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Synthesis of substituted 1*H*- and 3*H*-1-benzazepines: Rearrangement of 2-alkoxycarbonyl-1*H*-1-benzazepines to isoquinolines[§]

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Abstract- The $SnCl_2$-mediated reduction of nitro groups in 2-nitro-4-(2-nitro-benzylidene)-alkanoates and 4-nitro-2-(2-nitro-alkylidene)-alkanoates afforded via S_N2' reaction of ethyl nitroacetate and nitroethane with the acetyl derivatives of Baylis-Hillman adducts afforded by 2-nitro-substituted benzaldehydes leads to facile synthesis of substituted 1*H*-1-benzazepine and 3*H*-1-benzazepine. During the study an unprecedented rearrangement of 2-alkoxycarbonyl-1*H*-benzazepine to substituted isoquinoline has been observed.

Keywords: Baylis-Hillman reaction/ $SnCl_2.2H_2O$/ Nitrogen heterocycles/ Rearrangement.

Introduction

The products afforded by Baylis-Hillman reaction and their derivatives have served as an excellent source for the synthesis of several heterocyclic motifs.[1-10] In this context, our research group has successfully developed several simple, convenient and high yielding protocols for the synthesis of a variety of heterocyclic systems.[11-19] We have recently described syntheses of 3-methylene-2-pyrrolidinones and 3-(1-alkoxycarbonyl-vinyl)-1H-indole-2-carboxylates.[20] During this study we have discovered that a secondary nitro group attached to the carbon bearing the alkoxycarbonyl group undergoes a chemoselective reduction to an oxime in the presence of $SnCl_2.2H_2O$. Mechanistic considerations generated interest in extending the study to similar reduction in the substrates afforded by the S_N2' reaction between acetyl derivatives of the Baylis-Hillman adducts of 2-nitrobenzaldehyde and ethyl nitroacetate or nitroethane. It was reasoned that $SnCl_2.2H_2O$-mediated reduction of the nitro groups would result in an aromatic amino

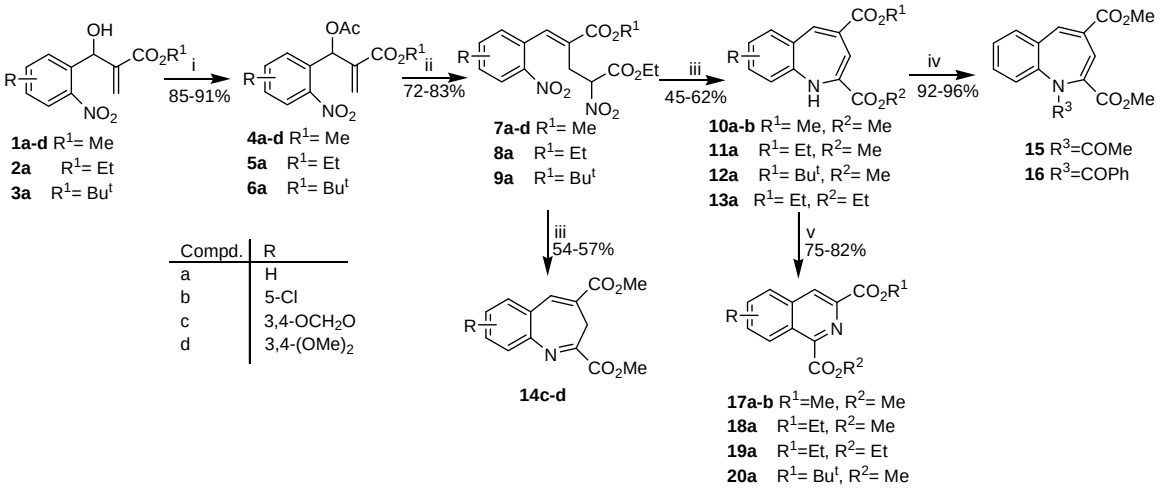
group and an oxime in the case of derivatives of ethyl nitroacetate and aliphatic amino group in the case of derivatives of nitroethane. Subsequently the intermediates in both cases would cyclize to yield a heterocyclic system. In order to investigate the outcome of this reaction, the acetyl derivatives of several Baylis-Hillman adducts were treated with ethyl nitroacetate or nitroethane and the resulting substrates were subjected to $SnCl_2.2H_2O$-promoted reductions. We were pleased to note that this reaction invariably led to the formation of 1*H*-1-benzazepine or 3*H*-1-benzazepine derivatives. Interestingly, we discovered that the 2-alkoxycarbonyl-1*H*-1-benzazepines are highly unstable and rearrange easily to isoquinolines which is unprecedented.

1*H*-1-Benzazepine derivatives are pharmacologically important class of heterocycles. They are potent antagonists of the glycine binding site associated with *N*-methyl-D-aspartate (NMDA),[21] antagonists for CC chemokine receptor-5 useful against HIV-1 infection[22-23] and show usefulness in illness related to melanocortin-4 receptor.[24] A survey of the literature revealed only a few methods for the synthesis of substituted 1*H*-benzazepines were known.[25-30] The approach developed by us is very simple and constitutes a practical route to this class of heterocycle. The results of our study are being reported in this paper.

Results and Discussion

The first part of our study deals with the substrates afforded from the reaction between acetyl derivatives of the Baylis-Hillman adducts and ethyl nitroacetate. Preparation of the starting material **1a-d,2-3a** in this synthetic sequence was achieved by carrying out the Baylis-Hillman reaction of 2-nitrobenzaldehyde or substituted 2-nitrobenzaldehydes with activated alkenes following the reported procedure.[20] The adducts **1a-d,2-3a** were transformed to the respective acetyl derivatives **4a-d,5-6a** by reaction with acetyl chloride in the presence of pyridine in dichloromethane at room temperature in excellent yields. The S_N2' reaction of acetates **4a-d,5-6a** with ethyl nitroacetate in the presence of K_2CO_3 in DMF at room temperature yielded stereoselectively the *E*-isomer of respective products **7a-d,8-9a** (Scheme 1) in good yields. Treatment of the nitroalkanoate **7a** with $SnCl_2.2H_2O$ in methanol at reflux temperature for 2h furnished a product which was found to be less polar as compared to the starting substrate. On the basis of spectral

analysis the structure of this product was established as substituted 1*H*-1-benzazepine **10a**. The formation of 1*H*-1-benzazepine **10a** asserts that the aromatic amino group attacks the carbon bearing the oxime as observed earlier.[20] The presence of the methoxycarbonyl group instead of the ethoxycarbonyl group at 3-position of the 1*H*-1-



