solid, mp 85-87 °C. R_f = 0.30 (EtOAc/Hexanes 1:4, v/v). 3_{max} (KBr): 1748 (CO_2Me) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.92-1.97 (m, 1H, CH_2), 2.06-2.13 (m, 2H, CH_2), 2.40-2.45 (m, 1H, CH_2), 3.13-3.20 (m, 1H, CH_2), 3.49-3.57 (m, 1H, CH_2), 3.69 (s, 3H, OCH_3), 4.39-4.44 (m, 1H, CH), 6.76-6.84 (m, 2H, ArH), 7.33-7.39 (m, 1H, ArH), 7.70 (dd, 1H, J_1 = 8.1 Hz, J_2 = 1.3 Hz, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.6, 30.9, 51.2, 52.4, 61.8, 116.5, 117.2, 126.6, 133.0, 138.3, 141.3, 173.2. MS (ES): *m/z* = 251.1 [M+1]$^{+}$. Anal. Calcd. for $C_{12}H_{14}N_2O_4$ (250.0954): C 57.59, H 5.64, N 11.19; found C 57.70, H 5.53, N 11.25.

Typical procedure for the synthesis of compound 19 - To a stirred solution of imidazole-2-carbaldehyde (0.76 g, 7.0 mmol) in dry DMF (15 mL), K_2CO_3 (1.75 g, 12.7 mmol) was added and the reaction was continued at room temperature for 30 min. Thereafter 2-chloro-3-nitro pyridine (1.00 g, 6.3 mmol) was added and the reaction was stirred for additional 3 h at room temperature. After completion as monitored by TLC, the contents were poured into water (150 mL) under stirring with glass rod. Thereafter the aqueous layer was extracted with EtOAc (4 × 50 mL). The organic layers were combined and washed with water (50 mL), then with brine (80 mL), dried (Na_2SO_4) and concentrated to yield the residue. Purification of the crude material via column chromatography over silica gel (100-200 mesh) using EtOAc/hexanes (1:1, v/v) as the eluent furnished **19** as an off white solid (0.74 g, 55%).

1-(2-Nitropyridin-3-yl)-1*H*-imidazole-2-carbaldehyde (19): Mp 189-190 °C. R_f = 0.30 (EtOAc/Hexanes 1:1, v/v). IR (KBr): 3_{max} = 1638 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.42 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.5 Hz, ArH), 7.49 (d, 1H, J = 0.7 Hz, ArH), 7.68-7.80 (m, 2H, ArH), 8.23 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.7 Hz, ArH), 9.76 (s, 1H, CHO) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 126.2, 126.8, 129.8, 131.0, 132.8, 134.5, 144.1, 181.3 ppm. MS (ES): *m/z* = 220.2 [M+1]$^{+}$. $C_9H_6N_4O_3$ (218.0440): Calcd.C 49.55, H 2.77, N 25.68; found C 49.72, H 2.63, N 25.79.

General procedure for the synthesis of compounds 3a-f, 4a,e, 7, 19 as exemplified for compound 3a- To a mixture of DABCO (0.30 g, 2.30 mmol) and methyl acrylate (0.30 mL, 0.35 mmol) that had been stirred at room temperature for 10 min was added the aldehyde **1** (0.50 g, 2.30 mmol) under stirring and the reaction was allowed to proceed for 2 h. Thereafter aq HCl (5%; 50 mL) was added to the reaction, and the mixture was extracted with EtOAc (2 × 50 mL). The organic layers were combined, washed with brine (75 mL), dried (Na_2SO_4) and evaporated under vacuum to yield an oily residue. The residue upon trituration with EtOAc-hexanes furnished pure product **3a** (0.49 g, 70%) as a white solid.

Methyl 2-{hydroxy[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}acrylate (3a): Mp 152-153 °C. R_f = 0.20 (EtOAc/Hexanes 3:2, v/v). IR (KBr): 3_{max}

= 1713 (CO_2Me), 3090 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 3.70 (s, 3H, OCH_3), 5.37 (s, 1H, CHOH), 5.98 (brs, 1H, =CH_2), 6.35 (s, 1H, =CH_2), 6.99 (s, 1H, ArH), 7.15 (s, 1H, ArH), 7.66-7.71 (m, 2H, ArH), 7.75-7.80 (m, 1H, ArH), 8.11 (d, 1H, *J* = 7.9 Hz, ArH) ppm. ^{13}C NMR (CD_3OD, 75 MHz): δ = 52.3, 65.4, 124.3, 126.5, 126.6, 128.3, 131.8, 132.1, 132.5, 135.1, 149.3, 167.3 ppm. MS (ES): *m/z* = 304.1 [M+1]$^+$. $C_{14}H_{13}N_3O_5$ (303.0855): Calcd. C 55.45, H 4.32, N 13.86; found C 55.25, H 4.42, N 13.73.

Ethyl 2-{hydroxy[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}acrylate (3b): This compound was isolated in 80% yield (0.35 g from 0.30 g) as a white solid, mp 118-120 °C. R$_f$ = 0.19 (EtOAc/Hexanes 3:2, v/v). IR (KBr): ʒ$_{max}$ = 1713 (CO_2Et), 3138 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 200 MHz): δ = 1.18 (t, 3H, *J* = 6.6 Hz, CH_3), 4.10 (d, 2H, *J* = 7.4 Hz, OCH_2), 4, 5.34 (s, 1H, CHOH), 5.91 (s, 1H, =CH_2), 6.27 (s, 1H, =CH_2), 7.03 (s, 1H, ArH), 7.23 (s, 1H, ArH), 7.66-7.89 (m, 3H, ArH), 8.19 (d, 1H, *J* = 7.9 Hz, ArH) ppm. ^{13}C NMR (CD_3OD, 50 MHz): δ = 13.4, 60.8, 64.4, 123.2, 125.2, 125.6, 127.2, 130.8, 131.0, 131.5, 134.1, 146.7, 148.3, 165.7 ppm. MS (ES): *m/z* = 318.1 [M+1]$^+$. $C_{15}H_{15}N_3O_5$ (317.1012): Calcd. C 56.78, H 4.76, N 13.24; found C 56.88, H 4.82, N 13.10.

Butyl 2-{hydroxy[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}acrylate (3c): This compound was isolated in 83% yield (0.40 g from 0.30 g) as reddish brown oil. R$_f$ = 0.23 (EtOAc/Hexanes 3:2, v/v). IR (Neat): ʒ$_{max}$ = 1711 ($CO_2{}^nBu$), 3428 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.91 (t, 3H, *J*= 7.4 Hz, CH_3), 1.32-1.40 (m, 2H, CH_2), 1.49-1.63 (m, 2H, CH_2), 4.10 (d, 2H, *J*= 6.4 Hz, OCH_2), 5.35 (s, 1H, CHOH), 5.95 (s, 1H, =CH_2), 6.34 (s, 1H, =CH_2), 6.98 (s, 1H, ArH), 7.12 (s, 1H, ArH), 7.67-7.80 (m, 3H, ArH), 8.10 (d, 1H, *J*= 8.5 Hz, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.1, 19.5, 30.9, 65.2, 125.8, 130.9, 131.2, 131.4, 134.1, 139.5, 148.6, 166.2 ppm. MS (ES): *m/z* = 346.1 [M+1]$^+$. $C_{17}H_{19}N_3O_5$ (345.1325): Calcd. C 59.12, H 5.55, N 12.17; found C 59.01, H 5.77, N 12.23.

