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[2,3]-Sigmatropic rearrangements of didehydropiperidinium ylids☆

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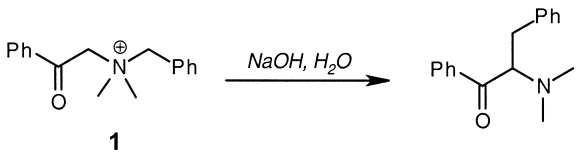
Abstract—The [2,3]-sigmatropic rearrangements of ammonium ylids derived from 1,2,5,6-tetrahydropyridine have been studied: both rearrangement and elimination processes are observed, with rearrangement favoured when aprotic solvents are used in the reaction. The presence of anion-stabilizing substituents on the nucleophilic carbon atom of the intermediate ylid species involved in the tranformation also engenders rearrangement; when certain aryl substituents or two anion-stabilizing groups are present, elimination is not observed, and electron-donating ylid substituents retard rearrangement whilst enhancing elimination. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction[1]

The rearrangement of an ammonium ylid was first described by Stevens et al., in 1928, when (whilst executing a study of protecting groups for nitrogen) they observed that *N*,*N*,*N*-benzyldimethyl-2′-aminoacetophenone, **1**, underwent a [1,2]-benzyl migration upon reaction with sodium hydroxide (Scheme 1).[2] After a series of largely inconclusive mechanistic studies,[3] Stevens concluded that the mechanism of the reaction involved an ion-pair, or an S_Ni process.[4]



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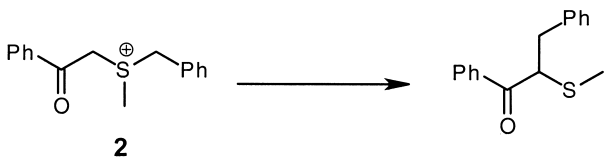
Scheme 1.



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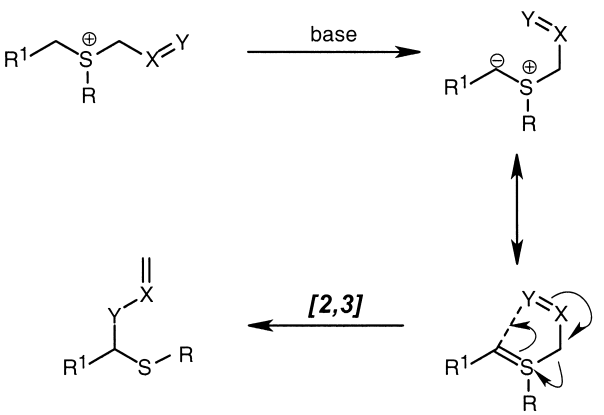
Scheme 2.

Thomson and Stevens subsequently observed a corresponding base-mediated [1,2]-benzyl migration when phenacylsulfonium salt **2** reacted with base (Scheme 2).[5]

The [2,3]-sigmatropic rearrangements of allylic ylids, first investigated (in the case of sulfonium salts) by Baldwin et al.[6] and subsequently by Ollis and his co-workers (sulfonium and ammonium ylids),[7] were described as a general class in the late 1960s: such processes were postulated to be in operation in squalene biosynthesis, and Baldwin drew attention to the fact that these reactions could be considered as a general class of electrocyclic rearrangements of such ylids (Scheme 3).[8]

Such reactions frequently exhibit high diastereoselectivity, arising from highly-ordered, cyclic transition states; in the



Scheme 3.

☆ It has been suggested[1(b)] that the prefix ('[3,2]' be used to describe these reactions, the justification for this terminology being derived from consideration of non-symmetry-controlled processes. For the sake of consistency, when referring to processes as 'sigmatropic rearrangements', we discourage the use of this nomenclature.

Keywords: ammonium ylids; [2,3]-rearrangement; vinyl proline.
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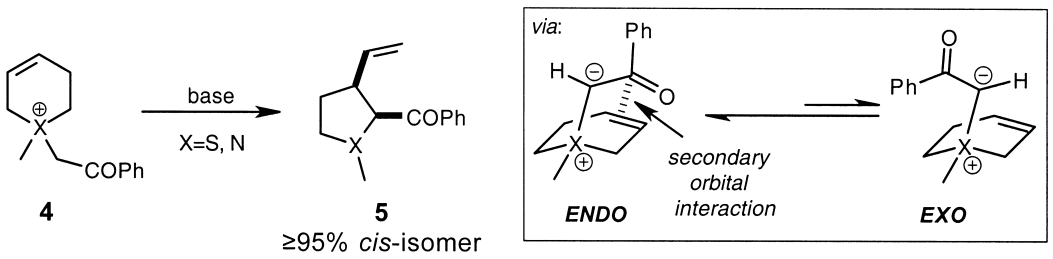
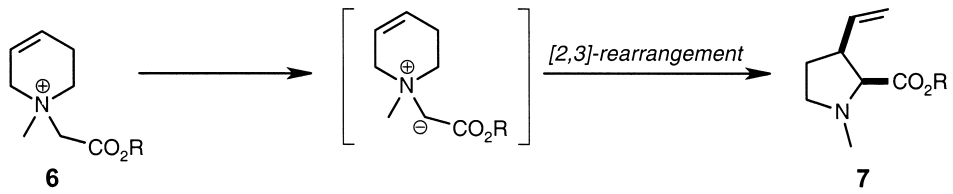


Scheme 4.



Scheme 5.

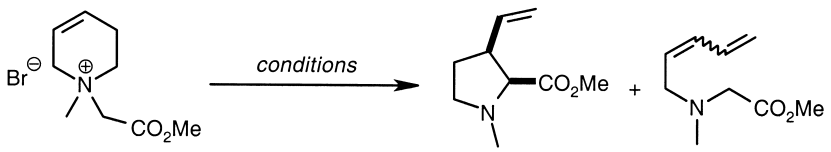
case of carbonyl-stabilized ylids derived from cyclic amines and sulfides (**4**), ring-contracted products **5** of almost exclusively *cis*-configuration are obtained. In addition to providing evidence which strongly supported the suggestion that Stevens rearrangement proceeded by means of a diradical mechanism,[9] Ollis et al. rationalized this selectivity by invoking a secondary orbital interaction between the anion-stabilizing carbonyl and the alkene subunit, favouring an *endo*-configured transition state (Scheme 4).[10]

If an ester, rather than a ketone, were used as the anion-stabilizing portion of the latter ammonium ylids, the reaction would then have an obvious potential utility in the synthesis of potent bioactive pyrrolidine carboxylic acids (such as acromelic, domoic and kainic acids).[11] Thus, we wished to investigate the rearrangement reaction of *N*-(alkoxycarbonyl)methyl-*N*-methyl-1,2,5,6-tetrahydropyridine ylids derived from salts such as **6**, reasoning that a successful [2,3]-rearrangement reaction would give rapid entry to esters of 3-vinylprolines **7** and that an analogous rearrangement of an appositely-functionalized ylid would enable us to prepare a range of kainoid-like compounds in short order (Scheme 5). We here report in full[12] the details of these studies.

2. Results and discussion

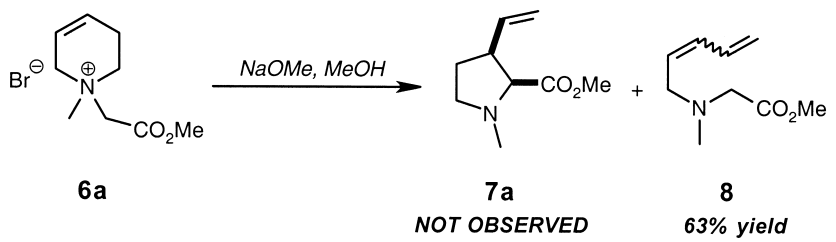
Examination of the literature revealed that this notion had already been examined from a practical perspective and found to be wanting: Stevenson et al. had previously reported that rearrangement of **6a** in alcoholic solvent

Table 1. Reaction of *N*-(methoxycarbonyl)methyl-*N*-methyl-1,2,5,6-tetrahydropyridinium salts with bases

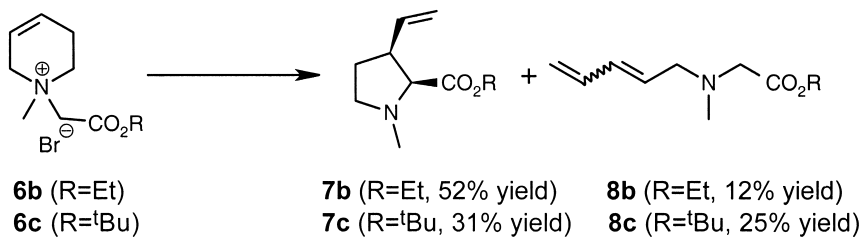


Entry	Solvent	Base	Reaction temperature	Yield (%)	
				7a	**8a**
1	THF	NaH	Ambient	No reaction	
2	THF	DBU	Ambient	No reaction	
3	MeOH	DBU	Ambient	No reaction	
4	THF	NaOMe	Ambient	No reaction	
5	MeOH	NaOMe	Ambient	0	63
6	THF	LDA	Reflux	20	8[a]
7	THF	^{n}BuLi	−78 °C→Reflux	21	7[a]
8	THF	DBU	Reflux	No reaction	
9	THF	NaOH	Reflux	No reaction	
10	THF	NaH	Reflux	50	8
11	THF	NaH (2 equiv.)	Reflux	37	18
12	DME	NaH	Reflux	58	5
13	Dioxane	NaH	Reflux	54	6
14	Toluene	NaH	Reflux	0	11

[a] Remainder unreacted starting material



Scheme 6.



Scheme 7.

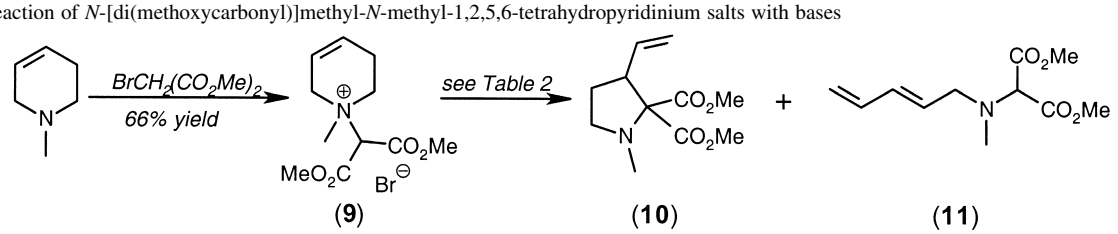
proceeded to give diene **8**, rather than proline **7a**.[13] However, no detailed analysis of the reaction was performed, and thus the authors, reasonably, speculated that the strain generated during attainment of the reactive conformation of **6a** precluded its rearrangement. We wondered whether a less-polar, aprotic reaction medium might circumvent production of diene whilst enhancing production of rearranged product; our observations are gathered in Table 1 (Scheme 6).

Thus, methyl ester **6a** (easily prepared formed by the reaction of *N*-methyl-3,4-didehydropiperidine and methyl bromoacetate) would not undergo reaction at room temperature with a variety of bases in a range of solvents, both protic and aprotic: only starting materials were isolated (entries 1–4). When the reaction was performed using the conditions adumbrated by Stevenson et al., i.e. with methanolic sodium methoxide (entry 5), a reaction did occur, and diene **8** was obtained in 63% yield, confirming the previous observations.[3] Using strong aprotic base (LDA) in THF, however, the major product of the reaction was rearranged product **7a** when the reaction mixture was heated to reflux, although the overall yield of the reaction was low due to incomplete reaction (entry 6). This vinylproline was obtained as a single *cis*-diastereoisomer (^3J=8.8 Hz).[14] The reaction yield was not improved by switching to a stronger base such as ^{n}BuLi (entry 7), but use of sodium hydride as base significantly improved the yield of rearrangement and replacement of THF by DME afforded a 58% yield of vinylproline. Roughly similar yields of rearranged product were obtained when dioxane was used in place of DME as solvent. The obtention of the *cis*-configured product is in agreement with the postulated preference for an *endo*-transition state in rearrangements of the analogous phenacyl ylids (vide supra).[10]

When ethyl and ^{t}butyl esters **6b** and **6c** reacted under the optimized conditions the proportion of elimination product was increased (Scheme 7), indicating that the steric demands of the ester group are of significance (due, no doubt, to involvement of the ester carbonyl in the secondary orbital interaction referred to previously).