Scheme 1. *Reagents and conditions*: i) AcCl, Pyridine, CH_2Cl_2, rt, 3 h. ii) $NO_2CH_2CO_2Et$, K_2CO_3, DMF, 3 h. iii) $SnCl_2.2H_2O$, MeOH/ EtOH, N_2, reflux, 2 h. iv) R_3COCl (R_3= Me, Ph), Et_3N, CH_2Cl_2, rt, 3 h. v) Silica gel (60-120 mesh), rt, 24 h or Silica gel (60-120 mesh), hυ, rt, 6 h.

benzazepine ring was attributed to the transesterification of the ethoxycarbonyl moiety due to the use of methanol as solvent in the reaction. In order to examine the general applicability of this reaction, other substrates **7b-d,8-9a** were also subjected to $SnCl_2.2H_2O$-promoted reductions in methanol or ethanol. Interestingly similar to **7a**, compounds **7b,8-9a** afforded the corresponding 1*H*-1-benzazepines **10b,11-12a** but compounds **7c-d** yielded 3*H*-benzazepines **14c-d** instead of the expected product. At this stage of the study it was assumed that possibly the substitution attributes of the phenyl ring have some role in the outcome of the products since compounds **7c-d** had electron donating substituents on the phenyl ring. Remarkably it was found that the transesterification was chemoselective since the ethoxycarbonyl group originating from the ethyl nitroacetate was only affected whereas no such phenomenon was observed with the other ester moiety present in the substrate. The reduction of **8a** indeed resulted in the

formation of the product **13a** when the reaction was performed in ethanol. In our efforts to provide chemical evidence towards the formation of substituted 1*H*-1-benzazepine, **10a** was treated with acetyl chloride and benzoyl chloride separately to furnish the N-substituted products **15** and **16**, respectively. It was interesting to note that both these products were obtained as mixture of rotational isomers (endo and exo forms). This observation has literature precedence since it is reported that the amides where the nitrogen is disubstituted, the hindered rotation about the N-C owing to its partial double bond character leads to steric interactions.[31]

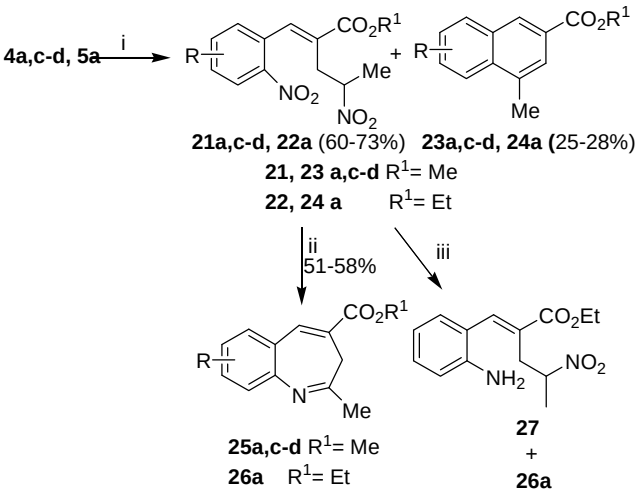
During the course of this work it was observed that the 1*H*-1-benzazepine derivatives **10a-b,11-13a** were unstable and even the pure solid compounds changed to oil within short span of time (ca. 12-24 h) at room temperature. Further this phenomenon was accelerated if compounds were left on silica-gel column. As compared to the starting 1*H*-1-benzazepine, the new product was found to be polar in the tlc analysis. Purification, isolation and characterization via detailed NMR spectroscopy led to elucidation of the structure of these products as substituted isoquinolines **17a-b,18-20a**. Although the oxidation of N-methyl benzazepines to naphthyl-1-amine[32] and acid-promoted rearrangement of 1*H*-1-benzazepine-2,5-dione to 2,4-dihydroxy quinoline[33] have been reported earlier, the ring contraction of 1*H*-1-benzazepine to isoquinoline derivative is unprecedented. However we are unable to propose a mechanism for this unusual observation at the present times. Nevertheless, with the objective to understand the possible reason behind such unusual rearrangement we carried out a set of experiments with **10a**. Table 1 summarizes the results of these experiments. It is evident from this study the 1*H*-benzazepine are stable only when stored at a temperature below 0^{o}C in dark. Since the transformation of 1*H*-1-benzazepine to isoquinoline proceeded smoothly on silica gel, compounds **10a-b,11-13a** were treated with silica gel at room temperature under uv light for 6 h or normal light for 24 h to furnish the corresponding isoquinoline derivatives **17a-b,18-20a** exclusively in excellent yields. In contrast to the behavior of 1*H*-1-benzazepine derivatives, the 3*H*-1-benzazepine derivatives were found to be stable at room temperature.

Table 1. Results of the transformation of 1*H*-1-benzazepine **10a** to isoquinoline **17a** under various conditions monitored for 12 h via HPLC

Entry	Condition for reaction of compound **10a**	Unreacted **10a** (%)	Product **17a** (%)
1	CCl_4, dark, rt	100	-
2	CCl_4, AIBN, hν, rt	3	28+ other mix.
3	CCl_4, hν, rt	80	4+ other mix.
4	CCl_4, Silica-gel, hν, rt	0	31+ other mix
5	Silica gel, open flask, rt	30	37+ other mix
6	Silica gel, hν, rt	0	100
7	Silica gel, dark, rt	30	70
8	AIBN, Toluene, reflux	5	45+ other mix
9	Left at 0^oC under nitrogen	100	-
10	Left at 0^oC	100	-

All HPLCs were performed on RP C-18 column (250x4.5mm, 5μ) using a gradient of 10-100% methanol containing 0.1% TFA and water in 25 min at a flow rate of 1mL/min.