tert-Butyl 2-{hydroxyl[1-(2-nitrophenyl)-1*H*-imidazol-2-yl}methyl}acrylate (3d): This compound was isolated in 95% yield (0.45 g from 0.30 g) as a yellow solid, mp 126-127 °C. R$_f$ = 0.21 (EtOAc/Hexanes 3:2, v/v). IR (KBr): ʒ$_{max}$ = 1715 ($CO_2{}^tBu$), 3428 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.43 (s, 9H, 3 x CH_3), 5.37 (s, 1H, CHOH), 5.75 (s, 1H, =CH_2), 6.13 (s, 1H, =CH_2), 6.97 (s, 1H, ArH), 7.09 (s, 1H, ArH), 7.59-7.76 (m, 3H, ArH), 8.09 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.2 Hz, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ = 27.9, 65.9, 81.4, 122.1, 125.1, 125.3, 128.1, 130.3, 131.0, 133.6, 140.5, 146.3, 148.2, 164.9 ppm. MS (ES): *m/z* = 346.1 [M+1]$^+$. $C_{17}H_{19}N_3O_5$ (345.1325): Calcd. C 59.12, H 5.55, N 12.17; found C 59.16, H 5.50, N 12.08.

2-{Hydroxy[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}acrylonitrile (3e): This compound was isolated in 73% yield (0.32 g from 0.35 g) as a white solid, mp 153-155 °C. R$_f$ = 0.25 (EtOAc/Hexanes 3:2, v/v). IR (KBr): ʒ$_{max}$ = 2225 (C≡N), 3146 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 200 MHz): δ = 5.22 (s, 1H, CHOH), 5.96 (s, 1H, =CH_2), 6.02 (s, 1H, =CH_2), 7.13 (s, 1H, ArH), 7.29 (s, 1H, ArH), 7.63 (d, 1H, *J* = 7.5 Hz, ArH), 7.69-7.85 (m, 2H, ArH), 8.20 (d, 1H, *J* = 7.7 Hz, ArH) ppm. ^{13}C NMR (CD_3OD, 50 MHz): δ = 67.0, 124.0, 125.5, 127.7, 130.8, 131.2, 131.3, 134.1, 136.3, 139.5, 146.3 ppm. MS (ES) *m/z* = 271.1 [M+1]$^+$. $C_{13}H_{10}N_4O_3$ (270.0753): Calcd. C 57.78, H 3.73, N 20.73; found C 57.92, H 3.81, N 20.64.

3-{Hydroxy[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}but-3-en-2-one (3f): This compound was isolated in 80% yield (0.74 g from 0.70 g) as reddish brown oil. R$_f$ = 0.15 (EtOAc). IR (Neat): ʒ$_{max}$ = 1710 (CO), 3406 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.33 (s, 3H, CH_3), 5.31 (d, 1H, *J* = 5.6 Hz, CH), 6.26 (brs, 2H, =CH_2), 6.97 (s, 1H, ArH), 7.08 (s, 1H, ArH), 7.65-7.78 (m, 3H, ArH), 8.10 (d, 1H, *J* = 8.0 Hz, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.1, 53.5, 125.4, 126.5 130.5, 130.6, 131.1, 133.9, 146.3, 147.2, 148.7 ppm. MS (ES): *m/z* = 288.2 [M+1]$^+$. $C_{14}H_{13}N_3O_4$ (287.0906): Calcd C 58.53, H 4.56, N 14.63; found C 58.32, H 4.68, N 14.39.

Methyl 2-{hydroxy[1-(5-methyl-2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}acrylate (4a): This compound was isolated in 76% yield (0.31 g from 0.30 g) as reddish brown oil. R$_f$ = 0.38 (EtOAc). IR (Neat): ʒ$_{max}$ = 1714 (CO_2Me), 3426 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.52 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 5.33 (s, 1H, CHOH), 5.97 (s, 1H, =CH_2), 6.42 (s, 1H, =CH_2), 6.93 (t, 2H, *J* = 5.5 Hz, ArH), 7.40-7.46 (m, 2H, ArH), 8.02 (d, 1H, *J* = 8.3 Hz, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.4, 52.1, 65.3, 120.3, 125.5, 125.8, 127.4, 130.6, 130.8, 131.4, 139.1, 145.6, 166.5 ppm. MS (ES): *m/z* = 318.1 [M+1]$^+$. $C_{15}H_{15}N_3O_5$ (317.1012): Calcd C 56.78, H 4.76, N 13.24; found C 56.99, H 4.59, N 13.06.

2-{Hydroxy[1-(5-methyl-2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}acrylonitrile (4e): This compound was isolated in 73% yield (0.45 g from 0.50 g) as brown oil. R$_f$ = 0.30 (EtOAc). IR (Neat): ʒ$_{max}$ =2222 (C≡N), 3417 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 200 MHz): δ = 2.51 (s, 3H, CH_3), , 5.20 (s, 1H, CH), 5.99 (s, 1H, =CH_2), 6.02 (d, 1H, *J*= 5.3 Hz, =CH_2), 7.12 (d, 1H, *J* = 1.3 Hz, ArH), 7.26 (d, 1H, *J* = 4.9 Hz, ArH), 7.43 (s, 1H, ArH), 7.58 (d, 1H, *J* = 7.3 Hz, ArH), 8.10 (d, 1H, *J* = 8.3 Hz, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 19.9, 67.0, 123.5, 125.2, 127.3, 130.6, 131.1, 131.2, 154.9 ppm. MS (ES): *m/z* = 285.2 [M+1]$^+$. $C_{14}H_{12}N_4O_3$ (284.0909): Calcd C 59.15, H 4.25, N 19.71; found C 59.43, H 4.07, N 19.93.

2-{Hydroxy[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}cyclohex-2-en-1-one (7): This compound was isolated in 73% yield (0.84 g from 0.80 g) as an orange solid, m.p. 144-145 °C. R$_f$ = 0.20 (EtOAc). IR (KBr): ʒ$_{max}$ = 1713 (CO), 3414 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 1.89-2.01 (m, 2H, CH_2), 231-2.37 (m, 4H, 2 x CH_2), 5.35 (s, 1H, CH), 7.02 (brs, 2H, =CHand ArH), 7.19 (s, 1H, ArH), 7.74-7.89 (m, 3H, ArH), 8.19 (d, 1H, *J* = 7.3 Hz, ArH) ppm. ^{13}C NMR (CD_3OD, 50 MHz): δ = 24.3, 27.5, 39.8, 64.4, 124.8, 127.4, 128.9, 132.8, 133.3, 135.9, 140.1, 148.5, 149.5, 150.7, 201.1 ppm. MS (ES): *m/z* = 314.2 [M+1]$^+$. $C_{16}H_{15}N_3O_4$ (313.1063): Calcd C 61.34, H 4.83, N 13.41; found C 61.45, H 4.73, N 13.29.

