Chemistry of Ethyl 2-{[*t*-Butoxycarbonyl(methyl)amino]methyl}-3-hydroxy-3-phenyl (or 3-vinyl)propionate: Mechanistic Considerations in the Formation of Tetrahydro-1,3-oxazin-2-ones

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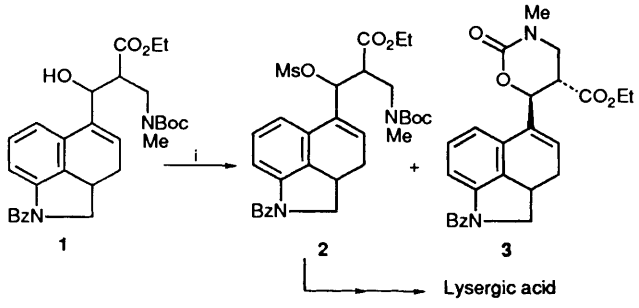
The *threo*- and *erythro*-selective aldol condensation of ethyl 3-[*t*-butoxycarbonyl(methyl)amino]-propionate with benzaldehyde gave the benzylic alcohol-substituted aminopropionate ethyl 2-{[*t*-butoxycarbonyl(methyl)amino]methyl}-3-hydroxy-3-phenylpropionate as a diastereoisomeric mixture. On treatment with methanesulphonyl chloride and triethylamine, the *threo*-isomer was converted into ethyl 3-methyl-2-oxo-6-phenyl-3,4,5,6-tetrahydro-2*H*-1,3-oxazine-5-carboxylate, and the *erythro*-isomer gave simply its corresponding mesate derivative. The mechanism for this transformation is discussed.

Our previous paper reported [1] the formal total synthesis of (±)-lysergic acid *via* the mesate **2** as the key compound, by treatment of the allyl alcohol **1** with methanesulphonyl chloride and triethylamine. In this reaction, however, the tetrahydro-1,3-oxazin-2-one derivative **3**, which caused a significant decrease in the yield of compound **2**, was isolated as a by-product in *ca.* 30% yield (Scheme 1). This paper presents in detail the mechanism for this side-reaction by using a simple model compound.[2]



Scheme 1 *Reagents:* i, MsCl, Et_3N. Abbreviations: Boc, *tert*-butoxycarbonyl; Ms, methylsulphonyl

Results and Discussion

The aldol condensation of ethyl 3-[*t*-butoxycarbonyl(methyl)-amino]propionate **4** with benzaldehyde **5a** in the presence of lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −78 °C gave the benzylic alcohol **6a** in quantitative yield. ^1H NMR spectroscopy indicated the product **6a** to be an inseparable mixture of diastereoisomers in the ratio 45:55 (based on *N*-methyl signals). Treatment of this mixture with MsCl (1.5 mol equiv.) in the presence of Et_3N in methylene dichloride at room temperature for 20 min gave the tetrahydro-1,3-oxazin-2-one **7a**† (36%) and mesate **8a** (47%), following purification by SiO_2 column chromatography. *trans*-Stereochemistry of the former product, having a stable 5,6-diequatorial configuration, was deduced from the coupling constant (*J* 7.8 Hz) of 6-H (δ 5.45, d) in the ^1H NMR spectrum.[3] *threo*-Selective[4] and *erythro*-selective[5] aldol condensations of diester **4** with benzaldehyde **5a**, followed by mesylation of the resulting alcohol **6a**, gave a mixture of compounds **7a** and **8a**, whose product ratios are indicated in Table 1. The *threo*-selective condensation product (*threo*/*erythro* 79/21) was clearly shown to yield the 1,3-oxazin-2-one **7a** predominantly, whereas mesate **8a** was the major component from the *erythro*-selective condensation product (*threo*/*erythro* 26/74). It is significant that the diastereoisomeric ratio was virtually the same as that of the products. Isolated mesate **8a** was not converted into the oxazinone **7a** under the same conditions of mesylation.‡ *threo*-**6a** Alone is converted into the 1,3-oxazin-2-one **7a**, possibly *via* the mesyl intermediate, while *erythro*-**6a** is converted into the corresponding mesate **8a** by treatment of compound **6a** with MsCl–Et_3N. Assignment of the stereochemistry of the alcohols *threo*-**6a** and *erythro*-**6a** was made as follows: reduction of the *threo*-selective condensation product with lithium borohydride–methanol[6] in diethyl ether to give diols which were subsequently separated by SiO_2 column chromatography afforded diols **9** (67%) and **10** (18%). Treatment of either diol **9** or **10** with 2,2-dimethoxypropane in the presence of toluene-*p*-sulphonic acid (TsOH) gave the corresponding 1,3-dioxane derivative **11** or **12** (Scheme 2). Coupling constants of the ring methine protons in compound **11** ($J_{4,5}$) had a value (12 Hz) exceeding that (3 Hz) for the corresponding protons of its isomer **12**. The major component of aldol condensation product **6a** is thus shown to be the *threo*-isomer and the minor one to be the *erythro*-one.