The second phase of our study relates to similar reduction of nitro group in substrates resulting from the S_N2' reaction of nitroethane with the acetyl derivatives of Baylis Hillman adducts **(4a,c-d,5a)**. The compounds **21a,c-d,22a** were prepared following the literature procedure. Contrary to the reactions of ethyl nitroacetate, all reactions of nitromethane led to isolation of another product along with the expected nitro derivatives (Scheme 2). The spectroscopic analysis led us to elucidate the structure of these products as naphthalenes **23a,c-d,24a**. The formation of naphthalenes via S_NAr in nitro derivatives of Baylis-Hillman derivatives is known in the literature.[34-35] Subsequent reduction of nitro groups in compounds **21a,c-d,22a** with $SnCl_2.2H_2O$ at reflux temperature was complete in 24 h to furnish the corresponding products which were established to be 3*H*-1-benzazepine derivatives **25a,c-d,26a**. Contrary to the observation made with the derivatives of ethyl nitroacetate, the substitution pattern of the phenyl ring bears no role



Scheme 2. *Reagents and conditions*: i) $EtNO_2$, K_2CO_3, DMF, rt, 3 h. ii) $SnCl_2.2H_2O$, MeOH/ EtOH, N_2, reflux, 24 h. iii) $SnCl_2.2H_2O$, MeOH, N_2, reflux, 4 h.

in the outcome of the final product in the reaction of these substrates. The prolonged duration for completion of reaction was in line with our earlier observation where we have found that the reduction of the aliphatic nitro group is slower than the reduction of the aromatic nitro group.[3] Indeed if the reduction is arrested after 3 h as exemplified in a model reaction with compound **22a**, we could isolate **27** beside the usual product **26a**.

Conclusions

In summary we have demonstrated a facile approach for the synthesis of substituted 1*H*-1-benzazepines and 3*H*-1-benzazepines via $SnCl_2$-mediated reduction of nitro groups in 2-nitro-4-(2-nitro-benzylidene)-alkanoates and 4-nitro-2-(2-nitroalkylidene)-alkanoates afforded by S_N2' reaction of ethyl nitroacetate and nitroethane with the acetyl derivatives of Baylis-Hillman adducts afforded by 2-nitro-substituted benzaldehydes. The protocol described herein is impressive due to the easy availability of starting materials and simple reaction conditions. We have for the first time discovered the unusual rearrangement of 2-alkoxycarbonyl-1*H*-1-benzazepine to isoquinoline.

Experimental

General- Melting points were recorded on hot stage melting point apparatus and are uncorrected. The IR spectra were recorded on a FTIR spectrophotometer. The ^{1}H- and

^{13}C-NMR spectra were recorded on 200MHz, 300MHz or 600 MHz spectrometer using TMS as internal standard. The mass spectra were recorded as FAB or LCMS having ES probe. The HRMS spectra were recorded as EI-HRMS. All the solvents and chemicals were used as procured from the suppliers. Compounds **23-24a** are already reported in the literature.[8b] Compounds **10a-b,11-13a** due to their unstable behavior were not subjected to chemical analyses or HR-EIMS. All HPLCs were performed on RP C-18 column (250x4.5mm, 5μ) using a gradient of 10-100% methanol containing 0.1% TFA and water in 25 min at a flow rate of 1mL/min.

General procedure for the preparation of compounds 7a-d,8-9a,21,23a,c-d,22,24a as exemplified for compound 7a

To a stirred solution of compound **4a** (1.5 g, 5.38 mmol) in DMF (10 mL) was added ethyl nitroacetate (0.73 mL, 6.56 mmol) and K_2CO_3 (1.11 g, 8.06 mmol) at room temperature and the reaction was allowed to proceed for 4 h. The reaction mixture was acidified to pH 5 with conc. HCl and extracted with EtOAc (3x40 mL). The organic layers were pooled, washed with brine (50 mL), dried (anhyd. Na_2SO_4) and evaporated to yield a residue, which was purified via silica gel column chromatography employing hexane–EtOAc (80:20, v/v) to afford 1.14 g (83%) of product **7a** as yellow oil.

1-Ethyl 5-methyl 2-nitro-4-[(*E*)-(2-nitrophenyl)methylidene]pentanedioate (7a)- ν_{max} (neat) 1716 (CO_2Et), 1740 (CO_2Me) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ= 1.24 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 3.18 (d, 2H, *J*= 7.5 Hz, C*H*$_2$CH), 3.89 (s, 3H, CO_2CH_3), 4.19 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 5.60 (t, 1H, *J*= 7.5 Hz, $CHNO_2$), 7.24-7.28 (m, 1H, ArH), 7.59-7.63 (m, 1H, ArH), 7.68-7. 73 (m, 1H, ArH), 8.19 (s, 1H, =CH), 8.24-8.28 (m, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 14.2, 29.2, 51.3, 86.4, 125.6, 127.9, 130.1, 130.9, 131.4, 134.3, 141.9, 147.6, 164.3, 165.7; mass (FAB+) *m/z* 353 (M^++1); $C_{15}H_{16}N_2O_8$ (352.29): Calcd. C, 51.14; H, 4.58; N, 7.95; found: C; 51.06, H, 4.64; N, 7.76.

5-Ethyl 1-methyl 2-[(*E*)-(5-chloro-2-nitrophenyl)methylidene]-4-nitropentanedioate (7b)- 1.5 g (78%) as yellow oil; ν_{max} (neat) 1719 (CO_2Et), 1750 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 1.25 (t, 3H, *J*= 7.1 Hz, C*H*$_3$CH$_2$), 3.17-3.20 (m, 1H, 1H of C*H*$_2$CH), 3.86-3.89 (m, 1H, 1H of C*H*$_2$CH), 3.90 (s, 3H, CO_2CH_3), 4.22 (q, 2H, *J*= 7.1 Hz, C*H*$_2$CH$_3$), 5.58-5.61 (m, 1H, $CHNO_2$), 7.25-7.33 (m, 1H, ArH), 7.55-7.59 (m, 1H, ArH), 8.12 (s, 1H, ArH), 8.23 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 12.5, 27.5,

33.7, 51.5, 62.0, 84.5, 124.6, 125.4, 128.6, 129.0, 131.2, 140.0, 144.2, 162.4, 164.9; mass (FAB+) *m/z* 387 (M^++1); $C_{15}H_{15}ClN_2O_8$ (386.74): Calcd. C, 46.58; H, 3.91; N, 7.24; found: C; 46.63, H, 3.67; N, 7.13.

