DOI: 10.1002/ejoc.200700175

Synthesis of Substituted 1*H*- and 3*H*-1-Benzazepines and Rearrangement of Alkyl 1*H*-1-Benzazepine-2-carboxylates into Isoquinolines[‡]

Vijay Singh[a] and Sanjay Batra*[a]

Keywords: Baylis–Hillman reaction / Nitrogen heterocycles / Rearrangement

The $SnCl_2$-mediated reduction of nitro groups in 2-nitro-4-(2-nitrobenzylidene)alkanoates and 4-nitro-2-(2-nitroalkylidene)alkanoates allows the facile synthesis of substituted 1*H*-1-benzazepines and 3*H*-1-benzazepines. This reaction proceeds via S_N2' reaction of ethyl nitroacetate and nitroethane with the acetyl derivatives of Baylis–Hillman adducts deriving from 2-nitro-substituted benzaldehydes. During the study, an unprecedented rearrangement of an alkyl 1*H*-benzazepine-2-carboxylate to a substituted isoquinoline has been observed.

Introduction

The products afforded by the Baylis–Hillman reaction and their derivatives have served as an excellent source 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-alkoxycarbonylvinyl)-1*H*-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 $SnCl_2{\cdot}2H_2O$. Mechanistic considerations generated interest in extending the study to a 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. We reasoned that the $SnCl_2{\cdot}2H_2O$-mediated reduction of the nitro groups would result in an aromatic amino group and an oxime in the case of ethyl nitroacetate derivatives and an aliphatic amino group in the case of nitroethane derivatives. Subsequently, the intermediates in both cases would cyclize to yield heterocyclic systems. 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 $SnCl_2{\cdot}2H_2O$-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 a pharmacologically important class of heterocycles. They are potent antagonists of the glycine binding site associated with *N*-methyl-D-aspartate (NMDA),[21] antagonists of the CC chemokine receptor-5, and therefore, useful against HIV-1 infection,[22–23] and show usefulness in illnesses related to the melanocortin-4 receptor.[24] A survey of the literature revealed that only a few methods for the synthesis of substituted 1*H*-benzazepines were known.[25–30] Our approach is very simple and constitutes a practical route to this class of heterocycle. The results of our study are being reported in this paper.

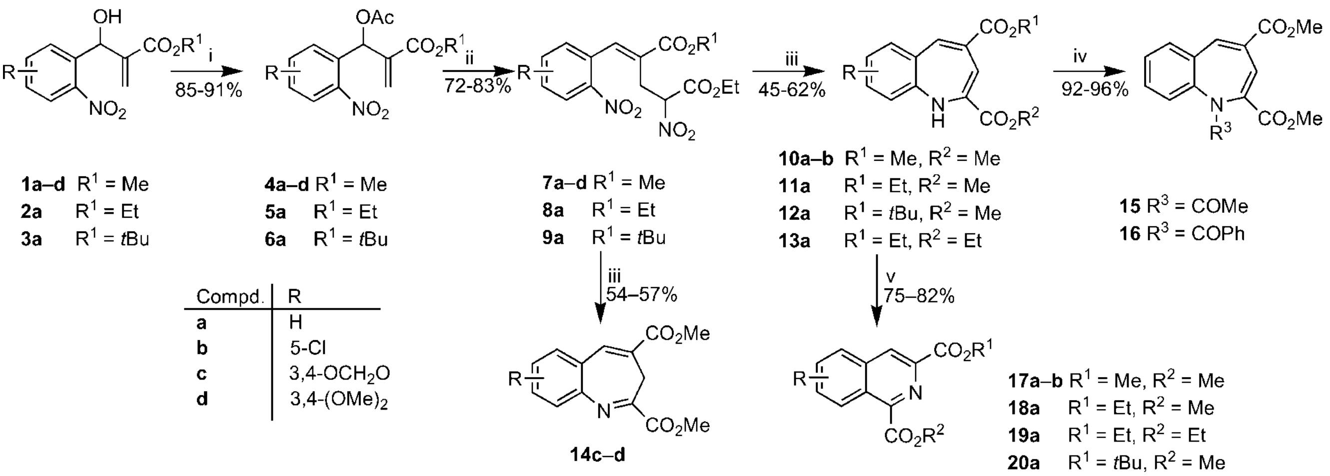
Results and Discussion

The first part of our study deals with the substrates afforded from the reaction between acetyl derivatives of Baylis–Hillman adducts and ethyl nitroacetate. The preparation of the starting materials **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 into 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 stereoselectively yielded the (*E*) isomer of the respective products **7a**–**d**,**8**–**9a** (Scheme 1) in good yields. Treatment of the nitroalkanoate **7a** with $SnCl_2{\cdot}2H_2O$ in methanol at reflux for 2 h furnished a product that was found to be less polar than the substrate.

[‡] CDRI communication no. 7149

[a] Medicinal and Process Chemistry Division, Central Drug Research Institute,
P. O. Box 173, Lucknow 226001, India

Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.



Scheme 1. Reagents and conditions: i) AcCl, pyridine, CH_2Cl_2, room temp., 3 h; ii) $NO_2CH_2CO_2Et$, K_2CO_3, DMF, 3 h; iii) $SnCl_2{\cdot}2H_2O$, MeOH or EtOH, N_2, reflux, 2 h; iv) R_3COCl (R_3 = Me, Ph), Et_3N, CH_2Cl_2, room temp., 3 h; v) silica gel (60–120 mesh), room temp., 24 h or silica gel (60–120 mesh), *hv*, room temp., 6 h.

