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Studies on the reduction of the nitro group in 3-aryl-2-methylene-4-nitro-alkanoates afforded by the Baylis–Hillman adducts: synthesis of 4-aryl-3-methylene-2-pyrrolidinones and 3-(1-alkoxycarbonyl-vinyl)-1*H*-indole-2-carboxylates☆

Vijay Singh,[a] Sanjeev Kanojiya[b] and Sanjay Batra[a,*]

[a]*Medicinal Chemistry Division, Central Drug Research Institute, PO Box 173, Lucknow 226001, Uttar Pradesh, India*
[b]*SAIF Division, Central Drug Research Institute, PO Box 173, Lucknow 226001, Uttar Pradesh, India*

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Abstract—The formation of substituted 2-pyrrolidinones and indoles by the reduction of the secondary nitro group in appropriate 3-aryl-2-methylene-4-nitroalkanoates afforded by Baylis–Hillman chemistry via different reducing agents is described. The 3-aryl-2-methylene-4-nitroalkanoate obtained from S_N2 nucleophilic reaction between the acetate of Baylis–Hillman adducts and ethyl nitroacetate upon reduction with indium–HCl furnishes a mixture of cis and trans substituted phenyl-3-methylene-2-pyrrolidinones. In contrast, similar reductions of analogous substrates derived from nitroethane stereoselectively furnished only the trans substituted phenyl-3-methylene-2-pyrrolidinones. On the other hand the $SnCl_2\cdot 2H_2O$-promoted reductions of substrates derived from nitro ethylacetate give oxime derivatives while the ones obtained from nitroethane yield a mixture of *cis* and *trans* 4-aryl-3-methylene-2-pyrrolidinones. Alternatively, the $SnCl_2\cdot 2H_2O$-promoted reduction of substituted 2-nitrophenyl-2-methylene-alkanoate furnished from ethyl nitroacetate yield 3-(1-alkoxycarbonyl-vinyl)-1*H*-indole-2-carboxylate while indium-promoted reaction of this substrate leads to a complex mixture. Analogous reactions with $SnCl_2\cdot 2H_2O$ of substituted 2-nitrophenyl-2-methylene-alkanoate obtained from nitroethane yield 4-alkyl-3-methylene-2-quinolones in moderate yields.

1. Introduction

Nitrogen-heterocycles are structural units of several natural products and represent compounds of pharmacological significance. Their prevalence and medicinal utility perhaps are the major driving force for attracting organic and medicinal chemists to formulate their diverse syntheses via novel, convenient, and efficient methods. The propensity of the Baylis–Hillman reaction to afford products with multifunctional backbone, which could be tailored further, has found profound application toward the construction of an array of useful synthons, heterocycles, and natural products.[1] In order to expand the synthetic utility of this reaction, for the last couple of years our group has been involved in a program to carry out convenient and efficient syntheses of diverse heterocyclic systems utilizing the Baylis–Hillman chemistry.[2,3] Based on our previous work in this area and on the results reported by Janecki et al.[4] and Yus et al.[5] we reasoned that the 3-aryl-2-methylene-4-nitroalkanoates, obtained by S_N2 nucleophilic reaction of the acetate of the Baylis–Hillman products with nitroalkanes, should in principle offer opportunities for constructing highly substituted 3-methylene-2-pyrrolidinones provided the nitro group is chemoselectively reduced and the resulting amine could be made to undergo intramolecular cyclization. Recently, Kim and co-workers have reported the synthesis of 2-amino-2,3-dihydrobenzofuran derivatives via oxidation of similar nitro compounds afforded via S_N2' reaction of ethyl nitroacetate on the allyl bromides afforded by the Baylis–Hillman adducts.[6] In addition, several groups have accomplished the facile synthesis of different heterocyclic compounds employing nitro derivatives afforded via Baylis–Hillman adducts.[7,8] In order to investigate our envisaged strategy, we have carried out selective reduction of the nitro group in nitroalkanoates with In to afford the 4-aryl-3-methylene-2-pyrrolidinones in good yields. Interestingly, we have observed that reduction of the secondary nitro group via $SnCl_2\cdot 2H_2O$ in these compounds occurs only partially leading to the oxime derivatives. This unique observation has led us to formulate a simple synthesis of substituted indoles from the nitroalkanoates obtained from the Baylis–Hillman adducts of 2-nitrobenzaldehyde. The details of the results of our studies are described herein.

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Keywords: Baylis–Hillman; Nitroalkanoate; 2-Pyrrolidinone; 1*H*-Indole-2-carboxylate; Indium; $SnCl_2\cdot 2H_2O$.

* Corresponding author. Tel.: +91 522 2262411/18×4368; fax: +91 522 2623405/2623938; e-mail: batra_san@yahoo.co.uk

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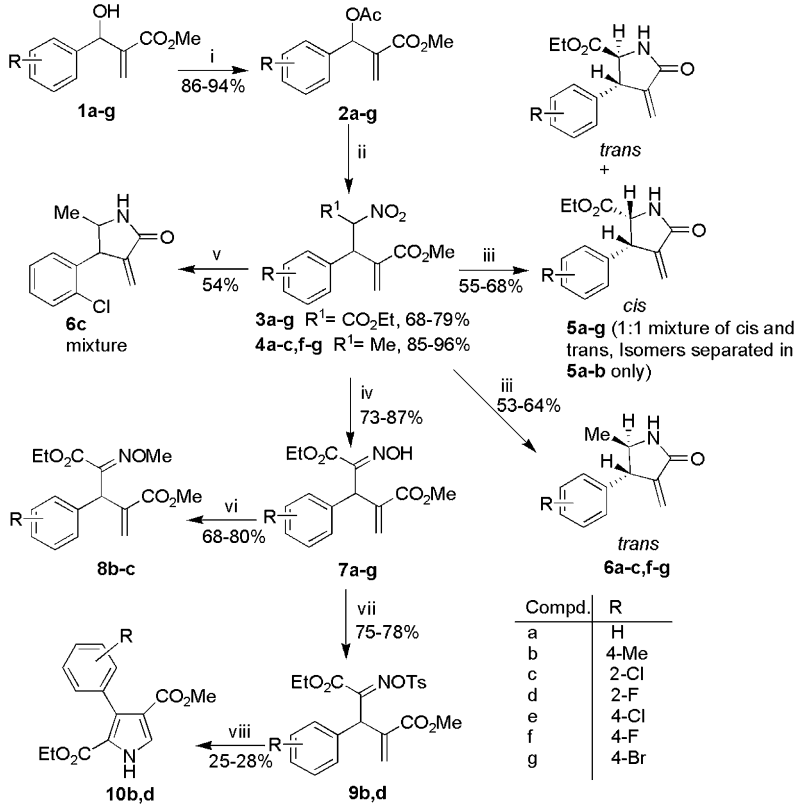
2. Results and discussion

The preparation of the starting materials in our synthetic sequence (Scheme 1), the acetates **2a–g**, was accomplished by acetylating Baylis–Hillman adducts **1a–g**, which in turn were afforded from substituted benzaldehydes following the literature procedure.[9] The S_N2 nucleophilic substitution of the acetate **2a–g** with ethyl nitroacetate in the presence of DABCO in a THF–water system yielded the nitroalkanoates **3a–g** in 4–6 h in 68–79% yields as diastereoisomeric mixtures. This observation is in contrast to the reactions carried out by Kim et al. who have reported the synthesis of similar derivatives after 2 days.[10] In the next step the products **3a–g** were subjected to chemoselective reduction of the nitro group without affecting the double bond. In a model reaction, the reduction of the nitro group of compound **3b** was examined with metallic In, Sn, Zn, and Fe in the presence of HCl or AcOH and $SnCl_2\cdot 2H_2O$.[11] The selection of these reagents was based on the fact that they are inexpensive, readily available, and do not require any elaborate reaction conditions. Results of our evaluation in this direction are illustrated in Table 1. The highest yield of the expected substituted 3-methylene-2-pyrrolidinone **4b** was achieved when the reaction was carried out in the presence of In using HCl in a THF–H_2O system at room temperature. Consequently all the substituted 3-methylene-2-pyrrolidinones **5a–g** were prepared by reducing the required nitro compound with In in the presence of aq HCl. In all cases these compounds were obtained as a mixture of cis and trans products. Our attempts to separate these diastereoisomers via silica gel column chromatography were successful with compounds **5a** and **5b**, whereas for compounds **5c–g** these could not be separated. The NOESY experiment of the polar isomer of compound **5b** indicated it to be the trans isomer.

Table 1. Results of optimization study for the synthesis of 4-aryl-3-methylene-2-pyrrolidinones

Entry	Metal/ metal salt	Condition	Product	Yield (%)
1	In	In/HCl in THF–H_2O for 2 h at rt	**5b**	64
2	Sn	Sn/HCl for 2 h at reflux	**5b**	42
3	Zn	Zn/HCl in EtOH for 24 h at rt	**5b**	39
4	Fe	Fe/AcOH for 2 h at rt	**5b**	45
5	$SnCl_2\cdot 2H_2O$	$SnCl_2\cdot 2H_2O$ in MeOH for 2 h at reflux	**7b**	78

However the reduction of compound **3b** with $SnCl_2\cdot 2H_2O$, instead of yielding the expected pyrrolidinone **5b**, gave the oxime **7b** (entry 5, Table 1). This was found to be the general course of reaction as substrates **3a–g** also furnished the corresponding oximes **7a–g** when subjected to the $SnCl_2$ reductive conditions. The spectroscopic data supported the structure assignments. Further support for the assigned structures of the oximes was made on the basis of an alternate synthesis. It is reported in the literature that the tin complexes generated from $SnCl_2\cdot 2H_2O$ in the presence of thiophenol and triethylamine reduces secondary aliphatic nitro compound to the corresponding oxime.[12] On the basis of this report, the compound **3a** was treated with $SnCl_2\cdot 2H_2O$, thiophenol, and triethylamine to yield a product, which was similar in all respect to the oxime **7a**. As would be expected,



Scheme 1. Reagents and conditions: (i) AcCl, Pyridine, CH_2Cl_2, rt, 3 h; (ii) DABCO, $R^1CH_2NO_2$, THF–H_2O, rt, 4–7 h; (iii) In, HCl, THF–H_2O, rt, 2 h; (iv) $SnCl_2\cdot 2H_2O$, MeOH, reflux, 1.5 h; (v) $SnCl_2\cdot 2H_2O$, MeOH, reflux, 24 h; (vi) MeI, Ag_2O, neat, reflux, 1 h; (vii) TsCl, Et_3N, CH_2Cl_2, rt, 3 h; and (viii) DBU, CH_2Cl_2, rt, 330 min.

the methylation of the oximes **7b**, **c** using methyl iodide in the presence of silver oxide furnished the methyl derivatives **8b**, **c**.[13] Although, the $SnCl_2\cdot 2H_2O$-promoted reduction of nitroalkenes to the corresponding oximes is documented,[14] the ability of $SnCl_2\cdot 2H_2O$ alone to transform the secondary aliphatic nitro compound to the oxime derivative is unreported.