1-Ethyl 5-methyl 2-nitro-4-[(*E*)-(6-nitro-1,3-benzodioxol-5-yl)methylidene] pentanedioate (7c)- 1.68g (72%) as yellow oil; ν_{max} (neat) 1709 (CO_2Et), 1739 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.27 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 3.18-3.22 (m, 2H, C*H*$_2$CH), 3.89 (s, 3H, CO_2CH_3), 4.22 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 5.59-5.64 (m, 1H, $CHNO_2$), 6.21 (s, 2H, OCH_2O), 6.62 (s, 1H, ArH), 7.75 (s, 1H, ArH), 8.11 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 12.5, 27.5, 51.4, 61.9, 84.5, 102.3, 104.6, 107.6, 123.8, 125.9, 140.3, 141.9, 147.3, 151.1, 162.7, 165.3; mass (FAB+) *m/z* 397 (M^++1); $C_{16}H_{16}N_2O_{10}$ (396.30): Calcd. C, 48.49; H, 4.07; N, 7.07; found: C; 48.61, H, 3.89; N, 7.31.

5-Ethyl 1-methyl 2-[(*E*)-(4,5-dimethoxy-2-nitrophenyl)methylidene]-4-nitro-pentanedioate (7d)- 1.1 g **(**75%) as yellow oil; ν_{max} (neat) 1706 (CO_2Et), 1755 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ= 1.26 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 3.18 (d, 2H, *J*= 7.9 Hz, C*H*$_2$CH), 3.89 (s, 3H, CO_2CH_3), 3.99 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.22 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 5.71 (t, 1H, *J*= 7.9 Hz, $CHNO_2$), 6.63 (s, 1H, ArH), 7.79 (s, 1H, ArH), 8.15 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 12.5, 27.8, 51.3, 55.2, 55.5, 61.9, 84.6, 106.6, 110.1, 123.7, 123.8, 138.5, 141.9, 147.8, 152.3, 162.6, 165.4; mass (FAB+) *m/z* 413 (M^++1); $C_{17}H_{20}N_2O_{10}$ (412.34): Calcd. C, 49.52; H, 4.89; N, 6.79; found: C; 49.73, H, 5.66; N, 6.89.

Diethyl 2-nitro-4-[(*E*)-(2-nitrophenyl)methylidene]pentanedioate (8a)- 1.34 g (80%) as yellow oil; ν_{max} (neat) 1709 (CO_2Et) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.26 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 1.38 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 3.18-3.21 (m, 2H, C*H*$_2$CH), 4.20 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 4.37 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 5.60-5.65 (m, 1H, $CHNO_2$), 7.27-7.30 (m, 1H, ArH), 7.60-7.63 (m, 1H, ArH), 7.71-7.73 (m, 1H, ArH), 8.19 (s, 1H, =CH), 8.26-8.28 (m, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 14.2, 14.6, 62.1, 63.5, 86.3, 125.6, 126.6, 130.2, 130.9, 131.2, 134.3, 142.5, 147.6, 164.3, 166.4; mass (FAB+) *m/z* 367 (M^++1); $C_{16}H_{18}N_2O_8$ (366.32): Calcd. C, 52.46; H, 4.95; N, 7.65; found: C; 52.33, H, 5.11; N, 7.74.

5-(*tert*-Butyl) 1-ethyl 2-nitro-4-[(*E*)-(2-nitrophenyl)methylidene]pentanedioate (9a)- 1.9 g (77%) as yellow oil; ν_{max} (neat) 1706 ($CO_2{}^tBu$), 1713 (CO_2Et) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ= 1.25 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 1.57 (s, 9H, $CO_2C(CH_3)_3$), 3.13 (d, 2H, *J*= 7.6 Hz, C*H*$_2$CH), 4.19 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 5.54 (t, 1H, *J*= 7.6 Hz, $CHNO_2$), 7.20-7.31 (m, 1H, ArH), 7.51-7.78 (m, 2H, ArH), 8.07 (s, 1H, =CH), 8.26 (d, 1H, *J*= 8.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 14.2, 28.5, 29.2, 63.5, 82.8, 86.4, 87.4, 125.5, 127.9, 130.0, 131.5, 134.3, 141.7, 147.7, 164.4, 165.5; mass (FAB+) *m/z* 395 (M^++1); $C_{18}H_{22}N_2O_8$ (394.37): Calcd. C, 54.82; H, 5.62; N, 7.10; found: C; 65.71, H, 5.84; N, 6.82.

Methyl (*E*)-3-(2-nitrophenyl)-2-(2-nitropropyl)prop-2-enoate (21a)- 1.92 g (69%) as yellow solid, mp 92-94^{o}C; ν_{max} (KBr) 1742 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.39 (d, 3H, *J*= 6.7 Hz, C*H*$_3$CH), 2.68-2.75 (m, 1H, 1H of C*H*$_2$CH), 2.89-2.96 (m, 1H, 1H of C*H*$_2$CH), 3.88 (s, 3H, CO_2CH_3), 4.88-4.91 (m, 1H, $CHNO_2$), 7.23-7.28 (m, 1H, ArH), 7.56-7.61 (m, 1H, ArH), 7.69-7.74 (m, 1H, ArH), 8.12 (s, 1H, =CH), 8.20-8.24 (m, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 17.6, 31.9, 51.2, 80.3, 123.8, 126.7, 128.4, 129.3, 132.0, 132.6, 139.8, 146.0, 165.4; mass (FAB+) *m/z* 295 (M^++1); $C_{13}H_{14}N_2O_6$ (294.26): Calcd. C, 53.06; H, 4.80; N, 9.52; found: C; 53.67, H, 4.41; N, 9.49.

Methyl (*E*)-3-(6-nitro-1,3-benzodioxol-5-yl)-2-(2-nitropropyl)prop-2-enoate (21c)- 1.8 g (60%) as yellow oil; ν_{max} (neat) 1715 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.40 (d, 3H, *J*= 6.6 Hz, C*H*$_3$CH), 2.69- 2.77 (m, 1H, 1H of C*H*$_2$CH), 2.92- 2.3.00 (m, 1H, 1H of C*H*$_2$CH), 3.87 (s, 3H, CO_2CH_3), 4.86-4.93 (m, 1H, $CHNO_2$), 6.02 (s, 2H, OCH_2O), 6.59 (s, 1H, ArH), 7.71 (s, 1H, ArH), 8.04 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 17.5, 31.9, 51.2, 80.3, 102.3, 104.5, 107.7, 125.9, 126.2, 139.6, 140.3, 147.2, 151.1, 165.5; mass (FAB+) *m/z* 339 (M^++1); $C_{14}H_{14}N_2O_8$ (338.26): Calcd. C, 49.71; H, 4.17; N, 8.28; found: C; 49.98, H, 3.94; N, 8.05.