On the basis of spectral analysis, the structure of this product was established as the substituted 1*H*-1-benzazepine **10a**. The formation of 1*H*-1-benzazepine **10a** indicates 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 the 3-position of the 1*H*-1-benzazepine ring was attributed to the transesterification of the ethoxycarbonyl moiety due to the use of methanol as the solvent in the reaction. In order to examine the general applicability of this reaction, other substrates **7b–d**,**8–9a** were also subjected to $SnCl_2{\cdot}2H_2O$-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 products. At this stage of the study, we reasoned that the substitution of the phenyl ring could have some role in the outcome of the reactions, since compounds **7c–d** had electron-donating substituents on the phenyl ring. Remarkably, we found that the transesterification was chemoselective, since only the ethoxycarbonyl group originating from the ethyl nitroacetate was 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 of the formation of a 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 of these products were obtained as a mixture of rotational isomers (*endo* and *exo* forms). This observation has literature precedence since it has been reported that the hindered rotation about the N–C, owing to its partial double bond character, leads to steric interactions in amides where the nitrogen is disubstituted.[31]

During the course of this work, we observed that the 1*H*-1-benzazepine derivatives **10a–b**,**11–13a** were unstable, and that even the pure solid compounds changed to oils within a short span of time (≈ 12–24 h) at room temperature. Furthermore, this phenomenon was accelerated if compounds were left on a silica gel column. As compared to the starting 1*H*-1-benzazepine, the new product was more polar by TLC analysis. Purification, isolation, and characterization by detailed NMR spectroscopy led to the elucidation of the structure of these products as substituted isoquinolines **17a–b**,**18–20a**. Although the oxidation of *N*-methylbenzazepines to naphthyl-1-amine[32] and the acid-promoted rearrangement of 1*H*-1-benzazepine-2,5-dione to 2,4-dihydroxyquinoline[33] have been previously reported, the ring contraction of 1*H*-1-benzazepines to isoquinoline derivatives is unprecedented. However, we are unable to propose a mechanism for this unusual observation at the present time. Nevertheless, with the objective to understand the possible reason behind such an 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 that the 1*H*-benzazepines are stable only when stored at a temperature below 0 °C in the dark. Since the transformation of a 1*H*-1-benzazepine to an 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** in excellent yields. In contrast to the behavior of 1*H*-1-benzazepine derivatives, the 3*H*-1-benzazepine derivatives were stable at room temperature.

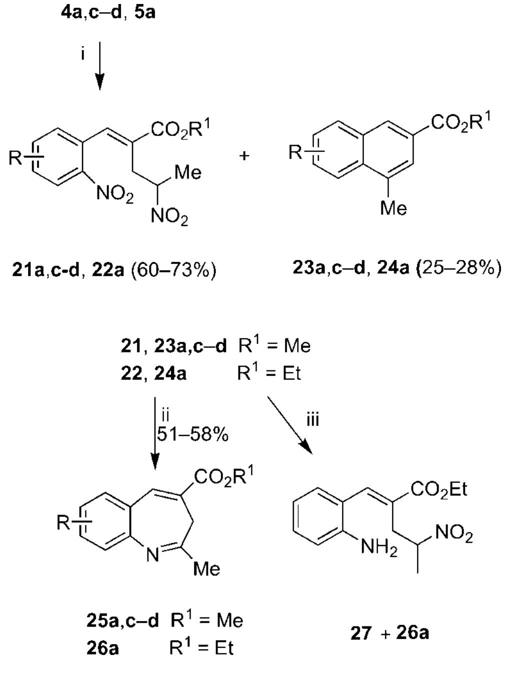
The second phase of our study relates to the similar reduction of a nitro group in substrates resulting from the S_N2' reaction of nitroethane with the acetyl derivatives of Baylis–Hillman adducts **4a**,**c–d**,**5a**. Compounds **21a**,**c–d**,**22a** were prepared following the literature procedure. In contrast to the reactions with ethyl nitroacetate, all reactions with nitromethane led to the isolation of unexpected products along with the expected nitro derivatives (Scheme 2). The spectroscopic analysis led us to elucidate the structure

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

Entry	Conditions for reactions of **10a**	% Yield of **10a**	% Yield of **17a**
1	CCl_4, dark, r.t.	100	–
2	CCl_4, AIBN, *hν*, r.t.	3	28
3	CCl_4, *hν*, r.t.	80	4
4	CCl_4, silica gel, *hν*, r.t.	0	31
5	silica gel, open flask, r.t.	30	37
6	silica gel, *hν*, r.t.	0	100
7	silica gel, darkness, r.t.	30	70
8	AIBN, toluene, reflux	5	45
9	left at 0 °C under nitrogen	100	–
10	left at 0 °C	100	–

[a] HPLC was performed with an RP C-18 column (250 × 4.5 mm, 5 μ) with a gradient of 10–100% methanol in 0.1% TFA/H_2O over 25 min at a flow rate of 1 mL/min.

of these unexpected products as naphthalenes **23a**,**c**–**d**,**24a**. The formation of naphthalenes by the S_NAr reaction of 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 $SnCl_2{\cdot}2H_2O$ at reflux was complete in 24 h and furnished the corresponding products, which were determined to be 3*H*-1-benzazepine derivatives **25a**,**c**–**d**,**26a**. In contrast to the observation made with the derivatives of ethyl nitroacetate, the substitution pattern of the phenyl ring played no role in the outcome of these reactions. The long reaction time was in line with our earlier observation, where we found that the reduction of the aliphatic nitro group was slower than the reduction of the aromatic nitro group.[20] Indeed, if the reduction is arrested after 3 h, as exemplified in a model reaction with compound **22a**, we could isolate **27** in addition to the usual product **26a**.