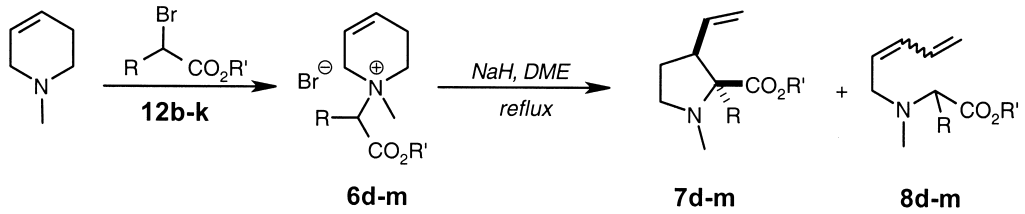
We next turned our attention to an examination of the extent to which electronic effects are a factor in the reaction. Thus, the use of *N*-methyl-*N*-di(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (**9**) in our optimized reaction conditions, confirmed that an increase in the stability of the intermediate ylid exerts a powerful influence upon the reaction, encouraging formation of rearrangement

Table 2. -Reaction of *N*-[di(methoxycarbonyl)]methyl-*N*-methyl-1,2,5,6-tetrahydropyridinium salts with bases



Entry	Solvent	Base	Reaction temperature	Yield (**10**) (%)	Yield (**11**) (%)
1	THF	NaH	Reflux	30	0
2	THF	BuLi	−78 °C→Reflux	46	0
3	THF	DBU	Reflux	73	0
4	DME	NaH	Reflux	57	0
5	DME	DBU	Reflux	79	0

Table 3. Rearrangement reaction of 2′-substituted *N*-(methoxycarbonyl)methyl-*N*-methyl-1,2,5,6-tetrahydropyridinium salts



Entry	R	Product (yield, %)	
1	H	**7a** (58)	**8a** (5)
2	Et	–	**8d** (41)
3	^{n}Hex	–	**8e** (45)
4	Ph	**7f** (71)	–
5	1-Naphthyl	**7g** (89)[a]	–
6	4-MeO-C_6H_4	**7h** (28)	**8h** (25)
7	4-NO_2-C_6H_4	**7i** (48)	–
8	4-Cl-C_6H_4	**7j** (32)	**8j** (11)
9	3-Cl-C_6H_4	**7k** (43)	**8k** (9)
10	4-F-C_6H_4	**7l** (58)	–
11	3-F-C_6H_4	**7m** (36)	–

[a] Obtained as a 4:1 mixture of *cis*- and *trans*-isomers.

product (**10**) and (under most conditions) completely suppressing the formation of the elimination product (**11**) (Table 2). In this rearrangement, best yields of pyrrolidine product were obtained using DBU as base and comparable results were obtained using either DME or THF as solvent.

Having examined the use of ylids bearing only 2′-protons or carboxylic substituents, we next turned our attention to rearrangements of ylids derived from ammonium salts prepared from 2-alkyl or 2-arylacetic esters (**12b–k**). These ammonium salts, (**6d–m**), were prepared in an exactly similar fashion to the original compounds, although in some cases, the synthesis was slightly lengthier due to the need to prepare the 2-bromoesters needed for the quaternization reaction. Armed with these compounds, we examined their rearrangements using conditions similar to those optimized for compound **6a**; the results are summarized in Table 3.

As can be seen from these data, the course of the reaction is highly dependent upon the nature of the 2′-substituent: in general, substituents incapable of stabilizing anions give only dienes (i.e. the products of elimination) upon reaction with base, whereas 2′-aryl substituents encourage rearrangement rather than elimination. In line with the notion that anion stabilization is an important factor in enhancing the yield of rearranged products, aryl substituents bearing strongly (such as a 4-methoxy substituent, compound **6f**) or moderately (such as a 4-chloro substituent, compound **6h**) electron-donating substituents react increasingly via

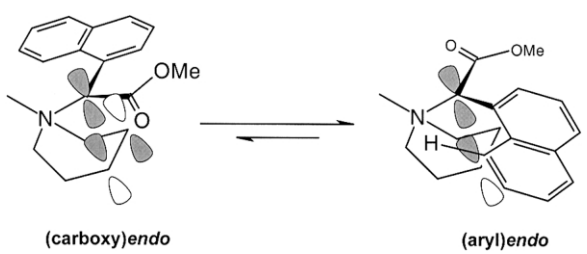


Figure 1. The equilibrium should favour the (carboxy)*endo* form.

elimination at the expense of rearrangement. Interestingly, and out of step with most of our observations in this series, the presence of a 3-chlorophenyl substituent also leads to a significant yield of elimination product. In this case, the dominating influence is perhaps steric rather than electronic, although it is not easy to visualize how this destabilization may occur. Also notable is the diminished diastereoselectivity in the case of the rearrangement of the 2′-(1-naphthyl)-substituted salt, **6e**, where a 4:1 ratio of *cis*/*trans* isomers of **7e** was observed: we rationalize this diminished diastereoselectivity as being due to a preference for an (aryl)*endo*-, rather than a (carboxy)*endo*-configured transition state (Fig. 1); this can be justified if one supposes the naphthyl moiety also to be capable of a secondary orbital. Here the larger aromatic system allows an interaction not possible in rearrangement of monocyclic compounds.

Thus, our studies have revealed certain factors affecting the balance between rearrangement and elimination processes during the reaction of didehydropiperidinium salts with a variety of bases. Further delineation of the controlling features of these transformations is currently underway in our laboratories.

3. Experimental

3.1. General techniques

Except where stated, chemicals were purchased from the Aldrich Chemical Company. Throughout the text, the term ‘petrol’ refers to the fraction of petroleum ether with the boiling range 40–60°C and ‘ether’ to diethyl ether. Ether and THF were distilled from sodium benzophenone ketyl, methanol from magnesium methoxide. All other solvents were provided as sure-seal® and were used without further purification.

Melting points were recorded on a Kofler hot-stage apparatus and are uncorrected. Infra-red spectra were

recorded on a Perkin–Elmer 881 or Paragon 1000 spectrophotometer. Mass spectra were recorded on a Fisons Autospec spectrometer. NMR spectra were recorded on a Bruker DPX-250, or Bruker AX-400 spectrometer. Unless otherwise stated, deuterochloroform was used as solvent and TMS was used as the internal standard. Chemical shifts in ^{1}H NMR spectra are expressed as ppm downfield from TMS, and in ^{13}C NMR, relative to the internal solvent standard. Coupling constants (*J*) are quoted in Hz.

Reactions involving chemicals or intermediates sensitive to air or moisture were conducted under a nitrogen or argon atmosphere in oven- or flame-dried apparatus. Column chromatography was performed using Merck Kieselgel 60 or Fluka Kieselgel 60 silica gel. Analytical thin-layer chromatography was performed using either precoated Merck Kieselgel 60 F_{254} glass-backed plates, or precoated Merck Kieselgel 60 F_{254} aluminium backed plates and were visualized under UV at 254 nm and by staining with iodine and/or an acidic ammonium molybdate dip.

3.1.1. Preparation of *N*-methyl-*N*-(methoxycarbonyl)-methyl-3,4-didehydropiperidinium bromide (6a). A solution of *N*-methyl-3,4-didehydropiperidine hydrochloride (Aldrich, 33,238-0) (5.0 g, 37.4 mmol) in 2 M aqueous sodium hydroxide (56.1 mL, 112.2 mmol, 3 equiv.) was extracted with pentane (4×25 mL). The combined extracts were dried ($MgSO_4$) and removal of the solvent in vacuo (without heating) gave *N*-methyl-3,4-didehydropiperidine as a colourless liquid (2.81 g, 77%); this material was used directly, without further purification.

Methyl bromoacetate (1.9 mL, 20.6 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (2.0 g, 20.6 mmol) in THF (40 mL) under an inert atmosphere. The mixture was heated at reflux for 1 h yielding a colourless precipitate, which was filtered and washed with ether (2×25 mL) to give *N-methyl-N-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide* (4.92 g, 96%) as a deliquescent colourless solid (Found: C, 43.2; H, 6.7; N, 5.5. $C_9H_{16}NO_2Br$ requires C, 43.2; H, 6.5; N, 5.6%); mp 167.9–168.1°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 1746, 732; δ_H ($CDCl_3$) 2.46 (1H, br. d, *J*=17.58 Hz), 2.59 (1H, br. d, *J*=17.58 Hz), 3.63 (3H, s), 3.82 (3H, s), 4.13 (1H, br. m), 4.20 (1H, br. m), 4.50 (1H, br. d, *J*=16.5 Hz), 4.78 (1H, ddd, *J*=16.5, 2.4, 2.4 Hz), 5.19 (1H, d, *J*=17.2 Hz), 5.33 (1H, d, *J*=17.2 Hz), 5.74 (1H, d, *J*=10.5 Hz), 6.02 (1H, d, *J*=10.5 Hz); δ_C ($CDCl_3$) 21.2, 47.5, 53.1, 57.1, 59.7, 60.6, 119.2, 124.3, 165.3; *m/z* (CI) 170.1172 (M^+-Br. $C_9H_{16}NO_2$ requires 170.1181), 156 (71%), 142 (21), 96 (100), 82 (30), 67 (12).

3.2. General procedure for the rearrangement of (6a)

Base (2.0 mmol) was added to a suspension of *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in the specified solvent (20 mL), vigorously stirred under argon. After the reaction was judged complete by tlc, the vessel was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with ether/petrol (2:1) to give *N-methyl-2-methoxycarbonyl-3-ethenylpyrrolidine (**7a**)* and *methyl-3-aza-3-methyl-octa-5,7-dienoate (**8a**)*, as colourless oils.

3.2.1. *N*-Methyl-2-methoxycarbonyl-3-ethenylpyrrolidine (7a). R_f 0.26 (ether/petrol 2:1); ν_{max} (cm^{-1}) 3081, 2952, 2845, 2787, 1736; δ_H ($CDCl_3$) 1.80 (1H, dddd, *J*=12.8, 5.1, 7.7, 8.1 Hz), 2.06 (1H, dddd, *J*=12.8, 6.6, 8.4, 8.8 Hz), 2.37 (3H, s), 2.38 (1H, m), 3.06 (1H, dddd, *J*=8.1, 8.1, 8.4, 8.8 Hz), 3.16 (1H, d, *J*=8.8 Hz), 3.18 (1H, m), 3.69 (3H, s), 4.96 (1H, dd, *J*=1.5, 10.3 Hz), 5.02 (1H, dd, *J*=1.5, 16.8 Hz), 5.73 (1H, ddd, *J*=8.1, 10.3, 16.8 Hz); δ_C ($CDCl_3$) 30.6, 40.7, 46.2, 51.4, 55.5, 72.3, 115.8, 138.3, 171.9; *m/z* (CI) 170.1185 (MH^+H. $C_9H_{16}NO_2$ requires 170.1181).

3.2.2. Methyl-3-aza-3-methyl-octa-5,7-dienoate (8a). R_f 0.40 (ether/petrol 2:1); ν_{max} (cm^{-1}) 2980, 2949 and 2740, 1736, 1658 and 1641; δ_H ($CDCl_3$) 2.38 (3H, s), 3.25 (2H, s), 3.30 (2H, dd, *J*=7.3, 1.5 Hz), 3.72 (3H, s), 5.16 (1H, br. d, *J*=10.1 Hz), 5.24 (1H, dd, *J*=1.9, 16.8 Hz), 5.54 (1H, ddt, *J*=7.3, 10.9, 1.1 Hz), 6.17 (1H, br. dd, *J*=10.9, 11.1 Hz), 6.65 (1H, dddd, *J*=10.1, 11.1, 16.8, 1.1 Hz); δ_C ($CDCl_3$) 42.5, 51.6, 53.7, 57.5, 118.8, 128.0, 131.6, 132.6, 171.4; *m/z* (CI) 170.1191 (MH^+. $C_9H_{16}NO_2$ requires 170.1181), 110 (59%), 85 (7), 49 (8).