The next phase of the study was aimed at determining the driving force responsible for the formation of the oximes. One possibility was the presence of the carboethoxy group on the α-carbon of the nitroalkane derivative as illustrated in Figure 1. In order to validate this concept experimentally, the S_N2 reaction of acetates **2a**–**c**, **f**, **g** with nitroethane in the presence of DABCO in a THF–H_2O system to afford products **4a**–**c**, **f**, **g** was accomplished. The nitro group in compound **4c** in the presence of $SnCl_2\cdot 2H_2O$ underwent reduction followed by cyclization to give 3-methylene-2-pyrrolidinones **6c** as a diastereoisomeric mixture, although the reaction took more than 24 h for completion. This supported our assumption that the presence of carboethoxy group was responsible for the formation of the oxime probably by the formation of an oximino intermediate. In order to establish that oxime was not the intermediate for the pyrrolidinone, in a model reaction the oxime **7c** was treated with $SnCl_2\cdot 2H_2O$ for more than 24 h. But this reaction failed indicating that the presence of the ester moiety stabilizes the oximes. Nevertheless, the reduction of the nitro group in compounds **4a**–**c**,**f**, **g** in the presence of In was complete in 2 h in a highly diastereoselective fashion to furnish the trans isomer of 4-aryl-5-methyl-3-methylene-2-pyrrolidinones **6a**–**c**, **f**, **g** exclusively in 53–64% yields.

Of particular relevance to **7**, it has been very recently reported that oximes obtained from α-aryl ketones can be transformed to indoles by an intermediate azirine in two steps.[15] In order to investigate such possibility with the oxime **7** generated during the present study, compounds **7b**, **d** were treated with tosyl chloride in the presence of triethylamine in dichloromethane at room temperature to yield the corresponding tosyl derivatives **9b**, **d**. Reaction of compounds **9b**, **d** with DBU in dichloromethane gave a complex mixture of products. The column chromatography of this mixture led to isolation of a pure product in low yield, the structure of which was established as substituted pyrroles **10a**, **d**. The formation of the pyrroles can be explained on the basis of the mechanism as shown in Figure 2.

Having demonstrated the utility of substrates such as **3a**–**g** and **4a**–**c**, **f**, **g** for the generation of the 3-methylene-2-pyrrolidinone system and oximes via selective reduction, we decided to explore the synthetic utility of similar substrates derived from 2-nitrophenyl benzaldehyde, such as **11a**–**c** (Scheme 2) for the following reasons. It is well established that the Baylis–Hillman derivatives obtained from 2-nitrobenzaldehyde and acrylates, upon reduction of the nitro moiety to amine invariably results in the formation of quinoline derivatives through an in situ intramolecular cyclization between the amino group on the phenyl ring and the ester group of the side chain.[16] However, in view of the findings of the present study, if compounds **11a**–**c** and **12** are reduced in the presence of $SnCl_2\cdot 2H_2O$, the aromatic nitro group will be chemoselectively reduced to an amino group, which will then compete for the two ester moieties for the intramolecular cyclization. Consequently compound **11a** was synthesized and reacted with $SnCl_2\cdot 2H_2O$ in methanol under reflux conditions. This reaction proceeded smoothly to be completed in 1.5 h to give a product, the structure of which was established as substituted 3-(1-methoxycarbonyl-vinyl)-1*H*-indole-2-carboxylic acid ethyl ester **14a** (Scheme 2). Subsequently other analogs **11b**, **c** and **12** were prepared and subjected to reaction with $SnCl_2\cdot 2H_2O$.

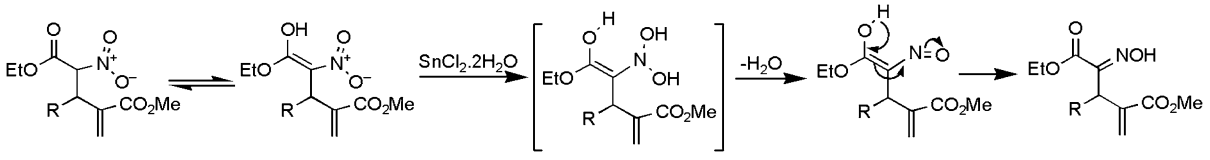


Figure 1. Mechanism for the formation of oximes.

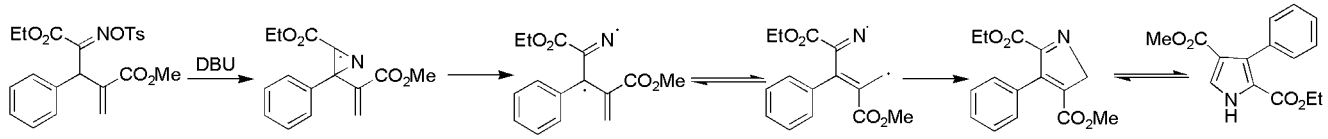
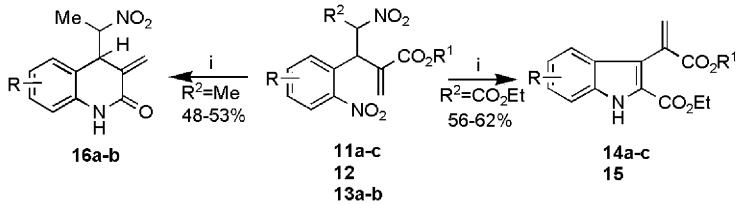


Figure 2. Mechanism for the formation of pyrroles.



Compd.	R	R^1
11a	H	Me
11b	3,4-OCH_2O	Me
11c	5-Cl	Me
12	H	Et
13a	H	Me
13b	5-Cl	Me

Scheme 2. Reagents and conditions: (i) $SnCl_2\cdot 2H_2O$, MeOH, reflux, 1.5–2 h.

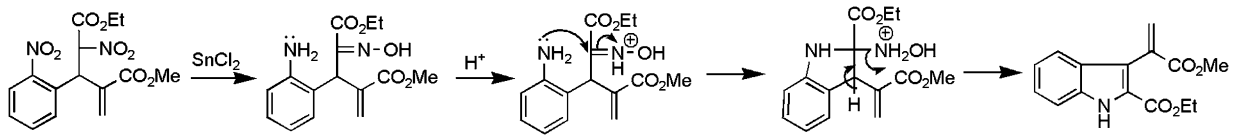


Figure 3. Mechanism for the formation of indole derivatives.

All these substrates afforded the respective indole derivatives **14b**, **c** and **15** indicating the general nature of this reaction and implying that this transformation invariably eliminates the aliphatic nitro group, presumably after reduction to the oxime. The expected mechanism for the formation of the indole derivative is shown in Figure 3. Unlike compounds **11** and **12**, compounds **13a**, **b** upon reduction in the presence of $SnCl_2 \cdot 2H_2O$ yielded the corresponding substituted 2-quinolones **16a**, **b** in 2 h in moderate yields. The formation of **16** was understandable since it has been previously observed that the aliphatic nitro group is reduced to an amino group only when the reaction is prolonged beyond 24 h. These results provoked us to evaluate the reactions of compounds **11** and **13a**, **b** with In in the presence of HCl in aqueous medium. However, this reaction led to a complex mixture, which could not be purified in all cases.

3. Conclusions

In summary, we demonstrated the scope of 3-aryl-2-methylene-4-nitroalkanoates obtained from the Baylis–Hillman chemistry for the generation of 4-aryl-3-methylene-2-pyrrolidinones and 3-(1-alkoxycarbonyl-vinyl)-1*H*-indole-2-carboxylates by the reduction of the secondary nitro group using different reducing conditions. The mechanistic details to account for the formation of different heterocyclic systems have also been proposed. All the synthetic achievements described herein were operationally simple and diversity oriented. We believe that the lactam and the indole derivatives described in this paper will serve as useful building blocks for the synthesis of compounds belonging to these classes.

4. Experimental

4.1. General

Melting points were recorded on a hot stage melting point apparatus and are uncorrected. The IR spectra were recorded on a FTIR spectrophotometer. The ^1H and ^{13}C NMR spectra were recorded on 200 MHz or 300 MHz spectrometer using TMS as an internal standard. The mass spectra were recorded as FAB or LCMS having ES probe. The HRMS spectra were recorded as EIHRMS. All the solvents and chemicals were used as procured from the suppliers. The compounds **3a–g**, **4a–c**, **f**, **g**, **5c–g**, **11a–c**, **12**, **13a**, **b**, and **16a**, **b** were obtained as diastereoisomeric mixtures. All yields indicated herein are the isolated yields after column chromatography.

4.2. General procedure for the preparation of compounds 3a–g and 4a–c, f, g

To the stirred solution of appropriate compound from **2a–g** (1.0 equiv) in THF–H_2O (10 mL for approx. 1.5 g of compound, 50:50, v/v) was added DABCO (1.5 equiv) at room temperature and the reaction was allowed to continue for 20 min. Thereafter ethyl nitroacetate or nitroethane (1.2 equiv) was added to the reaction mixture and the reaction was allowed to proceed at room temperature for 4 h. The THF was removed from the reaction mixture via rotary evaporation and the residue was diluted with water (100 mL) and extracted with EtOAc (3×40 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 chromatography employing hexane–EtOAc (80:20, v/v) to afford products as oils or solids.

4.2.1. 2-Methylene-4-nitro-3-phenylpentanedioic acid 5-ethyl ester 1-methyl ester (3a). Colorless oil 77% (1.0 g); ν_{max} (Neat) 1723 (CO_2Et), 1751 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=0.97 (t, 3H, J=7.1 Hz, CH_3CH_2), 1.27 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.71 (s, 3H, CO_2CH_3), 3.73 (s, 3H, CO_2CH_3), 3.99 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.26 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.89 (d, 1H, J=12.0 Hz, CHAr), 4.95 (d, 1H, J=12.0 Hz, CHAr), 5.80 (s, 1H, =CH), 5.86 (s, 1H, =CH), 5.87 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.05 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.34 (s, 1H, =CH), 6.38 (s, 1H, =CH), 7.28–7.30 (m, 10H, 2×5ArH); mass (ES+) m/z 330.0 (M^++Na); Anal. Calcd for $C_{15}H_{17}NO_6$: C, 58.63; H, 5.58; N, 4.56. Found: C, 58.38; H, 5.76; N, 4.64.