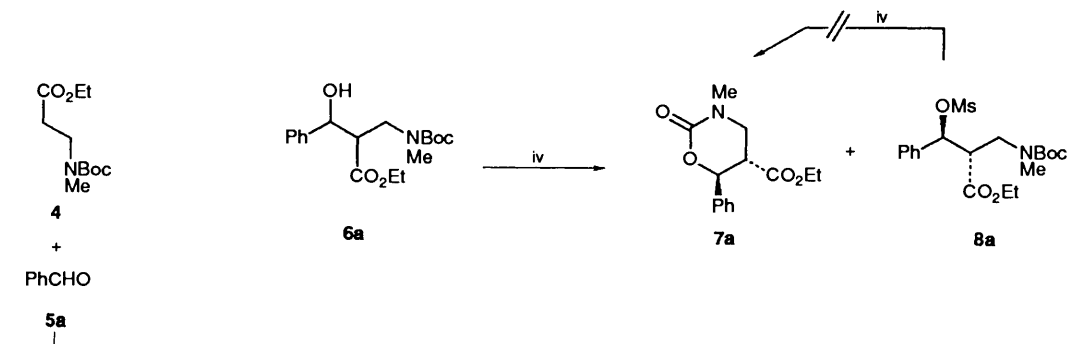
We then turned our attention to the reason why compound **7a** is obtained from the *threo*-**6a** alcohol only. A possible explanation is as follows: Fig. 1 shows the most stable of the three possible conformers of the *threo*- and *erythro*-mesate **8a**. Electrostatic repulsion between the mesyloxy and ethoxycarbonyl groups in the *threo*-isomer should accelerate elimination of the mesyloxy group to give the tetrahydro-1,3-oxazin-2-one **7a**.

On the other hand, effects of substitition on the benzene ring could be detected in the reaction of alcohols **6b–6f** with MsCl–Et_3N, as shown in Table 2. That is, electron-donating groups in the compounds **6** caused the exclusive formation of 1,3-oxazine-2-ones **7b–d** in high yields, whereas electron-withdrawing groups such as nitro resulted in the predominant formation of mesate **8f**, which was shown to be a mixture of *threo* and *erythro* isomers by its ^1H NMR spectrum. Similarly, treatment of allyl alcohols **16** and **19**, obtained by condensation of diester **4** with α,β-unsaturated aldehydes **13** and **14**, with MsCl–Et_3N gave a mixture of 1,3-oxazin-2-ones **17**, **20** and mesates **18**, **21**. However, saturated alcohol **22** prepared from cyclohexanecarbaldehyde **15** did not give any cyclised product under the same conditions (Table 2). These results strongly indicated that the

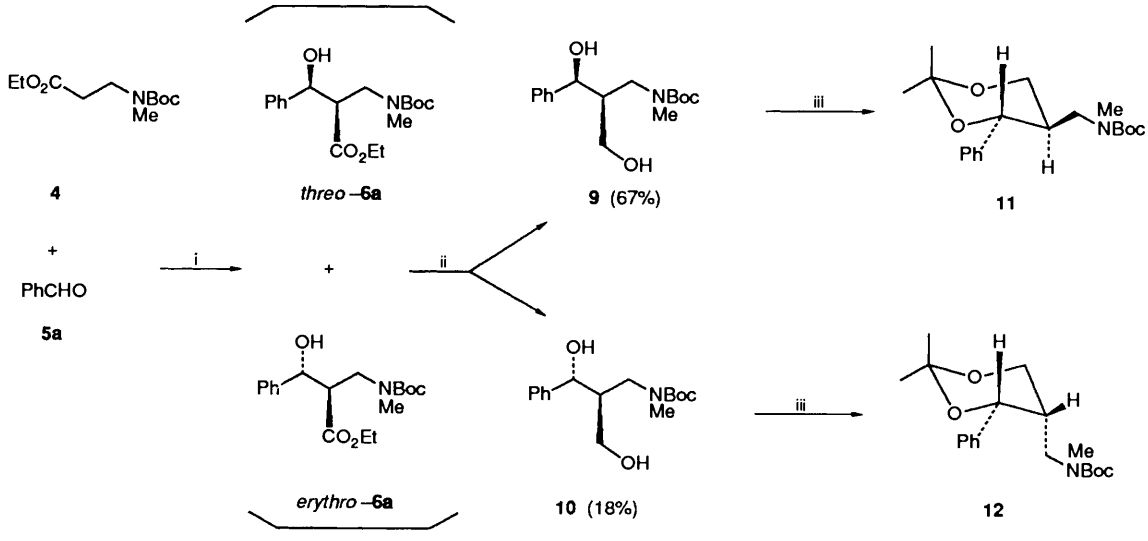
† Refluxing of compound **6a** with Et_3N in methylene dichloride did not give the 1,3-oxazine **7a**.

‡ Compound **8a** was recovered unchanged after being refluxed with Et_3N hydrochloride in methylene dichloride.