3.3. Reaction of (6a) with sodium methoxide in methanol

Sodium methoxide (108 mg, 2.0 mmol) was added to a solution of *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in methanol (20 mL) and the reaction was vigorously stirred at room temperature under argon for 16 h, yielding methyl-3-aza-3-methyl-octa-5,7-dienoate (213 mg, 63%).

3.4. Reaction of (6a) with lithium diisopropylamide in THF

LDA (1 mL, 2 M solution in THF, 2.0 mmol) and *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in THF (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2-methoxycarbonyl-3-ethenylpyrrolidine (68 mg, 20%) and methyl-3-aza-3-methyl-octa-5,7-dienoate (27 mg, 8%).

3.5. Reaction of (6a) with butyllithium in THF

BuLi (1 mL, 2 M solution in pentane, 2.0 mmol) was added dropwise over 5min to a stirred suspension of *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in THF (20 mL) at −78°C. The reaction was stirred at −78°C for 1 h after which it was allowed to warm to room temperature and then heated at reflux for 16 h, yielding *N*-methyl-2-methoxycarbonyl-3-ethenylpyrrolidine (71 mg, 21%) and methyl-3-aza-3-methyl-octa-5,7-dienoate (24 mg, 7%).

3.6. Reaction of (6a) with sodium hydride in THF

(1) Sodium hydride (48 mg, 2.0 mmol) and *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in THF (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2-methoxycarbonyl-3-ethenylpyrrolidine (168 mg, 50%) and methyl-3-aza-3-methyl-octa-5,7-dienoate (27 mg, 8%).

(2) Sodium hydride (96 mg, 2 equiv., 4.0 mmol) and *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in THF (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2-methoxycarbonyl-3-ethenylpyrrolidine (125 mg, 37%) and methyl-3-aza-3-methyl-octa-5,7-dienoate (61 mg, 18%), both colourless oils.

3.7. Reaction of (6a) with sodium hydride in DME

Sodium hydride (48 mg, 2.0 mmol) and *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in DME (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2-methoxycarbonyl-3-ethenylpyrrolidine (196 mg, 58%) and methyl-3-aza-3-methyl-octa-5,7-dienoate (17 mg, 5%).

3.8. Reaction of (6a) with sodium hydride in dioxane

Sodium hydride (48 mg, 2.0 mmol) and *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in THF (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2-methoxycarbonyl-3-ethenylpyrrolidine (183 mg, 54%) and methyl-3-aza-3-methyl-octa-5,7-dienoate (20 mg, 6%).

3.9. Reaction of (6a) with sodium hydride in toluene

Sodium hydride (48 mg, 2.0 mmol) and *N*-methyl-*N*-(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 2.0 mmol) in toluene (20 mL) were reacted as outlined in the general procedure to give methyl-3-aza-3-methyl-octa-5,7-dienoate (37 mg, 11%).

3.9.1. Preparation of *N*-methyl-*N*-(ethoxycarbonyl)-methyl-3,4-didehydropiperidinium bromide (6b). Ethyl bromoacetate (1.1 mL, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under a nitrogen atmosphere. The mixture was heated at reflux for 2 h during which the title compound precipitated; the crude solid was filtered and washed with ether (2×25 mL) to give *N-methyl-N-(ethoxycarbonyl)methyl-3,4-didehydropiperidinium bromide* (2.52 g, 93%) as a deliquescent colourless solid (Found: C, 45.4; H, 7.2; N, 5.2. $C_{10}H_{18}NO_2Br$ requires C, 45.5; H, 6.9; N, 5.3%); mp 144.6–145.2°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 3039, 2956, 1746, 736; δ_H ($CDCl_3$) 1.32 (3H, t, *J*=7.0 Hz), 2.46 (1H, br. d, *J*=18.3 Hz), 2.57 (1H, br. d, *J*=18.3 Hz), 3.65 (3H, s), 4.15 (1H, br. m), 4.22 (1H, br. m), 4.27 (3H, q, *J*=7.0 Hz), 4.52 (1H, br. d, *J*=15.8 Hz), 4.79 (1H, br. d, *J*=15.8 Hz), 5.02 (1H, d, *J*=16.9 Hz), 5.16 (1H, d, *J*=16.9 Hz), 5.75 (1H, br. d, *J*=9.7 Hz), 6.03 (1H, br. d, *J*=9.7 Hz); δ_C ($CDCl_3$) 14.0, 21.4, 48.1, 57.3, 60.1, 60.5, 62.8, 119.4, 124.4, 164.8; *m/z* (CI) 184.1328 (M^+-Br. $C_{10}H_{18}NO_2$ requires 184.1338), 156 (51%), 142 (33), 112 (51), 96 (75), 82 (20).

3.10. Rearrangement of *N*-methyl-*N*-(ethoxycarbonyl)-methyl-3,4-didehydropiperidinium bromide

Sodium hydride (45.4 mg, 1.89 mmol) was added to a suspension of *N*-methyl-*N*-(ethoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 1.89 mmol) in DME (20 mL), vigorously stirred under an inert atmosphere. The mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was removed and extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with (2:1) ether/petrol to give *N-methyl-2-ethoxycarbonyl-3-ethenylpyrrolidine (**7b**)* and *ethyl-3-aza-3-methyl-octa-5,7-dienoate (**8b**)*, both colourless oils.

3.10.1. *N*-Methyl-2-ethoxycarbonyl-3-ethenylpyrrolidine (7b). (180 mg, 52%), R_f 0.28 (ether/petrol 2:1); ν_{max} (cm^{-1}) 3081, 2952, 2845, 2787, 1736; δ_H ($CDCl_3$) 1.25, (3H, t, *J*=7.0 Hz), 1.80 (1H, dddd, *J*=12.8, 6.6, 7.0, 9.9 Hz), 2.06 (1H, dddd, *J*=12.8, 4.0, 8.4, 8.9 Hz), 2.35 (1H, m), 2.36 (3H, s), 3.05 (1H, dddd, *J*=7.0, 8.1, 8.4, 8.9 Hz), 3.11 (1H, d, *J*=8.4 Hz), 3.17 (1H, m), 4.16 (2H, br. q, *J*=7.0 Hz), 4.96 (1H, dd, *J*=1.8, 10.6 Hz), 5.03 (1H, dd, *J*=1.8, 17.9 Hz), 5.75 (1H, ddd, *J*=8.1, 10.6, 17.9 Hz); δ_C ($CDCl_3$) 14.3, 30.4, 40.5, 46.0, 55.3, 60.2, 71.9, 115.6, 138.3, 171.3; *m/z* (CI) 184.1333 (MH^+. $C_{10}H_{18}NO_2$ requires 184.1338), 110 (83%).

3.10.2. Ethyl-3-aza-3-methyl-octa-5,7-dienoate (8b). (40.0 mg, 11.5%), R_f 0.42 (ether/petrol 2:1); ν_{max} (cm^{-1}) 2953, 2949 and 2751, 1736, 1686 and 1632; δ_H ($CDCl_3$) 1.27 (3H, t, *J*=7.0 Hz), 2.39 (3H, s), 3.24 (2H, s), 3.32 (2H, dd, *J*=7.3, 1.1 Hz), 4.18 (2H, q, *J*=7.0 Hz), 5.16 (1H, br. d, *J*=10.3 Hz), 5.24 (1H, br. d, *J*=16.9 Hz), 5.54 (1H, dt, *J*=7.3, 11.0 Hz), 6.17 (1H, br. dd, *J*=11.0, 11.0 Hz), 6.65 (1H, dddd, *J*=10.3, 11.0, 16.9, 1.1 Hz); δ_C ($CDCl_3$): 14.3, 42.5, 53.6, 57.5, 60.6, 118.9, 127.9, 131.6, 132.8, 171.7; *m/z* (CI) 184.1338 (MH^+. $C_{10}H_{18}NO_2$ requires 184.1338), 110 (59%), 85 (7), 49 (8).

3.10.3. Preparation of *N*-methyl-*N*-(*tert*-butoxycarbonyl)-methyl-3,4-didehydropiperidinium bromide (6c). ^{t}Butyl bromoacetate (3.3 mL, 20.6 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (2.0g, 20.6 mmol) in THF (40 mL) under an inert atmosphere. The mixture was heated at reflux for 6 h yielding a colourless precipitate, which was filtered and washed with ether (2×25 mL) to give *N-methyl-N-(tert-butoxycarbonyl)methyl-3,4-didehydropiperidinium bromide* (4.87 g, 80%) as a deliquescent colourless solid (Found: C, 49.4; H, 7.9; N, 4.8. $C_{12}H_{22}NO_2Br$ requires C, 49.3; H, 7.6; N, 4.8%); mp 154.0–154.6°C (dichloromethane/petrol; ν_{max} (cm^{-1}) (dichloromethane) 2979, 2956, 1737; δ_H ($CDCl_3$) 1.51 (9H, s), 2.42 (1H, br. d, *J*=19.2 Hz), 2.55 (1H, br. d,

J=19.2 Hz), 3.66 (3H, s), 4.08 (1H, m), 4.21 (1H, m), 4.50 (1H, br. d, J=16.3 Hz), 4.70 (1H, d, J=17.0 Hz), 4.78 (1H, br. d, J=16.3 Hz), 4.86 (1H, d, J=17.0 Hz), 5.74 (1H, br. d, J=10.4 Hz), 6.03 (1H, br. d, J=10.4 Hz); δ_C ($CDCl_3$) 21.4, 28.1, 48.6, 57.2, 60.2, 60.4, 85.5, 119.5, 124.5, 163.8; *m/z* (CI) 212.1651 (M^+-Br. $C_{12}H_{22}NO_2$ requires 212.1651), 156 (71%), 142 (21), 96 (100), 82 (30), 67 (12).

3.11. Rearrangement of *N*-methyl-*N*-(*tert*-butoxycarbonyl)methyl-3,4-didehydropiperidinium bromide

Sodium hydride (41.0 mg, 1.71 mmol) was added to a suspension of *N*-methyl-*N*-(*tert*-butoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 1.71 mmol) in DME (20 mL), vigorously stirred under an inert atmosphere. The mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was removed and extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with (2:1) ether/petrol to give *N-methyl-2-tert-butoxycarbonyl-3-ethenylpyrrolidine (**7c**)* and *tert-butyl-3-aza-3-methyl-octa-5,7-dienoate (**8c**)*, both colourless oils.

3.11.1. *N*-Methyl-2-*tert*-butoxycarbonyl-3-ethenylpyrrolidine (7c). (111 mg, 31%), R_f 0.27 (ether/petrol 2:1); ν_{max} (cm^{-1}) 3077, 2976, 2842, 2784, 1743; δ_H ($CDCl_3$) 1.44, (9H, s), 1.79 (1H, dddd, J=12.8, 6.6, 7.0, 8.8 Hz), 2.03 (1H, dddd, J=12.8, 2.6, 8.1, 8.8 Hz), 2.37 (3H, s), 2.38 (1H, ddd, J=8.8, 6.6, 8.8 Hz), 3.01 (1H, m), 3.02 (1H, m), 3.12 (1H, ddd, J=8.8, 2.6, 8.8 Hz), 4.96 (1H, dd, J=1.8, 9.9 Hz), 5.03 (1H, dd, J=1.8, 16.9 Hz), 5.79 (1H, ddd, J=8.8, 9.9, 16.9 Hz); δ_C ($CDCl_3$) 28.1, 28.1, 28.31, 30.5, 40.3, 46.2, 55.2, 72.1, 80.8, 115.5, 138.7, 170.6; *m/z* (CI) 212.1652 (MH^+. $C_{12}H_{22}NO_2$ requires 212.1650).