4.2.2. 2-Methylene-4-nitro-3-*p*-tolylpentanedioic acid 5-ethyl ester 1-methyl ester (3b). Colorless oil 68% (1.4 g); ν_{max} (Neat) 1724 (CO_2Et), 1751 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.00 (t, 3H, J=7.1 Hz, CH_3CH_2), 1.27 (t, 3H, J=7.1 Hz, CH_3CH_2), 2.30 (s, 6H, 2×$ArCH_3$), 3.70 (s, 3H, CO_2CH_3), 3.72 (s, 3H, CO_2CH_3), 4.01 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.25 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.85 (d, 1H, J=12.0 Hz, CHAr), 4.91 (d, 1H, J=12.0 Hz, CHAr), 5.79 (s, 1H, =CH), 5.83 (s, 1H, =CH), 5.82 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.02 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.32 (s, 1H, =CH), 6.35 (s, 1H, =CH), 7.08–7.22 (m, 8H, 2×4ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=13.9, 14.2, 21.4, 48.2, 48.6, 52.6, 63.3, 63.6, 90.1, 90.7, 125.6, 127.5, 128.2, 129.0, 129.9, 130.0, 132.2, 133.5, 138.3, 138.4, 139.0, 163.5, 163.7, 166.1; mass (ES+) m/z 344.0 (M^++Na); Anal. Calcd for $C_{16}H_{19}NO_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 59.48; H, 5.82; N, 4.26.

4.2.3. 3-(2-Chlorophenyl)-2-methylene-4-nitro-pentanedioic acid 5-ethyl ester 1-methyl ester (3c). Colorless oil 79% (2.5 g); ν_{max} (Neat) 1724 (CO_2Et), 1751 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.03 (t, 3H, J=7.1 Hz, CH_3CH_2), 1.27 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.71 (s, 3H, CO_2CH_3), 3.73 (s, 3H, CO_2CH_3), 4.05 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.24 (q, 2H, J=7.1 Hz, CH_2CH_3), 5.34 (d, 1H, J=12.1 Hz, CHAr), 5.40 (d, 1H, J=12.1 Hz, CHAr), 5.98 (s, 1H, =CH), 5.99 (s, 1H, =CH), 6.14

(d, 1H, J=12.1 Hz, $CHCO_2Et$), 6.31 (d, 1H, J=12.1 Hz, $CHCO_2Et$), 6.39 (s, 1H, =CH), 6.42 (s, 1H, =CH), 7.20–7.25 (m, 4H, ArH), 7.36–7.41 (m, 3H, ArH), 7.48–7.52 (m, 1H, ArH); mass (FAB+) m/z 342 (M^++1); Anal. Calcd for $C_{15}H_{16}ClNO_6$: C, 52.72; H, 4.72; N, 4.14. Found: C, 53.08; H, 4.93; N, 4.24.

4.2.4. 3-(2-Fluorophenyl)-2-methylene-4-nitro-pentanedioic acid 5-ethyl ester 1-methyl ester (3d). Colorless oil 73% (1.4 g from 1.5 g); ν_{max} (Neat) 1724 (CO_2Et), 1753 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.02 (t, 3H, J=7.1 Hz, CH_3CH_2), 1.28 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.72 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 4.04 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.28 (q, 2H, J=7.1 Hz, CH_2CH_3), 5.10–5.19 (m, 2H, CHAr), 5.92 (d, 1H, J=1.0 Hz, =CH), 5.95 (s, 1H, =CH), 6.08 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.23 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.38 (s, 1H, =CH), 6.41 (s, 1H, =CH), 7.03–7.39 (m, 8H, 2×4ArH); mass (ES+) m/z 326.4 (M^++1); Anal. Calcd for $C_{15}H_{16}FNO_6$: C, 55.38; H, 4.96; N, 4.31. Found: C, 55.89; H, 5.21; N, 4.52.

4.2.5. 3-(4-Chlorophenyl)-2-methylene-4-nitro-pentanedioic acid 5-ethyl ester 1-methyl ester (3e). Pale yellow solid 78% (1.23 g), mp 96–98 °C; ν_{max} (KBr) 1724 (CO_2Et), 1751 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.04 (t, 3H, J=7.1 Hz, CH_3CH_2), 1.26 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.71 (s, 3H, CO_2CH_3), 3.73 (s, 3H, CO_2CH_3), 4.04 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.26 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.86 (d, 1H, J=12.1 Hz, CHAr), 4.91 (d, 1H, J=12.1 Hz, CHAr), 5.81 (s, 1H, =CH), 5.86 (s, 1H, =CH), 5.87 (d, 1H, J=12.1 Hz, $CHCO_2Et$), 6.02 (d, 1H, J=12.1 Hz, $CHCO_2Et$), 6.35 (s, 1H, =CH), 6.38 (s, 1H, =CH), 7.24–7.38 (m, 8H, 2×4ArH); mass (FAB+) m/z 342 (M^++1); Anal. Calcd for $C_{15}H_{16}ClNO_6$: C, 52.72; H, 4.72; N, 4.14. Found: C, 53.28; H, 4.54; N, 4.35.

4.2.6. 3-(4-Fluorophenyl)-2-methylene-4-nitro-pentanedioic acid 5-ethyl ester 1-methyl ester (3f). Pale yellow solid 72% (1.56 g), mp 82–84 °C; ν_{max} (KBr) 1723 (CO_2Et), 1750 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.00 (t, 3H, J=7.1 Hz, CH_3CH_2), 1.27 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.72 (s, 3H, CO_2CH_3), 3.73 (s, 3H, CO_2CH_3), 4.03 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.26 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.85 (d, 1H, J=12.0 Hz, CHAr), 4.98 (d, 1H, J=12.0 Hz, CHAr), 5.80 (s, 1H, =CH), 5.86 (s, 1H, =CH), 5.87 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.01 (d, 1H, J=12.0 Hz, $CHCO_3Et$), 6.35 (s, 1H, =CH), 6.38 (s, 1H, =CH), 6.96–7.04 (m, 4H, 2×2ArH), 7.21–7.30 (m, 4H, 2×2ArH); mass (FAB+) m/z 326 (M^++1); Anal. Calcd for $C_{15}H_{16}FNO_6$: C, 55.38; H, 4.96; N, 4.31. Found: C, 55.98; H, 5.11; N, 4.52.

4.2.7. 3-(4-Bromophenyl)-2-methylene-4-nitro-pentanedioic acid 5-ethyl ester 1-methyl ester (3g). Colorless oil 72% (1.5 g); ν_{max} (Neat) 1721 (CO_2Et), 1750 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.04 (t, 3H, J=7.1 Hz, CH_3CH_2), 1.26 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.71 (s, 3H, CO_2CH_3), 3.73 (s, 3H, CO_2CH_3), 4.05 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.26 (q, 2H, J=7.1 Hz, CH_2CH_3), 4.85 (d, 1H, J=12.0 Hz, CHAr), 4.89 (d, 1H, J=12.0 Hz, CHAr), 5.81 (s, 1H, =CH), 5.86 (s, 1H, =CH), 5.87 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.02 (d, 1H, J=12.0 Hz, $CHCO_2Et$), 6.34 (s, 1H, =CH), 6.38 (s, 1H, =CH), 7.14–7.22 (m, 4H, 2×2ArH), 7.42–7.57 (m, 4H, 2×2ArH); mass (ES+) m/z 386.2 (M^++1); Anal. Calcd for $C_{15}H_{16}BrNO_6$: C, 46.65; H, 4.18; N, 3.63. Found: C, 46.98; H, 4.25; N, 3.71.

4.2.8. 2-Methylene-4-nitro-3-phenylpentanoic acid methyl ester (4a). Colorless oil 96% (2.35 g); ν_{max} (Neat) 1721 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.40 (d, 3H, J=6.6 Hz, CH_3CH), 1.61 (d, 3H, J=6.6 Hz, CH_3CH), 3.73 (s, 6H, CO_2CH_3), 4.37 (d, 1H, J=12.0 Hz, CHAr), 4.44 (d, 1H, J=12.0 Hz, CHAr), 5.19–5.28 (m, 1H, $CHCH_3$), 5.42–5.60 (m, 1H, $CHCH_3$), 5.81 (s, 1H, =CH), 5.91 (d, 1H, J=1.8 Hz, =CH), 6.34 (s, 1H, =CH), 6.36 (s, 1H, =CH), 7.28–7.35 (m, 10H, 2×5ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=19.3, 19.5, 51.5, 52.5, 52.7, 85.5, 86.0, 125.2, 128.0, 128.2, 129.1, 129.4, 131.1, 137.8, 139.6, 139.9, 166.3, 166.6; mass (ES+) m/z 272.1 (M^++Na); Anal. Calcd for $C_{13}H_{15}F_3NO_5$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.97; H, 5.99; N, 5.53.

4.2.9. 2-(2-Nitro-1-*p*-tolylpropyl)-acrylic acid methyl ester (4b). Colorless oil 88% (0.73 g); ν_{max} (Neat) 1721 (CO_2Me) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=1.42 (d, 3H, J=6.0 Hz, CH_3CH), 1.62 (d, 3H, J=6.0 Hz, CH_3CH), 2.30 (s, 3H, $ArCH_3$), 2.34 (s, 3H, $ArCH_3$), 3.70 (s, 3H, CO_2CH_3), 3.75 (s, 3H, CO_2CH_3), 4.36 (d, 1H, J=12.0 Hz, CHAr), 4.43 (d, 1H, J=12.0 Hz, CHAr), 5.19–5.25 (m, 1H, $CHCH_3$), 5.44–5.50 (m, 1H, $CHCH_3$), 5.81 (s, 1H, =CH), 5.91 (d, 1H, J=3.0 Hz, =CH), 6.34 (s, 1H, =CH), 6.36 (s, 1H, =CH), 7.09–7.20 (m, 8H, 2×2ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=19.3, 19.5, 21.4, 51.2, 52.4, 52.5, 52.6, 85.6, 86.1, 125.0, 127.7, 128.3, 129.0, 130.1, 134.0, 134.8, 137.9, 138.1, 139.8, 140.0, 166.4, 166.7; mass (ES+) m/z 286.1 (M^++Na); Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 64.23; H, 6.89; N, 5.21.