Scheme 2. Reagents and conditions: i. $EtNO_2$, K_2CO_3, DMF, room temp., 3 h; ii. $SnCl_2{\cdot}2H_2O$, MeOH or EtOH, N_2, reflux, 24 h; iii. $SnCl_2{\cdot}2H_2O$, MeOH, N_2, reflux, 4 h.

Conclusion

In summary, we have demonstrated a facile approach for the synthesis of substituted 1*H*-1-benzazepines and 3*H*-1-benzazepines by the $SnCl_2$-mediated reduction of nitro groups in the 2-nitro-4-(2-nitrobenzylidene)alkanoates and 4-nitro-2-(2-nitroalkylidene)alkanoates afforded by the S_N2' reaction of ethyl nitroacetate and nitroethane with the acetyl derivatives of Baylis–Hillman adducts deriving from 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 an alkyl 1*H*-1-benzazepine-2-carboxylate to an isoquinoline derivative.

Experimental Section

General: Melting points were recorded with a hot-stage melting point apparatus and are uncorrected. IR spectra were recorded with an FTIR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded with a 200 MHz, 300 MHz, or 600 MHz spectrometer with TMS as an internal standard. Mass spectra were recorded with FAB or LCMS and an ES probe. HRMS spectra were recorded as EI-HRMS. All the solvents and chemicals were used as procured from the suppliers. Compounds **23**–**24a** were previously reported in the literature.[35] Due to their unstable behavior, **10a**–**b**,**11**–**13a** were not subjected to chemical analyses or HR-EIMS. HPLC was performed with an RP C-18 column (250 × 4.5 mm, 5 μ) with a gradient of 10–100% methanol in 0.1% TFA/H_2O over 25 min at a flow rate of 1 mL/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 concentrated aqueous HCl and extracted with EtOAc (3 × 40 mL). The organic layers were pooled, washed with brine (50 mL), dried (anhydrous Na_2SO_4), and evaporated to yield a residue, which was purified by silica gel column chromatography employing hexane/EtOAc (80:20, v/v) to afford 1.14 g (83% yield) of product **7a** as a yellow oil.

1-Ethyl 5-Methyl 2-Nitro-4-[(*E*)-(2-nitrophenyl)methylidene]pentanedioate (7a): IR (neat): $\tilde{\nu}$ = 1716 (CO_2Et), 1740 (CO_2Me) cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.24 (t, J = 7.2 Hz, 3 H, CH_3CH_2), 3.18 (d, J = 7.5 Hz, 2 H, CH_2CH), 3.89 (s, 3 H, CO_2CH_3), 4.19 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.60 (t, J = 7.5 Hz, 1 H, $CHNO_2$), 7.24–7.28 (m, 1 H, ArH), 7.59–7.63 (m, 1 H, ArH), 7.68–7. 73 (m, 1 H, ArH), 8.19 (s, 1 H, =CH), 8.24–8.28 (m, 1 H, ArH) ppm. ^{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 ppm. FAB-MS: 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% yield) as a yellow oil. IR (neat):