3.11.2. *tert*-Butyl-3-aza-3-methyl-octa-5,7-dienoate (8c). (91 mg, 25%), R_f 0.47 (ether/petrol 2:1); ν_{max} (cm^{-1}) 2953, 1736, 1685, 1654; δ_H ($CDCl_3$) 1.47 (9H, s), 2.39 (3H, s), 3.16 (2H, s), 3.32 (2H, d, J=7.5 Hz), 5.15 (1H, br. d, J= 10.3 Hz), 5.23 (1H, br. d, J=16.9 Hz), 5.55 (1H, dt, J=7.5, J=11.0 Hz), 6.17 (1H, br. dd, J=11.0, 11.0 Hz), 6.67 (1H, ddd, J=10.3, 11.0, 16.9 Hz); δ_C ($CDCl_3$): 28.1, 42.2, 53.3, 58.1, 81.0, 118.6, 128.4, 131.8, 132.4, 170.1; *m/z* (CI) 212.1648 (MH^+. $C_{12}H_{22}NO_2$ requires 212.1650), 110 (59%), 85 (7), 49 (8).

3.11.3. Preparation of *N*-methyl-*N*-di(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (9). Dimethyl bromomalonate (2.7 mL, 20.6 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (2.0 g, 20.6 mmol) in THF (40 mL) under argon. The reaction mixture was heated at reflux for 12 h during which the title compound precipitated; the crude solid was filtered and washed with ether (2×25 mL) to give *N*-methyl-*N*-di(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (4.31 g, 14.0 mmol, 68%) as a colourless deliquescent solid; mp 129.3–130.1°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 1759, 1736, 736; δ_H ($CDCl_3$) 2.45 (1H, br. d), 2.56 (1H, br. d, J=17.6 Hz), 3.66 (3H, s), 3.95 (3H, s), 4.01 (3H, s), 4.09 (1H, br. m), 4.15 (1H, br. m), 4.51 (1H, br. d), 4.70 (1H, m), 4.88 (1H, br. s, NC*H*$(CO_2CH_3)_2$), 5.77 (1H, d, J=10.5 Hz), 6.03 (1H, d, J=10.5 Hz); δ_C ($CDCl_3$) 21.1, 45.0, 54.6, 56.8, 58.8, 71.7, 118.5, 124.3, 162.1; *m/z* (CI) 228.1233 (M^+-Br. $C_{11}H_{18}NO_4$ requires 228.1236), 168 (80%), 156 (82), 110 (20), 96 (100).

3.11.4. General procedure for the rearrangement of (9): preparation of *N*-methyl-2,2-di(methoxycarbonyl)-3-ethenylpyrrolidine (10). Base (1.6 mmol) was added to a suspension of *N*-methyl-*N*-di(methoxycarbonyl)methyl-3,4-didehydropiperidinium bromide (500 mg, 1.6 mmol) in solvent (20 mL), vigorously stirred under an inert atmosphere. The mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The reaction mixture was concentrated in vacuo to yield a solid, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was removed and extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo to give a colourless solid which was purified by recrystalization (ethanol/water) to give *N-methyl-2,2-di(methoxycarbonyl)-3-ethenylpyrrolidine* as colourless crystals. R_f 0.36 (ether/petrol 2:1) (Found: C, 58.2; H, 7.9; N, 6.1. $C_{11}H_{17}NO_4$ requires C, 58.1; H, 7.5; N, 6.2%); mp 64.5°C (ethanol/water); ν_{max} (cm^{-1}) (dichloromethane) 3056, 2955, 2852, 1730, 1727; δ_H ($CDCl_3$) 1.83 (1H, dddd, J=12.7, 9.4, 6.5, 6.5 Hz), 2.21 (1H, dddd, J=12.7, 8.9, 8.9, 4.0 Hz), 2.46 (3H, s), 2.84 (1H, ddd, J=9.1, 6.5, 8.9 Hz), 3.07 (1H, ddd, J=9.1, 9.4, 4.0 Hz), 3.30 (1H, ddd, J=8.9, 8.8, 6.5 Hz), 3.70 (3H, s), 3.77 (3H, s), 5.01 (1H, dd, J=1.8, 10.1 Hz), 5.07 (1H, dd, J=1.8, 17.1 Hz), 5.80 (1H, ddd, J=17.1, 10.1, 8.8 Hz); δ_C ($CDCl_3$) 28.6, 37.1, 50.3, 51.8, 51.9, 53.5, 79.0, 116.5, 137.7, 168.8, 169.1; *m/z* (EI) 227.1158 (M^+ $C_{11}H_{17}NO_4$ requires 227.1158), 168 (96%), 109 (69).

3.12. Rearrangement of (9) with sodium hydride in THF

NaH (38 mg, 1.6 mmol) and (**9**) (500 mg, 1.6 mmol) in THF (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2,2-di(methoxycarbonyl)-3-ethenylpyrrolidine (110 mg, 30%).

3.13. Rearrangement of (9) with butyllithium in THF

^{n}BuLi (0.8 mL, 2 M solution in pentane, 1.6 mmol) was added dropwise over 5 min to a stirred suspension of (**9**) (500 mg, 1.6 mmol) in THF (20 mL) at −78°C. The reaction was stirred at −78°C for 1h after which it was allowed to warm to room temperature and then heated at reflux for 16h, yielding *N*-methyl-2,2-di(methoxycarbonyl)-3-ethenylpyrrolidine (169 mg, 46%).

3.14. Rearrangement of (9) with 1,8-diazabicyclo[5.4.0]-undec-7-ene in THF

DBU (0.24 mL, 1.6 mmol) (**9**) (500 mg, 1.6 mmol) in DME (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2,2-di(methoxycarbonyl)-3-ethenylpyrrolidine (213 mg, 58%).

3.15. Rearrangement of (9) with sodium hydride in DME

NaH (38 mg, 1.6 mmol) and (**9**) (500 mg, 1.6 mmol) in THF (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2,2-di(methoxycarbonyl)-3-ethenylpyrrolidine (209 mg, 57%).

3.16. Rearrangement of (9) with 1,8-diazabicyclo[5.4.0]-undec-7-ene in DME

DBU (0.24 mL, 1.6 mmol) and (**9**) (500 mg, 1.6 mmol) in DME (20 mL) were reacted as outlined in the general procedure to give *N*-methyl-2,2-di(methoxycarbonyl)-3-ethenylpyrrolidine (289 mg, 79%).

3.16.1. *N*-Methyl-*N*-((methoxycarbonyl)methyl(ethyl))-3,4-didehydropiperidinium bromide (6d). Methyl 2-bromobutyrate (1.18 mL, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The reaction mixture was heated at reflux for 6 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl-(ethyl))-3,4-didehydropiperidinium bromide* (2.23 g, 78%) as a colourless deliquescent solid; mp 104.1–104.5°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 2956, 1742, 731; δ_H ($CDCl_3$) 1.03 (3H, t, *J*=7.3 Hz), 1.83 (3H, t, *J*=7.3 Hz), 2.01 (2H, m), 2.10 (2H, m), 2.51 (2H, br. m), 2.62 (2H, br. d), 3.46 (3H, s), 3.47 (3H, s), 3.87 (3H, s), 3.88 (3H, s), 3.90 (1H, br. m), 3.93 (1H, br. m), 3.99 (1H, br. m), 4.10 (1H, br. m), 4.28 (1H, br. d, *J*=16.5 Hz), 4.40 (1H, br. d, *J*=16.5 Hz), 4.59 (1H, br. d, *J*=16.5 Hz), 4.63 (1H, br. d, *J*=16.5 Hz), 4.82 (1H, t, *J*=7.3 Hz), 4.84 (1H, t, *J*=7.3 Hz), 5.78 (2H, br. m), 6.06 (2H, br. m); δ_C ($CDCl_3$) 10.2, 11.8, 21.5, 21.7, 28.4, 45.5, 47.4, 52.8, 53.4, 56.5, 57.2, 58.0, 58.8, 72.9, 73.8, 118.8, 119.1, 124.6, 124.8, 168.2, 168.3; *m/z* (CI) 198.1506 (M^+-Br. $C_{11}H_{20}NO_2$ requires 198.1494), 139 (21%), 96 (100), 82 (42).

3.16.2. Rearrangement of *N*-methyl-*N*-((methoxycarbonyl)methyl(ethyl))-3,4-didehydropiperidinium bromide: preparation of methyl-3-aza-2-ethyl-3-methyl-octa-5,7-dienoate (8d). Sodium hydride (43 mg, 1.79 mmol) was added to a suspension of *N*-methyl-(methyl-2-*N*-butyrate)-3,4-didehydropiperidinium bromide (500 mg, 1.79 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with (1:2) ether/petrol to give *methyl-3-aza-2-ethyl-3-methyl-octa-5,7-dienoate* (146 mg, 41%) as a colourless oil R_f 0.46 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2955, 2924, 2871, 1736, 1686 and 1642; δ_H ($CDCl_3$) 0.92 (3H, t, *J*=7.3 Hz), 1.66 (1H, ddq, *J*=14.3, 6.9, 7.3 Hz), 1.78 (1H, ddq, *J*=14.3, 7.3, 7.7 Hz), 2.30 (3H, s), 3.21 (1H, dd, *J*=6.9, 7.7 Hz), 3.31 (2H, d, *J*=7.3 Hz), 3.71 (3H, s), 5.14 (1H, d, *J*=9.9 Hz), 5.22 (1H, d, *J*=16.9 Hz), 5.49 (1H, dt, *J*=7.3, 10.9 Hz), 6.14 (1H, dd, *J*=10.9, 10.9 Hz), 6.65 (1H, dddd, *J*=9.9, 10.9, 16.9, 1.1 Hz); δ_C ($CDCl_3$): 10.8, 22.7, 37.9, 51.0, 51.2, 67.1, 118.3, 129.3, 131.8, 131.9, 173.1; *m/z* (CI) 198.1506 (MH^+. $C_{11}H_{20}NO_2$ requires 198.1494), 138 (100%), 67 (27), 49 (13).

3.16.3. *N*-Methyl-*N*-(ethoxycarbonyl)methyl(hexyl))-3,4-didehydropiperidinium bromide (6e). Ethyl 2-bromooctanoate (2.21 mL, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The reaction mixture was heated at reflux for 12 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-(ethoxycarbonyl)methyl(hexyl))-3,4-didehydropiperidinium bromide* (2.01 g, 56%) as a colourless deliquescent solid; mp 99.8–101.7°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 2932, 2859, 1735, 732; δ_H ($CDCl_3$) 0.88 (6H, br. t, *J*=6.6 Hz), 1.21 (6H, t, *J*=6.9 Hz), 1.28 (4H, m), 1.29 (4H, m), 1.36 (4H, m), 1.39 (4H, m), 1.98 (2H, m), 2.17 (2H, m), 2.35 (1H, br. m), 2.41 (1H, br. m), 2.52 (1H, br. m), 2.55 (1H, br. d), 2.89 (6 h, s), 3.47 (2H, d, *J*=6.9 Hz), 3.49 (2H, d, *J*=6.9 Hz), 3.79 (1H, m), 3.81 (1H, m), 3.83 (1H, m), 4.09 (1H, m), 4.21 (1H, m), 4.35 (1H, m), 4.42 (1H, m), 4.66 (1H, m), 4.72 (1H, m), 4.78 (1H, m), 5.76 (2H, br. m), 6.04 (2H, br. m); δ_C ($CDCl_3$) 14.0, 14.1, 21.6, 22.0, 22.4, 25.7, 27.0, 28.7, 31.4, 42.6, 50.3, 51.5, 56.7, 57.5, 56.0, 58.8, 71.1, 72.7, 118.9, 119.2, 124.9, 125.6, 167.5, 168.0; *m/z* (CI) 268.2287 (M^+-Br. $C_{15}H_{28}NO_2$ requires 268.2276), 254 (82%), 240 (11), 226 (8), 194 (12), 180 (100), 98 (58), 82 (16).