4.2.10. 3-(2-Chlorophenyl)-2-methylene-4-nitro-pentanoic acid methyl ester (4c). Pale yellow oil 85% (1.8 g); ν_{max} (Neat) 1726 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.45 (d, 3H, J=6.6 Hz, CH_3CH), 1.63 (d, 3H, J=6.6 Hz, CH_3CH), 3.68 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 4.93 (d, 1H, J=11.0 Hz, CHAr), 5.08 (d, 1H, J=11.0 Hz, CHAr), 5.21–5.28 (m, 1H, $CHCH_3$), 5.64–5.73 (m, 1H, $CHCH_3$), 5.95 (s, 1H, =CH), 5.97 (s, 1H, =CH), 6.39 (s, 1H, =CH), 6.41 (s, 1H, =CH), 7.17–7.25 (m, 4H, 2×2ArH), 7.33–7.37 (m, 2H, 2×1ArH), 7.53–7.58 (m, 2H, 2×1ArH); mass (ES+) m/z 284.6 (M^++1); Anal. Calcd for $C_{13}H_{14}ClNO_4$: C, 55.04; H, 4.97; N, 4.94. Found: C, 54.78; H, 5.08; N, 4.86.

4.2.11. 3-(4-Fluorophenyl)-2-methylene-4-nitro-pentanoic acid methyl ester (4f). Pale yellow oil 85% (1.5 g); ν_{max} (Neat) 1721 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.40 (d, 3H, J=6.6 Hz, CH_3CH), 1.61 (d, 3H, J=6.6 Hz, CH_3CH), 3.70 (s, 3H, CO_2CH_3), 3.74 (s, 3H, CO_2CH_3), 4.35 (d, 1H, J=11.2 Hz, CHAr), 4.43 (d, 1H, J=11.2 Hz, CHAr), 5.18–5.25 (m, 1H, $CHCH_3$), 5.40–5.49 (m, 1H, $CHCH_3$), 5.83 (s, 1H, =CH), 5.90 (s, 1H, =CH), 6.34 (s, 1H, =CH), 6.37 (s, 1H, =CH), 6.92–7.06 (m, 4H, 2×2ArH), 7.21–7.30 (m, 4H, 2×2ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=19.3, 19.5, 51.5, 52.5, 52.7, 85.5,

86.0, 125.2, 128.0, 128.2, 129.1, 129.4, 131.1, 137.8, 139.6, 139.9, 166.3, 166.6; mass (FAB+) *m/z* 268 (M^++1); Anal. Calcd for $C_{13}H_{14}FNO_4$: C, 58.42; H, 5.28; N, 5.24. Found: C, 58.01; H, 5.52; N, 5.20.

4.2.12. 3-(4-Bromophenyl)-2-methylene-4-nitro-pentanoic acid methyl ester (4g). Colorless oil 92% (2.4 g); ν_{max} (Neat) 1725 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.41 (d, 3H, *J*=6.6 Hz, C*H*$_3$CH), 1.61 (d, 3H, *J*=6.6 Hz, C*H*$_3$CH), 3.68 (s, 3H, CO_2CH_3), 3.73 (s, 3H, CO_2CH_3), 4.32 (d, 1H, *J*=11.5 Hz, CHAr), 4.41 (d, 1H, *J*=11.5 Hz, CHAr), 5.14–5.22 (m, 1H, C*H*CH$_3$), 5.41–5.47 (m, 1H, C*H*CH$_3$), 5.81 (s, 1H, =CH), 5.90 (s, 1H, =CH), 6.35 (s, 1H, =CH), 6.37 (s, 1H, =CH), 7.13–7.19 (m, 4H, 2×2ArH), 7.39–7.48 (m, 4H, 2×2ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=19.3, 19.4, 51.1, 52.4, 52.6, 52.8, 85.0, 85.7, 122.3, 125.6, 128.3, 130.1, 130.8, 132.3, 132.5, 136.1, 136.9, 139.1, 139.4, 166.1, 166.4; mass (FAB+) *m/z* 328 (M^++1); Anal. Calcd for $C_{13}H_{14}BrNO_4$: C, 47.58; H, 4.30; N, 4.27. Found: C, 46.71; H, 4.53; N, 4.41.

4.3. General procedure for the reduction of 3a–g and 4a–c, f, g with indium

To the stirred solution of appropriate compound from **3a–g** and **4a–c**, **f**, **g** (1.0 equiv) in THF–H_2O (5 mL for approx. 0.5 g of compound, 1:3, v/v) was added In powder (4.0 equiv) followed by 6 N HCl (6.0 equiv). The reaction was allowed to proceed at room temperature and was monitored via TLC. On completion, approximately 2 h, THF was evaporated and the pH of the residue was made alkaline with saturated $NaHCO_3$ solution. The solution was diluted with EtOAc and filtered through a bed of Celite. The filtrate was then extracted with EtOAc (3×25 mL) and the combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography over silica gel using hexane–EtOAc (30:70, v/v) to yield products **5a–g** and **6a–c**, **f**, **g**.

4.3.1. 4-Methylene-5-oxo-3-phenylpyrrolidine-2-carboxylic acid ethyl ester (5a)-(*cis*). Total yield 68% (0.54 g) as a white solid, mp 122–124 °C; ν_{max} (KBr) 1692 (CONH), 1746 (CO_2Et), 3400 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.27 (t, 3H, *J*=7.1 Hz, C*H*$_3$CH$_2$), 4.18–4.27 (m, 4H, C*H*$_2$CH$_3$, CHAr and $CHCO_2Et$), 5.26 (s, 1H, =CH), 6.22 (s, 1H, =CH), 6.56 (s, 1H, NH), 7.29–7.38 (m, 5H, ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.5, 48.9, 61.9, 62.3, 119.8, 128.0, 128.4, 129.4, 141.7, 142.9, 170.1, 171.3; mass (ES+) *m/z* 246.1 (M^++1); HREIMS calculated for $C_{14}H_{15}NO_3$ 245.1052, found, 245.1052.

4.3.2. 4-Methylene-5-oxo-3-phenylpyrrolidine-2-carboxylic acid ethyl ester (5a)-(*trans*). Total yield 68% (0.54 g) as a white solid, mp 160–162 °C; ν_{max} (KBr) 1692 (CONH), 1738 (CO_2Et), 3445 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=0.83 (t, 3H, *J*=6.0 Hz, C*H*$_3$CH$_2$), 3.57–3.63 (m, 1H, CHAr), 3.75–3.81 (m, 1H, $CHCO_2Et$), 4.52–4.61 (m, 2H, C*H*$_2$CH$_3$), 5.33 (s, 1H, =CH), 6.26 (s, 1H, =CH), 6.76 (s, 1H, NH), 7.18–7.29 (m, 5H); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=13.9, 48.2, 59.7, 61.6, 119.6, 128.2, 128.9, 129.4, 138.6, 142.3, 170.4, 171.4; mass (ES+) *m/z* 246.1 (M^++1); HREIMS calculated for $C_{14}H_{15}NO_3$ 245.1052, found, 245.1052.

4.3.3. 4-Methylene-5-oxo-3-*p*-tolylpyrrolidine-2-carboxylic acid ethyl ester (5b)-(*cis*). Total yield 64% (0.268 g) as a white solid, mp 123–125 °C; ν_{max} (KBr) 1695 (CONH), 1738 (CO_2Et), 3445 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.28 (t, 3H, *J*=7.1 Hz, C*H*$_3$CH$_2$), 2.35 (s, 3H, ArCH$_3$), 4.15–4.27 (m, 4H, C*H*$_2$CH$_3$, CHAr and $CHCO_2Et$), 5.25 (d, 1H, *J*=1.8 Hz, =CH), 6.20 (d, 1H, *J*=2.6 Hz, =CH), 6.62 (s, 1H, NH), 7.17 (s, 4H, ArH); mass (FAB+) *m/z* 260 (M^++1); HREIMS calculated for $C_{15}H_{17}NO_3$ 259.1208, found, 259.1208.

4.3.4. 4-Methylene-5-oxo-3-*p*-tolylpyrrolidine-2-carboxylic acid ethyl ester (5b)-(*trans*). Total yield 64% (0.268 g) as a white solid, mp 162–164 °C; ν_{max} (KBr) 1695 (CONH), 1738 (CO_2Et), 3442 (NH) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ=0.85 (t, 3H, *J*=7.3 Hz, C*H*$_3$CH$_2$), 2.30 (s, 3H, ArCH$_3$), 3.57–3.64 (m, 1H, CHAr), 3.74–3.77 (m, 1H, CHAr), 4.46–4.54 (m, 2H, C*H*$_2$CH$_3$), 5.29 (d, 1H, *J*=3.0 Hz, =CH), 6.22 (d, 1H, *J*=3.0 Hz, =CH), 6.57 (s, 1H, NH), 7.04–7.10 (m, 4H, ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=13.9, 21.4, 48.0, 59.8, 61.6, 119.4, 129.3, 129.5, 135.5, 137.9, 142.4, 170.4, 171.4; mass (FAB+) *m/z* 260 (M^++1); HREIMS calculated for $C_{15}H_{17}NO_3$ 259.1208, found, 259.1208.

4.3.5. 3-(2-Chlorophenyl)-4-methylene-5-oxo-pyrrolidine-2-carboxylic acid ethyl ester (5c). White solid 56% (0.37 g), mp 110–112 °C; ν_{max} (KBr) 1710 (CONH), 1728 (CO_2Et), 3412 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=0.82 (t, 3H, *J*=7.1 Hz, C*H*$_3$CH$_2$), 1.27 (t, 3H, *J*=7.1 Hz, C*H*$_3$CH$_2$), 3.49–3.62 (m, 1H, CH*H*CH$_3$), 3.67–3.79 (m, 1H, C*H*HCH$_3$), 4.17–4.31 (m, 2H, C*H*$_2$CH$_3$), 4.68 (d, 2H, *J*=9.0 Hz, 2×CHAr), 5.13 (d, 2H, *J*=9.0 Hz, 2×$CHCO_2Et$), 5.23 (s, 1H, =CH), 5.35 (s, 1H, =CH), 6.16 (d, 1H, *J*=2.4 Hz, =CH), 6.31 (d, 1H, *J*=2.6 Hz, =CH), 6.69 (br s, 2H, 2×1NH), 7.20–7.27 (m, 6H, 2×3ArH), 7.40–7.41 (m, 2H, 2×1ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=13.9, 14.4, 44.2, 46.1, 58.2, 60.5, 61.1, 62.4, 119.1, 119.7, 127.4, 127.9, 129.4, 129.7, 130.0, 130.3, 130.4, 134.2, 135.9, 138.8, 140.9, 142.1, 170.0, 170.4, 171.2; mass (ES+) *m/z* 280.1 (M^++1), 282.1 (M^++3); HREIMS calculated for $C_{14}H_{14}ClNO_3$ 279.0662, found, 279.0664.