$\tilde{\nu}$ = 1719 (CO_2Et), 1750 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3 H, CH_3CH_2), 3.17–3.20 (m, 1 H, 1H of CH_2CH), 3.86–3.89 (m, 1 H, 1H of CH_2CH), 3.90 (s, 3 H, CO_2CH_3), 4.22 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.58–5.61 (m, 1 H, $CHNO_2$), 7.25–7.33 (m, 1 H, ArH), 7.55–7.59 (m, 1 H, ArH), 8.12 (s, 1 H, ArH), 8.23 (s, 1 H, =CH) ppm. ^{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 ppm. FAB-MS: 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): 1.68 g (72% yield) as a yellow oil. IR (neat): $\tilde{\nu}$ = 1709 (CO_2Et), 1739 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (t, J = 7.2 Hz, 3 H, CH_3CH_2), 3.18–3.22 (m, 2 H, CH_2CH), 3.89 (s, 3 H, CO_2CH_3), 4.22 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.59–5.64 (m, 1 H, $CHNO_2$), 6.21 (s, 2 H, OCH_2O), 6.62 (s, 1 H, ArH), 7.75 (s, 1 H, ArH), 8.11 (s, 1 H, =CH) ppm. ^{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 ppm. FAB-MS: 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-nitropentanedioate (7d): 1.1 g (75% yield) as a yellow oil. IR (neat): $\tilde{\nu}$ = 1706 (CO_2Et), 1755 (CO_2Me) cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.26 (t, J = 7.2 Hz, 3 H, CH_3CH_2), 3.18 (d, J = 7.9 Hz, 2 H, CH_2CH), 3.89 (s, 3 H, CO_2CH_3), 3.99 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 4.22 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.71 (t, J = 7.9 Hz, 1 H, $CHNO_2$), 6.63 (s, 1 H, ArH), 7.79 (s, 1 H, ArH), 8.15 (s, 1 H, =CH) ppm. ^{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 ppm. FAB-MS: 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% yield) as a yellow oil. IR (neat): $\tilde{\nu}$ = 1709 (CO_2Et) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.26 (t, J = 7.2 Hz, 3 H, CH_3CH_2), 1.38 (t, J = 7.2 Hz, 3 H, CH_3CH_2), 3.18–3.21 (m, 2 H, CH_2CH), 4.20 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 4.37 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.60–5.65 (m, 1 H, $CHNO_2$), 7.27–7.30 (m, 1 H, ArH), 7.60–7.63 (m, 1 H, ArH), 7.71–7.73 (m, 1 H, ArH), 8.19 (s, 1 H, =CH), 8.26–8.28 (m, 1 H, ArH) ppm. ^{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 ppm. FAB-MS: 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% yield) as a yellow oil. IR (neat): $\tilde{\nu}$ = 1706 (CO_2tBu), 1713 (CO_2Et) cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.2 Hz, 3 H, CH_3CH_2), 1.57 [s, 9 H, $CO_2C(CH_3)_3$], 3.13 (d, J = 7.6 Hz, 2 H, CH_2CH), 4.19 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 5.54 (t, J = 7.6 Hz, 1 H, $CHNO_2$), 7.20–7.31 (m, 1 H, ArH), 7.51–7.78 (m, 2 H, ArH), 8.07 (s, 1 H, =CH), 8.26 (d, J = 8.0 Hz, 1 H) ppm. ^{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 ppm. FAB-MS: 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% yield) as a yellow solid, m.p. 92–94 °C. IR (KBr): $\tilde{\nu}$ = 1742 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.39 (d, J = 6.7 Hz, 3 H, CH_3CH), 2.68–2.75 (m, 1 H, 1H of CH_2CH), 2.89–2.96 (m, 1 H, 1H of CH_2CH), 3.88 (s, 3 H, CO_2CH_3), 4.88–4.91 (m, 1 H, $CHNO_2$), 7.23–7.28 (m, 1 H, ArH), 7.56–7.61 (m, 1 H, ArH), 7.69–7.74 (m, 1 H, ArH), 8.12 (s, 1 H, =CH), 8.20–8.24 (m, 1 H, ArH) ppm. ^{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 ppm. FAB-MS: 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% yield) as a yellow oil. IR (neat): $\tilde{\nu}$ = 1715 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 (d, J = 6.6 Hz, 3 H, CH_3CH), 2.69–2.77 (m, 1 H, 1H of CH_2CH), 2.92–2.3.00 (m, 1 H, 1H of CH_2CH), 3.87 (s, 3 H, CO_2CH_3), 4.86–4.93 (m, 1 H, $CHNO_2$), 6.02 (s, 2 H, OCH_2O), 6.59 (s, 1 H, ArH), 7.71 (s, 1 H, ArH), 8.04 (s, 1 H, =CH) ppm. ^{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 ppm. FAB-MS: 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% yield) as a yellow solid, m.p. 130–132 °C. IR (KBr): $\tilde{\nu}$ = 1715 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (d, J = 6.6 Hz, 3 H, CH_3CH), 2.67–2.85 (m, 2 H, CH_2CH), 3.87 (s, 3 H, CO_2CH_3), 3.98 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 4.94–5.01 (m, 1 H, $CHNO_2$), 6.54 (s, 1 H, ArH), 7.75 (s, 1 H, ArH), 8.07 (s, 1 H, =CH) ppm. ^{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 ppm. FAB-MS: 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% yield) as a yellow oil. IR (neat): $\tilde{\nu}$ = 1709 (CO_2Et) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.36–1.41 (m, 6 H, CH_3CH and CH_3CH_2), 2.73 (dd, J = 5.7 Hz, J = 5.8 Hz, 1 H, 1H of CH_2CH), 2.93 (dd, J = 8.3 Hz, J = 7.9 Hz, 1 H, 1H of CH_2CH), 4.34 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 4.89–4.92 (m, 1 H, $CHNO_2$), 7.24–7.28 (m, 1 H, ArH), 7.56–7.61 (m, 1 H, ArH), 7.69–7.72 (m, 1 H, ArH), 8.12 (s, 1 H, =CH), 8.21–8.24 (m, 1 H, ArH) ppm. ^{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 ppm. FAB-MS: 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): Column chromatography with hexane/EtOAc, 90:10, v/v; 0.54 g (25% yield) as a pale yellow solid, m.p. 152–154 °C. IR (KBr): $\tilde{\nu}$ = 1722 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.60 (s, 3 H, CH_3), 3.96 (s, 3 H, CO_2CH_3), 6.07 (s, 2 H, OCH_2O), 7.17 (s, 1 H, ArH), 7.24 (s, 1 H, ArH), 7.77 (s, 1 H, ArH), 8.24 (s, 1 H, ArH) ppm. ^{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 ppm. FAB-MS: m/z = 245 [M + 1]$^+$. $C_{14}H_{12}O_4$ (244.24): calcd. C 68.85, H 4.95; found C 68.86, H 4.99.