Table 1 *Reagents:* i, LDA; ii, LDA, TMSCl, $TiCl_4$; iii, LDA, Cp_2ZrCl_2; iv, MsCl, Et_3N



	threo/erythro	(%)	(%)	(%)	Quotient **7a**/**8a**
i →	45/55	99	36	47	43/57
ii →	79/21	62	67	20	77/23
iii →	26/74	90	21	64	25/75



Scheme 2 *Reagents:* i, LDA, TMSCl, $TiCl_4$; ii, $LiBH_4$–MeOH; iii, $MeCH(OMe)_2Me$, TsOH

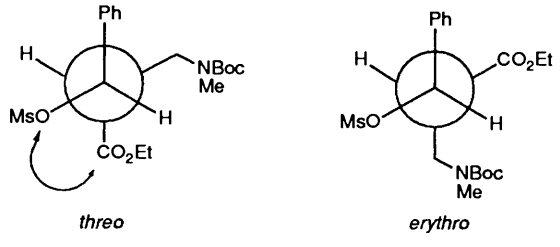
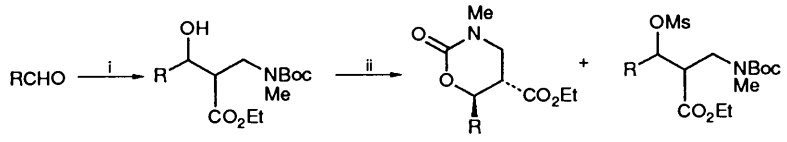


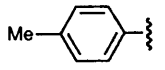
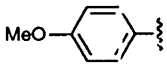
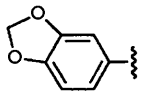
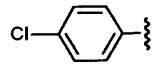
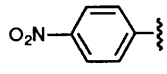
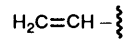
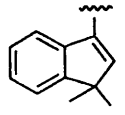
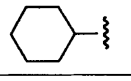
Fig. 1 Newman projections of *threo*- and *erythro*-mesates **8a**

stability of the carbocation that may be generated by elimination of a mesyloxy group may also be a fundamental factor in the preferential formation of 1,3-oxazin-2-ones (Scheme 3). The benzylic or allylic mesates must therefore be formed in order to give the corresponding 1,3-oxazin-2-one. It therefore follows that the mechanism of 1,3-oxazin-2-one formation from benzylic or allylic mesates may be as follows: elimination of the mesyloxy anion promoted by electrostatic repulsion and/or presence of electron-donating groups on the benzene ring as mentioned above leads to the formation of the stabilised benzylic or allylic carbocations. Abstraction of a proton from the *t*-butyl group by the mesyloxy anion, with subsequent liberation of isobutene followed by cyclisation of the *N*-carboxylate anion thus produced, gives the corresponding 1,3-oxazin-2-one *via* an S_N1 process.

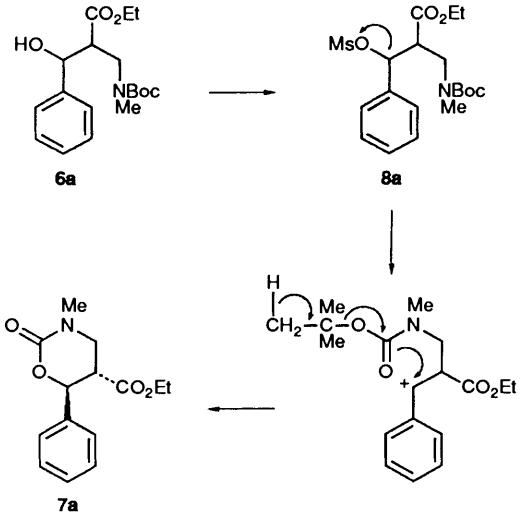
Previously, Kano *et al.*[7] reported a simple diastereoselective conversion of chiral *N*-benzyloxycarbonyl 1,2-amino alcohols by treatment of thionyl dichloride at 60 °C, followed by ring cleavage of the resulting oxazolidin-2-ones, of which cyclocarbamation was thought to proceed through S_N2-type C–O bond formation. 1,3-Oxazin-2-one formation was found to occur in one case apparently *via* an S_N2 process. Condensation of acrylaldehyde **13** with ethyl 3-[*t*-butoxycarbonyl(methyl)-amino]-2-methylpropionate **24** under the same conditions as for the preparation of compound **6a** gave *threo*-alcohol **25** and *erythro*-alcohol **26** in 47 and 40% yield, respectively. These could be separated by SiO_2 column chromatography. Determination of *threo* and *erythro* stereochemistry for compounds **25** and **26** were conducted by the same method as that used in the determination of compound **6a** by which 1,3-dioxanes **27** and **28** were obtained. The nuclear Overhauser