3.16.4. Rearrangement of *N*-methyl-*N*-(ethoxycarbonyl)-methyl(hexyl))-3,4-didehydropiperidinium bromide: preparation of ethyl-3-aza-2-hexyl-3-methyl-octa-5,7-dienoate (8e). Sodium hydride (34.5 mg, 1.44 mmol) was added to a suspension of *N*-methyl-*N*-(ethoxycarbonyl)-methyl(hexyl))-3,4-didehydropiperidinium bromide (500 mg, 1.44 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with (1:2) ether/petrol to give *ethyl-3-aza-2-hexyl-3-methyl-octa-5,7-dienoate* (174 mg, 45%) as a colourless oil R_f 0.49 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2951, 2845, 2793, 1725, 1686, 1641; δ_H ($CDCl_3$) 0.89 (3H, m), 1.19 (3H, m), 1.25 (2H, m), 1.30 (2H, m), 1.57 (2H, m), 1.60 (2H, m), 1.81 (2H, m), 2.36 (3H, br. s), 3.27 (1H, br. m), 3.36 (2H, br. d), 4.22 (3H, q, *J*=7.1 Hz), 5.18 (1H, d, *J*=10.3 Hz), 5.26 (1H, d, *J*=16.5 Hz), 5.56 (1H, m), 6.19 (1H, dd, *J*=10.8, 11.08 Hz), 6.70 (1H, ddd, *J*=10.3, 11.08, 16.5 Hz); δ_C ($CDCl_3$): 14.1, 14.5, 22.6, 26.2, 29.1, 29.7, 31.7, 37.9, 51.2, 60.1, 65.5, 118.1, 125.9, 132.0, 132.0, 174.9; *m/z* (CI) 268.2275 (MH^+. $C_{16}H_{30}NO_2$ requires 268.2276), 110 (78%), 96 (53), 85 (13), 45 (10).

3.17. General procedure for preparation of methyl-α-bromoarylacetates (12g–m)[15–18]

(1) Concentrated sulfuric acid (2 mL) was added to a stirred solution of arylacetic acid (13 mmol) in methanol (20 mL) and the solution was heated at reflux for 3 h. The solvents were removed in vacuo, the resultant product was partitioned between ether (20 mL) and water (20 mL). The organic layer was washed with saturated sodium carbonate solution (2×20 mL), dried ($MgSO_4$) and the solvent removed in vacuo to leave the arylacetic acid.

(2) AIBN (0.50 mmol, 5 mol%) was added to a stirred solution of methyl arylacetate (10 mmol) and *N*-bromosuccinimide (11 mmol, 1.1 equiv.) in carbon tetrachloride (20 mL) under argon. The reaction mixture was heated at reflux for 5 h after which it was cooled and petrol (20 mL) was added to the reaction mixture. Solids were removed by filtration, and the solvents removed in vacuo to give the methyl-α-bromoarylacetate which was purified by column chromatography, eluting with 1:2 ether/petrol.

3.17.1. Methyl-α-bromo-1-naphthylacetate (12g). Methyl-1-naphthylacetate (2.0 g, 10.0 mmol), *N*-bromosuccinimide (1.95 g, 11.0 mmol) and AIBN (82 mg, 0.50 mmol) were reacted as outlined above to give *methyl-α-bromo-1-naphthylacetate* (2.66 g, 95%) as a colourless oil; R_f 0.42 (ether/petrol 1:2); ν_{max} (cm^{-1}) 1751, 1686, 1637; δ_H ($CDCl_3$) 3.75 (3H, s), 6.16 (1H, s), 7.43 (1H, m) 7.50 (1H, m) 7.57 (1H, m), 7.76 (1H, m), 7.83 (1H, m), 7.85 (1H, m), 8.09 (1H, m); δ_C ($CDCl_3$) 45.0, 53.6, 123.0, 125.4, 126.2, 126.9, 127.2, 129.0, 130.2, 130.2, 131.5, 134.0, 168.8; *m/z* (CI) 277.9946 (M^+ $C_{13}H_{11}O_2Br$ requires 277.9942), 232 (18%), 199 (100), 139 (52).

3.17.2. Methyl-α-bromo-*p*-methoxyphenylacetate (12h). Methyl *p*-methoxyphenylacetate (2.0 g, 11.1 mmol), *N*-bromosuccinimide (2.17 g, 12.2 mmol) and AIBN (91 mg, 0.55 mmol) were reacted as outlined above to give *methyl-α-bromo-p-methoxyphenylacetate* (2.71 g, 94%) as a colourless oil; R_f 0.43 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2954, 1739, 1609br; δ_H ($CDCl_3$) 3.78 (3H, s), 3.80 (3H, s), 5.37 (1H, s), 6.89 (2H, d, *J*=8.8 Hz), 7.48 (2H, d, *J*=8.8 Hz); δ_C ($CDCl_3$) 46.3, 53.3, 55.4, 114.3, 127.7, 130.1, 160.3, 168.9; *m/z* (CI) 257.9894 (M^+ $C_{10}H_{11}O_3Br$ requires 257.9891), 195 (6%), 179 (100), 151 (13), 135 (6), 121 (5).

3.17.3. Methyl-α-bromo-*p*-nitrophenylacetate (12i). (1) *p*-Nitrophenyl acetic acid (2.0 g, 11.0 mmol) was reacted as outlined above to give methyl *p*-nitrophenyl acetate (2.05 g, 95%) as a colourless solid; mp 40.8–41.2°C (dichloromethane/petrol); ν_{max} (cm^{-1}) 3055, 1739, 1608 br., 1523, 1349; δ_H ($CDCl_3$) 3.73 (3H, s), 3.75 (2H, s), 7.46 (1H, d, *J*=8.8 Hz), 8.19 (1H, d, *J*=8.8 Hz); δ_C ($CDCl_3$) 40.8, 52.4, 123.8, 130.3, 141.3, 147.3, 170.6; *m/z* (CI) 195.0525 (M^+ $C_9H_9NO_4$ requires 195.0532), 179 (27%), 166 (94), 120 (100).

(2) Methyl *p*-nitrophenylacetate (2.0 g, 10.3 mmol), *N*-bromosuccinimide (2.01 g, 11.3 mmol) and AIBN (84 mg, 0.21 mmol) were reacted as outlined above to give *methyl-α-bromo-p-nitrophenylacetate* (2.69 g, 95%) as a colourless solid; mp 32.9–33.1°C (dichloromethane/petrol); R_f 0.43 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2980, 1741, 1607 br., 1520, 1348; δ_H ($CDCl_3$) 3.82 (3H, s), 5.46 (1H, s), 7.76 (1H, d, *J*=8.8 Hz), 8.22 (1H, d, *J*=8.8 Hz); δ_C ($CDCl_3$) 44.2, 53.8, 123.9, 129.9, 130.4, 142.6, 167.9; *m/z* (CI) 272.9837 (M^+ $C_9H_8NO_4Br$ requires 272.9837), 194 (91%), 120 (54), 89 (86).

3.17.4. Methyl-α-bromo-*p*-chlorophenylacetate (12j). (1) *p*-Chlorophenyl acetic acid (2.0 g, 11.7 mmol) was reacted as outlined above to give methyl *p*-chlorophenyl acetate (2.01 g, 93%) as a colourless oil ν_{max} (cm^{-1}) 3005, 1740, 1609 br.; δ_H ($CDCl_3$) 3.61 (2H, s), 3.66 (3H, s), 7.18 (2H, d, *J*=8.8 Hz), 7.26 (2H, d, *J*=8.8 Hz); δ_C ($CDCl_3$) 40.6, 52.3, 128.9, 130.9, 132.6, 133.3, 171.8; *m/z* (CI) 184.0295 (M^+ $C_9H_9NO_2Cl$ requires 184.0291), 125 (100%).

(2) Methyl *p*-chlorophenylacetate (1.5 g, 8.2 mmol), *N*-bromosuccinimide (1.59 g, 9.0 mmol) and AIBN (67 mg, 0.41 mmol) were reacted as outlined above to give *methyl-α-bromo-p-chlorophenylacetate* (2.06 g, 96%) as a colourless oil; R_f 0.42 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2955, 1746, 1645 br.; δ_H ($CDCl_3$) 3.77 (3H, s), 5.33 (1H, s), 7.31 (2H, d, *J*=8.8 Hz), 7.48 (2H, d, *J*=8.8 Hz); δ_C ($CDCl_3$) 45.1, 53.3, 128.8, 129.9, 134.1, 135.1, 168.2; *m/z* (CI) 261.9392 (M^+ $C_9H_8O_2ClBr$ requires 261.9392), 183 (100%), 155 (56), 140 (19), 125 (14), 89 (41).

3.17.5. Methyl-α-bromo-*m*-chlorophenylacetate (12k). (1) *m*-Chlorophenyl acetic acid (2.0 g, 11.7 mmol) was reacted as outlined above to give methyl *m*-chlorophenyl acetate (2.05 g, 95%) as a colourless oil ν_{max} (cm^{-1}) 2953, 1740, 1599, 1576; δ_H ($CDCl_3$) 3.60 (2H, s), 3.69 (3H, s), 7.16 (1H, m), 7.24 (1H, m), 7.25 (1H, m), 7.29 (1H, m); δ_C ($CDCl_3$) 40.4, 51.9, 127.1, 127.3, 129.3, 129.8, 134.1, 135.7, 171.1; *m/z* (CI) 184.0293 (M^+ $C_9H_9NO_2Cl$ requires 184.0291), 125 (100%).

(2) Methyl *m*-chlorophenylacetate (1.5 g, 8.2 mmol), *N*-bromosuccinimide (1.59 g, 9.0 mmol) and AIBN (67 mg, 0.41 mmol) were reacted as outlined above to give *methyl-α-bromo-m-chlorophenylacetate* (2.01 g, 94%) as a colourless oil; R_f 0.43 (ether/petrol 1:2); ν_{max} (cm^{-1}) 3002, 1746, 1615, 1592; δ_H ($CDCl_3$) 3.78 (3H, s), 5.31 (1H, s), 7.29 (1H, m), 7.30 (1H, m), 7.41 (1H, ddd, *J*=6.9, 1.8, 1.8 Hz), 7.55 (1H, d, *J*=1.8 Hz); δ_C ($CDCl_3$) 45.1, 53.4, 126.7, 128.7, 129.3, 129.9, 134.4, 137.5, 168.2; *m/z* (CI) 261.9399 (M^+ $C_9H_8O_2ClBr$ requires 261.9396), 183 (100%), 155 (89), 140 (35), 125 (18), 89 (79).

3.17.6. Methyl-α-bromo-*p*-fluorophenylacetate (12l). (1) *p*-Fluorophenyl acetic acid (2.0 g, 13.0 mmol) was reacted as outlined above to give methyl *p*-fluorophenyl acetate (2.08 g, 95%) as a colourless oil ν_{max} (cm^{-1}) 2955, 1739, 1609 br.; δ_H ($CDCl_3$) 3.59 (2H, s), 3.67 (3H, s), 7.00 (2H, dd, *J*=8.4, 8.8 Hz), 7.24 (2H, dd, *J*=5.5, 8.8 Hz); δ_C ($CDCl_3$) 39.9, 51.7, 115.2 (d, *J*=22.1 Hz), 129.6 (d, *J*=3.7 Hz), 130.6 (d, *J*=7.4 Hz), 161.8 (d, *J*=244.5 Hz), 171.6; *m/z* (CI) 168.0592 (M^+ $C_9H_9O_2F$ requires 168.0587), 168 (82%), 109 (100).

(2) Methyl *p*-fluorophenylacetate (1.5 g, 8.9 mmol), *N*-bromosuccinimide (1.75 g, 9.8 mmol) and AIBN (73 mg,

0.45 mmol) were reacted as outlined above to give *methyl-α-bromo-p-fluorophenylacetate* (2.16 g, 98%) as a colourless oil; R_f 0.42 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2955, 1750, 1614 br; δ_H ($CDCl_3$) 3.77 (3H, s), 5.38 (1H, s), 7.04 (2H, dd, J=8.4, 8.8 Hz), 7.55 (2H, dd, J=5.5, 8.8 Hz); δ_C ($CDCl_3$) 45.1, 53.1, 115.6 (d, J=22.1 Hz), 130.5 (d, J=7.3 Hz), 131.5 (d, J=3.7 Hz), 162.8 (d, J=250.0 Hz), 168.4; *m/z* (CI) 246.9692 (M^+ $C_9H_8O_2FBr$ requires 245.9691), 184 (22%), 167 (100), 139 (43), 108 (14).