Methyl 6,7-Dimethoxy-4-methyl-2-naphthoate (23d): 0.61 g (28% yield) as a brown solid, m.p. 114–116 °C. IR (KBr): $\tilde{\nu}$ = 1728 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.63 (s, 3 H, CH_3), 3.94 (s, 3 H, CO_2CH_3), 3.99 (s, 3 H, OCH_3), 4.02 (s, 3 H, OCH_3), 7.15 (s, 1 H, ArH), 7.19 (s, 1 H, ArH), 7.77 (s, 1 H, ArH), 8.29 (s, 1 H, ArH) ppm. ^{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 ppm. FAB-MS: 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, Exemplified for Compound 10a: To a solution of compound **7a** (0.8 g, 2.27 mmol) in methanol (10 mL) was added $SnCl_2\cdot 2H_2O$ (2.56 g, 11.36 mmol), and the reaction mixture was heated at reflux with stirring at 80 °C for 2 h under a nitrogen atmosphere. Upon completion, methanol was evaporated, and the residue was made alkaline with saturated aqueous $NaHCO_3$, and then EtOAc (100 mL) was added. The suspension was passed through a bed of Celite, and the filtrate was partitioned in a separatory funnel. The organic layer was separated, dried (anhydrous Na_2SO_4), and concentrated to afford a residue, which was purified by silica gel column chromatography with hexane/EtOAc (90:10, v/v or 80:20, v/v) as the eluent to yield 0.32 g (55%) of product **10a** as a black solid.

Dimethyl 1*H*-1-Benzazepine-2,4-dicarboxylate (10a): M.p. 110–112 °C. IR (KBr): ṽ = 1731 (CO_2Me), 3350 (NH) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, CO_2CH_3), 3.81 (s, 3 H, CO_2CH_3), 5.35 (s, 1 H, NH), 6.23 (d, *J* = 7.9 Hz, 1 H, ArH), 6.42 (s, 1 H, ArH), 6.78–6.80 (m, 2 H, ArH), 7.05–7.08 (m, 1 H, ArH), 7.32 (s, 1 H, ArH) ppm. ^{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; ESI-MS: *m*/*z* = 260.1 $[M + 1]^+$.

Dimethyl 7-Chloro-1*H*-1-benzazepine-2,4-dicarboxylate (10b): 0.44 g (58% yield) as a black solid, m.p. 103–105 °C. IR (KBr): ṽ = 1709 (CO_2Me), 3329 (NH) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 6 H, $2\times CO_2CH_3$), 5.35 (s, 1 H, NH), 6.24 (d, *J* = 7.8 Hz, 1 H, ArH), 6.40 (s, 1 H, ArH), 6.74 (s, 1 H, ArH), 7.02 (d, *J* = 7.8 Hz, 1 H, ArH), 7.20 (s, 1 H, ArH) ppm. ^{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; ESI-MS: *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% yield) as a black solid, m.p. 98–100 °C. IR (KBr): ṽ = 1711 (CO_2Et), 1731 (CO_2Me), 3350 (NH) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.36 (t, *J* = 7.2 Hz, 3 H, CH_3CH_2), 3.81 (s, 3 H, CO_2CH_3), 4.26 (s, 2 H, CH_2CH_3), 5.35 (s, 1 H, NH), 6.32 (d, *J* = 7.9 Hz, 1 H, ArH), 6.44 (s, 1 H, ArH), 6.79–6.80 (m, 2 H, ArH), 7.05–7.10 (m, 1 H, ArH), 7.32 (s, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: *m*/*z* = 274.1 $[M + 1]^+$.

4-(*tert*-Butyl) 2-Methyl 1*H*-1-Benzazepine-2,4-dicarboxylate (12a): 0.48 g (45% yield) as a black oil. IR (neat): ṽ = 1706 (CO_2tBu), 1722 (CO_2Me), 3424 (NH) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.55 [s, 9 H, $C(CH_3)_3$], 3.79 (s, 3 H, CO_2CH_3), 5.36 (s, 1 H, NH), 6.33 (d, *J* = 7.8 Hz, 1 H, ArH), 6.45 (s, 1 H, ArH), 6.74 (s, 1 H, ArH), 6.79–6.81 (m, 2 H, ArH), 7.05–7.09 (m, 1 H, ArH), 7.26 (s, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: *m*/*z* = 302.0 $[M + 1]^+$.

Diethyl 1*H*-1-Benzazepine-2,4-dicarboxylate (13a): 0.38 g (62% yield) as a black oil. IR (neat): ṽ = 1714 (CO_2Et), 3352 (NH) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28–1.36 (m, 6 H, $2\times CH_3CH_2$), 4.22–4.29 (m, 4 H, $2\times CH_2CH_3$), 5.38 (s, 1 H, NH), 6.32 (d, *J* = 7.9 Hz, 1 H, ArH), 6.44 (s, 1 H, ArH), 6.78–6.80 (m, 2 H, ArH), 7.05–7.10 (m, 1 H, ArH), 7.35 (s, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: *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% yield) as a black oil. IR (neat): ṽ = 1738 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.24 (s, 2 H, CH_2), 3.88 (s, 3 H, CO_2CH_3), 3.95 (s, 3 H, CO_2CH_3), 6.10 (s, 2 H, OCH_2O), 6.91 (s, 1 H, ArH), 7.06 (s, 1 H, ArH), 7.73 (s, 1 H, =CH) ppm. ^{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 ppm. ESI-MS: *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 (7% yield) as a yellow oil. IR (neat): ṽ = 1732 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.26 (s, 2 H, CH_2), 3.87 (s, 3 H, CO_2CH_3), 3.95 (s, 3 H, CO_2CH_3), 3.96 (s, 6 H, $2\times OCH_3$), 4.05 (s, 2 H, CH_2), 6.91 (s, 1 H, ArH), 7.11 (s, 1 H, ArH), 7.79 (s, 1 H, =CH) ppm. ^{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 ppm. ESI-MS: *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 that heating was continued for 12 h.