4.3.6. 3-(2-Fluorophenyl)-4-methylene-5-oxo-pyrrolidine-2-carboxylic acid ethyl ester (5d). White solid 57% (0.12 g), mp 105–107 °C; ν_{max} (KBr) 1704 (CONH), 1743 (CO_2Et), 3332 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=0.85 (t, 3H, *J*=7.2 Hz, C*H*$_3$CH$_2$), 1.29 (t, 3H, *J*=7.2 Hz, C*H*$_3$CH$_2$), 3.48–3.61 (m, 2H, C*H*$_2$CH$_3$), 4.23–4.39 (m, 5H, C*H*$_2$CH$_3$, 2×CHAr and $CHCO_2Et$), 4.71–4.84 (m, 1H, $CHCO_2Et$), 5.28 (d, 1H, *J*=1.3 Hz, =CH), 5.36 (d, 1H, *J*=0.6 Hz, =CH), 6.20 (d, 1H, *J*=1.1 Hz, =CH), 6.38 (d, 1H, *J*=1.0 Hz, =CH), 7.04–7.30 (m, 8H, 2×4ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=13.9, 14.4, 40.0, 43.0, 58.8, 60.8, 61.7, 61.9, 115.3, 115.7, 116.1, 116.5, 119.7, 119.8, 124.7, 125.0, 125.1, 125.7, 129.8, 130.0, 130.2, 130.3, 138.9, 140.8, 142.0, 169.9, 170.2, 171.0, 171.5; mass (ES+) *m/z* 264.3 (M^++1); HREIMS calculated for $C_{14}H_{14}FNO_3$ 263.0958, found, 263.0954.

4.3.7. 3-(4-Chlorophenyl)-4-methylene-5-oxo-pyrrolidine-2-carboxylic acid ethyl ester (5e). White solid 61% (0.174 g), mp 106–108 °C; ν_{max} (KBr) 1713 (CONH),

1748 (CO_2Et), 3445 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=0.88 (t, 3H, J=7.2 Hz, CH_3CH_2), 1.29 (t, 3H, J=7.2 Hz, CH_3CH_2), 3.51–3.92 (m, 2H, 2×CHAr), 4.14–4.27 (m, 4H, 2×CH_2CH_3), 4.40–4.68 (m, 2H, 2×$CHCO_2Et$), 5.25 (d, 1H, J=1.9 Hz, =CH), 5.31 (d, 1H, J=1.6 Hz, =CH), 6.22 (d, 1H, J=2.9 Hz, =CH), 6.26 (d, 1H, J=2.6 Hz, =CH), 6.98 (s, 2H, 2×NH), 7.11–7.37 (m, 8H, 2×4ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.0, 14.5, 47.5, 48.2, 59.6, 61.8, 61.9, 62.6, 119.5, 120.1, 129.0, 129.6, 129.7, 129.8, 130.8, 133.9, 134.2, 137.1, 138.9, 140.0, 141.9, 142.6, 169.9, 170.1, 171.0, 171.3; mass (ES+) m/z 280.1 (M^++1); HREIMS calculated for $C_{14}H_{14}ClNO_3$ 279.0662, found, 279.0658.

4.3.8. 3-(4-Fluorophenyl)-4-methylene-5-oxo-pyrrolidine-2-carboxylic acid ethyl ester (5f). White solid 63% (0.315 g), mp 114–116 °C; ν_{max} (KBr) 1705 (CONH), 1743 (CO_2Et), 3214 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.21–1.39 (m, 6H, 2×CH_3CH_2), 3.70–3.98 (m, 2H, 2×CHAr), 4.05–4.38 (m, 6H, 2×CH_2CH_3 and 2×$CHCO_2Et$), 5.27–5.32 (m, 2H, 2×=CH), 6.23–6.28 (m, 2H, 2×=CH), 7.01–7.43 (m, 8H, 2×4ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.0, 14.5, 44.3, 45.8, 62.0, 62.6, 66.2, 67.9, 115.7, 116.1, 116.2, 116.7, 120.0, 120.3, 129.8, 130.0, 131.5, 131.7, 136.1, 139.2, 139.7, 142.0, 160.3, 164.7, 165.2, 168.2, 169.8; mass (FAB+) m/z 264 (M^++1); HREIMS calculated for $C_{14}H_{14}FNO_3$ 263.0958, found, 263.0958.

4.3.9. 3-(4-Bromophenyl)-4-methylene-5-oxo-pyrrolidine-2-carboxylic acid ethyl ester (5g). White solid 55% (0.21 g), mp 159–161 °C; ν_{max} (KBr) 1712 (CONH), 1750 (CO_2Et), 3430 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=0.88 (t, 3H, J=7.1 Hz, CH_3CH_2), 1.29 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.60–3.91 (m, 2H, 2×CHAr), 4.21–4.27 (m, 4H, 2×CH_2CH_3), 4.38–4.60 (m, 2H, 2×$CHCO_2Et$), 5.25 (d, 1H, J=2.0 Hz, =CH), 5.30 (d, 1H, J=1.7 Hz, =CH), 6.22 (d, 1H, J=2.9 Hz, =CH), 6.25 (d, 1H, J=2.5 Hz, =CH), 6.66 (br s, 2H, 2×NH), 7.06–7.57 (m, 8H, 2×4ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.0, 14.5, 47.5, 48.3, 59.4, 61.8, 62.4, 120.0, 122.0, 122.3, 130.2, 131.1, 131.5, 132.0, 132.5, 134.4, 137.7, 140.6, 141.9, 142.6, 170.2, 171.1, 171.9; mass (ES+) m/z 324.1 (M^++1), 326.1 (M^++3); HREIMS calculated for $C_{14}H_{14}BrNO_3$ 323.0157, found, 323.0155.

4.3.10. 5-Methyl-3-methylene-4-phenylpyrrolidin-2-one (6a). An off white solid 62% (0.144 g), mp 118–120 °C; ν_{max} (KBr) 1674 (CONH), 3413 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.45 (d, 3H, J=6.2 Hz, CH_3CH), 3.55–3.58 (m, 1H, CHAr), 3.82–3.88 (m, 1H, $CHCH_3$), 5.13 (d, 1H, J=2.4 Hz, =CH), 6.09 (d, 1H, J=3.0 Hz, =CH), 7.19 (m, 5H, ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=18.4, 51.2, 63.0, 117.8, 128.0, 128.8, 129.3, 140.4, 163.6; mass (ES+) 188.2 (M^++1); HREIMS calculated for $C_{12}H_{13}NO$ 187.0997, found, 187.0991.

4.3.11. 5-Methyl-3-methylene-4-*p*-tolylpyrrolidin-2-one (6b). Brown solid 60% (0.107 g), mp 155–157 °C; ν_{max} (KBr) 1686 (CONH), 3431 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.32 (d, 3H, J=6.0 Hz, CH_3CH), 2.35 (s, 3H, $ArCH_3$), 3.54 (d, 1H, J=2.7 Hz, CHAr), 3.68 (t, 1H, J=6.1 Hz, $CHCH_3$), 5.12 (s, 1H, =CH), 6.08 (d, 1H, J=2.7 Hz, =CH), 6.92 (s, 1H, NH), 7.11 (d, 2H, J=8.0 Hz, ArH), 7.17 (d, 2H, J=8.0 Hz, ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=18.3, 21.4, 50.9, 62.9, 117.9, 128.7, 130.0, 137.3, 137.7, 163.8; mass (ES+) 188.2 (M^++1); HREIMS calculated for $C_{13}H_{15}NO$ 201.1155, found, 201.1148.

4.3.12. 4-(2-Chlorophenyl)-5-methyl-3-methylenepyrrolidin-2-one (6c). Brown solid 58% (0.09 g), mp 117–119 °C; ν_{max} (KBr) 1684 (CONH), 3433 (NH) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ=0.76 (d, 3H, J=6.0 Hz, CH_3CH), 4.20–4.25 (m, 1H, CHAr), 4.85–4.90 (m, 1H, $CHCH_3$), 5.33 (d, 1H, J=3.0 Hz, =CH), 6.30 (d, 1H, J=3.0 Hz, =CH), 7.18–7.25 (m, 2H, ArH), 7.38–7.44 (m, 2H, ArH); mass (ES+) 222.1 (M^++1); HREIMS calculated for $C_{12}H_{12}ClNO$ 221.0607, found, 221.0606.

4.3.13. 4-(2-Chlorophenyl)-5-methyl-3-methylenepyrrolidin-2-one (6c) (diastereoisomeric mixture as obtained from reaction of $SnCl_2\cdot 2H_2O$). Brown solid 54% (0.13 g), mp 96–98 °C; ν_{max} (KBr) 1670 (CONH), 3415 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=0.77 (d, 3H, J=6.5 Hz, CH_3CH), 0.89 (d, 3H, J=6.5 Hz, CH_3CH), 3.60–3.65 (m, 1H, CHAr), 4.22–3.29 (m, 1H, CHAr), 4.35–4.39 (m, 1H, $CHCH_3$), 4.87–4.92 (m, 1H, $CHCH_3$), 5.26 (s, 1H, =CH), 5.37 (d, 1H, J=2.5 Hz, =CH), 6.14 (s, 1H, =CH), 6.34 (d, 1H, J=2.5 Hz, =CH), 6.96 (br s, 2H, 2×NH), 7.17–7.27 (m, 6H, 2×3ArH), 7.33–7.45 (m, 2H, 2×1ArH); mass (FAB+) 222 (M^++1); HREIMS calculated for $C_{12}H_{12}ClNO$ 221.0607, found, 221.0608.

4.3.14. 4-(4-Fluoro-phenyl)-5-methyl-3-methylenepyrrolidin-2-one (6f). White solid 53% (0.13 g), mp 162–164 °C; ν_{max} (KBr) 1667 (CONH), 3413 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.45 (d, 3H, J=6.2 Hz, CH_3CH), 3.54–3.57 (m, 1H, CHAr), 3.75–3.84 (m, 1H, $CHCH_3$), 5.12 (d, 1H, J=2.3 Hz, =CH), 6.08 (d, 1H, J=2.8 Hz, =CH), 6.99–7.08 (m, 2H, ArH), 7.14–7.21 (m, 2H, ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=18.3, 50.5, 63.1, 116.1, 116.5, 118.0, 130.2, 130.4, 131.4, 136.1, 141.8, 165.0; mass (ES+) m/z 206.1 (M^++1); HREIMS calculated for $C_{12}H_{12}FNO$ 205.0903, found, 205.0905.

