General procedures and instrumentation

Flash column chromatography was carried out using geduran silica gel 60 (40-63 μm) supplied by Merck Chemicals. Thin-layer chromatography was conducted using aluminium pre-coated silica gel plates (Macherey-Nagek 818133, 0.20 mm thickness) supplied by Merck chemicals. All reagents were obtained from commercial sources and were used without further purification. Infra-red spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer. Vibrational frequencies are reported in wavenumbers (cm^{-1}). Melting points were recorded on a Reichert hotstage apparatus and are reported uncorrected. Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on a 300 / 75 MHz Bruker DPX300 or a 500 / 125 MHz Bruker Advance 500 fourier transform spectrometer as indicated, using an internal deuterium lock. Chemical shifts are reported in parts per million (ppm) and are reported with reference to tetramethylsilane (TMS) as an internal standard. For proton spectra, the integration (e.g. 1H), multiplicities (e.g. d = doublet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublets of doublets, m = multiplet s = singlet, t = triplet, tt = triplet of triplets, q = quartet) and coupling constants (*J*, measured in Hertz) are given where the abbreviation Ar = aromatic. Samples were prepared in deuterated chloroform ($CDCl_3$) as indicated. Solvents for this purpose were obtained from Sigma-Aldrich chemical company Ltd. Only n.O.e. data relevent to stereochemical assignment is provided where α refers to downwards stereochemistry and β refers to upwards stereochemistry.

General Procedures

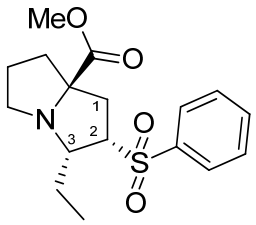
General Procedure (A)

A mixture of proline ester (1 mmol), dipolarophile (1 mmol) and $(PPh_3)_3RhCl$ (10 mol%) was stirred in refluxing toluene for 24 hours. The progression of the reaction was monitored by TLC. Upon completion of reaction, the mixture was filtered, solvent removed under reduced pressure and the crude product purified by column chromatography (ethyl acetate/hexanes approx 1:3 ratio).

General Procedure (B)

A mixture of proline ester (1 mmol), dipolarophile (1 mmol) and $(PPh_3)_3RhCl$ (10 mol%) was stirred in refluxing xylene for 24 hours. The progression of the reaction was monitored by TLC. Upon completion of reaction, the mixture was filtered, solvent removed under reduced pressure and the crude product purified by column chromatography (ethyl acetate/hexanes approx 1:3 ratio).

Preparation of methyl 3-ethyl-2-(phenylsulfonyl)hexahydro-1H-pyrrolizine-7a-carboxylate (3)

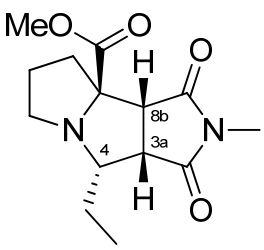


Methyl 1-allylpyrrolidine-2-carboxylate (1 mmol) and (vinylsulfonyl)benzene (1 mmol) were reacted following general procedure A to afford methyl 3-ethyl-2-(phenylsulfonyl)hexahydro-1H-pyrrolizine-7a-carboxylate (307 mg, 0.91 mmol, 91 %) as an orange solid. **δ_H (500 MHz, $CDCl_3$);** 7.89-7.86 (2H, m, Ar-H), 7.64 (1H, tt, *J* 7.5, 1.5 Hz, Ar-H), 7.58-7.55 (2H, m, Ar-H), 3.80 (1H, dd *J* 8.0 Hz, 2-H), 3.69 (3H, s, O-CH_3), 3.69-3.63 (1H, m, 3-H), 3.17-3.12 (2H, m, N-CH_2), 2.37-2.30 (3H, m, 1-CH_2 and CH), 2.10-1.92 (5H, m, CH_2, CH_2 and CH), 1.15 (3H, t, *J* 7.5, CH_3); **δ_C (125 MHz, $CDCl_3$);** 175.3, 140.5, 133.5, 129.3, 128.1, 76.0, 68.3, 67.6, 52.8, 47.0, 38.5, 34.8, 23.9, 21.3, 13.3; **ν_{max}/cm^{-1} (solid);** 3443, 2967, 2876, 1731, 1446, 1379; **H.R.M.S. [ES^+]** found MNa^+, 338.1529. $C_{17}H_{23}N_4NaS$ requires *MNa* 338.1536; **n.O.e data**:

% enhancement

Irradiated hydrogen	1_β	2_β	3_β	ArH
2_β	6		10	7
3_β	-	9		-

Preparation of methyl 4-ethyl-2-methyl-1,3-dioxodecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (4)

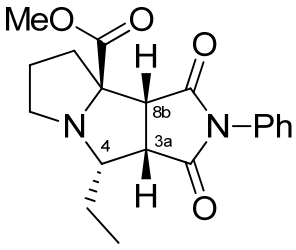


Methyl 1-allylpyrrolidine-2-carboxylate (1 mmol) and N-methyl maleimide (1 mmol) were reacted following general procedure A to afford methyl 4-ethyl-2-methyl-1,3-dioxodecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (199 mg, 0.71 mmol, 71 %) as a yellow oil. **Δ_H (500 MHz, $CDCl_3$);** 3.87 (1H, d, *J* 8.0 Hz, 8b-H), 3.78 (3H, s, O-CH_3), 3.39 (1H, q, *J* 8.0 Hz, 4-H), 3.30 (1H, t, *J* 8.0 Hz, 3a-H), 3.06 (1H, ddd, *J* 9.5, 8.0, 3.0 Hz, N-CH), 2.91 (3H, s, N-CH_3), 2.60 (1H, ddd, *J* 14.0, 9.0, 7.0 Hz, CH), 3.36-2.30 (2H, m, N-CH and CH), 2.02-1.92 (2H, m, CH and CH), 1.87-1.81 (1H, m, CH), 1.74-1.67 (1H, m, CH), 1.18 (3H, t, *J* 7.5 Hz, CH_3); **δ_C (125 MHz, $CDCl_3$);** 177.5, 177.1, 174.3, 79.2, 65.6, 53.1, 51.4, 49.5, 47.7, 30.3, 25.0, 24.2, 21.7, 12.4; **ν_{max}/cm^{-1} (film);** 3607, 3452, 2968, 2879, 1726, 1698, 1434, 1382; **H.R.M.S. [ES^+]** found MH^+, 281.1507. $C_{14}H_{21}N_2O_4$ requires *MH* 281.1496; **n.O.e data**:

% enhancement

irradiated hydrogen	$3a_\beta$	4_β	$8b_\beta$
$3a_\beta$		5	9
4_β	8		-
$8b_\beta$	8	-	

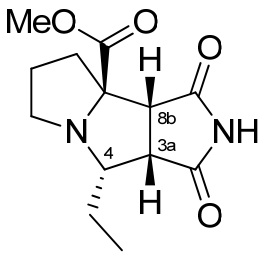
Preparation of methyl 4-ethyl-1,3-dioxo-2-phenyl-decahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (5)



Methyl 1-allylpyrrolidine-2-carboxylate (1 mmol) and N-Phenyl maleimide (1 mmol) were reacted following general procedure A to afford methyl 4-ethyl-1,3-dioxo-2-phenyl-decahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (277 mg, 0.81 mmol, 81 %) as a yellow oil. **Δ_H (500 MHz, $CDCl_3$);** 7.50 (2H, t, *J* 7.5 Hz, ArH), 7.43 (1H, t, *J* 7.5 Hz, ArH), 7.22 (2H, d, *J* 7.5 Hz, ArH), 4.07 (1H, d, *J* 8.0 Hz, 8b-H), 3.82 (3H, s, O-CH_3), 3.53-3.45 (2H, m, 4-H and 3a-H), 3.22-3.18 (1H, m, N-CH), 2.73 (1H, ddd, *J* 14.0, 8.5, 7.5 Hz, N-CH), 2.56 (1H, q, *J* 9.5 Hz, CH), 2.44-2.38 (1H, m, CH), 2.06-1.98 (2H, m, CH and CH), 1.96-1.80 (2H, m, CH and CH), 1.22 (3H, t, *J* 7.5 Hz, CH_3); **δ_C (75 MHz, $CDCl_3$);** 176.4, 175.9, 174.2, 131.8, 129.3, 128.7, 126.0, 79.8, 66.1, 53.3, 51.3, 49.4, 48.1, 30.2, 24.2,

21.7, 12.4; ; **ν_{max}/cm^{-1} (film);** 3607, 3463, 2969, 2878, 1713, 1597, 1499, 1380; **H.R.M.S. [ES$^+$]** found MH$^+$, 343.1666. $C_{19}H_{23}N_2O_4$ requires *MH* 343.1652.