Methyl 2-Methyl-3*H*-1-benzazepine-4-carboxylate (25a): 0.63 g (58% yield) as a brown oil. IR (neat): ṽ = 1733 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 2.87 (s, 2 H, CH_2), 3.88 (s, 3 H, CO_2CH_3), 7.22–7.25 (m, 1 H, ArH), 7.41–7.48 (m, 3 H, ArH), 7.79 (s, 1 H, =CH) ppm. ^{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 ppm. ESI-MS: *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% yield) as a yellow oil. IR (neat): ṽ = 1723 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.34 (s, 3 H, CH_3), 2.84 (s, 2 H, CH_2), 3.93 (s, 3 H, CO_2CH_3), 6.00 (s, 2 H, OCH_2O), 6.76 (s, 1 H, ArH), 6.84 (s, 1 H, ArH), 7.48 (s, 1 H, =CH) ppm. ^{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 ppm. ESI-MS: *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% yield) as a brown oil. IR (neat): ṽ = 1728 (CO_2Me) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3 H, CH_3), 2.84 (s, 2 H, CH_2), 3.85 (s, 3 H, CO_2CH_3), 3.91 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 6.84 (s, 1 H, ArH), 6.92 (s, 1 H, ArH), 7.70 (s, 1 H, =CH) ppm. ^{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 ppm. ESI-MS: *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% yield) as a yellow oil. IR (neat): ṽ = 1703 (CO_2Et) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.2 Hz, 3 H, CH_3CH_2), 2.35 (s, 3 H, CH_3), 2.85 (s, 2 H, CH_2), 4.33 (q, *J* = 7.2 Hz, 2 H, CH_2CH_3), 7.19–7.24 (m, 1 H, ArH), 7.41–7.48 (m, 3 H, ArH), 7.78 (s, 1 H, =CH) ppm. ^{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 ppm. ESI-MS: *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% yield) as a yellow oil. IR (neat): ṽ = 1713 (CO_2Et) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.44 (d, *J* = 6.7 Hz, 3 H, CH_3CH), 2.86 (dd, *J* = 5.7 Hz, *J* = 5.8 Hz, 1 H, 1H of CH_2CH), 3.21 (dd, *J* = 8.3 Hz, *J* = 7.9 Hz, 1 H, 1H of CH_2CH), 4.31 (q, *J* = 7.2 Hz, 2 H, CH_2CH_3), 4.85–4.92 (m, 1 H, $CHNO_2$), 6.72–6.81

(m, 2 H, ArH), 6.98 (d, J = 7.5 Hz, 1 H, ArH), 7.14–7.20 (m, 1 H, ArH), 7.78 (s, 1 H, =CH) ppm. ^{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 ppm. ESI-MS: m/z = 279.2 $[M + 1]^+$. $C_{14}H_{18}N_2O_4$ (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, 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 °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. Upon completion (monitored by TLC), the mixture was extracted with water and dichloromethane. The organic layer was separated and dried (Na_2SO_4), and the solvents were evaporated to dryness to yield the crude product, which was purified by silica gel column chromatography with hexane/EtOAc (70:30, v/v) to yield 0.16 g (92%) of pure product **15** as a pale yellow solid.

Dimethyl 1-Acetyl-1*H*-1-benzazepine-2,4-dicarboxylate (15, rotamer ratio of 1:2, as evident from ^{1}H NMR): M.p. 144–146 °C. IR (KBr): $\tilde{\nu}$ = 1710 (COMe), 1735 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85 (s, 3 H, $OCOCH_3$), 2.05 (s, 3 H, $OCOCH_3$), 3.85 (s, 3 H, CO_2CH_3), 3.89 (s, 3 H, CO_2CH_3), 3.90 (s, 3 H, CO_2CH_3), 3.92 (s, 3 H, CO_2CH_3), 7.39–7.57 (m, 6 H, 2 × 3ArH), 7.62–7.68 (m, 2 H, 2 × 1ArH), 7.68 (s, 1 H, ArH), 7.78 (s, 1 H, ArH), 8.21 (s, 1 H, ArH), 8.30 (s, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: m/z = 302.0 $[M + 1]^+$. HRMS (EI): 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 of 1:2, as evident from ^{1}H NMR): 0.13 g (96% yield) as an off-white solid, m.p. 164–166 °C. IR (KBr): $\tilde{\nu}$ = 1707 (COPh), 1738 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.93 (s, 3 H, CO_2CH_3), 3.96 (s, 3 H, CO_2CH_3), 4.11 (s, 3 H, CO_2CH_3), 4.14 (s, 3 H, CO_2CH_3), 7.11–7.26 (m, 8 H, 2 × 4ArH), 7.27–7.38 (m, 8 H, 2 × 4ArH), 7.44–7.46 (m, 1 H, ArH), 7.52–7.55 (m, 1 H, ArH), 7.68 (s, 1 H, ArH), 7.73 (s, 1 H, ArH), 8.35 (s, 1 H, ArH), 8.40 (s, 1 H, ArH) ppm. ^{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 ppm. FAB-MS: m/z = 364 $[M + 1]^+$. HRMS (EI): Calcd. for $C_{21}H_{17}NO_5$ 363.1107; found 363.1105.