Methyl 2-{hydroxy[1-(3-methoxy-3-oxopropyl)-1*H*-imidazol-2-yl]methyl}acrylate (19): This compound was isolated in 58% yield (0.36 g from 0.50 g) as reddish brown oil. R$_f$ = 0.30 (EtOAc). IR (Neat): ʒ$_{max}$ = 1727 (CO_2Me), 3415 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.87 (t, 2H, *J* = 6.8 Hz, CH_2), 3.70 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 4.35-4.41 (m, 2H, CH_2), 5.65 (s, 1H, CHOH), 6.03 (s, 1H, =CH_2), 6.43 (s, 1H, =CH_2), 6.90 (s, 2H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 35.4, 41.5, 51.96, 52.04, 65.3, 120.3, 125.8, 127.3, 139.7, 147.2, 166.5, 171.3 ppm. MS (ES+): *m/z* = 269.1 [M+1]$^+$. $C_{12}H_{16}N_2O_5$ (268.1059): Calcd. C 53.73, H 6.01, N 10.44; found C 53.62, H 5.84, N 10.58.

General procedure for the synthesis of compounds 5a-f, 6a,e, 8, 12, 13, 23, 32 as exemplified for compound 5a- To a solution of compound **3a** (0.30 g, 1.00 mmol) in AcOH (2 mL), Fe powder (0.28 g, 5.00 mmol) was added and the mixture was heated at 90 °C for 20 min. Then the reaction mixture was cooled to room temperature and poured in ice water followed by neutralization with saturated aqueous $NaHCO_3$ solution. The precipitated solid was separated by filtration through a Celite bed which was repeatedly washed with EtOAc. The organic layers were pooled, washed with brine, dried (Na_2SO_4) and concentrated to obtain a crude product. Purification via column chromatography using EtOAc/hexanes (1:1, v/v) as the eluent furnished **5a** (0.20 g, 74%).as a white solid.

Methyl 4-hydroxy-4,5,6,7-tetrahydroimidazo[1,2-*a*][1,6]benzodiazocine-5-carboxylate (5a): Mp 187-188 °C. R$_f$ = 0.25 (EtOAc/Hexanes 7:3, v/v). IR (KBr): ʒ$_{max}$ = 1726 (CO_2Me), 3426 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 2.52-2.60 (m, 2H, CH_2), 3.26 (s, 1H, CH), 3.78 (s, 3H, OCH_3), 5.29 (d, 1H, *J* = 9.8 Hz, CH), 6.64-6.72 (m, 2H, ArH), 7.02-7.14 (m, 3H, ArH), 7.23 (d, 1H, *J* = 1.3 Hz, ArH) ppm. ^{13}C NMR (DMSO-d$_6$, 75 MHz): δ = 42.8, 52.5, 53.8, 65.1, 116.8, 118.4, 129.1, 129.5, 143.8, 172.7 ppm. MS (ES): *m/z* = 274.2 [M+1]$^+$. DART-HRMS [ES+]: calcd. for $C_{14}H_{16}N_3O_3$ 274.1192; found 274.1171.

Ethyl 4-hydroxy-4,5,6,7-tetrahydroimidazo[1,2-*a*][1,6]benzodiazocine-5-carboxylate (5b): This compound was isolated in 70% yield (0.11 g from 0.18 g) as a white solid, mp 155-157 °C. R$_f$ = 0.26 (EtOAc/Hexanes 7:3, v/v). IR (KBr): ɜ$_{max}$ = 1726 (CO_2Et), 3429 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 1.36 (t, 3H, *J*= 7.1 Hz, CH_3), 2.58-2.63 (m, 2H, CH_2), 3.32 (s, 1H, CH), 4.23-4.33 (m, 2H, OCH_2), 5.36 (d, 1H, *J* = 9.7 Hz, CH), 6.70-6.78 (m, 2H, ArH), 7.08-7.20 (m, 3H, ArH), 7.28 (s, 1H, ArH) ppm. ^{13}C NMR (CD_3OD, 75 MHz): δ = 14.6, 43.7, 54.9, 62.2, 66.2, 118.1, 119.3, 120.4, 122.9, 129.2, 129.5, 130.5, 144.5, 149.9, 173.8 ppm. MS (ES): *m/z* = 288.2 [M+1]$^+$. DART-HRMS [ES+]: Calcd. for $C_{15}H_{18}N_3O_3$ 288.1348; found 288.1336.

Butyl 4-hydroxy-4,5,6,7-tetrahydroimidazo[1,2-*a*][1,6]benzodiazocine-5-carboxylate (5c): This compound was isolated in 68% yield (0.22 g from 0.35 g) as a white solid, mp 160-162 °C. R$_f$ = 0.26 (EtOAc/Hexanes 7:3, v/v). IR (KBr): ɜ$_{max}$ = 1723 ($CO_2{}^nBu$), 3415 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 1.03 (t, 3H, *J*= 7.3 Hz, CH_3), 1.43-1.53 (m, 2H, CH_2), 1.70-1.79 (m, 2H, CH_2), 2.61-2.66 (m, 2H, CH_2), 3.33 (s, 1H, CH), 4.17-4.34 (m, 2H, OCH_2), 5.38 (d, 1H, *J* = 9.7 Hz, CH), 6.72-6.80 (m, 2H, ArH), 7.12 (d, 1H, *J* = 8.0 Hz, ArH), 7.16-7.22 (m, 2H, ArH), 7.30 (s, 1H, ArH) ppm. ^{13}C NMR (CD_3OD, 75 MHz): δ = 12.7, 18.9, 30.4, 42.2, 53.5, 60.2, 64.6, 116.6, 117.8, 121.4, 127.7, 128.0, 129.0, 143.0, 149.4, 172.4 ppm. MS (ES): *m/z* = 316.3 [M+1]$^+$. DART-HRMS [ES+]: Calcd. for $C_{17}H_{22}N_3O_3$ 316.1661; found 316.1658.

tert-Butyl 4-hydroxy-4,5,6,7-tetrahydroimidazo[1,2-*a*][1,6]benzodiazocine-5-carboxylate (5d): This compound was isolated in 78% yield (0.28 g from 0.40 g) as a white solid, mp 189-190 °C. R$_f$ = 0.29 (EtOAc/Hexanes 7:3, v/v). IR (KBr): ɜ$_{max}$= 1725 ($CO_2{}^tBu$), 3422 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 1.52 (s, 9H, 3 x CH_3), 2.50-2.55 (m, 2H, CH_2), 3.25 (s, 1H, CH), 5.25 (s, 1H, CH), 6.66-6.76 (m, 2H, 7.04-7.15 (m, 4H, ArH) ppm. ^{13}C NMR (DMSO, 75 MHz): δ = 19.9, 35.4, 52.2, 65.9, 120.2, 121.3, 125.9, 127.3, 128.3, 128.5, 130.3, 139.5, 148.1, 173.1 ppm. MS (ES): *m/z* = 316.1 (M$^+$+1)$^+$. HR-EIMS [EI+]: Calcd. for $C_{17}H_{21}N_3O_3$ 315.1583; found 315.1571.

4-Hydroxy-4,5,6,7-tetrahydroimidazo[1,2-*a*][1,6]benzodiazocine-5-carbonitrile (5e): This compound was isolated in 70% yield (0.19 g from 0.30 g) as a white solid, mp 117-118 °C. R$_f$ = 0.27 (EtOAc/Hexanes 7:3, v/v). IR (KBr): ɜ$_{max}$ = 2224 (C≡N), 3423 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 2.53 (dd, 1H, J_1 = 15.8 Hz, J_2 = 2.6 Hz, CH_2), 2.82 (d, 1H, *J* = 10.0 Hz, CH_2), 3.28 (s, 1H, CH), 5.03 (d, 1H, *J* = 10.1 Hz, CH), 6.70-6.75 (m, 1H, ArH), 6.83 (d, 1H, *J* = 8.3 Hz, ArH), 7.07 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.3 Hz, ArH), 7.14-7.20 (m, 2H, ArH), 7.26 (d, 1H, *J* = 1.1 Hz, ArH) ppm. ^{13}C NMR (CD_3OD, 75 MHz): δ = 41.0, 65.4, 117.0, 117.7, 119.8, 121.9, 128.0, 128.1, 129.2, 142.4, 146.3 ppm. MS (ES): *m/z* = 241.2 [M+1]$^+$. DART-HRMS [ES+]: Calcd. for $C_{13}H_{13}N_4O$ 241.1089; found 241.1089.