3.17.7. Methyl-α-bromo-*m*-fluorophenylacetate (12m). (1) *m*-Fluorophenyl acetic acid (2.0 g, 13.0 mmol) was reacted as outlined above to give methyl *m*-fluorophenyl acetate (1.99 g, 91%) as a colourless oil ν_{max} (cm^{-1}) 2953, 1740, 1600, 1577; δ_H ($CDCl_3$) 3.59 (2H, s), 3.67 (3H, s), 6.93 (1H, m), 6.97 (1H, m), 7.01 (1H, m), 7.25 (1H, m); δ_C ($CDCl_3$) 40.5, 51.8, 113.8 (d, J=22.1 Hz), 116.1 (d, J=20.2 Hz), 124.8 (d, J=3.6 Hz), 129.8 (d, J=9.2 Hz), 136.1 (d, J=7.3 Hz), 162.6 (d, J=246.4 Hz), 171.2; *m/z* (CI) 168.0583 (MH^+. $C_9H_9NO_2F$ requires 168.0587), 109 (100%), 83 (10).

(2) Methyl *m*-fluorophenylacetate (1.5 g, 8.9 mmol), *N*-bromosuccinimide (1.75 g, 9.8 mmol) and AIBN (73 mg, 0.45 mmol) were reacted as outlined above to give *methyl-α-bromo-m-fluorophenylacetate* (2.19 g, 98%) as a colourless oil; R_f 0.42 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2955, 1750, 1614, 1591; δ_H ($CDCl_3$) 3.77 (3H, s), 5.34 (1H, s), 7.03 (1H, m), 7.27 (1H, m), 7.29 (1H, m), 7.32 (1H, m); δ_C ($CDCl_3$) 45.1, 53.3, 115.7 (d, J=23.9 Hz), 116.2 (d, J=20.2 Hz), 124.2, 130.2 (d, J=9.2 Hz), 137.8 (d, J=9.2 Hz), 162.5 (d, J=246.3 Hz), 168.2; *m/z* (CI) 245.9696 (M^+ $C_9H_8O_2FBr$ requires 245.9691), 184 (24%), 167 (100), 139 (47), 108 (12).

3.17.8. *N*-Methyl-*N*-((methoxycarbonyl)methyl(phenyl))-3,4-didehydropiperidinium bromide (6f). Methyl-α-bromophenylacetate (2.94 mL, 20.6 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (2.0 g, 20.6 mmol) in THF (40 mL) under argon. The reaction mixture was heated at reflux for 6 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl(phenyl))-3,4-didehydropiperidinium bromide* (5.36 g, 83%) as a colourless deliquescent solid; mp 166.5–166.8°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 2952, 2926, 2843, 1747, 1699, 1634, 1538; δ_H ($CDCl_3$) 2.47 (2H, br. d, J=17.5 Hz), 2.57 (2H, br. m), 3.41 (3H, s), 3.44 (3H, s), 3.75 (3H, s), 3.77 (3H, s), 4.02 (2H, br. m), 4.07 (2H, br. m), 4.28 (2H, br. m), 4.76 (1H, br. d, J=16.5 Hz), 5.69 (2H, br. d, J=10.3 Hz), 5.99 (2H, br. m), 7.13 (2H, s), 7.52 (4H, m), 7.54 (2H, m), 7.82 (4H, br. s); δ_C ($CDCl_3$) 21.2, 21.4, 43.2, 43.3, 53.5, 51.6, 54.5, 55.2, 56.9, 57.1, 73.9, 74.5, 119.0, 119.2, 124.2, 124.5, 126.1, 129.6, 131.6, 132.3, 167.5; *m/z* (CI) 246.1487 (M^+-Br. $C_{15}H_{20}NO_2$ requires 246.1494), 232 (4%), 188 (14), 132 (10), 98 (100).

3.17.9. *cis*-*N*-Methyl-2-methoxycarbonyl-2-phenyl-3-ethenylpyrrolidine (7f). Sodium hydride (38 mg, 1.60 mmol) was added to a suspension of *N*-methyl-*N*-((methoxycarbonyl)methyl(phenyl))-3,4-didehydropiperidinium bromide (500 mg, 1.60 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with ether/petrol (1:2) to give *cis-N-methyl-2-methoxycarbonyl-2-phenyl-3-ethenylpyrrolidine* (27 mg, 71%) as a colourless oil. R_f 0.43 (ether/petrol 1:2); ν_{max} (cm^{-1}) 3026, 2951, 2839, 1723, 1688, 1678, 1658, 1641; δ_H ($CDCl_3$) 2.08 (2H, m), 2.24 (3H, s), 2.65 (1H, ddd, J=9.2, 9.2, 9.2 Hz), 2.78 (1H, ddd, J=9.2, 7.7, 8.1 Hz), 3.27 (1H, ddd, J=6.2, 8.6, 8.8 Hz), 3.69 (3H, s), 4.71 (1H, dd, J=1.2, 17.2 Hz), 4.98 (1H, dd, J=1.2, 9.9 Hz), 5.97 (1H, ddd, J=8.8, 9.9, 17.2 Hz), 7.25 (2H, m), 7.31 (1H, m), 7.33 (2H, m); δ_C ($CDCl_3$) 28.7, 36.5, 50.6, 53.0, 57.0, 78.6, 117.5, 127.1, 127.4, 127.6, 137.2, 139.6, 170.4; *m/z* (CI) 246.1498 (MH^+. $C_{15}H_{20}NO_2$ requires 246.1494), 186 (100%).

3.17.10. *N*-Methyl-*N*-((methoxycarbonyl)methyl(1-naphthyl))-3,4-didehydro-piperidinium bromide (6g). Methyl-α-bromo(1-naphthyl)acetate (2.87 g, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The reaction mixture was heated at reflux for 6 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl(1-naphthyl))-3,4-didehydropiperidinium bromide* (2.55 g, 66%) as a colourless deliquescent solid; mp 168.4–168.8°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 3046, 2956, 1745, 1698, 1633, 1651, 1615, 732; δ_H ($CDCl_3$) 2.45 (1H, br. m), 2.50 (2H, br. m), 2.64 (1H, br. m), 3.52 (3H, s), 3.64 (3H, s), 3.74 (3H, s), 3.76 (3H, s), 4.07 (2H, br. m), 4.12 (2H, br. m), 4.38 (2H, br. d, J=16.1 Hz), 4.50 (2H, br. m), 5.69 (2H, br. d, J=10.3 Hz), 5.96 (1H, br. m), 6.03 (1H, br. m), 7.16 (2H, s), 7.56 (2H, m), 7.63 (2H, m), 7.69 (2H, m), 7.86 (2H, m), 7.93 (1H, d, J=9.1 Hz), 7.95 (1H, d, J=9.1 Hz), 8.07 (1H, d, J=6.6 Hz), 8.08 (1H, d, J=7.3 Hz), 9.22 (1H, d, J=8.8 Hz), 9.47 (1H, d, J=8.4 Hz); δ_C ($CDCl_3$) 21.3, 21.6, 45.0, 53.7, 53.8, 55.7, 56.9, 57.2, 68.5, 70.8, 119.4, 119.7, 122.2, 122.6, 124.1, 124.3, 124.4, 124.5, 125.4, 127.4, 128.9, 129.2, 129.4, 129.7, 130.1, 133.1, 133.2, 133.7, 134.3, 167.7, 167.8; *m/z* (CI) 296.1652 (M^+-Br. $C_{19}H_{22}NO_2$ requires 296.1651), 282 (7%), 238 (28), 141 (29), 98 (100).

3.17.11. *cis*- and *trans*-*N*-Methyl-2-methoxycarbonyl-2-(1-naphthyl)-3-ethenylpyrrolidine (7g). Sodium hydride (32 mg, 1.33 mmol) was added to a suspension of *N*-methyl-*N*-((methoxycarbonyl)methyl(1-naphthyl))-3,4-didehydropiperidinium bromide (500 mg, 1.33 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL).

The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with 1:2 ether/petrol to give an inseparable 4:1 mixture of *cis*- and *trans-N-methyl-2-methoxycarbonyl-2-(1-naphthyl)-3-ethenylpyrrolidine* (35 mg, 89%) as a colourless oil R_f 0.44 (ether/petrol 1:2); Data for the trans-isomer is indicated by the symbol $*$. ν_{max} (cm^{-1}) 2947, 2841, 1718, 1677, 1656, 1639, 734; δ_H ($CDCl_3$) 1.71 (1H, dddd, J=13.4, 3.6, 7.9, 8.8 Hz)*, 2.13 (8H, m), 2.25 (12H, s), 2.36 (3H, s)*, 2.43 (1H, m)*, 2.69 (1H, m)*, 2.81 (4H, m), 2.88 (4H, ddd, J=8.8, 9.2, 9.2 Hz), 3.30 (1H, m)*, 3.35 (4H, m), 3.46 (3H, s)*, 3.53 (12H, s), 3.83 (1H, ddd, J=5.5, 9.5, 9.5 Hz)*, 4.15 (1H, dd, J=1.8, 9.9 Hz)*, 4.46 (1H, dd, J=1.8, 16.8 Hz)*, 4.59 (4H, br. d, J=16.9 Hz), 4.80 (4H, dd, J=1.5, 10.3 Hz), 5.03 (1H, ddd, J=9.5, 9.9, 16.8 Hz)*, 6.31 (4H, ddd, J=8.8, 10.3, 16.9 Hz), 6.31 (4H, m), 7.25 (1H, m)*, 7.32 (4H, m), 7.35 (1H, m)*, 7.37 (4H, m), 7.39 (1H, m)*, 7.42 (1H, m)*, 7.46 (4H, m), 7.56 (1H, m)*, 7.72 (1H, m)*, 7.76 (4H, m), 7.79 (4H, m), 7.83 (4H, m), 7.9, (1H, m),)*; δ_C ($CDCl_3$) 29.0, 30.7*, 36.9, 37.5*, 50.4, 50.7*, 50.8*, 52.6, 53.4*, 57.0, 76.8*, 77.2, 113.0*, 117.3, 124.4, 124.5*, 124.7*, 124.8, 124.8, 124.9, 124.9, 125.2, 126.4*, 128.0*, 128.4, 128.7, 128.8*, 131.7, 131.8*, 133.8*, 134.2, 135.1, 136.2*, 138.2, 139.4*, 169.9, 172.2*; 296.1657 (MH^+. $C_{19}H_{22}NO_2$ requires 296.1651), 236 (100%), 220 (6).

3.17.12. *N*-Methyl-*N*-((methoxycarbonyl)methyl(*p*-methoxyphenyl))-3,4-didehydro-piperidinium bromide (6h). Methyl-α-bromo-*p*-methoxyphenylacetate (2.68 g, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The reaction mixture was heated at reflux for 6 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl(p-methoxyphenyl))-3,4-didehydropiperidinium bromide* (2.91 g, 79%) as a colourless deliquescent solid; mp 142.1–142.9°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 2954 and 2838, 1748, 1608, 1583; δ_H ($CDCl_3$) 2.50 (4H, br. m), 3.38 (3H, s), 3.41 (3H, s), 3.77 (6H, s), 3.85 (6H, s), 3.98 (2H, br. m), 4.06 (2H, br. m), 4.25 (2H, br. m), 4.73 (2H, br. m), 5.71 (2H, br. m), 6.01 (2H, m), 6.91 (1H, s), 7.00 (4H, d, J=9.2 Hz), 7.09 (1H, s), 7.73 (4H, br. m); δ_C ($CDCl_3$) 21.7, 22.0, 43.6, 43.8, 54.0, 54.7, 55.6, 56.1, 57.2, 57.3, 74.2, 74.9, 115.5, 115.6, 118.0, 118.1, 119.5, 119.7, 124.8, 125.1, 134.2, 162.5, 168.2; *m/z* (CI) 276.1608 (M^+−Br. $C_{16}H_{22}NO_3$ requires 276.1600), 202 (8%), 179 (82), 151 (16), 137 (7), 121 (20), 98 (100), 82 (17).