Preparation of methyl 4-ethyl-1,3-dioxodecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (6)

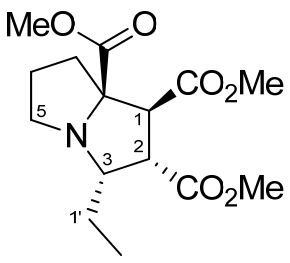


Methyl 1-allylpyrrolidine-2-carboxylate (1 mmol) and maleimide (1 mmol) were reacted following general procedure A to afford methyl 4-ethyl-1,3-dioxodecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (141 mg, 0.62 mmol, 62 %) as an off-white powder m.p. 195-197 ^{o}C; **δ_H (500 MHz, $CDCl_3$);** 7.92 (1H, s, N-H), 3.84 (1H, d, *J* 7.5 Hz, 8b-H), 3.70, (3H, s, O-CH_3), 3.33-3.26 (2H, m, 3a-H and 4-H), 3.05-3.01 (1H, m, N-CH), 2.58-2.50 (2H, m, N-CH and CH), 2.31-2.25 (1H, m, CH), 1.99-1.86 (2H, m, CH and CH), 1.84-1.74, (2H, m, CH and CH), 1.10 (3H, t, *J* 7.5 Hz, CH_3); **δ_C (125 MHz, $CDCl_3$);** 177.3, 177.0, 174.2, 79.14, 65.5, 53.2, 52.6, 50.74, 47.8, 30.4, 24.4, 21.6, 12.4; **ν_{max}/cm^{-1} (solid);** 3455, 2938, 2720, 1713, 1432, 1296; **H.R.M.S. [ES$^+$]** found MH$^+$, 267.1333. $C_{13}H_{19}N_2O_4$ requires *MH* 267.1339.

Preparation of trimethyl 3-ethylhexahydro-1H-pyrrolizine-1,2,7a-tricarboxylates (7) (8)

Methyl 1-allylpyrrolidine-2-carboxylate (1 mmol) and dimethyl fumarate (1 mmol) were reacted following general procedure A to afford trimethyl 3-ethylhexahydro-1H-pyrrolizine-1,2,7a-tricarboxylate **(7)** and trimethyl 3-ethylhexahydro-1H-pyrrolizine-1,2,7a-tricarboxylate **(8)** with combined yield of (197 mg, 0.63 mmol, 63 %) in a 3:1 ratio both as yellow oils.

Trimethyl 3-ethylhexahydro-1H-pyrrolizine-1,2,7a-tricarboxylate (7)



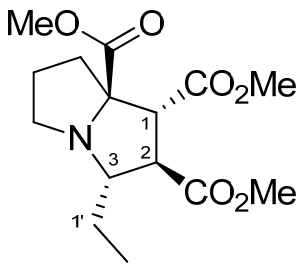
δ_H (500 MHz, $CDCl_3$); 3.70 (3H, s, O-CH_3), 3.68 (3H, s, O-CH_3), 3.66 (3H, s, O-CH_3), 3.68-3.66 (2H, m, 2-H and 3-H) 3.49 (1H, d, *J* 7.0 Hz, 1-H), 2.99-2.94 (1H, m, N-CH), 2.89 (1H, dd, *J* 7.0, 9.5 Hz, N-CH), 2.63-2.58 (1H, m, CH), 2.35 (1H, dt, *J* 13.5, 8.5 Hz, CH), 2.01-1.94 (2H, m, CH and CH), 1.79-1.52 (2H, m, CH_2), 1.01 (3H, t, *J* 7.5

Hz, CH_3); **δ_C (125 MHz, $CDCl_3$);** 175.3, 173.1, 172.2, 79.9, 65.3, 56.3, 52.5, 52.0, 51.9, 51.2, 47.1, 34.2, 23.9, 21.9, 12.3; **ν_{max}/cm^{-1} (film);** 3451, 2954, 2258, 1732, 1436, 1381; **H.R.M.S. [ES^+]** found MH^+, 314.1612. $C_{15}H_{24}NO_6$ requires *MH* 314.1598. **n.O.e data**:

% enhancement

irradiated hydrogen	1'	2_β	3_β	5_α	5_β	CH_3
1_α	-	4	-	4	-	-
3_β	2	-		-	-	2
5_α	4	-	-		12	-

Trimethyl 3-ethylhexahydro-1H-pyrrolizine-1,2,7a-tricarboxylate (8)