4.3.15. 4-(4-Bromophenyl)-5-methyl-3-methylenepyrrolidin-2-one (6g). Yellow oil 64% (0.23 g); ν_{max} (Neat) 1688 (CONH), 3427 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.44 (d, 3H, J=6.2 Hz, CH_3CH), 3.53–3.58 (m, 1H, CHAr), 3.76–3.86 (m, 1H, $CHCH_3$), 5.13 (d, 1H, J=2.4 Hz, =CH), 6.07 (d, 1H, J=2.9 Hz, =CH), 7.08 (d, 2H, J=8.4 Hz, ArH), 7.48 (d, 2H, J=8.4 Hz, ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=18.5, 51.2, 62.8, 117.9, 128.9, 130.2, 137.3, 137.9, 164.5; mass (ES+) m/z 266.0 (M^++1); HREIMS calculated for $C_{12}H_{12}BrNO$ 265.0102, found, 265.0108.

4.4. General procedure for reduction of compounds 3a–g with $SnCl_2\cdot 2H_2O$

To the solution of compounds from **3a–g** (1.0 equiv) in methanol (10 mL) was added $SnCl_2\cdot 2H_2O$ (5.0 equiv) and the reaction mixture was heated at reflux with stirring at 80 °C for 1.5 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 (Na_2SO_4), and concentrated to afford a residue, which was purified by silica gel chromatography using hexane–EtOAc (90:10, v/v) or (20:80, v/v) as eluent to yield products **7a–g** as oils.

4.4.1. 2-Hydroxyimino-4-methylene-3-phenylpentanedioic acid 1-ethyl ester 5-methyl ester (7a). Pale yellow oil 73% (0.83 g); ν_{max} (Neat) 1630 (C=N), 1735 (CO_2Me and CO_2Et), 3425 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.26 (t, 3H, J=7.2 Hz, CH_3CH_2), 3.75 (s, 3H, CO_2CH_3), 4.21 (q, 2H, J=7.2 Hz, CH_2CH_3), 5.32 (d, 1H, J=2.1 Hz, =CH), 5.48 (s, 1H, CHAr), 6.35 (s, 1H, =CH), 7.31 (s, 5H, ArH), 9.20 (br s, 1H, OH); mass (ES+) m/z 291.9 (M^++1); HREIMS calculated for $C_{15}H_{17}NO_5$ 291.1107, found, 291.1110.

4.4.2. 2-Hydroxyimino-4-methylene-3-*p*-tolylpentanedioic acid 1-ethyl ester 5-methyl ester (7b). 78% (1.48 g); ν_{max} (Neat) 1631 (C=N), 1731 (CO_2Me and CO_2Et), 3425 (OH) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ=1.19–1.30 (m, 3H, CH_3CH_2), 2.33 (s, 3H, $ArCH_3$), 3.75 (s, 3H, CO_2CH_3), 4.07–4.28 (m, 2H, CH_2CH_3), 5.32 (d, 1H, J=1.2 Hz, =CH), 5.42 (s, 1H, CHAr), 6.33 (d, 1H, J=1.2 Hz, =CH), 7.13 (d, 2H, J=8.2 Hz, ArH), 7.20 (d, 2H, J=8.2 Hz, ArH), 9.20 (br s, 1H, OH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.2, 21.5, 45.1, 52.5, 62.2, 126.9, 129.8, 134.2, 137.4, 137.4, 140.4, 151.5, 163.6, 167.5; mass (FAB+) m/z 306 (M^++1); HREIMS calculated for $C_{16}H_{19}NO_5$ 305.1263, found, 305.1249.

4.4.3. 3-(2-Chlorophenyl)-2-hydroxyimino-4-methylenepentanedioic acid 1-ethyl ester 5-methyl ester (7c). Colorless oil 79% (0.45 g); ν_{max} (Neat) 1627 (C=N), 1726 (CO_2Et and CO_2Me), 3497 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.27–1.29 (m, 3H, CH_3CH_2), 3.75 (s, 3H, CO_2CH_3), 4.11–4.28 (m, 2H, CH_2CH_3), 5.29 (s, 1H, =CH), 5.86 (s, 1H, CHAr), 6.40 (s, 1H, =CH), 7.20–7.34 (m, 3H, ArH), 7.38–7.41 (m, 1H, ArH), 9.21 (br s, 1H, OH); mass (FAB+) m/z 326 (M^++1); HREIMS calculated for $C_{15}H_{16}ClNO_5$ 325.0717, found, 325.0717.

4.4.4. 3-(2-Fluorophenyl)-2-hydroxyimino-4-methylenepentanedioic acid 1-ethyl ester 5-methyl ester (7d). Colorless oil 77% (0.73 g); ν_{max} (Neat) 1630 (C=N), 1724 (CO_2Et and CO_2Me), 3452 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.26 (t, 3H, J=7.0 Hz, CH_3CH_2), 3.76 (s, 3H, CO_2CH_3), 4.24 (q, 2H, J=7.0 Hz, CH_2CH_3), 5.31 (s, 1H, =CH), 5.77 (s, 1H, CHAr), 6.38 (s, 1H, =CH), 7.01–7.10 (m, 2H, ArH), 7.14–7.32 (m, 2H, ArH), 9.26 (br s, 1H, OH); mass (ES+) m/z 310.1 (M^++1); HREIMS calculated for $C_{15}H_{16}FNO_5$ 309.1013, found, 309.1015.

4.4.5. 3-(4-Chlorophenyl)-2-hydroxyimino-4-methylenepentanedioic acid 1-ethyl ester 5-methyl ester (7e). Colorless oil 75% (0.47 g); ν_{max} (Neat) 1627 (C=N), 1722 (CO_2Et and CO_2Me), 3341 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.26 (t, 3H, J=7.2 Hz, CH_3CH_2), 3.75 (s, 3H, CO_2CH_3), 4.07–4.29 (m, 2H, CH_2CH_3), 5.33 (d, 1H, J=1.8 Hz, =CH), 5.45 (s, 1H, CHAr), 6.36 (d, 1H, J=1.6 Hz, =CH), 7.22–7.33 (m, 4H, ArH), 9.28 (br s, 1H, OH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.2, 44.8, 52.6, 62.4, 127.2, 129.2, 131.3, 133.7, 135.8, 139.7, 151.3, 163.3, 167.3; mass (FAB+) m/z 326; HREIMS calculated for $C_{15}H_{16}ClNO_5$ 325.0717, found, 325.0718.

4.4.6. 3-(4-Fluorophenyl)-2-hydroxyimino-4-methylenepentanedioic acid 1-ethyl ester 5-methyl ester (7f). Colorless oil 87% (0.24 g); ν_{max} (Neat) 1628 (C=N), 1722 (CO_2Et and CO_2Me), 3367 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.27 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.75 (s, 3H, CO_2CH_3), 4.23 (q, 2H, J=7.1 Hz, CH_2CH_3), 5.32 (d, 1H, J=1.6 Hz, =CH), 5.45 (s, 1H, CHAr), 6.35 (d, 1H, J=1.6 Hz, =CH), 6.97–7.09 (m, 2H, ArH), 7.29–7.33 (m, 2H, ArH), 9.35 (br s, 1H, OH); mass (ES+) m/z 310.0; HREIMS calculated for $C_{15}H_{16}FNO_5$ 309.1013, found, 309.1016.

4.4.7. 3-(4-Bromophenyl)-2-hydroxyimino-4-methylenepentanedioic acid 1-ethyl ester 5-methyl ester (7g). Pale yellow oil 73% (0.7 g from 1.0 g); ν_{max} (Neat) 1633 (C=N), 1722 (CO_2Et and CO_2Me), 3450 (OH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.27 (t, 3H, J=7.2 Hz, CH_3CH_2), 3.75 (s, 3H, CO_2CH_3), 4.23 (q, 2H, J=7.2 Hz, CH_2CH_3), 5.34 (d, 1H, J=1.9 Hz, =CH), 5.43 (s, 1H, CHAr), 6.37 (d, 1H, J=1.6 Hz, =CH), 7.19 (d, 2H, J=8.4 Hz, ArH), 7.45 (d, 2H, J=8.4 Hz, ArH), 9.26 (br s, 1H, OH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.3, 44.8, 52.7, 62.4, 127.3, 131.7, 132.2, 141.8, 144.6, 152.2, 164.3, 166.7; mass (ES+) m/z 370.2 (M^++1); HREIMS calculated for $C_{15}H_{16}BrNO_5$ 369.0212, found, 369.0210.

4.5. Reaction of 3a with $Sn(SPh)_2$ complex

To a stirred solution of $SnCl_2\cdot 2H_2O$ (0.81 g, 3.61 mmol) in MeCN (5 mL), PhSH (1.12 mL, 12.1 mmol) and Et_3N (1.67 mL, 12.1 mmol) were added at room temperature. Subsequently a solution of compound **3a** (0.74 g, 2.25 mmol) in MeCN (2 mL) was added and the reaction was allowed to continue for 30 min. Thereafter, the reaction mixture was concentrated and the residue was purified by column chromatography over silica gel using hexane–EtOAc (90:10, v/v) as an eluent to give compound (0.42 g) (60%) **7a** as a pale yellow oil.

4.6. General procedure for the preparation of methyl derivatives 8b, c

To the flask charged with oxime **7b** or **7c** (1.0 equiv) and Ag_2O (1.0 equiv) was added MeI (5 mL for approx. 0.3 g substrate) with stirring at room temperature. After the initial exothermic reaction has subsided, the reaction mixture was heated at reflux for 1 h. The reaction mixture was cooled to room temperature and filtered through a bed of Celite with the help of $CHCl_3$. The combined filtrates were evaporated and the residue was purified via silica gel column chromatography. Elution with hexane–EtOAc (90:10, v/v) gave pure **8b** or **8c**.

4.6.1. 2-Methoxyimino-4-methylene-3-*p*-tolylpentanedioic acid 1-ethyl ester 5-methyl ester (8b). Pale yellow oil 80% (0.25 g); ν_{max} (Neat) 1625 (C=N), 1735 (CO_2Me and CO_2Et) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.25 (t, 3H, J=7.1 Hz, CH_3CH_2), 2.32 (s, 3H, $ArCH_3$), 3.74 (s, 3H, CO_2CH_3), 3.98 (s, 3H, NCH_3), 4.23 (q, 2H, J=7.1 Hz, CH_2CH_3), 5.32 (d, 1H, J=1.5 Hz, =CH), 5.39 (s, 1H, CHAr), 6.30 (s, 1H, =CH), 7.12 (s, 4H, ArH); mass

(FAB+) *m/z* 320 (M^++1); EIHRMS calculated for $C_{17}H_{21}NO_5$ 319.1420, found, 319.1421.