3.17.13. *cis-N*-Methyl-2-methoxycarbonyl-2-(*p*-methoxyphenyl)-3-ethenylpyrrolidine (7h) and methyl-3-aza-2-(*p*-methoxyphenyl)-3-methyl-octa-5,7-dienoate (8h). Sodium hydride (34 mg, 1.40 mmol) was added to a suspension of *N*-methyl-*N*-((methoxycarbonyl)methyl-(*p*-methoxyphenyl))-3,4-didehydropiperidinium bromide (500 mg, 1.40 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with 1:2 ether/petrol to give *cis-N-methyl-2-methoxycarbonyl-2-(p-methoxyphenyl)-3-ethenylpyrrolidine* (111 mg, 28%), and *methyl-3-aza-2-(p-methoxyphenyl)-3-methyl-octa-5,7-dienoate* (98 mg, 25%) both as colourless oils.

cis-N-Methyl-2-methoxycarbonyl-2-(p-methoxyphenyl)-3-ethenylpyrrolidine. R_f 0.44 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2957, 2851, 1736, 1641 br.; δ_H ($CDCl_3$) 2.08 (2H, m), 2.22 (3H, s), 2.64 (1H, ddd, J=9.5, 9.2, 9.2 Hz), 2.77 (1H, ddd, J=9.5, 4.0, 9.2 Hz), 3.25 (1H, ddd, J=5.9, 8.4, 9.2 Hz), 3.69 (3H, s), 3.79 (3H, s), 4.73 (1H, dd, J=1.8, 17.2 Hz), 4.98 (1H, dd, J=1.8, 10.3 Hz), 5.95 (1H, ddd, J=9.2, 10.3, 17.2 Hz), 6.86 (2H, d, J=9.2 Hz), 7.26 (2H, d, J=9.2 Hz); δ_C ($CDCl_3$) 28.6, 36.4, 50.6, 51.9, 55.2, 57.0, 78.2, 113.0, 117.4, 128.4, 131.6, 137.3, 158.6, 170.7; *m/z* (CI) 276.1599 (M^++H. $C_{16}H_{22}NO_3$ requires 276.1600), 216 (100%), 179 (45), 148 (8), 96 (4), 67 (21).

Methyl-3-aza-2-(p-methoxyphenyl)-3-methyl-octa-5,7-dienoate. R_f 0.36 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2951 and 2837, 1735, 1654 br., 1610; δ_H ($CDCl_3$) 2.25 (3H, s), 3.13 (1H, dd, J=14.1, 6.9 Hz), 3.28 (1H, dd, J=14.1, 7.3 Hz), 3.69 (3H, s), 3.80 (3H, s), 4.16 (1H, s), 5.12 (1H, br. d, J=9.9 Hz), 5.21 (1H, dd, J=1.7, 16.8 Hz), 5.54 (1H, ddd, J=6.9, 7.3, 10.9 Hz), 6.15 (1H, dd, J=11.3, 10.9 Hz), 6.52 (1H, ddd, J=9.9, 11.3, 16.8 Hz), 6.87 (1H, d, J=8.7 Hz), 7.33 (1H, d, J=8.7 Hz); δ_C ($CDCl_3$): 39.5, 51.3, 51.9, 55.3, 71.7, 113.0, 118.5, 128.2, 128.6, 130.1, 131.8, 132.3, 159.6, 172.5; *m/z* (CI) 276.1590 (MH^+. $C_{16}H_{22}NO_3$ requires 276.1600), 216 (100%), 85 (7), 49 (8).

3.17.14. *N*-Methyl-*N*-((methoxycarbonyl)methyl-(*p*-nitrophenyl))-3,4-didehydro-piperidinium bromide (6i). Methyl-α-bromo-*p*-nitrophenylacetate (2.82 g, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The reaction mixture was heated at reflux for 12 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl(p-nitrophenyl))-3,4-didehydropiperidinium bromide* (3.11 g, 81%) as a colourless deliquescent solid; mp 121.9–122.3°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 3054, 2986, 2957, 2934, 1745, 1699, 1651, 1634, 1605, 1535, 1520 and 1353; δ_H ($CDCl_3$) 2.55 (4H, br. m), 3.45 (3H, s), 3.54 (3H, s), 3.81 (6 h, s), 4.02 (2H, br. m), 4.19 (2H, br. m), 4.29 (2H, br. m), 4.86 (2H, br. m), 5.76 (2H, br. m), 6.04 (2H, br. m), 7.29 (2H, s), 8.17 (4H, br. m), 8.35 (4H, d, J=8.8 Hz); δ_C ($CDCl_3$) 21.1, 21.4, 43.3, 54.0, 54.1, 55.1, 55.6, 57.4, 59.0, 71.7, 72.7, 118.6, 118.8, 124.4, 124.5, 125.7, 133.0, 133.7, 150.0, 166.7, 166.8; *m/z* (CI) 291.1352 (M^+−Br. $C_{15}H_{19}N_2O_4$ requires 291.1345), 231 (66%), 185 (9), 153 (27), 136 (35), 98 (100), 96 (36).

3.17.15. *cis-N*-Methyl-2-methoxycarbonyl-2-(*p*-nitrophenyl)-3-ethenylpyrrolidine (7i). Sodium hydride (32.3 mg, 1.35 mmol) was added to a suspension of

N-methyl-*N*-((methoxycarbonyl)methyl(*p*-nitrophenyl))-3,4-didehydropiperidinium bromide (500 mg, 1.35 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with 1:2 ether/petrol to give *cis-N-methyl-2-methoxycarbonyl-2-(p-nitrophenyl)-3-ethenylpyrrolidine* (190 mg, 48%) as a colourless oil R_f 0.40 (ether/petrol 1:2); (Found: C, 62.0; H, 6.3; N, 9.3. $C_{15}H_{18}N_2O_4$ requires C, 62.1; H, 6.25; N, 9.65%); ν_{max} (cm^{-1}) 3078, 2951, 2845, 2792, 1725, 1640, 1958, 1521 and 1352; δ_H ($CDCl_3$) 2.12 (2H, m), 2.24 (3H, s), 2.54 (1H, ddd, *J*=9.5, 9.5, 9.5 Hz), 2.82 (1H, ddd, *J*=9.5, 5.6, 9.5 Hz), 3.41 (1H, ddd, *J*=5.1, 8.8, 9.2 Hz), 3.76 (3H, s), 4.68 (1H, dd, *J*=1.8, 17.2 Hz), 5.03 (1H, dd, *J*=1.8, 10.3 Hz), 5.93 (1H, ddd, *J*=9.2, 10.3, 17.2 Hz), 7.58 (1H, d; *J*=9.2 Hz), 8.17 (1H, d, *J*=9.2 Hz); δ_C ($CDCl_3$) 28.0, 36.5, 51.0, 53.3, 57.8, 78.6, 118.9, 122.8, 128.3, 136.0, 147.0, 147.9, 169.5; *m/z* (CI) 291.1344 (MH^+. $C_{15}H_{19}N_2O_4$ requires 291.1345), 261 (8%), 321 (100), 201 (12), 185 (18).

3.17.16. *N*-Methyl-*N*-((methoxycarbonyl)methyl-(*p*-chlorophenyl))-3,4-didehydro-piperidinium bromide (6j). Methyl-α-bromo-*p*-chlorophenylacetate (2.71 g, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The reaction mixture was heated at reflux for 12 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl(p-chlorophenyl))-3,4-didehydro-piperidinium bromide* (2.81 g, 76%) as a colourless deliquescent solid; mp 147.9–148.1°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 2939, 2845, 1747, 1639 br., 734; δ_H ($CDCl_3$) 2.52 (4H, br. m), 3.40 (3H, s), 3.42 (3H, s), 3.78 (6H, s), 4.03 (4H, br. m), 4.28 (2H, br. m), 4.80 (2H, br. d, *J*=16.7 Hz), 5.72 (2H, br. m), 6.01 (2H, m), 7.19 (1H, d, *J*=3.6 Hz), 7.32 (1H, d, *J*=3.3 Hz), 7.50 (4H, d, *J*=6.8 Hz), 7.82 (4H, br. m); δ_C ($CDCl_3$) 21.2, 21.5, 43.3, 53.8, 54.7, 55.4, 57.0, 57.2, 73.2, 73.6, 118.8, 119.1, 124.4, 124.7, 126.0, 130.0, 133.7, 138.4, 167.3; *m/z* (CI) 280.1112 (M^+−Br. $C_{15}H_{19}NO_2Cl$ requires 280.1104), 222 (100%), 166 (23), 125 (32), 98 (58), 82 (9).

3.17.17. *cis-N*-Methyl-2-methoxycarbonyl-2-(*p*-chlorophenyl)-3-ethenylpyrrolidine (7j) and methyl-3-aza-2-(*p*-chlorophenyl)-3-methyl-octa-5,7-dienoate (8j). Sodium hydride (33 mg, 1.39 mmol) was added to a suspension of *N*-methyl-*N*-((methoxycarbonyl)methyl(*p*-chlorophenyl))-3,4-didehydropiperidinium bromide (500 mg, 1.39 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with 1:2 ether/petrol to give *cis-N-methyl-2-methoxycarbonyl-2-(p-chlorophenyl)-3-ethenylpyrrolidine* (130 mg, 32%), and *methyl-3-aza-2-(p-chlorophenyl)-3-methyl-octa-5,7-dienoate* (45 mg, 11%) both as colourless oils.

cis-N-Methyl-2-methoxycarbonyl-2-(p-chlorophenyl)-3-ethenylpyrrolidine. R_f 0.46 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2950, 2846, 2788, 1722, 1640 br.; δ_H ($CDCl_3$) 2.07 (2H, m), 2.22 (3H, s), 2.56 (1H, m), 2.77 (1H, m), 3.32 (1H, ddd, *J*=6.9, 7.7, 8.8 Hz), 3.71 (3H, s), 4.71 (1H, br. d, 17.2 Hz), 5.00 (1H, dd, *J*=1.8, 9.9 Hz), 5.92 (1H, ddd, *J*=8.8, 9.9, 17.2 Hz), 7.29 (4H, 2×d, *J*=9.5 Hz); δ_C ($CDCl_3$) 28.7, 36.4, 50.7, 53.1, 57.3, 78.3, 118.1, 127.8, 128.7, 129.5, 132.7, 136.6, 170.1; *m/z* (CI) 280.1105 (MH^+. $C_{15}H_{18}NO_2Cl$ requires 280.1104), 220 (100%), 152 (8), 119 (6).

Methyl-3-aza-2-(p-chlorophenyl)-3-methyl-octa-5,7-dienoate. R_f 0.40 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2932, 2855, 1737, 1654br. and 1641 br.; δ_H ($CDCl_3$) 2.26 (3H, s), 3.15 (1H, m), 3.26 (1H, br. m), 3.70 (3H, s), 4.21 (1H, br. s), 5.13 (1H, br. d, *J*=10.1 Hz), 5.22 (1H, br. d, *J*=16.7 Hz), 5.53 (1H, ddd, *J*=7.1, 7.3, 11.0 Hz), 6.16 (1H, dd, *J*=11.1, 11.1 Hz), 6.53 (1H, dddd, *J*=10.1, 11.1, 16.7, 1.0 Hz), 7.31 (1H, d, *J*=8.6 Hz), 7.36 (1H, d, *J*=8.6 Hz); δ_C ($CDCl_3$): 39.4, 51.3, 52.09, 71.4, 118.8, 125.3, 127.8, 128.8, 130.2, 131.6, 132.5, 134.2, 171.8; *m/z* (CI) 280.1100 (MH^+. $C_{15}H_{18}NO_2Cl$ requires 280.1104), 220 (100%), 206 (27), 183 (7), 152 (11), 96 (10), 67 (51).

3.17.18. *N*-Methyl-*N*-((methoxycarbonyl)methyl(*m*-chlorophenyl))-3,4-didehydro-piperidinium bromide (6k). Methyl-α-bromo-*m*-chlorophenylacetate (2.71 g, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The mixture was stirred at room temperature for 12h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl(m-chlorophenyl))-3,4-didehydro-piperidinium bromide* (2.89 g, 78%) as a colourless deliquescent solid; mp 151.2–151.8°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 2954, 2844, 1744, 1699, 1615 and 1590, 732; δ_H ($CDCl_3$) 2.54 (4H, br. m), 3.43 (3H, s), 3.45 (3H, s), 3.80 (6H, s), 4.08 (4H, br. m), 4.26 (2H, br. m), 4.82 (2H, br. d, *J*=16.3 Hz), 5.73 (2H, br. m, *J*=10.2 Hz), 6.03 (2H, br. d, *J*=10.2 Hz), 7.29 (1H, s), 7.30 (1H, s), 7.51 (2H, m), 7.54 (2H, m), 7.82 (2H, br. s), 7.88 (2H, br. d, *J*=7.8 Hz); δ_C ($CDCl_3$) 21.2, 21.5, 43.4, 53.9, 54.6, 55.4, 56.9, 57.3, 73.1, 73.5, 118.8, 119.1, 124.4, 124.6, 128.0, 127.2, 127.3, 128.8, 129.1, 129.5, 131.8, 131.8, 134.2, 142.1, 171.0, 128.1, 131.1, 132.1, 135.6, 142.2, 167.2; *m/z* (CI) 280.1117 (M^+−Br. $C_{15}H_{19}NO_2Cl$ requires 280.1104), 222 (93%), 166 (21), 98 (100), 96 (31), 82 (7).