Methyl (*E*)-3-(4,5-dimethoxy-2-nitrophenyl)-2-(2-nitropropyl)prop-2-enoate (21d)- 1.8 g (61%) as yellow solid, mp 130-132^{o}C; ν_{max} (KBr) 1715 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.42 (d, 3H, *J*= 6.6 Hz, C*H*$_3$CH), 2.67- 2.85 (m, 2H, C*H*$_2$CH), 3.87 (s, 3H, CO_2CH_3), 3.98 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.94-5.01 (m, 1H, $CHNO_2$), 6.54 (s, 1H, ArH), 7.75 (s, 1H, ArH), 8.07 (s, 1H, =CH); ^{13}C NMR (75 MHz,

$CDCl_3$) δ= 17.6, 32.6, 51.2, 55.2, 55.4, 80.3, 106.5, 110.3, 124.0, 125.9, 138.5, 140.5, 147.7, 152.3, 165.6; mass (FAB+) *m/z* 355 (M^++1); $C_{15}H_{18}N_2O_8$ (354.31): Calcd. C, 50.85; H, 5.12; N, 7.91; found: C; 50.88, H, 5.29; N, 8.06.

Ethyl (*E*)-3-(2-nitrophenyl)-2-(2-nitropropyl)prop-2-enoate (22a)- 1.6 g (73%) as yellow oil; ν_{max} (neat) 1709 (CO_2Et) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.36-1.41 (m, 6H, C*H*$_3$CH and C*H*$_3$CH$_2$), 2.73 (dd, 1H, *J*= 5.7 Hz, *J*= 5.8 Hz, 1H of C*H*$_2$CH), 2.93 (dd, 1H, *J*= 8.3 Hz, *J*= 7.9 Hz, 1H of C*H*$_2$CH), 4.34 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 4.89-4.92 (m, 1H, $CHNO_2$), 7.24-7.28 (m, 1H, ArH), 7.56-7.61 (m, 1H, ArH), 7.69-7.72 (m, 1H, ArH), 8.12 (s, 1H, =CH), 8.21-8.24 (m, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 14.6, 19.3, 33.6, 62.0, 82.0, 125.5, 129.1, 130.0, 131.1, 134.3, 141.1, 147.8, 166.7; mass (FAB+) *m/z* 309 (M^++1); $C_{14}H_{16}N_2O_6$ (308.28): Calcd. C, 54.54; H, 5.23; N, 9.09; found: C; 54.37, H, 5.26; N, 8.91.

Methyl 8-methylnaphtho[2,3-*d*][1,3]dioxole-6-carboxylate (23c)- (hexane-EtOAc, 90:10, v/v) 0.54 g (25%) as pale yellow solid, mp 152-154°C; ν_{max}(KBr) 1722 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 25% as pale yellow solid, mp 152-154°C; ν_{max} (KBr) 1722 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 2.60 (s, 3H, CH_3), 3.96 (s, 3H, CO_2CH_3), 6.07 (s, 2H, OCH_2O), 7.17 (s, 1H, ArH), 7.24 (s, 1H, ArH), 7.77 (s, 1H, ArH), 8.24 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 18.5, 50.8, 99.4, 100.2, 104.2, 123.5, 124.2, 126.9, 128.4, 131.2, 132.2, 146.4, 148.3, 166.2; mass (FAB+) *m/z* 245 (M^++1); $C_{14}H_{12}O_4$ (244.24): Calcd. C, 68.85; H, 4.95; fFound: C; 68.86, H, 4.99.

Methyl 6,7-dimethoxy-4-methyl-2-naphthoate (23d)- 0.61 g (28%) as a brown solid, mp 114-116°C; ν_{max} (KBr) 1728 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 2.63 (s, 3H, CH_3), 3.94 (s, 3H, CO_2CH_3), 3.99 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 7.15 (s, 1H, ArH), 7.19 (s, 1H, ArH), 7.77 (s, 1H, ArH), 8.29 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 18.3, 50.7, 54.6, 101.5, 106.7, 123.1, 124.0, 126.5, 127.1, 129.7, 131.6, 148.2, 149.8, 166.4; mass (FAB+) *m/z* 261 (M^++1); $C_{15}H_{16}O_4$ (260.28): Calcd. C, 69.22; H, 6.20; found: C; 69.41, H, 6.17.

General procedure for the preparation of compounds 10a-b,11-13a,14c-d as exemplified for compound 10a

To a solution of compound **7a** (0.8 g, 2.27 mmol) in methanol (10 mL) was added $SnCl_2.2H_2O$ (2.56 gm, 11.36 mmol) and the reaction mixture was heated at reflux with

stirring at 80°C for 2 h in a nitrogen atmosphere. On completion, methanol was evaporated and the residue was made alkaline with saturated $NaHCO_3$ and then EtOAc (100 mL) was added. The suspension was passed through a bed of Celite and the filtrate was partitioned in a separating funnel. The organic layer was separated, dried (anhyd. Na_2SO_4), and concentrated to afford a residue, which was purified by silica gel column chromatography using hexane–EtOAc (90:10, v/v) or (80:20, v/v) as eluent to yield 0.32 g (55%) of products **10a** as a black solid.

Dimethyl 1*H*-1-benzazepine-2,4-dicarboxylate (10a)- mp 110-112°C; ν_{max} (KBr) 1731 (CO_2Me), 3350 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 3.80 (s, 3H, CO_2CH_3), 3.81 (s, 3H, CO_2CH_3), 5.35 (s, 1H, NH), 6.23 (d, 1H, *J*= 7.9 Hz, ArH), 6.42 (s, 1H, ArH), 6.78-6.80 (m, 2H, ArH), 7.05-7.08 (m, 1H, ArH), 7.32 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 51.0, 51.6, 114.2, 118.7, 122.6, 126.9, 128.7, 131.7, 131.8, 136.2, 144.5, 148.2, 162.1, 164.4; mass (ES+) *m/z* 260.1 (M^++1).