Table 2 *Reagents*: i, **4**, LDA; ii, MsCl, Et_3N



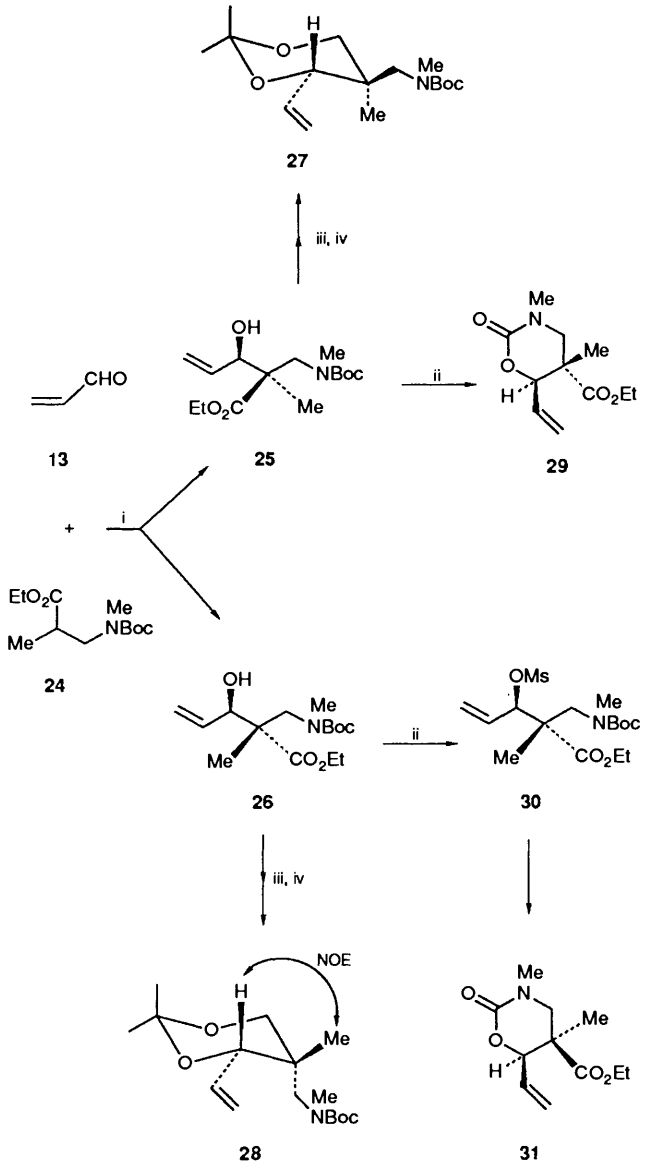
R	Comp.	Comp.	Comp. (Yield %)[a]	Comp. (Yield %)[a]
	**5b**	**6b**	**7b** (74)	
	**5c**	**6c**	**7c** (82)	
	**5d**	**6d**	**7d** (83)	
	**5e**	**6e**	**7e** (34)	**8e** (53)
	**5f**	**6f**	**7f** (19)	**8f** (60)[b]
	**13**	**16**	**17** (40)	**18** (42)
	**14**	**19**	**20** (37)	**21** (51)
	**15**	**22**		**23** (60)[c,d]

[a] Isolated yield by column chromatography. [b] This was a mixture of *threo* and *erythro* isomers prior to purification by recrystallisation. [c] This was a mixture of *threo* and *erythro* isomers. [d] Starting material **22** was recovered in 20% yield.



Scheme 3

effect (NOE) between 5-Me and 4-H was thereby shown to be stronger in compound **28** than in compound **27**. The usual treatment of compounds **25** and **26** with MsCl–Et_3N gave the 1,3-oxazin-2-one **29** as a single product in 83% yield from the former, and the mesate **30** in 79% yield from the latter, as an oil. However, the mesate **30** was surprisingly transformed into the 1,3-oxazin-2-one **31** as a single product by just being kept at room temperature for a few days, presumably because of the presence of a quaternary centre in a position adjacent to a mesyloxy group. The transformation of compound **30** presumably proceeds *via* the S_N1 process to give the more stable isomer **31** (Scheme 4). The *cis*-stereochemistry between 5-Me and 6-H of compound **31** was clarified based on the NOE enhancement. ^1H NMR spectrum of compound **29** was virtually the same as that of its diastereoisomer **31**, though there was no NOE enhancement between 5-Me and 6-H; compound **29** is therefore shown to have *trans*-stereochemistry. Though details have yet to be clarified, the transformation of the alcohol **25** *via* its mesate intermediate into the *trans* oxazine isomer **29**, should be explainable as being due to the S_N2 process.



Scheme 4 *Reagents*: i. LDA; ii, MsCl. Et_3N; iii, $LiBH_4$; iv, MeCH-$(OMe)_2$Me, TsOH

Experimental

IR spectra were recorded on a Shimadzu IR-435 spectrophotometer. ^{1}H NMR spectra were determined with a Varian Gemini-200 spectrometer (tetramethylsilane as internal standard), and mass spectra with a Hitachi M-80 instrument. The solvent for extraction was a mixture of benzene–EtOAc (1:1), unless otherwise stated, and was dried over anhydrous sodium sulphate. For column chromatography, SiO_2 (Merck, Art 9385) was used. Light petroleum refers to the fraction boiling in the range 30–60 °C.