3.17.19. *cis-N*-Methyl-2-methoxycarbonyl-2-(*m*-chlorophenyl)-3-ethenylpyrrolidine (7k) and methyl-3-aza-2-(*m*-chlorophenyl)-3-methyl-octa-5,7-dienoate (8k). Sodium hydride (33 mg, 1.39 mmol) was added to a

suspension of *N*-methyl-*N*-(methoxycarbonyl)methyl-(*m*-chlorophenyl))-3,4-didehydropiperidinium bromide (500 mg, 1.39 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with 1:2 ether/petrol to give *cis-N-methyl-2-methoxycarbonyl-2-(m-chlorophenyl)-3-ethenylpyrrolidine* (165 mg, 43%), and *methyl-3-aza-2-(m-chlorophenyl)-3-methyl-octa-5,7-dienoate* (34 mg, 9%) both as colourless oils.

cis-N-Methyl-2-methoxycarbonyl-2-(m-chlorophenyl)-3-ethenylpyrrolidine. R_f 0.44 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2948, 2849, 2785, 1723, 1638 br.; δ_H ($CDCl_3$) 2.09 (2H, m), 2.23 (3H, s), 2.59 (1H, br. m), 2.78 (1H, m), 3.33 (1H, ddd, *J*=6.8, 7.4, 8.3 Hz), 3.72 (3H, s), 4.72 (1H, dd, *J*=1.9, 17.09 Hz), 5.02 (1H, dd, *J*=1.9, 10.1 Hz), 5.92 (1H, ddd, *J*=8.3, 10.1, 17.09 Hz), 7.17–7.28 (3H, m), 7.42 (1H, m); δ_C ($CDCl_3$) 28.7, 36.5, 50.8, 53.1, 57.3, 78.4, 118.2, 126.0, 127.1, 127.2, 133.7, 136.5, 136.6, 142.1, 169.9; *m/z* (CI) 280.1105 (MH^+. $C_{15}H_{18}NO_2Cl$ requires 280.1104), 220 (100%), 169 (28), 152 (10), 119 (9).

Methyl-3-aza-2-(m-chlorophenyl)-3-methyl-octa-5,7-dienoate. R_f 0.38 (ether/petrol 1:2); ν_{max} (cm^{-1}) 3065, 2932, 2855, 1735, 1686, 1678, 1668, 1638; δ_H ($CDCl_3$) 2.22 (3H, s), 3.19 (2H, d, *J*=7.04 Hz), 3.49 (3H, s), 5.17 (1H, br. d, *J*=10.1 Hz), 5.25 (1H, dd, *J*=1.7, 16.8 Hz), 5.59 (1H, dt, *J*=10.9, 7.04 Hz), 6.18 (1H, dd, *J*=11.1, 10.9 Hz), 6.62 (1H, dddd, *J*=10.1, 11.1, 16.8, 1.1 Hz), 7.22-7.24 (3H, m), 7.25 (1H, s), 7.34 (1H, m); δ_C ($CDCl_3$): 42.2, 54.0, 61.0, 77.7, 118.6, 127.2, 127.3, 128.8, 129.0, 129.5, 131.8, 132.2, 134.2, 142.1, 171.0; *m/z* (CI) 280.1101 (MH^+. $C_{15}H_{19}NO_2Cl$ requires 280.1104), 220 (100%).

3.17.20. *N*-Methyl-*N*-((methoxycarbonyl)methyl(*p*-fluorophenyl))-3,4-didehydro-piperidinium bromide (6l). Methyl-α-bromo-*p*-fluorophenylacetate (2.54 g, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The reaction mixture was heated at reflux for 12 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl(p-fluorophenyl))-3,4-didehydropiperidinium bromide* (2.76 g, 78%) as a colourless deliquescent solid; mp 158.2–158.6°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 2958, 1742, 1640 br., 730; δ_H ($CDCl_3$) 2.53 (2H, br. m), 2.60 (2H, br. m), 3.40 (3H, s), 3.42 (3H, s), 3.79 (6 h, s), 4.02 (4H, br. m), 4.23 (2H, br. m), 4.78 (2H, br. d, *J*=15.7 Hz), 5.73 (2H, br. m), 6.02 (2H, br. m), 7.15 (1H, s), 7.22 (4H, dd, *J*=8.1, 7.7 Hz), 7.30 (1H, s), 7.89 (4H, br. m); δ_C ($CDCl_3$) 21.3, 21.5, 43.2, 43.3, 53.8, 54.6, 55.3, 57.0, 57.2, 73.1, 73.6, 117.0 (d, *J*=22.0 Hz), 118.9, 119.1, 122.1, 124.5, 124.7, 134.6, 164.5 (d, *J*=253.7 Hz), 167.4; *m/z* (CI) 264.1401 (M^+−Br. $C_{15}H_{19}NO_2F$ requires 264.1400), 250 (49%), 206 (42), 190 (28), 167 (8), 150 (9), 109 (50), 98 (100), 82 (18).

3.17.21. *cis-N*-Methyl-2-methoxycarbonyl-2-(*p*-fluorophenyl)-3-ethenylpyrrolidine (7l). Sodium hydride (35.0 mg, 1.45 mmol) was added to a suspension of *N*-methyl-*N*-((methoxycarbonyl)methyl(*p*-fluorophenyl))-3,4-didehydropiperidinium bromide (500 mg, 1.45 mmol) in DME (20 mL), vigorously stirred under argon. The reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with 1:2 ether/petrol to give *cis-N-methyl-2-methoxycarbonyl-2-(p-fluorophenyl)-3-ethenylpyrrolidine* (220 mg, 58%) as a colourless oil R_f 0.44 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2950, 2842, 2790, 1723, 1639, 1639, 1609; δ_H ($CDCl_3$) 2.07 (2H, m), 2.22 (3H, s), 2.54 (1H, m), 2.77 (1H, ddd, *J*=8.8, 7.7, 8.1 Hz), 3.31 (1H, ddd, *J*=6.6, 7.7, 8.1 Hz), 3.71 (3H, s), 4.70 (1H, br. d, *J*=16.5 Hz), 4.99 (1H, br. d, *J*=9.9 Hz), 5.92 (1H, ddd, *J*=7.7, 9.9, 16.5 Hz), 6.99 (1H, dd, *J*=8.4, 8.8 Hz), 7.30 (1H, dd, *J*=5.5, 8.8 Hz); δ_C ($CDCl_3$) 28.6, 36.4, 50.6, 53.0, 57.4, 78.1, 114.3 (d, *J*=20.2 Hz), 117.9, 128.8 (d, *J*=7.4 Hz), 135.5, 136.7, 161.8 (d, *J*=244.5 Hz), 170.3; *m/z* (CI) 264.1407 (MH^+. $C_{15}H_{19}NO_2F$ requires 264.1400), 204 (100%), 49 (25).

3.17.22. *N*-Methyl-*N*-((methoxycarbonyl)methyl-(*m*-fluorophenyl))-3,4-didehydro-piperidinium bromide (6m). Methyl-α-bromo-*m*-fluorophenylacetate (2.54 g, 10.3 mmol) was added dropwise over 5 min to a stirred solution of *N*-methyl-3,4-didehydropiperidine (1.0 g, 10.3 mmol) in THF (20 mL) under argon. The mixture was stirred at room temperature for 12 h resulting in the precipitation of the title compound, which was filtered and washed with ether (2×25 mL) under argon to give *N-methyl-N-((methoxycarbonyl)methyl(m-fluorophenyl))-3,4-didehydropiperidinium bromide* (2.81 g, 76%) as a colourless deliquescent solid; mp 160.8–160.9°C (dichloromethane/petrol); ν_{max} (cm^{-1}) (dichloromethane) 2955, 1746, 1614, 1591, 730; δ_H ($CDCl_3$) 2.54 (4H, br. m), 3.43 (3H, s), 3.45 (3H, s), 3.79 (6 h, s), 4.06 (4H, br. m), 4.24 (2H, br. m), 4.80 (2H, br. m), 5.73 (2H, br. m), 6.02 (2H, br. m), 7.22 (1H, s), 7.28 (2H, br. m), 7.31 (1H, s), 7.52 (2H, br. m), 7.55 (2H, br. d, *J*=8.1 Hz), 7.72 (2H, br. m); δ_C ($CDCl_3$) 21.3, 21.5, 43.4, 43.4, 53.9, 54.9, 55.5, 57.2, 57.4, 73.1, 73.6, 118.8, 118.9 (d, *J*=20.2 Hz), 119.0, 124.5, 124.7, 125.6, 128.2 (d, *J*=20.2 Hz), 128.3 (d, *J*=3.7 Hz), 131.6 (d, *J*=9.2 Hz), 162.7 (d, *J*=250.1 Hz), 167.2; *m/z* (CI) 164.1398 (M^+−Br. $C_{15}H_{19}NO_2F$ requires 264.1400), 250 (21%), 206 (7), 190 (7), 167 (10), 109 (22), 98 (100), 82 (22).

3.17.23. *cis-N*-Methyl-2-methoxycarbonyl-2-(*m*-fluorophenyl)-3-ethenylpyrrolidine (7m). Sodium hydride (35 mg, 1.45 mmol) was added to a suspension of *N*-methyl-*N*-(methoxycarbonyl(*m*-fluorophenyl))methyl-3,4-didehydropiperidinium bromide (500 mg, 1.45 mmol) in DME (20 mL), vigorously stirred under argon. The

reaction mixture was heated at reflux for 16 h, after which it was cooled and excess base quenched by careful addition of methanol. The mixture was concentrated in vacuo yielding a solid product, which was partitioned between water (20 mL) and ether (20 mL). The organic layer was separated and the aqueous layer was further extracted with ether (4×20 mL). The combined extracts were dried ($MgSO_4$) and the solvent removed in vacuo yielding a yellow oil which was purified by column chromatography, eluting with 1:2 ether/petrol to give *cis-N-methyl-2-methoxycarbonyl-2-(m-fluorophenyl)-3-ethenylpyrrolidine* (140 mg, 36%) as a colourless oil, R_f 0.41 (ether/petrol 1:2); ν_{max} (cm^{-1}) 2951, 2849, 1723, 1653, 1639, 1617, 1589; δ_H ($CDCl_3$) 2.08 (2H, m), 2.24 (3H, s), 2.59 (1H, m), 2.78 (1H, ddd, J=8.8, 7.7, 8.1 Hz), 3.32 (1H, ddd, J=6.9, 7.3, 8.4 Hz), 3.72 (3H, s), 4.72 (1H, br. d, J=16.8 Hz), 5.01 (1H, dd, J=1.8, 10.3 Hz), 5.93 (1H, ddd, J=8.4, 10.3, 16.8 Hz), 6.95 (1H, ddd; J=8.4, 8.05, 2.5 Hz), 7.10 (1H, m), 7.13 (1H, ddd, J=8.4, 2.5, 1.8 Hz), 7.27 (1H, m); δ_C ($CDCl_3$) 28.7, 36.5, 50.8, 53.1, 57.3, 78.4, 113.9 (d, J=20.2 Hz), 114.1 (d, J=22.1 Hz), 118.1, 123.3, 125.5, 128.9 (d, J=7.3 Hz), 136.7, 162.6 (d, J=244.5 Hz), 170.0; m/z (CI) 264.1402 (MH^+. $C_{15}H_{19}NO_2F$ requires 264.1400), 204 (67%), 136 (4).

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