Dimethyl 7-chloro-1*H*-1-benzazepine-2,4-dicarboxylate (10b)- 0.44 g (58%) as black solid, mp 103-105°C; ν_{max} (KBr) 1709 (CO_2Me), 3329 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 3.80 (s, 6H, 2 x CO_2CH_3), 5.35 (s, 1H, NH), 6.24 (d, 1H, *J*= 7.8 Hz, ArH), 6.40 (s, 1H, ArH), 6.74 (s, 1H, ArH), 7.02 (d, 1H, *J*= 7.8 H, ArH), 7.20 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 51.1, 51.7, 114.0, 119.8, 127.7, 128.5, 130.0, 130.9, 136.5, 142.7, 146.8, 162.0, 164.1; mass (ES+) *m/z* 294.1 (M^++1), 296.1 (M^++3).

4-Ethyl 2-methyl 1*H*-1-benzazepine-2,4-dicarboxylate (11a)- 0.56 g (54%) as a black solid, mp 98-100°C; ν_{max} (KBr) 1711 (CO_2Et), 1731 (CO_2Me), 3350 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.36 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 3.81 (s, 3H, CO_2CH_3), 4.26 (s, 2H, C*H*$_2$CH$_3$), 5.35 (s, 1H, NH), 6.32 (d, 1H, *J*= 7.9 Hz, ArH), 6.44 (s, 1H, ArH), 6.79-6.80 (m, 2H, ArH), 7.05-7.10 (m, 1H, ArH), 7.32 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ=14.6, 53.2, 61.6, 116.1, 120.3, 124.2, 128.7, 130.7, 133.3, 133.4, 137.8, 145.9, 149.9, 164.4, 166.2; mass (ES+) *m/z* 274.1 (M^++1).

4-(*tert*-Butyl) 2-methyl 1*H*-1-benzazepine-2,4-dicarboxylate (12a)- 0.48 g (45%) as black oil; ν_{max} (neat) 1706 ($CO_2{}^tBu$), 1722 (CO_2Me), 3424 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.55 (s, 9H, $C(CH_3)_3$), 3.79 (s, 3H, CO_2CH_3), 5.36 (s, 1H, NH), 6.33 (d, 1H, *J*= 7.8 Hz, ArH), 6.45 (s, 1H, ArH), 6.74 (s, 1H, ArH), 6.79-6.81 (m, 2H, ArH), 7.05-

7.09 (m, 1H, ArH), 7.26 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 26.8, 51.5, 115.0, 118.6, 122.5, 127.1,130.4, 131.4, 1315, 135.8, 143.4, 148.2, 163.1; mass (ES+) *m/z* 302.0 (M^++1).

Diethyl 1*H*-1-benzazepine-2,4-dicarboxylate (13a)- 0.38g (62%) as black oil; ν_{max} (neat) 1714 (CO_2Et), 3352 (NH) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 1.28-1.36 (m, 6H, 2 x C*H*$_3$CH$_2$), 4.22-4.29 (m, 4H, 2 x C*H*$_2$CH$_3$), 5.38 (s, 1H, NH), 6.32 (d, 1H, *J*= 7.9 Hz, ArH), 6.44 (s, 1H, ArH), 6.78-6.80 (m, 2H, ArH), 7.05-7.10 (m, 1H, ArH), 7.35 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 12.9, 13.0, 59.9, 60.8, 114.2, 118.7, 122.5, 127.0, 129.5, 131.6, 131.7, 136.4, 144.1, 148.3, 161.7, 164.4; mass (ES+) *m/z* 288.0 (M^++1).

Dimethyl 7*H*-[1,3]dioxolo[4,5-*h*][1]benzazepine-6,8-dicarboxylate (14c)- 0.58 g (54%) as black oil; ν_{max} (neat) 1738 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 3.24 (s, 2H, CH_2), 3.88 (s, 3H, CO_2CH_3), 3.95 (s, 3H, CO_2CH_3), 6.10 (s, 2H, OCH_2O), 6.91 (s, 1H, ArH), 7.06 (s, 1H, ArH), 7.73 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 28.4, 51.1, 51.4, 82.3, 91.7, 99.3, 99.8, 104.8, 118.9, 128.5, 137.2, 142.2, 145.2, 163.5, 164.1; mass (ES+) *m/z* 304.0 (M^++1); $C_{15}H_{13}NO_6$ (303.26): Calcd. C, 59.41; H, 4.32; N, 4.62; found: C; 59.21, H, 4.59; N, 4.48.

Dimethyl 7,8-dimethoxy-3*H*-1-benzazepine-2,4-dicarboxylate (14d)- 0.41 (07%) yellow oil; ν_{max} (neat) 1732 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 3.26 (s, 2H, CH_2), 3.87 (s, 3H, CO_2CH_3), 3.95 (s, 3H, CO_2CH_3), 3.96 (s, 6H, 2 x OCH_3), 4.05 (s, 2H, CH_2), 6.91 (s, 1H, ArH), 7.11 (s, 1H, ArH), 7.79 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 26.6, 51.1, 52.1, 54.8, 54.9, 109.6, 110.2, 120.2, 135.7, 140.1, 145.9, 146.5, 148.9, 162.2, 164.2; mass (ES+) *m/z* 320.0 (M^++1); $C_{16}H_{17}NO_6$ (319.30): Calcd. C, 60.18; H, 5.37; N, 4.39; found: C; 60.03, H, 5.49; N, 4.50.

General procedure for the preparation of compounds 25a,c-d,26a.

These compounds were prepared following the experimental procedure described for compound **10a** except for that the heating was continued for 12 h.

Methyl 2-methyl-3*H*-1-benzazepine-4-carboxylate (25a)- 0.63 g **(**58%) as brown oil; ν_{max} (neat) 1733 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 2.36 (s, 3H, CH_3), 2.87 (s, 2H, CH_2), 3.88 (s, 3H, CO_2CH_3), 7.22-7.25 (m, 1H, ArH), 7.41-7.48 (m, 3H, ArH), 7.79 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 26.1, 32.2, 51.0, 116.2, 117.2, 122.8,

125.9, 127.6, 129.7, 135.7, 146.8, 162.1, 164.9; mass (ES+) *m/z* 216.1 (M^++1); $C_{13}H_{13}NO_2$ (215.24): Calcd. C, 72.54; H, 6.09; N, 6.51; found: C; 72.47, H, 5.97; N, 6.66.