Ethyl 2-{[t-*Butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-*hydroxy*-3-*phenylpropionate* **6a**.—*Method A*. A solution of compound **4** (2.08 g, 9 mmol) in THF (5 cm^3) was added to a solution of LDA [prepared from diisopropylamine (1.4 cm^3, 10 mmol) and BuLi (1.6 mol dm^{-3} hexane solution; 6.4 cm^3, 10 mmol)] in THF (5 cm^3) at −78 °C under N_2, and the mixture was stirred for 20 min. A solution of benzaldehyde **5a** (1.06 g, 10 mmol) in THF (5 cm^3) was added dropwise to the mixture at −78 C, and the whole was stirred for 10 min. The reaction was quenched by the addition of water, and THF was removed by evaporation. The residue was extracted, and the extract was washed successively with water and brine, dried, and evaporated. The residue was purified by column chromatography [benzene–EtOAc (5:1)] to give *compound* **6a** (3.0 g, 99%) as an oil, ν_{max}(neat)/cm^{-1} 3420 (OH), 1730 and 1690 (CO). The ^{1}H NMR spectrum was not sufficiently well resolved for assignment of the signals. Selected ^{1}H NMR spectral data are as follows: $\delta_H(CDCl_3)$ 1.12 (3 H, br, CO_2CH_2Me), 1.44 (9 H, s, Bu^t, 2.75 and 2.84 (ratio 55:45) (3 H, each s, NMe), 3.0–3.50 (3 H, m, CH_2CH), 4.75–4.80 (1 H, m, $CHOH$) and 7.34 (5 H, s, ArH) (Found: M$^+$, 337.1886. $C_{18}H_{27}NO_5$ requires M, 337.1890).

Method B. A solution of compound **4** (693 mg, 3 mmol) in THF (5 cm^3) was added to a solution of LDA [prepared from diisopropylamine (0.5 cm^3, 3.6 mmol) and BuLi (1.6 mol dm^{-3} hexane solution; 2.2 cm^3, 3.6 mmol)] in THF (5 cm^3) at −78 °C under N_2, and the mixture was stirred for 20 min. A solution of chlorotrimethylsilane (TMSCl) (0.47 cm^3, 3.6 mmol) in THF (4 cm^3) was added dropwise to the mixture at −78 °C, and the whole was stirred for 30 min, then for an additional 30 min at room temperature. The reaction was quenched by the addition of water. and THF was removed by evaporation. The residue was extracted with light petroleum and the extract was washed successively with water and brine, dried, and evaporated to give a crude silyl enol ether as an oil. A solution of titanium tetrachloride (0.33 cm^3, 3 mmol) in methylene dichloride (6 cm^3), cooled to −78 °C, was added to a solution of benzaldehyde **5a** (223 mg, 2.1 mmol) in methylene dichloride (15 cm^3) at such a rate that the temperature of the reaction mixture remained between −70 and −75 °C. After the mixture had been stirred for 15 min, a solution of the silyl enol ether obtained above in methylene dichloride (3 cm^3) was added dropwise to the mixture at this temperature, and the whole was stirred for 2.5 h at −78 °C. The reaction mixture was quenched by the addition of 5% aq. potassium carbonate (25 cm^3), then diluted with chloroform (30 cm^3). The insoluble material was removed by filtration, and the filtrate was washed successively with water and brine, dried, and evaporated. The residue was purified by column chromatography [benzene–EtOAc (5:1)] to give a *threo*-predominant product **6a** (440 mg, 62%) as an oil, whose ^{1}H NMR spectrum showed the NMe signals at δ 2.75 and 2.84 with the ratio *erythro*:*threo* 21:79 (Found: M$^+$, 337.1882).

Method C. A solution of compound **4** (693 mg, 3 mmol) in THF (5 cm^3) was added to a solution of LDA [prepared from diisopropylamine (0.46 cm^3, 3.3 mmol) and BuLi (1.6 mol dm^{-3} hexane solution; 2.1 cm^3, 3.3 mmol) in THF (5 cm^3) at −78 °C under N_2, and the mixture was stirred for 30 min. A solution of bis(cyclopentadienyl)zirconium dichloride (Cp_2ZrCl_2) (964 mg, 3.3 mmol) in THF (15 cm^3) was then added at such a rate that the temperature of the reaction mixture remained between −70 and −75 °C, followed by a solution of benzaldehyde **5a** (223 mg, 2.1 mmol) in THF (1 cm^3), and the whole was stirred for 2 h at −78 °C. The reaction mixture was quenched by the addition of saturated aq. ammonium chloride (3 cm^3), and was then stirred for 30 min at room temperature, then extracted. The extract was washed successively with water and brine, dried, and evaporated. The residue was purified by column chromatography [benzene–EtOAc (5:1)] to give an *erythro*-predominant product **6a** (634 mg, 90%) as an oil, whose ^{1}H NMR spectrum showed the NMe signals at δ 2.75 and 2.84 with the ratio *erythro*:*threo* (74:26) (Found: M$^+$, 337.1888).

threo-*and*erythro-t-*Butyl* N-[3-*Hydroxy*-2-(*hydroxymethyl*)-3-*phenyl*]-N-*methylcarbamate* **9** *and* **10**.—To an ice-cooled solution of *threo*-predominant diester **6a** (309 mg, 0.92 mmol), prepared by Method B, in diethyl ether (6 cm^3) containing methanol (88 mg, 2.67 mmol) was added $LiBH_4$ (58 mg, 2.76 mmol), and the mixture was refluxed for 2 h, quenched by the addition of water (10 cm^3) and extracted. The extract was

washed successively with water and brine, dried, and evaporated. The residue was chromatographed [benzene–EtOAc (3:1)] to give compound **9** (182 mg, 67%) from the first fraction and compound **10** (48 mg, 18%) from the second fraction.