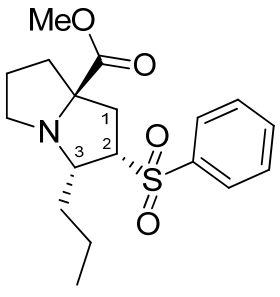


δ_H (500 MHz, $CDCl_3$); 4.06 (1H, d, *J* 11.0 Hz, 1-H), 3.80 (3H, s, O-CH_3), 3.72 (3H, s, O-CH_3), 3.68 (3H, s, O-CH_3), 3.32-3.28 (1H, m, 3-H), 3.01-2.96 (2H, m, 2-H and N-CH), 2.64-2.59 (1H, m, N-CH), 2.46-2.43 (1H, m, CH), 1.87-1.75 (1H, m, CH), 1.74-1.63 (3H, m, CH and CH_2), 1.39-1.33 (1H, m, CH), 0.99 (3H, t, *J* 7.5 Hz, CH_3); **δ_C (125 MHz, $CDCl_3$);** 174.7, 172.9, 171.9, 75.5, 67.6, 56.0, 52.8, 52.0, 52.0, 49.0, 48.6, 33.1, 25.3, 22.7, 11.9; **ν_{max}/cm^{-1} (film);** 3451, 2954, 2258, 1732, 1436, 1381; **H.R.M.S. [ES^+]** found MH^+, 314.1612. $C_{15}H_{24}NO_6$ requires *MH* 314.1598. **n.O.e data**:

% enhancement

irradiated hydrogen	1'	1_β	2_α	3_β	CH_3
1_β	-		1	4	-
3_β	2	7	1		2

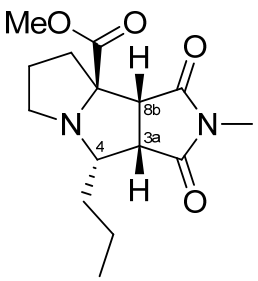
Preparation methyl 2-(benzenesulfonyl)-3-propyl-hexahydro-1H-pyrrolizine-7a-carboxylate (9)



(E)-methyl 1-(but-2-en-1-yl)pyrrolidine-2-carboxylate (1 mmol) and (vinylsulfonyl)benzene (1 mmol) were reacted following general procedure B to afford methyl 2-(benzenesulfonyl)-3-propyl-hexahydro-1H-pyrrolizine-7a-carboxylate (176 mg, 0.50 mmol, 50

%) as a thick yellow oil. **δ_H (500 MHz, $CDCl_3$);** 7.94-7.88 (2H, m, ArH), 7.69-7.63 (1H, m, ArH), 7.63-7.55 (2H, m, ArH), 3.84-3.74 (2H, m, 2-H and 3-H), 3.71 (1H, s O-CH_3), 3.23-3.08 (2H, m, N-CH and N-CH'), 2.40-2.33 (2H, m, 1-CH and 1-CH'), 2.25-2.15 (1H, m, CH), 2.10-1.92 (5H, CH_2, CH_2 and CH), 1.69-1.60 (1H, m, CH), 1.57-1.47 (1H, m, CH), 1.01 (t, *J* 7.5 Hz, CH_3; **δ_C (125 MHz, $CDCl_3$);** 175.3, 140.6, 13.4, 129.5, 128.1, 76.0, 68.3, 65.5, 52.7, 47.2, 38.4, 34.8, 30.0, 23.9, 21.8, 14.1; **ν_{max}/cm^{-1} (film);** 3454, 2959, 2876, 1729, 1446, 1307; **H.R.M.S. [ES^+]** found MH^+, 352.1590. $C_{18}H_{26}NO_4S$ requires *MH* 352.1577.

Preparation of methyl 2-methyl-1,3-dioxo-4-propyldecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (10)