1-(4-Hydroxy-4,5,6,7-tetrahydroimidazo[1,2-*a*][1,6]benzodiazocin-5-yl)ethan-1-one (5f): This compound was isolated in 68% yield (0.43 g from 0.70 g) as a yellow solid, mp 119-120 °C. R$_f$ = 0.22 (MeOH/EtOAc 1:9, v/v). IR (KBr): ɜ$_{max}$ = 1695(CO), 3375 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 2.30 (s, 3H, CH_3), 2.55 (dd, 1H, J_1 = 16.2 Hz, J_2 = 2.8 Hz, CH_2), 2.76 (dd, 1H, J_1 = 7.2 Hz, J_2 = 2.4 Hz, CH_2), 3.34 (s, 1H, CH), 5.32 (d, 1H, *J* = 9.8 Hz, CH), 6.64-6.69 (m, 2H, ArH), 7.02-7.13 (m, 3H, ArH), 7.22 (s, 1H, ArH) ppm. ^{13}C NMR (CD_3OD, 75 MHz): δ = 30.8, 43.5, 61.7, 66.3, 118.8, 120.0, 121.1, 123.5, 129.8, 130.2, 131.2, 145.1, 151.2, 210.9 ppm. MS (ES): *m/z* = 258.1 [M+1]$^+$. DART-HRMS [ES+]: Calcd. for $C_{14}H_{15}N_3O_2$ 258.1117; found 258.1142.

Methyl 4-hydroxy-10-methyl-4,5,6,7-tetrahydroimidazo[1,2-*a*][1,6]benzodiazocine-5-carboxylate (6a): This compound was isolated in 68% yield (0.28 g from 0.45 g) as a white solid, mp 191-192 °C. R$_f$ = 0.25 (EtOAc). IR (KBr): ɜ$_{max}$ = 1726 (CO_2Me), 3426 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.24 (s, 3H, CH_3), 2.72-2.76 (m, 2H, CH_2), 3.26-3.31 (m, 1H, CH), 3.80 (m, 3H, OCH_3), 5.25 (d, 1H, *J* = 9.8 Hz, CH), 6.57 (d, 1H, *J* = 8.3 Hz, ArH), 6.89-6.97 (m, 2H, ArH), 7.11 (dd, 2H, J_1 = 13.8 Hz, J_2 = 1.3 Hz, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.9, 43.1, 52.2, 65.0, 120.2, 125.8, 127.2, 128.3, 128.5, 130.2, 139.5, 139.9, 166.5, 173.1 ppm. MS (ES+): *m/z* = 288.2 [M+1]$^+$. DART-HRMS [ES+]: Calcd. for $C_{15}H_{18}N_3O_3$: 288.1348. Found: 288.1128.

4-Hydroxy-10-methyl-4,5,6,7-tetrahydroimidazo[1,2-*a*][1,6]benzodiazocine-5-carbonitrile (6e): This compound was isolated in 70% yield (0.19 g from 0.30 g) as a white solid, mp 209-210 °C. R$_f$ = 0.21 (EtOAc). IR (KBr): ɜ$_{max}$ =2240 (C≡N), 3390 (OH) cm^{-1}. ^{1}H NMR (CD_3OD, 300 MHz): δ = 2.23 (s, 3H, CH_3), 2.49-2.54 (m, 1H, CH_2), 2.81 (d, 1H, *J* = 9.0 Hz, CH_2), 3.27 (s, 1H, CH), 5.02 (d, 1H, *J* = 9.5 Hz, CH), 6.74 (d, 1H, *J* = 8.4 Hz, ArH), 6.89 (s, 1H, ArH), 7.01 (d, 1H, *J* = 7.6 Hz, ArH), 7.12 (d, 1H, *J* = 5.6 Hz, ArH), 7.26 (s, 1H, ArH) ppm. ^{13}C NMR (DMSO, 75 MHz): δ = 20.2, 41.7, 41.9, 66.1, 118.6, 119.2, 121.8, 122.7, 126.3, 129.1, 129.5, 130.6, 140.9, 146.6 ppm. MS (ES): *m/z* = 255.2 [M+1]$^+$. DART-HRMS Calcd. for $C_{14}H_{15}N_4O$: 255.1246. Found: 255.1253.

14-hydroxy-9a,10,11,12,13a,14-hexahydrodibenzo[*b*,*g*]imidazo[1,2-*d*][1,4]diazocin-13(9*H*)-one (8): This compound was isolated in 70% yield (0.51 g from 0.80 g) as a yellow solid, mp 105-106 °C. R$_f$ = 0.24 (MeOH/EtOAc 1:9, v/v). IR (KBr): ɜ$_{max}$ = 1705 (CO), 3429 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.93 (d, 2H, *J* = 3.4 Hz, CH_2), 2.34 (s, 4H, 2 x CH_2), 3.72 (s, 1H, CH), 4.08 (s, 1H, CH), 5.35 (d, 1H, *J* = 8.9 Hz, CH), 6.80-6.90 (m, 3H, ArH), 7.02-7.12 (m, 2H, ArH), 7.19-7.24 (m, 1H, ArH) ppm. ^{13}C NMR (CD_3OD, 75 MHz): δ = 24.4, 27.5, 40.0, 64.2, 64.5, 118.7, 119.6, 123.9, 129.1, 130.7, 132.2, 140.2, 146.4, 149.3, 201.8 ppm. MS (ES): *m/z* = 284.2 [M+1]$^+$. DART-HRMS [ES+]: Calcd. for $C_{16}H_{18}N_3O_2$ 284.1399; found 284.1401.

Imidazo[1,2-a]quinoxaline (12): 121-122 °C [Lit. 124 °C][8c]

Ethyl 2-{[1-(2-aminophenyl)-1*H*-imidazol-2-yl]methyl}acrylate (13): This compound was isolated in 74% yield (0.10 g from 0.15 g) as brown oil. R$_f$ = 0.20 (EtOAc/Hexanes 3:2, v/v). IR (Neat): ɜ$_{max}$ = 1718 (CO_2Et), 3437 (NH_2) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.86 (t, 3H, *J*= 7.5 Hz, CH_3), 3.51-3.57 (m, 2H, CH_2), 4.10 (s, 1H, NH), 4.10-4.17 (m, 2H, CH_2), 5.61 (d, 1H, *J* = 5.9 Hz, =CH_2), 6.29 (d, 1H, *J* = 5.9 Hz, =CH_2), 6.76-6.85 (m, 2H, ArH), 6.94 (d, 1H, *J* = 1.1 Hz, ArH), 7.66-7.89 (m, 3H, ArH), 8.19 (d, 1H, *J* = 7.9 Hz, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz) δ = 14.0, 29.3, 61.1, 116.9, 118.3, 121.0, 125.4, 128.05, 128.1, 130.9, 142.3, 143.0, 143.2, 147.1, 176.5 ppm. MS (ES): *m/z* = 272.2 [M+1]$^+$. $C_{15}H_{17}N_3O_2$ (271.1321): Calcd. C 66.40, H 6.32, N 15.49; found C 66.54, H 6.17, N, 15.64.