Compound **9** was an oil; ν_{max}(neat)/cm^{-1} 3350 (OH) and 1660 (CO); δ_H($CDCl_3$) 1.46 (9 H, s, Bu^t), 1.90 (1 H, m, C*H*CH_2OH), 2.70 (3 H. s, NMe), 2.80 (1 H, dd, *J* 14.0 and 4.0, C*H*HNBoc), 3.54 and 3.78 (each 1 H, each d, *J* 12.0, CH_2OH), 3.94 and 4.44 (each 1 H, each br s, 2 × OH), 4.04 (1 H, dd, *J* 14.0 and 12.0, CH*H*NBoc), 5.08 (1 H, d, *J* 5.0, ArCH) and 7.20–7.40 (5 H, m, ArH); *m/z* 296 (M^+ + 1) [Found: (M + 1) 296.1862. $C_{16}H_{26}NO_4$ requires *m/z* 296.1862].

Compound **10** was an oil; ν_{max}(neat)/cm^{-1} 3400 (OH) and 1660 (CO); δ_H($CDCl_3$) 1.47 (9 H, s, Bu^t), 1.89 (1 H, m, C*H*CH_2OH), 2.88 (3 H, s, NMe), 3.27 (1 H, dd, *J* 15.0 and 7.0, C*H*NBoc), 3.42 and 3.71 (each 1 H, each dd, *J* 12.0 and 7.0, CH_2OH), 3.83 (1 H, dd, *J* 15.0 and 10.0, CH*H*NBoc), 3.95 (1 H, t, *J* 7.0, CH_2O*H*), 4.93 (1 H. d, *J* 6.0, ArCHO*H*), 4.81 (1 H, dd, *J* 6.0 and 5.0, ArCH) and 7.20–7.40 (5 H, m, ArH) (Found: M^+, 295.1786. $C_{16}H_{25}NO_4$ requires M, 295.1785).

trans-t-*Butyl* N-[(2,2-*Dimethyl*-4-*phenyl*-1,3-*dioxan*-5-*yl*)-*methyl*]-N-*methylcarbamate* **11**.—A solution of compound **9** (65 mg, 0.22 mmol) and 2,2-dimethoxypropane (1.64 cm^3, 13.2 mmol) in the presence of TsOH (42 mg, 0.22 mmol) in diemthylformamide (DMF) (3 cm^3) was stirred at room temperature for 2 h. After the reaction mixture had been quenched by the addition of 2% aq. potassium carbonate (10 cm^3), it was extracted with EtOAc. The extract was washed with water, dried, and evaporated. The residue was purified by column chromatography [benzene–EtOAc (10:1)] to give *compound* **11** (58 mg, 79%) as an oil; ν_{max}(neat)/cm^{-1} 1690 (CO); δ_H($CDCl_3$) 1.42 (9 H, s, Bu^t), 1.48 and 1.55 (each 3 H, each s, 2 × Me), 2.05–2.56 (2 H, m, C*H*NBoc and 5-H), 2.58 (3 H, s, NMe), 3.29 (1 H, m, C*H*NBoc), 3.88 (2 H, d, *J* 8.0, OCH_2), 4.53 (1 H, d, *J* 12.0, 4-H) and 7.25–7.45 (5 H, m, ArH) (Found: M^+, 335.2094. $C_{19}H_{29}NO_4$ requires M, 335.2098).

cis-t-*Butyl* N-[(2,2-*Dimethyl*-4-*phenyl*-1,3-*dioxan*-5-*yl*)*methyl*]-N-*methylcarbamate* **12**.—A solution of compound **10** (145 mg, 0.5 mmol) was treated with 2,2-dimethoxypropane (3.7 cm^3, 30 mmol), as described for the preparation of compound **11**, to give *compound* **12** (128 mg, 76%) as an oil; ν_{max}(neat)/cm^{-1} 1675 (CO); δ_H($CDCl_3$) 1.39 (9 H, s, Bu^t), 1.54 and 1.55 (each 3 H, each s, 2 × Me), 1.98 (1 H, m, 5-H), 2.72 (4 H, br s, NMe and C*H*NBoc), 3.49 (1 H, br t, *J* 12.0, C*H*NBoc), 3.85 and 4.16 (each 1 H, each d, *J* 12.0, OCH_2), 5.24 (1 H, d, *J* 2.6, 4-H) and 7.16–7.40 (5 H, m, ArH) (Found: M^+, 335.2096).