Methyl 6-methyl-7*H*-[1,3]dioxolo[4,5-*h*][1]benzazepine-8-carboxylate (25c)- 0.66 (51%) as yellow oil; ν_{max} (neat) 1723 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 2.34 (s, 3H, CH_3), 2.84 (s, 2H, CH_2), 3.93 (s, 3H, CO_2CH_3), 6.00 (s, 2H, OCH_2O), 6.76 (s, 1H, ArH), 6.84 (s, 1H, ArH), 7.48 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 26.0, 31.6, 49.7, 81.9, 90.7, 99.2, 99.7, 104.5, 119.3, 128.2, 138.0, 143.4, 144.2, 164.8; mass (ES+) *m/z* 260.3 (M^++1); $C_{14}H_{13}NO_4$ (259.25): Calcd. C, 64.86; H, 5.05; N, 5.40; found: C; 64.70, H, 4.98; N, 5.42.

Methyl 7,8-dimethoxy-2-methyl-3*H*-1-benzazepine-4-carboxylate (25d)- 0.61 (53%) as brown oil; ν_{max} (neat) 1728 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 2.33 (s, 3H, CH_3), 2.84 (s, 2H, CH_2), 3.85 (s, 3H, CO_2CH_3), 3.91 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.84 (s, 1H, ArH), 6.92 (s, 1H, ArH), 7.70 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 25.8, 32.3, 50.9, 54.6, 54.7, 108.1, 110.1, 118.9, 119.2, 135.2, 142.0, 148.7, 151.8, 159.5; mass (ES+) *m/z* 276.2 (M^++1); $C_{15}H_{17}NO_4$ (275.29): Calcd. C, 65.44; H, 6.22; N, 5.09;. found: C; 65.66, H, 6.25; N, 4.90.

Ethyl 2-methyl-3*H*-1-benzazepine-4-carboxylate (26a)- 0.62 g (56%) as yellow oil; ν_{max} (neat) 1703 (CO_2Et) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.39 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 2.35 (s, 3H, CH_3), 2.85 (s, 2H, CH_2), 4.33 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 7.19-7.24 (m, 1H, ArH), 7.41-7.48 (m, 3H, ArH), 7.78 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 13.0, 26.0, 32.1, 60.0, 122.6, 123.2, 125.9, 126.0, 127.5, 129.6, 135.4, 148.6, 162.2, 164.4; mass (ES+) *m/z* 230.1 (M^++1); $C_{14}H_{15}NO_2$ (229.27): Calcd. C, 73.34; H, 6.59; N, 6.11; found: C; 73.19, H, 6.41; N, 5.88.

Ethyl (*E*)-3-(2-aminophenyl)-2-(2-nitropropyl)prop-2-enoate (27)- 0.50 g (37%) as yellow oil; ν_{max} (neat) 1713 (CO_2Et) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ= 1.44 (d, 3H, *J*= 6.7 Hz, C*H*$_3$CH), 2.86 (dd, 1H, *J*= 5.7 Hz, *J*= 5.8 Hz, 1H of C*H*$_2$CH), 3.21 (dd, 1H, *J*= 8.3 Hz, *J*= 7.9 Hz, 1H of C*H*$_2$CH), 4.31 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 4.85-4.92 (m, 1H, $CHNO_2$), 6.72-6.81 (m, 2H, ArH), 6.98 (d, 1H, *J*= 7.5 Hz, ArH), 7.14-7.20 (m, 1H, ArH), 7.78 (s, 1H, =CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 12.9, 17.5, 32.0, 60.0, 80.7, 114.5, 117.2, 119.1, 127.5, 128.2, 128.7, 138.8, 143.1, 165.6; mass (ES+) *m/z* 279.2 (M^++1).

Anal. for $C_{14}H_{18}N_2O_4$ (278.30): Calcd. C, 60.42; H, 6.52; N, 10.07; found: C; 60.31, H, 6.66; N, 9.84.

General procedure for the preparation of compounds (15-16) as exemplified for compound 15.

To a stirred solution of compound **10a** (0.15 g, 0.58 mmol) in dry dichloromethane (5 mL) was added Et_3N (0.121 mL, 0.87 mmol) and the reaction was allowed to continue for 20 min at 0^{o}C. Thereafter acetyl chloride (1.16 g, 1.0 mmol) was added to the reaction mixture at the same temperature and the stirring was continued for another 2 h at room temperature. On completion (monitored by tlc), the mixture was extracted with water and dichloromethane. The organic layer was separated, dried (Na_2SO_4), and evaporated to dryness to yield the crude product, which was purified via silica gel column chromatography using hexane–EtOAc (70:30, v/v) to yield 0.16 g (92%) of pure product **15** as pale yellow solid.

Dimethyl 1-acetyl-1*H*-1-benzazepine-2,4-dicarboxylate (15) (rotamer ratio 1:2 as evident from ^{1}H-NMR)- mp 144-146^{o}C; ν_{max} (KBr) 1710 (COMe), 1735 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 1.85 (s, 3H, $OCOCH_3$), 2.05 (s, 3H, $OCOCH_3$), 3.85 (s, 3H, CO_2CH_3), 3.89 (s, 3H, CO_2CH_3), 3.90 (s, 3H, CO_2CH_3), 3.92 (s, 3H, CO_2CH_3), 7.39-7.57 (m, 6H, 2 x 3ArH), 7.62-7.68 (m, 2H, 2 x 1ArH), 7.68 (s, 1H, ArH), 7.78 (s, 1H, ArH), 8.21 (s, 1H, ArH), 8.30 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 19.7, 19.9, 51.3, 51.4, 51.5, 51.6, 126.1, 126.5, 126.6, 127.0, 127.3, 127.7, 127.8, 129.4, 129.9, 130.0, 130.4, 131.0, 131.6, 131.7, 131.8, 138.5, 138.8, 140.7, 143.6, 161.5, 161.8, 164.6, 164.7, 168.3, 168.6; mass (Es+) *m/z* 302.0 (M^++1); HR-EIMS Calcd. for $C_{16}H_{15}NO_5$: 301.0950. Found: 301.0954.