4.6.2. 3-(2-Chlorophenyl)-2-methoxyimino-4-methylene-pentanedioic acid 1-ethyl ester 5-methyl ester (8c). Colorless oil 68% (0.05 g); ν_{max} (Neat) 1627 (C=N), 1728 (CO_2Et and CO_2Me) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.24 (t, 3H, *J*=7.1 Hz, C*H*$_3$CH$_2$), 3.74 (s, 3H, CO_2CH_3), 3.97 (s, 3H, NCH_3), 4.23 (q, 2H, *J*=7.1 Hz, CH$_2$CH$_3$), 5.29 (d, 1H, *J*=1.5 Hz, =CH), 5.80 (s, 1H, CHAr), 6.37 (s, 1H, =CH), 7.18–7.25 (m, 3H, ArH), 7.37–7.40 (m, 1H, ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.4, 43.4, 52.6, 62.3, 63.8, 127.3, 129.0, 130.0, 130.6, 134.7, 135.8, 138.2, 151.1, 163.4, 167.0; mass (FAB+) *m/z* 340 (M^++1); HREIMS calculated for $C_{16}H_{18}ClNO_5$ 339.0871, found, 339.0868.

4.7. General procedure for the preparation of tosyl derivatives 9b, d

To the stirred solution of appropriate oxime from **7b**, **d** (1.0 equiv) in dry dichloromethane (10 mL) was added Et_3N (1.5 mmol). The reaction mixture was brought to 0 °C via ice-bath and to it was added tosyl chloride (1.1 equiv) and the reaction was continued for 2 h at room temperature. Thereafter, 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 by silica gel column chromatography using hexane–EtOAc (80:20, v/v) to yield pure products.

4.7.1. 2-Tosyloxyimino-4-methylene-3-*p*-tolylpentanedioic acid 1-ethyl ester 5-methyl ester (9b). Yellow oil 75% (0.61 g); ν_{max} (Neat) 1628 (C=N), 1732 (CO_2Et and CO_2Me) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.25 (t, 3H, *J*=7.2 Hz, C*H*$_3$CH$_2$), 2.34 (s, 3H, ArCH$_3$), 2.44 (s, 3H, ArCH$_3$), 3.69 (s, 3H, CO_2CH_3), 4.17 (q, 2H, *J*=7.2 Hz, CH$_2$CH$_3$), 5.35 (two s merged, 2H, CHAr and =CH), 6.37 (s, 1H, =CH), 7.09 (s, 4H, ArH), 7.27 (d, 2H, *J*=8.0 Hz, ArH), 7.69 (d, 2H, *J*=8.0 Hz, ArH); mass (ES+) *m/z* 460.2 (M^++1); HREIMS calculated for $C_{23}H_{25}NO_7S$ 459.1352, found, 459.1364.

4.7.2. 3-(4-Fluorophenyl)-2-hydroxyimino-4-methylene pentanedioic acid 1-ethyl ester 5-methyl ester (9d). Yellow oil 78% (0.20 g); ν_{max} (Neat) 1630 (C=N), 1729 (CO_2Et and CO_2Me) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.23 (t, 3H, *J*=7.1 Hz, C*H*$_3$CH$_2$), 2.45 (s, 3H, ArCH$_3$), 3.70 (s, 3H, CO_2CH_3), 4.20 (q, 2H, *J*=7.1 Hz, CH$_2$CH$_3$), 5.33 (two s merged, 2H, CHAr and =CH), 6.39 (d, 1H, *J*=1.3 Hz, =CH), 7.11–7.15 (m, 2H, ArH), 7.23–7.34 (m, 4H, ArH), 7.64–7.68 (m, 2H, ArH); mass (ES+) *m/z* 464.1 (M^++1); HREIMS calculated for $C_{22}H_{22}FNO_7S$ 463.1101, found, 463.1124.

4.8. General procedure for the reaction of 9b, d with DBU

To the stirred solution of appropriate tosyl derivatives from **9b**, **d** (1.0 mmol) in dry dichloromethane (5 mL), a solution of DBU (1.2 mmol) in dichloromethane (4.0 mL) was added dropwise at room temperature. After 30 min, organic layer was washed with water, dried (anhyd Na_2SO_4), and evaporated to furnish a residue, which was purified via silica gel column chromatography using hexane–EtOAc (85:15, v/v) to give the pyrroles in low yields.

4.8.1. 3-*p*-Tolyl-1*H*-pyrrole-2,4-dicarboxylic acid 2-ethyl ester 4-methyl ester (10b). White solid 28% (0.11 g), mp 150–152 °C; ν_{max} (KBr) 1730 (CO_2Et and CO_2Me), 3429 (NH) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.37 (t, 3H, *J*=7.2 Hz, C*H*$_3$CH$_2$), 2.40 (s, 3H, ArCH$_3$), 3.77 (s, 3H, CO_2CH_3), 4.33 (q, 2H, *J*=7.2 Hz, CH$_2$CH$_3$), 7.25 (d, 2H, *J*=7.8 Hz, ArH), 7.38 (d, 1H, *J*=2.8 Hz, =CH), 7.52 (d, 2H, *J*=7.8 Hz, ArH), 9.36 (s, 1H, NH); mass (FAB+) *m/z* 288 (M^++1); HREIMS calculated for $C_{16}H_{17}NO_4$ 287.1158, found, 287.1146.

4.8.2. 3-(4-Fluorophenyl)-1*H*-pyrrole-2,4-dicarboxylic acid 2-ethyl ester 4-methyl ester (10d). White solid 25% (0.023 g), mp 156–158 °C; ν_{max} (KBr) 1728 (CO_2Et and CO_2Me), 3441 (NH) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.38 (t, 3H, *J*=7.2 Hz, C*H*$_3$CH$_2$), 3.77 (s, 3H, CO_2CH_3), 4.32 (q, 2H, *J*=7.2 Hz, CH$_2$CH$_3$), 7.10–7.18 (m, 2H, ArH), 7.38 (d, 1H, *J*=2.8 Hz, =CH), 7.59–7.65 (m, 2H, ArH), 9.38 (s, 1H, NH); mass (ES+) *m/z* 292.0 (M^++1); HREIMS calculated for $C_{15}H_{14}FNO_4$ 291.0907, found, 291.0919.

4.9. General procedure for the preparation of compounds 11a–c, 12, and 13a, b

The compounds **11a**–**c**, **12**, and **13a**, **b** were prepared following the procedure as described for compounds **3a**–**g** and the reactions were worked up after 1 h.

4.9.1. 2-Methylene-4-nitro-3-(2-nitrophenyl)-pentanedioic acid 5-ethyl ester 1-methyl ester (11a). An off white solid 72% (1.36 g), mp 116–118 °C; ν_{max} (KBr) 1721 (CO_2Et), 1755 (CO_2Me) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.07 (t, 3H, *J*=7.1 Hz, C*H*$_3$CH$_2$), 3.68 (s, 3H, CO_2CH_3), 4.09 (q, 2H, *J*=7.1 Hz, CH$_2$CH$_3$), 5.53 (d, 1H, *J*=11.5 Hz, CHAr), 5.99 (s, 1H, =CH), 6.08 (d, 1H, *J*=11.5 Hz, CHCO$_2$Et), 6.46 (s, 1H, =CH), 7.42–7.49 (m, 1H, ArH), 7.52–7.58 (m, 2H, ArH), 7.82–7.84 (d, 1H, *J*=7.6 Hz, ArH); ^{13}C NMR (50.632 MHz, $CDCl_3$) δ=13.8, 42.9, 52.8, 63.8, 89.3, 125.4, 128.5, 129.5, 130.1, 130.8, 133.2, 137.0, 150.5, 163.0, 165.7; mass (ES+) *m/z* 375.0 (M^++Na); HREIMS calculated for $C_{15}H_{16}N_2O_6$ 352.0907, found, 352.0909.

4.9.2. 2-Methylene-4-nitro-3-(6-nitrobenzo[1,3]dioxol-5-yl)-pentanedioic acid 5-ethyl ester 1-methyl ester (11b). Yellow solid 68% (0.42 g), mp 148–150 °C; ν_{max} (KBr) 1722 (CO_2Et), 1749 (CO_2Me) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ=1.17 (t, 3H, *J*=7.2 Hz, C*H*$_3$CH$_2$), 3.71 (s, 3H, CO_2CH_3), 4.15 (q, 2H, *J*=7.2 Hz, CH$_2$CH$_3$), 5.63 (d, 1H, *J*=12.0 Hz, CHAr), 5.99 (d, 1H, *J*=12.0 Hz, CHCO$_2$Et), 6.02 (s, 1H, =CH), 6.12 (s, 2H, CH_2), 6.47 (s, 1H, =CH), 6.93 (s, 1H, ArH), 7.38 (s, 1H, ArH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.2, 42.8, 52.9, 63.9, 89.3, 103.7, 106.4, 109.3, 126.3, 128.4, 137.2, 144.7, 148.0, 151.8, 163.0, 165.8; mass (ES+) *m/z* 419.0 (M^++Na); HREIMS calculated for $C_{16}H_{16}N_2O_{10}$ 396.0805, found, 396.0806.

4.9.3. 3-(5-Chloro-2-nitro phenyl)-2-methylene-4-nitro-pentanedioic acid 5-ethyl ester 1-methyl ester (11c). Brown solid 75% (0.80 g), mp 130–132 °C; ν_{max} (KBr)

1725 (CO_2Et), 1750 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.12 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.70 (s, 3H, CO_2CH_3), 4.12 (q, 2H, J=7.1 Hz, CH_2CH_3), 5.56 (d, 1H, J=11.6 Hz, CHAr), 6.00–6.06 (m, 2H, $CHCO_2Et$ and =CH), 6.49 (s, 1H, =CH), 7.39–7.44 (m, 1H, ArH), 7.52 (d, 1H, J=2.1 Hz, ArH), 7.83 (d, 1H, J=8.7 Hz, ArH); mass (ES+) m/z 409.0 (M^++Na); HREIMS calculated for $C_{15}H_{15}ClN_2O_8$ 386.0517, found, 386.0515.