General Procedure for the Preparation of Benzylic and Allylic Alcohols **6b–f**, **16**, **19** *and* **22**.—By a similar procedure (Method A) to that described for the preparation of compound **6a**, the crude product which was obtained from aldehydes **5b–f**, **13**, **14** and **15** and diester **4** was purified by column chromatography [benzene–EtOAc (5:1)] to give a benzylic or allylic alcohols, which were inseparable mixtures of diastereoisomers. The ^{1}H NMR spectra of these compounds were not sufficiently well resolved for assignment of the total signals.

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-*hydroxy*-3-(4-*methylphenyl*)*propionate* **6b** was an oil (92%), ν_{max}(neat)/cm^{-1} 3420 (OH), 1720 and 1680 (CO); δ_H($CDCl_3$) *inter alia* 1.05 (3 H, t, *J* 7.0, CO_2CH_2*Me*), 1.38 (9 H, s, Bu^t), 2.45 (3 H, s, Me), 2.73 and 2.78 (total 3 H, each s, NMe), 4.07 (2 H, m, CO_2CH_2Me), 4.65–4.80 (1 H, m, C*H*OH) and 7.15–7.30 (4 H, m, ArH) (Found: M^+, 351.2046. $C_{19}H_{29}NO_5$ requires M, 351.2044).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-*hydroxy*-3-(4-*methoxyphenyl*)*propionate* **6c** was an oil (91%), ν_{max}(neat)/cm^{-1} 3420 (OH), 1725 and 1690 (CO); δ_H($CDCl_3$) *inter alia* 1.03 (3 H, t, *J* 7.0, CO_2CH_2*Me*), 1.37 (9 H, s, Bu^t), 2.71 (3 H, s, NMe), 3.73 and 3.75 (total 3 H, each s, OMe), 4.05 (2 H, m, CO_2CH_2Me), 4.65–4.80 (1 H, m, C*H*OH), 6.80 (2 H, m, ArH) and 7.20 (2 H, m, ArH) (Found: M^+, 367.1994. $C_{19}H_{29}NO_6$ requires M, 367.1996).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-*hydroxy*-3-(3,4-*methylenedioxyphenyl*)*propionate* **6d** was an oil (97%), ν_{max}(neat)/cm^{-1} 3420 (OH), 1725 and 1690 (CO); δ_H($CDCl_3$) *inter alia* 1.05 (3 H, t, *J* 7.0, CO_2CH_2*Me*), 1.35 (9 H, s, Bu^t), 2.72 (3 H, s, NMe), 4.65–4.85 (1 H, m, C*H*OH), 5.85 and 5.87 (total 2 H, each s, OCH_2O) and 6.68–6.85 (3 H, m, ArH) (Found: M^+, 381.1785. $C_{19}H_{27}NO_7$ requires M, 381.1788).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-(4-*chlorophenyl*)-3-*hydroxypropionate* **6e** was an oil (100%), ν_{max}(neat)/cm^{-1} 3420 (OH), 1720 and 1680 (CO); δ_H($CDCl_3$) 1.13 (3 H, br, CO_2CH_2*Me*), 1.45 (9 H, s, Bu^t), 2.75 and 2.85 (total 3 H, each s, NMe), 3.10–3.50 (3 H, m, $CHCH_2N$) 4.04 (2 H, br, CO_2CH_2Me), 4.60–4.68 (1 H, m, C*H*OH) and 7.30 (4 H, m, ArH) (Found: M^+, 372.1578. $C_{18}H_{27}ClNO_5$ requires M, 372.1576).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-*hydroxy*-3-(4-*nitrophenyl*)*propionate* **6f** was an oil (97%), ν_{max}(neat)/cm^{-1} 3420 (OH), 1730 and 1690 (CO), 1545 and 1380 (NO_2); δ_H($CDCl_3$) 1.09 (3 H, t, *J* 7.0, CO_2CH_2*Me*), 1.40 (9 H, s, Bu^t), 2.71 and 2.85 (total 3 H, each s, NMe), 3.08 (1 H, m, C*H*CO_2Et), 3.96 (2 H, m, CO_2CH_2Me), 4.80–5.10 (1 H, m, C*H*OH) and 7.50 and 8.15 (each 2 H, each m, ArH) (Found: M^+, 382.1738. $C_{18}H_{26}N_2O_7$ requires M, 382.1741).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-*hydroxypent*-4-*enoate* **16** was an oil (96%), ν_{max}(neat)/cm^{-1} 3420 (OH), 1725 and 1680 (CO); δ_H($CDCl_3$) *inter alia* 1.20 (3 H, t, *J* 7.0, CO_2CH_2*Me*), 1.42 (9 H, s, Bu^t), 2.77 and 2.81 (total 3 H, each s, NMe), 4.10 (2 H, q, *J* 7.0, CO_2CH_2Me), 5.30–5.35 (2 H, m, =CH_2) and 5.70–5.92 (1 H, m, =CH) (Found: M^+, 287.1731. $C_{14}H_{25}NO_5$ requires M, 287.1736).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-(1,1-*dimethyl*-1H-*inden*-3-*yl*)-3-*hydroxypropionate* **19** was an oil (64%), ν_{max}(neat)/cm^{-1} 3400 (OH), 1730 and 1690 (CO); δ_H($CDCl_3$) *inter alia* 1.18 (3 H, m, CO_2CH_2*Me*), 1.28 and 1.30 (each 3 H, each s, 2 × Me), 1.45 (9 H, s, Bu^t), 2.74 and 2.91 (total 3 H, each s, NMe), 4.09 (2 H, m, CO_2CH_2Me), 4.82 and 5.04 (total 1 H, each m, C*H*OH) and 6.29 (1 H, s, =CH) (Found: M^+, 403.2357. $C_{23}H_{33}NO_5$ requires M, 403.2360).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-*cyclohexyl*-3-*hydroxypropionate* **22** was an oil (98%), ν_{max}(neat)/cm^{-1} 3420 (OH), 1725 and 1690 (CO); δ_H($CDCl_3$) *inter alia* 1.25 (3 H, t, *J* 7.5, CO_2CH_2*Me*), 1.46 (9 H, s, Bu^t), 2.82 and 2.88 (total 3 H, each s, NMe), 3.0–3.4 (1 H, m, C*H*CO_2Et), 3.5–3.7 (2 H, m, CH_2N), and 4.13 (2 H, q, *J* 7.5, CO_2CH_2Me) (Found: M^+, 343.2356. $C_{18}H_{33}NO_5$ requires M, 343.2357).