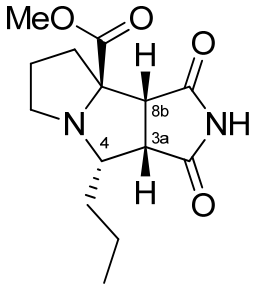


(E)-methyl 1-(but-2-en-1-yl)pyrrolidine-2-carboxylate (1 mmol) and N-methylmaleimide (1 mmol) were reacted following general method B to afford methyl 2-methyl-1,3-dioxo-4-propyldecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (209 mg, 0.71 mmol, 71 %) as a yellow oil. **δ_H (500 MHz, $CDCl_3$);** 3.84 (1H, d, *J* 8.0 Hz, 8b-CH), 3.76 (3H, s, O-CH_3), 3.45 (1H, q, *J* 8.0 Hz, 4-CH), 3.25 (1H, t, *J* 8.0 Hz, 3a-CH), 3.03 (1H, ddd, *J* 9.5, 8.0, 3.0 Hz, N-CH), 2.89 (3H, s, N-CH_3), 2.59 (1H, ddd, *J* 14.0, 9.5, 7.0 Hz, CH), 2.34-2.28 (2H, m, N-CH and CH), 1.99-1.86 (2H, m, CH and CH), 1.79-1.73 (1H, m, CH), 1.72-1.61 (2H, m, CH and CH), 1.56-1.47 (2H, m, CH and CH) 0.98 (3H, t, *J* 7.5 Hz, CH_3); **δ_C (125 MHz, $CDCl_3$);** 177.5, 177.1, 174.3, 79.2, 63.4, 53.1, 51.3, 49.6, 47.8, 30.5, 30.2, 25.0, 24.1, 21.0, 14.1; **ν_{max}/cm^{-1} (film);** 2958, 1701, 1434, 1381; **H.R.M.S. [ES^+]** found MH^+, 295.1646. $C_{15}H_{23}N_2O_4$ requires *MH* 295.1652; **n.O.e data**:

% enhancement

irradiated hydrogen	$3a_\beta$	4_β	$8b_\beta$
$3a_\beta$		10	12
4_β	10		-
$8b_\beta$	7	-	

Preparation of methyl 1,3-dioxo-4-propyldecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (11)

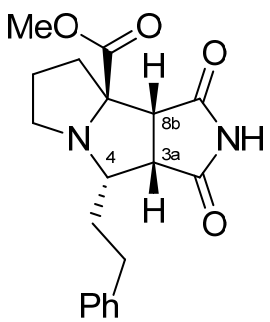


(E)-methyl 1-(but-2-en-1-yl)pyrrolidine-2-carboxylate (1 mmol) and maleimide (1 mmol) were reacted following general procedure B to afford methyl 1,3-dioxo-4-propyldecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (140 mg, 0.50 mmol, 50 %) as an off-white powder m.p 153-156 ^{o}C; **δ_H (500 MHz, $CDCl_3$);** 8.05 (1H, s, N-H), 3.90 (1H, d, *J* 8.0 Hz, 8b-H), 3.77 (3H, s, O-CH_3), 3.46 (1H, q, *J* 8.0 Hz, 4-H), 3.33 (1H, t, *J* 8.0 Hz, 3a-H), 3.11-3.07 (1H, m, N-CH), 2.66-2.57 (2H, m, N-CH and CH), 2.38-2.32 (1H, m, CH), 2.04-1.98 (1H, m, CH), 1.94-1.88 (1H, m, CH), 1.86-1.76 (2H, m, CH and CH), 1.69-1.63 (1H, m, CH), 1.55-1.51 (1H, m, CH), 0.99 (3H, t, *J* 7.5 Hz, CH_3); **δ_C (125 MHz, $CDCl_3$);** 177.6, 177.2, 174.2, 79.4, 63.4, 53.2, 52.6, 50.8, 47.9, 30.4, 30.3, 24.3, 21.0, 14.2; **ν_{max}/cm^{-1} (film);** 3454, 2970, 1738, 1435, 1365, 1217; **H.R.M.S. [ES$^+$]** found MH^+, 281.1507. $C_{14}H_{21}N_2O_4$ requires *MH* 281.1496.

Preparation of methyl 1,3-dioxo-4-phenethyldecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (14) and (E)-methyl 1,3-dioxo-4-styryldecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylates (15) (16)

Methyl 1-cinnamylpyrrolidine-2-carboxylate (1 mmol) and maleimide (1 mmol) were reacted following general procedure B to afford pure methyl 1,3-dioxo-4-((E)-styryl)decahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate **(16)** (109 mg, 0.50 mmol) as a yellow oil and two inseparable mixtures of methyl 1,3-dioxo-4-phenethyldecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate **(14)** and methyl 1,3-dioxo-4-((E)-styryl)decahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate **(15)** (109 mg combined mass) in which one mixture was a 5:2 ratio mixture of **(14)** to **(15)** and the other a 2:5 ratio mixture of **(14)** to **(15)**

Methyl 1,3-dioxo-4-phenethyldecahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (14):