General Procedure for the Preparation of Compounds 17a–b,18–20a, 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 a UV lamp (Philips, 500 W flash light) for 6 h. The silica gel was transferred to a column, and elution with hexane/EtOAc (80:20, v/v) yielded 0.15 g (80%) of pure **17a** as an off-white solid.

Dimethyl Isoquinoline-1,3-dicarboxylate (17a): Mp 118–120 °C. IR (KBr): $\tilde{\nu}$ = 1742 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.09 (s, 3 H, CO_2CH_3), 4.13 (s, 3 H, CO_2CH_3), 7.79–7.89 (m, 2 H, ArH), 8.39 (d, J = 8.4 Hz, 1 H, ArH), 8.71 (s, 1 H, ArH), 8.87 (d, J = 8.4 Hz, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: m/z = 246.0 $[M + 1]^+$. HRMS (EI): Calcd. for $C_{13}H_{11}NO_4$ 245.0688; found 245.0687.

Dimethyl 6-Chloroisoquinoline-1,3-dicarboxylate (17b): 0.14 g (75% yield) as a yellow oil. IR (neat): $\tilde{\nu}$ = 1732 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (s, 3 H, CO_2CH_3), 4.06 (s, 3 H, CO_2CH_3), 7.78 (d, J = 8.0 Hz, 1 H, ArH), 8.02 (s, 1 H, ArH), 8.70 (s, 1 H, ArH), 8.89 (d, J = 8.0 Hz, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: m/z = 280.1 $[M + 1]^+$. HRMS (EI): Calcd. for $C_{13}H_{10}ClNO_4$ 279.0298; found 279.0296.

3-Ethyl 1-Methyl Isoquinoline-1,3-dicarboxylate (18a): 0.212 (78% yield) as a pale yellow solid, m.p. 85–87 °C, IR (KBr): $\tilde{\nu}$ = 1712 (CO_2Et), 1740 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.51 (t, J = 7.2 Hz, 3 H, CH_3CH_2), 4.13 (s, 3 H, CO_2CH_3), 4.56 (q, J = 7.2 Hz, 2 H, CH_2CH_3), 7.78–7.87 (m, 2 H, ArH), 8.37–8.40 (m, 1 H, ArH), 8.69 (s, 1 H, ArH), 8.83 (d, J = 1.2 Hz, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: m/z = 260.0 $[M + 1]^+$. HRMS (EI): Calcd. for $C_{14}H_{13}NO_4$ 259.0845; found 259.0847.

Diethyl Isoquinoline-1,3-dicarboxylate (19a): 0.29 (82% yield) as a pale yellow oil, IR (neat): $\tilde{\nu}$ = 1723 (CO_2Et) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.46–1.55 (m, 6 H, 2 × CH_3CH_2), 4.49–4.64 (m, 4 H, 2 × CH_2CH_3), 7.74–7.88 (m, 2 H, ArH), 8.39 (d, J = 8.2 Hz, 1 H, ArH), 8.66 (s, 1 H, ArH), 8.84 (d, J = 8.2 Hz, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: m/z = 274.1 $[M + 1]^+$. HRMS (EI): Calcd. for $C_{15}H_{15}NO_4$ 273.1001; found 273.1002.

3-(*tert*-Butyl) 1-Methyl Isoquinoline-1,3-dicarboxylate (20a): 0.40 g (77% yield) as a pale yellow oil, IR (neat): $\tilde{\nu}$ = 1703 (CO_2tBu), 1733 (CO_2Me) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71 [s, 9 H, $C(CH_3)_3$], 4.12 (s, 3 H, CO_2CH_3), 7.34–7.87 (m, 2 H, ArH), 8.36 (d, J = 8.1 Hz, 1 H, ArH), 8.56 (s, 1 H, ArH), 8.73 (d, J = 8.1 Hz, 1 H, ArH) ppm. ^{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 ppm. ESI-MS: m/z = 287.9 $[M + 1]^+$. HRMS (EI): Calcd. for $C_{16}H_{17}NO_4$ 287.0058; found 287.0059.

Supporting Information (see also the footnote on the first page of this article): Copies of ^{1}H NMR, ^{13}C NMR, and mass spectra of several new compounds are being provided. Copies of HSQC and HMBC spectra for compound **18a** is also provided.

Acknowledgments

One of the authors (V. S.) acknowledges the financial support from the Department of Science and Technology (DST), New Delhi, in the form of a fellowship. This work was supported by a financial grant from DST. The authors acknowledge Dr. R. Roy and Dr. A. Arora for carrying out the NOESY, HMBC, and HSQC experiments.