Dimethyl 1-benzoyl-1*H*-1-benzazepine-2,4-dicarboxylate (16) (rotamer ratio 1:2 as evident from ^{1}H-NMR)- 0.13 g (96%) as off white solid, mp 164-166^{o}C; ν_{max} (KBr) 1707 (COPh), 1738 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 3.93 (s, 3H, CO_2CH_3), 3.96 (s, 3H, CO_2CH_3), 4.11 (s, 3H, CO_2CH_3), 4.14 (s, 3H, CO_2CH_3), 7.11-7.26 (m, 8H, 2 x 4ArH), 7.27-7.38 (m, 8H, 2 x 4ArH), 7.44-7.46 (m, 1H, ArH), 7.52-7.55 (m, 1H, ArH), 7.68 (s, 1H, ArH), 7.73 (s, 1H, ArH), 8.35 (s, 1H, ArH), 8.40 (s, 1H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 51.2, 51.4, 51.5, 51.6, 126.3, 126.4, 126.6, 126.8, 126.9, 127.2, 127.3, 127.6, 128.1, 128.5, 129.1, 129.4, 129.8, 131.1, 131.2, 131.3, 131.5, 132.5,

133.5, 138.1, 140.1, 141.0, 143.9, 161.5, 161.6, 164.7, 164.9, 168.3, 168.6; mass (FAB+) *m/z* 364 (M^++1); HR-EIMS Calcd. for $C_{21}H_{17}NO_5$: 363.1107. Found: 363.1105.

General procedure for the preparation of compounds 17a-b,18-20a as exemplified for 17a.

To a solution of compound **10a** (0.2 g, 0.77 mmol) in dichloromethane (1.0 mL) was added silica gel (60-120 mesh, 0.1 g) and the mixture was evaporated to dryness. The flask was exposed to uv lamp (Philips, 500W flash light) for 6 h. The silica gel was taken in a column and elution with hexane-EtOAc (80:20, v/v) yielded 0.15 g (80%) of pure **17a** as off white solid.

Dimethyl isoquinoline-1,3-dicarboxylate (17a)- mp 118-120^{o}C; ν_{max} (KBr) 1742 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 4.09 (s, 3H, CO_2CH_3), 4.13 (s, 3H, CO_2CH_3), 7.79-7.89 (m, 2H, ArH), 8.39 (d, 1H, *J*= 8.4 Hz, ArH), 8.71 (s, 1H, ArH), 8.87 (d, 1H, *J*= 8.4 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 51.1, 51.9, 119.0, 122.6, 126.9, 128.8, 131.7, 131.8, 136.3, 144.5, 148.3, 162.2, 164.5; (ES+) *m/z* 246.0 (M^++1); HR-EIMS $C_{13}H_{11}NO_4$: Calcd. 245.0688, found: 245.0687.

Dimethyl 6-chloroisoquinoline-1,3-dicarboxylate (17b)- 0.14 g (75%) as yellow oil; ν_{max} (neat) 1732 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= .96 (s, 3H, CO_2CH_3), 4.06 (s, 3H, CO_2CH_3), 7.78 (d, 1H, *J*= 8.0 Hz, ArH), 8.02 (s, 1H, ArH), 8.70 (s, 1H, ArH), 8.89 (d, 1H, *J*= 8.0 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 51.1, 51.7, 119.8, 124.3, 126.9, 128.5, 131.0, 131.8, 136.5, 144.2, 147.3, 162.0, 164.2; (ES+) *m/z* 280.1 (M^++1); HR-EIMS $C_{13}H_{10}ClNO_4$: Calcd. 279.0298, found: 279.0296.

3-Ethyl 1-methyl isoquinoline-1,3-dicarboxylate (18a)- 0.212 (78%) pale yellow solid, mp 85-87^{o}C, ν_{max} (KBr) 1712 (CO_2Et), 1740 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 1.51 (t, 3H, *J*= 7.2 Hz, C*H*$_3$CH$_2$), 4.13 (s, 3H, CO_2CH_3), 4.56 (q, 2H, *J*= 7.2 Hz, C*H*$_2$CH$_3$), 7.78-7.87 (m, 2H, ArH), 8.37-8.40 (m, 1H, ArH), 8.69 (s, 1H, ArH), 8.83 (d, 1H, *J*= 1.2 Hz, ArH); ^{13}C NMR (150 MHz, $CDCl_3$) δ= 14.3, 53.4, 62.2, 122.1, 125.5, 126.3, 130.3, 130.5, 131.2, 136.6, 147.5, 148.6, 165.4, 165.6; mass (ES+) *m/z* 260.0 (M^++1); HR-EIMS $C_{14}H_{13}NO_4$: Calcd. 259.0845, found: 259.0847.

Diethyl isoquinoline-1,3-dicarboxylate (19a)- 0.29 **(**82%) as pale yellow oil, ν_{max} (neat) 1723 (CO_2Et) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 1.46-1.55 (m, 6H, 2 x C*H*$_3$CH$_2$),

4.49-4.64 (m, 4H, 2 x C*H*$_2$CH$_3$), 7.74-7.88 (m, 2H, ArH), 8.39 (d, 1H, *J*= 8.2 Hz, ArH), 8.66 (s, 1H, ArH), 8.84 (d, 1H, *J*= 8.2 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 13.0, 13.1, 60.9, 61.2, 120.8, 124.2, 125.0, 128.9, 129.1, 130.1, 135.2, 146.6, 147.4, 163.6, 164.4; mass (ES+) *m/z* 274.1 (M^++1); HR-EIMS $C_{15}H_{15}NO_4$: Calcd. 273.1001, found: 273.1002.

3-(*tert*-Butyl) 1-methyl isoquinoline-1,3-dicarboxylate (20a)- 0.40 g **(**77%) as pale yellow oil, ν_{max} (neat) 1703 ($CO_2{}^tBu$), 1733 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ= 1.71 (s, 9H, C $(CH_3)_3$), 4.12 (s, 3H, CO_2CH_3), 7.34-7.87 (m, 2H, ArH), 8.36 (d, 1H, *J*= 8.1 Hz, ArH), 8.56 (s, 1H, ArH), 8.73 (d, 1H, *J*= 8.1 Hz, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ= 26.8, 52.0, 82.3, 120.4, 124.2, 125.0, 128.7, 129.1, 129.9, 137.2, 147.2, 163.7, 164.2; mass (ES+) *m/z* 287.9 (M^++1); HR-EIMS $C_{16}H_{17}NO_4$: Calcd. 287.0058, found: 287.0059.

Supporting Information: Copies of ^{1}H NMR, ^{13}C NMR and Mass spectra of several new compounds are being provided. The copy of HSQC and HMBC spectra for compound **18a** is also provided.

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