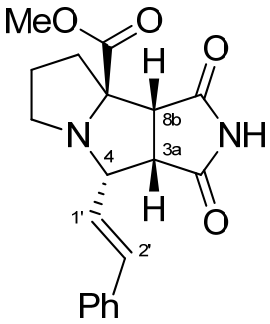
δ_H (500 MHz, $CDCl_3$); 8.60 (1H, s, N-H), 7.32-7.25 (4H, m, ArH), 7.21-7.16 (1H, m, ArH), 3.78 (1H, d, *J* 8.5 Hz, 8b-H), 3.75 (3H, s, O-CH_3), 3.51-3.44 (1H, m, 4-H), 3.34 (1H, t, *J* 8.5 Hz, 3a-H), 3.10-3.06 (1H, m, N-CH), 3.00-2.94 (1H, m, CH), 2.81-2.75 (1H, m, N-CH), 2.66-2.53 (2H, m,

CH_2), 2.37-2.32 (1H, m, CH), 2.24-2.19 (1H, m, CH), 2.18-2.11 (1H, m, CH), 2.04-1.89 (1H, m, CH), 1.89-1.80 (1H, m, CH); **n.O.e data:**

% enhancement

irradiated hydrogen	$3a_\beta$	4_β	$8b_\beta$
$3a_\beta$		5	10
4_β	5		-
$8b_\beta$	5	-	

Methyl 1,3-dioxo-4-((E)-styryl)decahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (15)

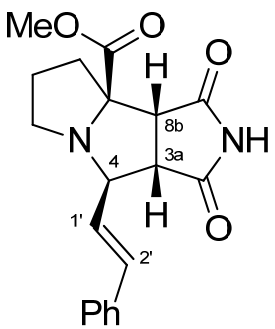


δ_H (500 MHz, $CDCl_3$); 8.57 (1H, s, N-H), 7.40 (2H, d, *J* 7.5 Hz, ArH), 7.32-7.16 (3H, m, ArH), 6.75 (1H, d, *J* 15.5 Hz, 2-H), 6.37 (1H, dd, *J* 9.5, 15.5 Hz, 1-H), 4.12 (1H, t, *J* 8.0 Hz, 4-H), 3.90 (1H, d, *J* 8.0 Hz, 8b-H), 3.76 (3H, s, O-CH_3), 3.49 (1H, t, *J* 8.0 Hz, 3a-H), 3.11-3.07 (1H, m, N-CH), 2.78-2.73 (1H, m, N-CH), 2.63-2.51 (1H, m, CH), 2.39-2.33 (1H, m, CH), 2.10-1.98 (1H, m, CH), 1.91-1.85 (1H, m, CH); **n.O.e data:**

% enhancement

irradiated hydrogen	1’	2’	$3a_\beta$	4_β	$8b_\beta$
$3a_\beta$	-	-		6	8
4_β	2	10	10		-
$8b_\beta$	-	-	5	-	

Methyl 1,3-dioxo-4-((E)-styryl)decahydropyrrolo[3,4-a]pyrrolizine-8a-carboxylate (16)



δ_H (500 MHz, $CDCl_3$); 7.69 (1H, s, N-H), 7.41 (2H, d, *J* 7.0 Hz, ArH), 7.35-7.32 (2H, m, ArH), 7.29-7.26 (1H, m, ArH), 6.84 (1H, d, *J* 15.5 Hz, 2-H), 6.32 (1H, dd, *J* 15.5, 7.0 Hz, 1-H), 4.52 (1H, t, *J* 8.5 Hz, 4-H), 3.75 (3H, s, O-CH_3), 3.60 (1H, dd, *J* 8.5, 9.5 Hz, 3a-H), 3.44 (1H, d, *J* 9.5 Hz, 8b-H), 3.10-3.06 (1H, m, N-CH), 3.05-3.00 (1H, m, CH), 2.73 (1H, q, *J* 8.5 Hz, N-CH), 1.99-1.86 (3H, m, CH_2, CH); **δ_C (125 MHz, $CDCl_3$);** 175.8, 175.7, 172.4, 172.1, 136.3, 135.0, 128.6, 128.1, 126.7, 125.0, 67.5,

58.5, 52.7, 52.1, 49.5, 36.3, 25.3, **ν_{max}/cm^{-1} (film);** 3851, 2952, 1717, 1340; **H.R.M.S. [ES$^+$]** found MH$^+$, 341.1511. $C_{19}H_{21}N_2O_4$ requires *MH* 341.1496. **n.O.e data**:

% enhancement

irradiated hydrogen	1’	2’	3a$_\beta$	4$_\alpha$	8b$_\beta$
1’		-	4	-	-
3a$_\beta$	3	5		2	7
4$_\alpha$	3	8	2		-
8b$_\beta$	-	-	5	-	