Ethyl (*E*)-3-[1-(2-aminophenyl)-1*H*-pyrrol-2-yl]prop-2-enoate (23): This compound was isolated in 77% yield (0.35 g from 0.50 g) as a yellow solid, mp 105-106 °C. R$_f$ = 0.65 (EtOAc/Hexanes 1:4, v/v). IR (KBr) ɜ$_{max}$ = 1698 (CO_2Et) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.25 (t, 3H, *J* = 7.1 Hz, CH_3), 3.53 (brs, 2H, NH_2), 4.11-4.18 (m, 2H, CH_2), 5.98 (d, 1H, *J* = 15.8 Hz, CH), 6.38 (t, 1H, *J* = 2.9 Hz, ArH), 6.80-6.85 (m, 4H, ArH), 7.08-7.11 (m, 1H, ArH), 7.22-7.27 (m, 2H, CH and ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.3, 60.1, 110.9, 112.4, 113.3, 116.2, 118.5, 124.4, 126.7, 128.7, 129.7, 130.0, 132.8, 143.3, 167.6 ppm. MS (ES): *m/z* = 256.9 [M+1]$^+$. $C_{15}H_{16}N_2O_2$ (256.1212): Calcd. C 70.29, H 6.29, N 10.93; found C 70.42, H 5.93, N 11.12.

Ethyl 2-[(3a*S*,4*S*)-1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*]quinoxalin-4-yl]acetate (32): This compound was isolated in 68% yield (0.49 g from 0.80 g) as brown oil, R$_f$ = 0.38 (EtOAc/Hexanes 1:4, v/v). $[\alpha]^{31}{}_{D}$ = 101.2 ° (c 0.08, MeOH). (ɜ$_{max}$ (Neat): 1723 (CO_2Et), 3467 (NH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.30 (t, 3H, *J* = 7.0 Hz, CH_3), 1.45-1.51 (m, 1H, CH_2), 1.90-2.00 (m, 1H, CH_2), 2.05-2.09 (m, 2H, CH_2), 2.38 (dd, 1H, J_1 = 16.2 Hz, J_2 = 9.4 Hz, CH_2), 2.65 (d, 1H, *J* = 14.6 Hz, CH_2), 3.14 (d, 2H, *J* = 5.0 Hz, CH_2), 3.26-3.34 (m, 2H, CH), 4.16-4.23 (m, 2H, OCH_2), 6.43 (d, 1H, *J* = 7.7 Hz, ArH), 6.56 (d, 2H, *J* = 8.3 Hz, ArH), 6.70 (d, 1H, *J* = 7.0 Hz, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ =14.2, 23.3, 29.4, 38.0, 47.3, 51.8, 60.9, 61.2, 110.9, 113.7, 116.8, 119.6, 132.8, 134.5, 171.9. MS (ES): *m/z* = 261.1 [M+1]$^+$. Anal. Calcd. for $C_{15}H_{20}N_2O_2$ (260.1525): C 69.20, H 7.74, N 10.76; found C 69.13, H 7.64, N, 10.82.

Typical procedure for the synthesis of compound 10- To a stirred suspension of **9** (1.00 g, 2.79 mmol) in dry ethanol (10 mL), NaBH$_4$ (0.53 g, 13.92 mmol) was added in small portions at 0 ^{o}C. After the addition was complete, the reaction was continued for 50 min. at room temperature. Upon completion (TLC), the precipitated solid was filtered and dried in air. The filtrate was evaporated in vacuo and the residue was dissolved in EtOAc (30 mL). Thereafter water (30 mL) was added to it and the organic layer was partitioned in a separating funnel. The aqueous layer was further extracted with EtOAc (2 × 20 mL). The organic layers were combined and washed with brine (30 mL), dried over anhydrous Na$_2$SO$_4$ and concentrated to yield the crude product. The crude product was further purified via column chromatography using EtOAc/ hexanes (1:4, v/v) as the eluent to afford **10** (0.53 g, 63%) as an off white solid.

Ethyl (*E*,*Z*)-2-methyl-3-[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]prop-2-enoate (10) Diastereomeric mixture-1:0.2: Mp 125-126 °C. R$_f$ = 0.35 (EtOAc/Hexanes 3:7, v/v). IR (KBr): з$_{max}$ = 1730 (CO$_2$Et) cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 1.23 (t, 3H, J = 7.1 Hz, CH$_3$), 1.34 (t, 3H, J = 7.1 Hz, CH$_3$), 2.44-2.47 (m, 6H, 2 x CH$_3$), 4.11-4.18 (m, 2H, OCH$_2$), 4.23-4.30 (m, 2H, OCH$_2$), 6.94 (d, 1H, J = 1.2 Hz, CH), 7.02 (s, 1H, CH), 7.07 (d, 1H, J = 1.1 Hz, ArH), 7.19 (s, 1H, ArH), 7.36-7.47 (m, 4H, ArH), 7.66-7.80 (m, 4H, ArH), 8.10 (dd, 2H, J_1 = 8.0 Hz, J_2 = 1.5 Hz, ArH) ppm. ^{13}C NMR (CDCl$_3$, 50 MHz): δ = 14.1, 14.3, 14.4, 61.0, 121.2, 121.9, 125.7, 129.1, 130.0, 130.38, 130.40, 130.6, 131.0, 133.1, 133.9, 134.0, 144.6, 168.0 ppm.MS (ES): *m/z* = 302.2 [M+1]$^+$. C$_{15}$H$_{15}$N$_3$O$_4$ (301.1063): Calcd. C 59.79, H 5.02, N 13.95; found C 59.93, H 4.82, N 14.05.

Typical procedure for the synthesis of compound 11- To a stirred solution of **9** (1.00 g, 2.79 mmol) in a mixture of THF/water (15 mL, 1:1, v/v), was added DABCO (0.37 g, 3.34 mmol) and reaction was continued for 15 min at room temperature. Thereafter NaBH$_4$ (0.16g, 4.18 mmol) was added and the reaction was continued for 2 h. After completion of the reaction (checked by TLC), THF was evaporated under vacuum and the residue was extracted with EtOAc (3 x 30 mL). The organic layers were combined, washed with brine (50 mL), dried over anhydrous Na$_2$SO$_4$ and concentrated to yield a residue. Purification of this residue via column chromatography using EtOAc/hexanes (3:7, v/v) afforded **11** (0.64 g, 76%) as an off white solid.