---

[1] D. Basavaiah, A. Jaganmohan Rao, T. Satyanarayana, *Chem. Rev.* **2003**, *103*, 811–890.

[2] T. P. Majhi, A. Neogi, S. Ghosh, A. K. Mukherjee, P. Chattopadhyay, *Tetrahedron* **2006**, *62*, 12003–12010.

[3] R. Rios, H. Sunden, I. Ibrahem, G.-L. Zhao, A. Cordova, *Tetrahedron Lett.* **2006**, *47*, 8679–8682.

[4] F. Coelho, D. Veronese, C. H. Pavam, V. I. de Paula, R. Buffon, *Tetrahedron* **2006**, *62*, 4563–4572.

[5] S. Chandrasekhar, D. Basu, Ch. Rambabu, *Tetrahedron Lett.* **2006**, *47*, 3059–3063.

[6] G. W. Kabalka, B. Venkataiah, C. Chen, *Tetrahedron Lett.* **2006**, *47*, 4187–4189.

[7] L. Jean, A. Marinetti, *Tetrahedron Lett.* **2006**, *47*, 2141–2145.

[8] P. Wasnaire, M. Wiaux, R. Touillaux, I. E. Marko, *Tetrahedron Lett.* **2006**, *47*, 985–989.

[9] J. Jayashankaran, R. Durga, R. S. Manian, M. Sivaguru, R. Raghunathan, *Tetrahedron Lett.* **2006**, *47*, 5535–5538.

[10] D. Basavaiah, R. J. Reddy, J. S. Rao, *Tetrahedron Lett.* **2006**, *47*, 73–77.

[11] V. Singh, R. Saxena, S. Batra, *J. Org. Chem.* **2005**, *70*, 353–356.

[12] R. Pathak, A. K. Roy, S. Batra, *Synlett* **2005**, 848–850.

[13] V. Singh, S. Batra, *Synthesis* **2006**, 63–72.

[14] S. Nag, R. Pathak, M. Kumar, P. K. Shukla, S. Batra, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3824–3828.

[15] V. Singh, G. P. Yadav, P. R. Maulik, S. Batra, *Tetrahedron* **2006**, *62*, 8731–8739.

[16] R. Pathak, S. Nag, S. Batra, *Synthesis* **2006**, 4205–4211.

[17] R. Pathak, S. Madapa, S. Batra, *Tetrahedron* **2007**, *63*, 451–460.

[18] S. Madapa, V. Singh, S. Batra, *Tetrahedron* **2006**, *62*, 8740–8747.

[19] V. Singh, S. Batra, *Tetrahedron Lett.* **2006**, *47*, 7043–7045.

[20] V. Singh, S. Kanojiya, S. Batra, *Tetrahedron* **2006**, *62*, 10100–10110.

[21] R. D. Fabio, F. Micheli, D. Baraldi, B. Bertani, N. Conti, G. D. Forno, A. Feriani, D. Donati, C. Marchioro, T. Messeri, A. Missio, A. Pasquarello, G. Pentassuglia, D. A. Pizzi, S. Provera, A. M. Quaglia, F. M. Sabbatini, *Il Farmaco* **2003**, *58*, 723–738.

[22] Y. Aramaki, M. Seto, T. Okawa, T. Oda, N. Kanazaki, M. Shiraishi, *Chem. Pharm. Bull.* **2004**, *52*, 254–258.

[23] M. Seto, N. Miyamoto, K. Aikawa, Y. Aramaki, N. Kanazaki, Y. Iizawa, M. Baba, M. Shiraishi, *Bioorg. Med. Chem.* **2005**, *13*, 363–368.

[24] J. R. Szewczyk, K. H. Donaldson, US Patent 2006003991, **2006**.

[25] H. J. Teuber, G. Emmerich, *Tetrahedron Lett.* **1970**, *11*, 4069–4070.

[26] V. N. Gogte, K. M. More, B. D. Tilak, *Ind. J. Chem.* **1974**, *12*, 1238–1241.

[27] E. Gonzalez, *Bull. Chem. Soc. Fr.* **1993**, *130*, 143–145.

[28] J. S. Yadav, B. V. Subba Reddy, M. K. Gupta, A. Prabhakar, B. Jagadeesh, *Chem. Commun.* **2004**, 2124–2125.

[29] W. M. Abdou, A. A. Kamel, M. D. Khidre, *Synth. Commun.* **2004**, *34*, 4119–4134.

[30] W. M. Abdou, N. A. Ganoub, A. F. Fahmy, A. M. Shaddy, *Heteroat. Chem.* **2005**, *16*, 56–64.

[31] G. V. Garner, O. Meth-Cohn, H. Suschitzky, *J. Chem. Soc., C* **1971**, 1234–1236.

[32] B. Kharraz, P. Uriac, S. Sinbandhit, L. Toupet, *Tetrahedron* **1996**, *52*, 4423–4434.

[33] T. A. Geissman, A. K. Cho, *J. Org. Chem.* **1959**, *24*, 41–43.

[34] K. Y. Lee, S. Gowrisankar, Y. J. Lee, J. N. Kim, *Tetrahedron* **2006**, *62*, 8798–8804 and references cited therein.

[35] J. N. Kim, Y. J. Im, J. H. Gong, K. Y. Lee, *Tetrahedron Lett.* **2001**, *42*, 4195–4197.

Received: February 25, 2007