4.9.4. 2-Methylene-4-nitro-3-(2-nitrophenyl)-pentanedioic acid diethyl ester (12). Yellow solid 71% (0.44 g), mp 90–92 °C; ν_{max} (KBr) 1728 (CO_2Et) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.03–1.30 (m, 6H, 2×CH_3CH_2), 4.03–4.28 (m, 4H, 2×CH_2CH_3), 5.52–5.59 (m, 2H, 2×CHAr), 5.96 (two s merged, 2H, =CH), 5.08 (d, 1H, J=11.5 Hz, $CHCO_2Et$), 6.29 (d, 1H, J=11.5 Hz, $CHCO_2Et$), 6.41 (s, 1H, =CH), 6.47 (s, 1H, =CH), 7.44–7.49 (m, 2H, 2×1ArH), 7.55–7.58 (m, 4H, 2×2ArH), 7.68–7.71 (m, 1H, ArH), 7.85 (d, 2H, J=7.8 Hz, ArH); mass (ES+) m/z 389.0 (M^++Na); HREIMS calculated for $C_{15}H_{16}N_2O_8$ 366.1063, found, 366.1059.

4.9.5. 2-Methylene-4-nitro-3-(2-nitrophenyl)-pentanoic acid methyl ester (13a). Brown solid 65% (0.58 g), mp 110–112 °C; ν_{max} (KBr) 1722 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.56 (d, 3H, J=6.6 Hz, CH_3CH), 1.63 (d, 3H, J=6.6 Hz, CH_3CH), 3.63 (s, 3H, CO_2CH_3), 3.75 (s, 3H, CO_2CH_3), 5.08 (d, 1H, J=11.0 Hz, CHAr), 5.21–5.35 (m, 2H, CHAr and $CHCO_2Et$), 5.64–5.68 (m, 1H, $CHCO_2Et$), 5.96 (s, 1H, =CH), 6.00 (s, 1H, =CH), 6.41 (two s merged, 2H, 2×=CH), 7.34–7.47 (m, 4H, 2×2ArH), 7.57 (t, 2H, J=7.2 Hz, 2×1ArH), 7.79 (t, 2H, J=7.2 Hz, 2×1ArH); mass (ES+) m/z 395.1 (M^++1); HREIMS calculated for $C_{15}H_{15}ClN_2O_8$ 294.0852, found, 294.0853.

4.9.6. 3-(5-Chloro-2-nitrophenyl)-2-methylene-4-nitropentanoic acid methyl ester (13b). Brown solid 66% (0.50 g), mp 104–106 °C; ν_{max} (KBr) 1724 (CO_2Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.57 (d, 3H, J=6.6 Hz, CH_3CH), 1.63 (d, 3H, J=6.6 Hz, CH_3CH), 3.65 (s, 3H, CO_2CH_3), 3.77 (s, 3H, CO_2CH_3), 5.06 (d, 1H, J=11.1 Hz, CHAr), 5.24–5.34 (m, 2H, CHAr and $CHCO_2Et$), 5.63–5.68 (m, 1H, $CHCO_2Et$), 5.99 (s, 1H, =CH), 6.04 (s, 1H, =CH), 6.45 (two s merged, 2H, 2×=CH), 7.30–7.31 (m, 2H, 2×1ArH), 7.38–7.44 (m, 2H, 2×1ArH), 7.76–7.83 (m, 2H, 2×1ArH); mass (ES+) m/z 329.1 (M^++1); HREIMS calculated for $C_{15}H_{15}ClN_2O_8$ 328.0462, found, 328.0458.

4.10. General procedure for the preparation of compounds 14a–c, 15, and 16a, b

To the solution of appropriate compounds from **11a–c**, **12**, and **13a**, **b** (1.0 equiv) in methanol (10 mL) was added $SnCl_2\cdot 2H_2O$ (10 equiv) and the reaction mixture was heated at reflux with stirring at 80 °C for 1 h in a nitrogen atmosphere. After completion, methanol was evaporated and the residue was made basic with saturated $NaHCO_3$ and taken up in EtOAc (100 mL). The suspension formed was filtered through a bed of Celite and the filtrate was partitioned in a separating funnel. The organic layer was separated, dried (Na_2SO_4), and concentrated to give a residue, which was purified by silica gel chromatography using hexane–EtOAc (80:20, v/v) as an eluent to yield the final products.

4.10.1. 3-(1-Methoxycarbonyl-vinyl)-1*H*-indole-2-carboxylic acid ethyl ester (14a). Yellow oil 56% (0.183 g); ν_{max} (Neat) 1723 (CO_2Et and CO_2Me), 3315 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.36 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.75 (s, 3H, CO_2CH_3), 4.40 (q, 2H, J=7.1 Hz, CH_2CH_3), 5.93 (s, 1H, =CH), 6.66 (s, 1H, =CH), 7.16–7.19 (m, 1H, ArH), 7.34–7.41 (m, 1H, ArH), 7.54–7.61 (m, 2H, ArH), 10.64 (s, 1H, NH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.4, 52.5, 61.7, 110.1, 114.2, 119.6, 120.9, 121.8, 126.4, 129.4, 133.3, 133.9, 164.3, 167.9; mass (ES+) m/z 274.0 (M^++1); HREIMS calculated for $C_{15}H_{15}NO_4$ 273.1001, found, 273.1004.

4.10.2. 3-(1-Methoxycarbonyl-vinyl)-5*H*-[1,3]dioxolo[4,5-*f*]indole-6-carboxylic acid ethyl ester (14b). Pale yellow solid 58% (0.093 g), mp 116–118 °C; ν_{max} (KBr) 1732 (CO_2Et and CO_2Me), 3308 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.23–1.36 (m, 3H, CH_3CH_2), 3.73 (s, 3H, CO_2CH_3), 4.31 (q, 2H, J=7.2 Hz, CH_2CH_3), 5.85 (t, 1H, J=2.8 Hz, =CH), 5.97 (s, 2H, CH_2), 6.60 (t, 1H, J=4.1 Hz, =CH), 6.85 (two s merged, 2H, ArH), 8.92 (s, 1H, NH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.6, 52.5, 62.5, 100.3, 102.7, 106.2, 115.3, 115.8, 120.4, 128.9, 136.9, 148.1, 151.6, 165.2, 168.3; mass (ES+) m/z 318.0 (M^++1), 340.1 (M^++Na); HREIMS calculated for $C_{16}H_{15}NO_6$ 317.0899, found, 317.0899.

4.10.3. 5-Chloro-3-(1-methoxycarbonyl-vinyl)-1*H*-indole-2-carboxylic acid ethyl ester (14c). Yellow oil 62% (0.103 g); ν_{max} (Neat) 1723 (CO_2Et and CO_2Me), 3372 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.36 (t, 3H, J=7.1 Hz, CH_3CH_2), 3.75 (s, 3H, CO_2CH_3), 4.40 (q, 2H, J=7.1 Hz, CH_2CH_3), 5.91 (s, 1H, =CH), 6.67 (s, 1H, =CH), 7.36 (s, 1H, ArH), 7.48–7.65 (m, 2H, ArH), 10.72 (s, 1H, NH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=13.8, 52.5, 61.8, 124.4, 125.6, 127.2, 130.6, 131.1, 131.4, 136.2, 141.7, 145.9, 165.2, 167.3; mass (ES+) m/z 308.0 (M^++1); HREIMS calculated for $C_{15}H_{14}ClNO_4$ 307.0611, found, 307.0612.

4.10.4. 3-(1-Ethoxycarbonyl-vinyl)-1*H*-indole-2-carboxylic acid ethyl ester (15). Brown solid 59% (0.10 g), mp 104–106 °C; ν_{max} (KBr) 1713 (CO_2Et), 3331 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.14–1.47 (m, 6H, 2×CH_3CH_2), 4.10–4.44 (m, 4H, 2×CH_2CH_3), 5.92 (s, 1H, =CH), 6.66 (s, 1H, =CH), 7.12–7.23 (m, 1H, ArH), 7.34–7.41 (m, 1H, ArH), 7.54–7.62 (m, 2H, ArH), 10.60 (s, 1H, NH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=14.4, 14.6, 61.4, 62.3, 110.1, 112.3, 114.2, 121.0, 121.7, 126.4, 129.1, 133.2, 134.2, 164.5, 167.7; mass (ES+) m/z 288.0 (M^++1); HREIMS calculated for $C_{16}H_{17}NO_4$ 287.1158, found, 287.1156.

4.10.5. 3-Methylene-4-(1-nitro-ethyl)-3,4-dihydro-1*H*-quinolin-2-one (16a). White solid 53% (0.062 g), mp 166–168 °C; ν_{max} (KBr) 1664 (CONH), 3218 (NH) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ=1.47 (d, 3H, J=4.7 Hz, CH_3CH), 1.50 (d, 3H, J=4.7 Hz, CH_3CH), 4.15 (d, 1H, J=7.6 Hz, CHAr), 4.23 (d, 1H, J=7.6 Hz, CHAr), 4.61–4.72 (m, 2H, 2×$CHCH_3$), 5.68 (two s merged, 2H,

2×=CH), 6.41 (s, 1H, =CH), 6.49 (s, 1H, =CH), 6.89–6.94 (m, 2H, 2×1ArH), 7.01–7.08 (m, 2H, 2×1ArH), 7.14–7.17 (m, 2H, 2×1ArH), 7.23–7.33 (m, 2H, 2×1ArH), 8.95 (s, 1H, NH), 9.10 (s, 1H, NH); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ=19.3, 19.4, 51.2, 52.4, 85.6, 86.1, 124.9, 127.7, 128.3, 129.0, 129.8, 130.1, 134.0, 134.8, 137.9, 138.1, 139.8, 140.0, 166.4, 166.7; mass (FAB+) *m/z* 233 (M^++1); HREIMS calculated for $C_{12}H_{12}N_2O_3$ 232.0848, found, 232.0848.

4.10.6. 6-Chloro-3-methylene-4-(1-nitro-ethyl)-3,4-dihydro-1*H*-quinolin-2-one (16b). Pale yellow solid 48% (0.116 g), mp>250 °C; ν_{max} (KBr) 1672 (CONH), 3391 (NH) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ=1.46 (d, 3H, *J*=4.6 Hz, C*H*$_3$CH), 1.52 (d, 3H, *J*=4.6 Hz, C*H*$_3$CH), 4.14 (d, 1H, *J*=7.8 Hz, CHAr), 4.22 (d, 1H, *J*=7.8 Hz, CHAr), 4.60–4.74 (m, 2H, 2×C*H*CH$_3$), 5.69 (two s merged, 2H, 2×=CH), 6.42 (s, 1H, =CH), 6.47 (s, 1H, =CH), 6.90–6.95 (m, 2H, 2×1ArH), 7.06–7.09 (m, 2H, 2×1ArH), 7.16–7.17 (m, 2H, 2×1ArH), 8.93 (s, 1H, NH), 9.08 (s, 1H, NH); mass (ES+) *m/z* 266.9 (M^++1), 289.0 (M^++Na); HREIMS calculated for $C_{13}H_{14}N_2O_3$ 266.0458, found, 266.0455.

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