Ethyl 2-{[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]methyl}acrylate (11): Mp 167-168 °C. R$_f$ = 0.35 (EtOAc/Hexanes 3:7, v/v). IR (KBr): з$_{max}$ = 1730 (CO$_2$Et) cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 1.23 (t, 3H, J = 7.1 Hz, CH$_3$), 3.53 (s, 2H, CH$_2$), 4.09-4.16 (m, 2H, OCH$_2$), 5.66 (t, 1H, J = 1.0 Hz, =CH$_2$), 6.28 (s, 1H, =CH$_2$), 6.94 (t, 1H, J = 1.4 Hz, ArH), 7.12 (d, 1H, J = 1.4 Hz, ArH), 7.50-7.53 (m, 1H, ArH), 7.63-7.68 (m, 1H, ArH), 7.72-7.77 (m, 1H, ArH), 8.06 (dd, 1H, J_1 = 8.1 Hz, J_2 = 1.4 Hz, ArH) ppm. ^{13}C NMR (CDCl$_3$, 50 MHz) δ = 14.1, 29.5, 60.8, 121.0, 125.3, 127.6, 128.7, 130.4, 130.5, 130.7, 133.9, 135.9, 146.2, 166.0 ppm. MS (ES): *m/z* = 302.2 [M+1]$^+$. C$_{15}$H$_{15}$N$_3$O$_4$ (301.1063): Calcd. C 59.79, H 5.02, N 13.95; found C 59.81, H 4.81, N 14.15.

General procedure for the synthesis of compounds 14, 22, 31as exemplified for compound 14- To a stirred suspension of NaH (0.08 g, 3.46 mmol) in THF (15mL), at 0 ^{o}C was added triethyl phosphonoacetate (0.36 mL, 1.80 mmol) under nitrogen atmosphere at room temperature and the reaction was continued for 1 h. Thereafter a solution of aldehyde **1** (0.30 g, 1.38 mmol) in dry THF (10 mL) was added drop wise to the reaction mixture via syringe at 0^{o}C and the reaction was continued for 4 h at room temperature. On completion (checked by TLC) excess THF was evaporated under vacuum and the residue was extracted with EtOAc (3 x 30 mL). The organic layers were combined, washed with brine (50 mL), dried over anhydrous Na$_2$SO$_4$ and concentrated to yield the crude product. Purification via column chromatography using EtOAc/hexanes (3:7, v/v) afforded **14** (0.30 g, 75%) as colorless oil.

Ethyl (*E*)-3-[1-(2-nitrophenyl)-1*H*-imidazol-2-yl]prop-2-enoate (14): R$_f$ = 0.30 (EtOAc/Hexanes 1:1, v/v). IR (Neat): з$_{max}$ = 1689 (CO$_2$Et) cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 1.27 (t, 3H, J = 7.0 Hz, CH$_3$), 4.15-4.23 (m, 2H, OCH$_2$), 6.77 (d, 1H, J = 15.6 Hz, CH), 7.07 (d, 1H, J = 14.9 Hz, CH), 7.24-7.48 (m, 3H, ArH), 7.70-7.83 (m, 2H, ArH), 8.18 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.5 Hz, ArH) ppm. ^{13}C NMR (CDCl$_3$, 50 MHz): δ = 14.6, 61.1, 122.8, 123.7, 126.1, 126.2, 126.8, 128.5, 129.8, 130.3, 130.8, 130.9, 131.4, 131.7, 132.7, 134.6, 144.4, 166.8 ppm. MS (ES): *m/z* = 288.2 [M+1]$^+$. C$_{14}$H$_{13}$N$_3$O$_4$ (287.0906): Calcd. C 58.53, H 4.56, N 14.63; found C 58.81, H 4.25, N 14.84.

Ethyl (*E*)-3-[1-(2-nitrophenyl)-1*H*-pyrrol-2-yl]prop-2-enoate (22): This compound was isolated in 83% yield (1.10 g from 1.00 g) as colorless oil. R$_f$ = 0.25 (EtOAc/Hexanes 1:4, v/v). IR (Neat): з$_{max}$ = 1696 (CO$_2$Et) cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 1.26 (t, 3H, J = 9.1 Hz, CH$_3$), 4.12-4.19 (m, 2H, CH$_2$), 5.96 (d, 1H, J = 15.8 Hz, CH), 6.39 (t, 1H, J = 3.1 Hz, ArH), 6.81-6.84 (m, 2H, ArH), 7.18 (d, 1H, J = 15.8 Hz, CH), 7.46 (dd, 1H, J_1 = 7.7 Hz, J_2 = 1.4 Hz, ArH), 7.62-7.68 (m, 1H, ArH), 7.71-7.77 (m, 1H, ArH), 8.04 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.5 Hz, ArH) ppm. ^{13}C NMR (CDCl$_3$, 50 MHz): δ = 14.7, 60.7, 112.0, 113.5, 114.9, 125.8, 127.1, 130.4, 131.2, 132.2, 132.6, 134.1, 147.3, 167.7 ppm. MS (ES): *m/z* = 287.1 [M+1]$^+$. C$_{15}$H$_{14}$N$_2$O$_4$ (286.0954): Calcd. C 62.93, H 4.93, N 9.79; found C 62.87, H 4.76, N 9.82.

Ethyl (*E*)-3-[(2*S*)-1-(2-nitrophenyl)pyrrolidin-2-yl]prop-2-enoate (31): This compound was isolated in 90% yield (1.20 g from 1.30 g) as reddish brown oil. R$_f$ = 0.30 (EtOAc/Hexanes 1:4, v/v). з$_{max}$ (Neat): 1722 (CO$_2$Et) cm^{-1}. ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 1.27 (t, 3H, J = 7.1 Hz, CH$_3$), 1.80-1.91 (m, 2H, CH$_2$), 2.04-2.09 (m, 1H, CH$_2$), 2.35-2.39 (m, 1H, CH$_2$), 2.82-2.91 (m, 1H, CH$_2$), 3.58-3.71 (m, 1H, CH$_2$), 4.12-4.22 (m, 2H, OCH$_2$), 4.43-4.54 (m, 1H, CH), 5.99 (dd, 1H, J_1 = 15.7 Hz, J_2 = 1.1 Hz, CH), 6.75-6.93 (m, 3H, ArH), 7.30-7.39 (m, 1H, ArH), 7.77 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.7 Hz, CH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ = 26.3, 29.8, 60.6, 64.4, 122.1, 125.6, 126.7, 128.2, 130.7, 131.3, 134.0, 147.3, 199.4. MS (ES): *m/z* = 291.1 [M+1]$^+$. Anal. Calcd. for C$_{15}$H$_{18}$N$_2$O$_4$ (290.1267): C 62.06, H 6.25, N 9.65; found C 62.18, H 6.34, N 9.49.

General procedure for the synthesis of compounds 15, 25, as exemplified for compound 15- To the solution of compound **12** (0.20g, 0.70mmol) in EtOH was added Raney-Ni (50 mg in EtOH) and subjected to hydrogenation in Parr assembly at 50 psi at room temperature. The reaction was allowed to continue for 2 h. On completion, the catalyst was removed by filtering the contents through a celite bed with ethanol. The filtrate was evaporated to obtain an oily crude product (0.16 g, 89%) which was utilized for the next step without any purification. For analytical grade, purification via short silica gel (100-200 mesh) column chromatography (EtOAc/hexanes, 1:1, v/v) afforded **13** as reddish brown oil.

Ethyl 3-[1-(2-aminophenyl)-1*H*-pyrrol-2-yl]propanoate (15): R$_f$ = 0.20 (EtOAc/Hexanes 1:1, v/v). IR (Neat) з$_{max}$ = 1721 (CO$_2$Et), 3400 (NH$_2$) cm^{-1}. ^{1}H NMR (CDCl$_3$, 200 MHz): δ = 1.21 (t, 3H, J = 7.1 Hz, CH$_3$), 2.76-2.80 (m, 2H, CH$_2$), 3.71 (m, 2H, CH$_2$), 4.03-4.13 (m, 2H, CH$_2$), 6.74-6.84 (m, 2H, ArH), 6.90 (d, 1H, J = 1.3 Hz, ArH), 7.04-7.10 (m, 2H, ArH), 7.18-7.26 (m, 1H, ArH) ppm. ^{13}C NMR (CDCl$_3$, 50 MHz): δ = 14.5, 22.2, 31.8, 60.9, 116.7, 118.8, 120.9, 123.2, 128.6, 128.8, 130.6, 143.5, 148.0, 173.2 ppm. MS (ES): *m/z* = 260.1 [M+1]$^+$. C$_{14}$H$_{17}$N$_3$O$_2$ (259.1321): Calcd. C 64.85, H 6.61, N 16.20; found C 65.00, H 6.52, N 15.95.

Ethyl 3-[1-(2-aminophenyl)-1*H*-pyrrol-2-yl]propanoate (25): This compound was isolated in 72% yield (0.65 g from 1.00 g) as reddish brown oil. R$_f$ = 0.34 (EtOAc/Hexanes 3:7, v/v). IR (Neat) з$_{max}$ = 1720 (CO$_2$Et) cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz): δ = 1.18-1.23 (m, 3H, CH$_3$), 2.47-2.53 (m, 2H, CH$_2$), 2.67-2.69 (m, 2H, CH$_2$), 3.55 (brs, 2H, NH$_2$), 4.04-4.11 (m, 2H, CH$_2$), 6.04 (s, 1H, ArH), 6.22 (s, 1H, ArH), 6.61 (d, 1H, J = 1.4 Hz, ArH), 6.77-6.80 (m, 2H, ArH), 7.09 (d, 1H, J = 7.4 Hz, ArH), 7.16-7.25 (m, 1H, ArH) ppm. ^{13}C NMR (CDCl$_3$, 50 MHz): δ = 14.6, 22.1, 33.9, 60.8, 106.7, 108.9, 116.3, 118.6, 121.9, 125.9, 129.1, 129.9, 132.8, 144.2, 173.4 ppm. MS (ES): *m/z* = 259.1 [M+1]$^+$. C$_{15}$H$_{18}$N$_2$O$_2$ (258.1368): Calcd. C 69.74, H 7.02, N 10.84; found C 69.92, H 6.88, N 10.95.

General procedure for the synthesis of compounds 16, 26, as exemplified for compound 26- To a stirred solution of **25** (0.50g, 1.94 mmol) in THF (10 mL) was added an aqueous solution of LiOH (0.23g, 9.69 mmol, 3 mL) at room temperature and the mixture was continued for 1 h. There after the reaction mixture was acidified to pH 2 with 10% HCl. The organic layer was separated and the aqueous layer was further washed with EtOAc (2 x 50 mL). The pooled organic extracts were washed with brine (50 mL), dried (Na_2SO_4) and concentrated in vacuum to get the crude product which was recrystallized with EtOAc-hexanes to afford pure **26** (0.41g, 91%) as a yellow solid.

3-[1-(2-Aminophenyl)-1*H*-pyrrol-2-yl]propanoic acid (26): Mp 117-118 °C. R$_f$ = 0.20 (EtOAc). IR (KBr): ʒ$_{max}$ = 1720 (CO_2Et) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.57 (t, 2H, *J* = 5.8 Hz, CH_2), 2.70 (t, 2H, *J* = 6.7 Hz, CH_2), 6.08 (d, 1H, *J* = 1.7 Hz, ArH), 6.25 (t, 1H, *J* = 3.0 Hz, ArH), 6.64 (t, 1H, *J* = 1.8 Hz, ArH), 6.79-6.85 (m, 2H, ArH), 7.11 (dd, 2H, J_1 = 7.7 Hz, J_2 = 1.3 Hz, ArH), 7.19-7.25 (m, 1H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.3, 33.1, 106.6, 108.8, 117.0, 119.6, 121.7, 126.5, 128.8, 129.6, 132.1, 141.9, 178.0 ppm. MS (ES): *m/z* = 231.1 [M+1]$^+$. $C_{13}H_{14}N_2O_2$ (230.1055): Calcd. C 67.81, H 6.13, N 12.17; found C 67.90, H 6.05, N 12.29.

General procedure for the synthesis of compounds 17, 27 as exemplified for compound 27- To a stirred solution of compound **26** (0.40g, 1.74 mmol) in dry CH_2Cl_2 (15 mL) was added NMM (0.21 mL, 1.91 mmol) and the mixture was cooled to -10 ^{0}C in an ice salt bath. Then EDC (0.37 g, 1.91 mmol) was added to the reaction over 10 min. and stir for another 2 h. There after cold 1N HCl (30 mL) was added to the reaction mixture and extracted with CH_2Cl_2 (20 mL). The aqueous phase was washed with CH_2Cl_2 (2 × 20 mL). The organic phases were combined washed with brine, dried (Na_2SO_4) and concentrated in vacuo, to get the crude product which was further purified via column chromatography (EtOAc/hexanes, 2:3, v/v) to obtain (0.30 g, 81%) **27** as an off white solid.

7,8-Dihydropyrrolo[1,2-*a*][1,6]benzodiazocin-6(5*H*)-one (27): Mp 169-170 °C. R$_f$ = 0.24 (EtOAc/Hexanes 1:1, v/v). IR (KBr): ʒ$_{max}$ = 1665 (CO), 3427 (NH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.42-2.49 (m, 1H, CH_2), 2.61-2.71 (m, 1H, CH_2), 2.78-2.87 (m, 1H, CH_2), 3.14-3.25 (m, 1H, CH_2), 6.08 (s, 1H, ArH), 6.19 (t, 1H, *J* = 3.0 Hz, ArH), 6.57 (s, 1H, ArH), 7.23-7.28 (m, 2H, ArH), 7.40-7.47 (m, 2H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 22.5, 31.5, 108.9, 109.2, 123.4, 127.3, 127.8, 128.4, 128.8, 131.6, 134.2, 138.8, 175.2 ppm. MS (ES+): *m/z* = 213.1 [M+1]$^+$. DART-HRMS [ES+]: Calcd. for $C_{13}H_{13}N_2O$ 213.1028; found 213.1038.

4,5-Dihydroimidazo[1,2-*a*][1,6]benzodiazocin-6(7*H*)-one (17): This compound was isolated in 65% yield (0.24 g from 0.40 g) as an off white solid, mp 115-116 °C. R$_f$ = 0.20 (EtOAc). IR (KBr): ʒ$_{max}$ = 1676 (CO), 3400 (NH) cm^{-1}. ^{1}H NMR (DMSO-d$_6$, 300 MHz): δ = 2.15-2.25 (m, 1H, CH_2), 2.39-2.55 (m, 1H, CH_2), 2.89-3.02 (t, 1H, *J* = 15.7 Hz, CH_2), 3.11-3.25 (m, 1H, CH_2), 6.91 (d, 1H, *J* = 1.9 Hz, ArH), 7.08 (s, 1H, ArH), 7.27-7.31 (m, 1H, ArH), 7.46-7.54 (m, 3H, ArH), 9.59 (s, 1H, NH) ppm. ^{13}C NMR (DMSO-d$_6$, 50 MHz): δ = 25.1, 30.4, 124.1, 127.9, 128.3, 128.4, 128.7, 130.2, 135.1, 135.9, 146.7, 173.7 ppm. MS (ES+): *m/z* = 214.3 [M+1]$^+$. DART-HRMS [ES+]: Calcd. for $C_{12}H_{12}N_3O$ 214.0980; found 214.0995.

Typical Procedure for the preparation of 29- To a stirred solution of **28** (1.20 g, 4.80 mmol) in toluene (20 mL), was added DIBAL-H (7.20 mL, 7.20 mmol, 1.0 M in toluene) at 0 ^{o}C under nitrogen atmosphere. The reaction was allowed to continue at room temperature for 30 min. Thereafter on completion as monitored by TLC, the reaction mixture was quenched with MeOH (15 mL) and the separated precipitate was filtered through a Celite bed. The filtrate was evaporated to afford the crude product as oil. Purification of the crude via column chromatography using EtOAc/ hexanes (1:4, v/v) as the eluent furnished **29** as an orange solid (1.00 g, 94%).

[(2*S*)-1-(2-nitrophenyl)pyrrolidin-2-yl]methanol (29): This compound was isolated in 94% yield (1.00 g from 1.20 g) as an orange solid, mp 80-81 °C. R$_f$ = 0.17 (EtOAc/Hexanes 1:4, v/v). ʒ$_{max}$ (KBr): 3428 (OH) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.72-1.88 (m, 2H, CH_2), 1.99-2.06 (m, 1H, CH_2), 2.09-2.19 (m, 2H, CH_2), 2.74 (t, 1H, *J* = 9.1 Hz, CH_2), 3.51-3.56 (m, 2H, CH_2), 3.82-3.85 (m, 1H, CH_2), 4.11-4.16 (m, 1H, CH), 6.80-6.85 (m, 1H, ArH), 7.11 (d, 1H, *J* = 8.5 Hz, ArH), 7.36-7.42 (m, 1H, ArH), 7.77 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.5 Hz, ArH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.2, 27.9, 53.4, 59.8, 61.8, 117.3, 117.6, 126.7, 133.0, 142.2. MS (ES): *m/z* = 223.1 [M+1]$^+$. Anal. Calcd. for $C_{11}H_{14}N_2O_3$ (222.1004): C 59.45, H 6.35, N 12.60; found C 59.64, H 6.23, N 12.67.

Typical Procedure for the preparation of 30- Oxalyl chloride (0.58 mL, 6.76 mmol) dissolve in dry CH_2Cl_2 was stirred at -78 ^{o}C for 10 min in a two neck round bottom flask under nitrogen atmosphere. Then DMSO (0.96 mL, 13.50 mmol) was added to it via syringe and allowed to stir at same temperature for 30 min. Thereafter **29** (1.00 g, 4.50 mmol) dissolved in dry CH_2Cl_2 was added to it and stirring was continued at -78 ^{o}C for 1h. Et_3N (3.16 mL, 22.52 mmol) was added to the mixture and the reaction was allowed to proceed at room temperature. After 30 min the reaction mixture was washed with water and extracted with CH_2Cl_2 (2 x 30 mL). The organic layers were combined, washed with brine (60 mL), dried (Na_2SO_4) and evaporated under vacuum to yield an oily residue. Purification of this residue via column chromatography using EtOAc/ hexanes (1:4, v/v) as the eluent furnished **30** as a yellow solid (0.89 g, 90%).

(2*S*)-1-(2-nitrophenyl)pyrrolidine-2-carbaldehyde (30): This compound was isolated in 90% yield (0.89 g from 1.00 g) as a yellow solid, mp 100-101 °C. R$_f$ = 0.35 (EtOAc/Hexanes 1:4, v/v). ʒ$_{max}$ (KBr): 1684 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.93-2.11 (m, 3H, CH_2), 2.29-2.32 (m, 1H, CH_2), 2.95-2.99 (m, 1H, CH_2), 3.63-3.69 (m, 1H, CH_2), 4.19-4.23 (m, 1H, CH), 6.82-6.87 (m, 2H, ArH), 7.35-7.41 (m, 1H, ArH), 7.73-7.77 (m, 1H, ArH), 9.41 (d, 1H, *J* = 4.1 Hz, CHO). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.0, 27.8, 52.4, 67.8, 116.1, 117.9, 126.8, 133.3, 201.1. MS (ES): *m/z* = 221.1 [M+1]$^+$. Anal. Calcd. for $C_{11}H_{12}N_2O_3$ (220.0848): C 59.99, H 5.49, N 12.72; found C 59.82, H 5.62, N 12.61.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H and ^{13}C- NMR of all new compounds are provided.

Acknowledgments

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[6] Crystal structure refinement details for **5a**: Crystal was coated with light hydrocarbon oil and mounted in the 100 K dinitrogen stream of a Bruker SMART APEX CCD diffractometer equipped with CRYO Industries low-temperature apparatus, and intensity data were collected using graphite-monochromated Mo Kα radiation (λ= 0.71073 Å). Crystal data of compound **5a** (crystallized from MeOH): $C_{14}H_{15}N_3O_3$, M = 273.29, Triclinic, P-1, a = 6.462(2) , b = 9.073(3), c = 11.997(4)Å, α = 69.394(5), β = 77.686(6), γ = 77.722(6), V = 635.9(4)Å^3, Z = 2, D_c = 1.427g cm^{-3}, μ (Mo-K$_\alpha$) = 0.103mm^{-1}, F (000) = 288 colorless block, dimension 0.23x 0.22x 0.20mm, 3514 reflections measured (R_{int} = 0.0375), 2421 unique, wR_2 = 0.1806, conventional R = 0.0601on F^2 values of 2421 reflections with I>2σ(I), (φ/ů)$_{max}$ = 000), S = 1.129 for all data and 184 parameters. The data integration and reduction were processed with the SAINT software. An absorption correction was applied. Structures were solved by the direct method using SHELXS-97 and refined on F^2 by a full-matrix least-squares technique using the SHELXL-97 program package. Non-hydrogen atoms were refined anisotropically. In the refinement, hydrogens were treated as riding atoms using the SHELXL default parameters. CCDC contains the supplementary crystallographic data for this paper with a deposition number of CCDC **772747**. Copies of this information can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK. [Fax: +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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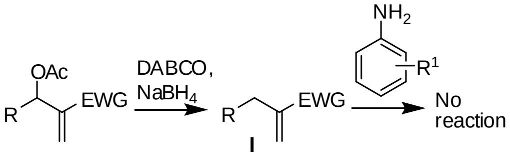
[8] The MBH-derivative (I) does not undergo Michael addition with aniline or substituted anilines as shown below.



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Entry for the Table of Contents (Please choose one layout)

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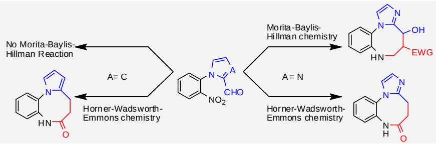

Expeditious strategies for obtaining fused-benzodiazocines and fused-benzodiazocinones via Morita-Baylis-Hillman and Horner-Wadsworth-Emmons chemistries, respectively have been developed.

Fused-Benzodiazocine

Amita Mishra, Sanjay Batra * é é ....

Page No. ï Page No.

Expeditious synthesis of fused-benzodiazocines

Keywords: Morita-Baylis-Hillman / Horner-Wadsworth-Emmons / fused-benzodiazocines / fused-benzodiazocinones / Reductive cyclization