General Procedure for the Preparation of 1,3-*Oxazines* **7**, **17** *and* **20** *and Mesates* **8**, **18**, **21** *and* **23**.—To an ice-cooled solution of an alcohol **6**, **16**, **19**, or **22** (3 mmol) and Et_3N (9 mmol) in methylene dichloride (10 cm^3) was added MsCl (3.6 mmol). After being stirred at room temperature for 10 min, the reaction mixture was quenched by the addition of cold water. The organic layer was washed with water, dried, and evaporated. The residue was chromatographed [benzene–EtOAc (5:1)] to give the mesate from the first fraction and the 1,3-oxazine from the latter fraction (see Tables 1 and 2).

Ethyl 3-*Methyl*-2-*oxo*-6-*phenyl*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **7a** was an oil; ν_{max}(neat)/cm^{-1} 1720 and 1705 (CO); δ_H($CDCl_3$) 1.05 (3 H, t, *J* 7.3, CO_2CH_2Me), 3.06 (3 H, s, NMe), 3.15 (1 H, ddd, *J* 8.9, 7.8 and 5.2, 5-H), 3.38 (1 H, dd, *J* 11.5 and 5.2, 4-H), 3.71 (1 H, dd, *J* 11.5 and 8.9, 4-H), 4.03 (2 H, q, *J* 7.3, CO_2CH_2Me), 5.45 (1 H, d, *J* 7.8, 6-H) and 7.35 (5

H, m, ArH) (Found: M^+, 263.1155. $C_{14}H_{17}NO_4$ requires M, 263.1158).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-*methylsulphonyloxy*-3-*phenylpropionate* **8a** had m.p. 73–75 °C (from benzene–light petroleum); ν_{max}(Nujol)/cm^{-1} 1730 and 1690 (CO), and 1365 and 1170 (SO_2); δ_H($CDCl_3$) 0.96 (3 H, t, *J* 7.4, CO_2CH_2*Me*), 1.45 (9 H, s, Bu^t), 2.62 (3 H, s, NMe), 2.87 [3 H, s, $S(O)_2Me$], 3.38 (1 H, m, CHCO), 3.68 (1 H, m, C*H*HNBoc), 3.82 (1 H, dd, *J* 12.0 and 4.3, CH*H*NBoc), 3.90 (2 H, q, *J* 7.4, CO_2CH_2Me), 5.60 (1 H, d, *J* 11.0, $CHOSO_2$) and 7.39 (5 H, m, ArH); *m/z* 415 (M^+) (Found: C, 54.9; H, 7.3; N, 3.4. $C_{19}H_{29}NO_7S$ requires C, 54.86; H, 6.90; N, 3.39%).

Ethyl 3-*methyl*-6-(4-*methylphenyl*)-2-*oxo*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **7b** had m.p. 69–71 °C (from benzene–light petroleum); ν_{max}(neat)/cm^{-1} 1720 and 1700 (CO); δ_H($CDCl_3$) 1.07 (3 H, t, *J* 7.3, CO_2CH_2*Me*), 2.34 (3 H, s, Me), 3.05 (3 H, s, NMe), 3.13 (1 H, ddd, *J* 8.8, 8.5, and 5.3, 5-H), 3.36 (1 H, dd, *J* 12.0 and 5.3, 4-H), 3.69 (1 H, dd, *J* 12.0 and 8.8, 4-H), 4.04 (2 H, q, *J* 7.3, CO_2CH_2Me), 5.42 (1 H, d, *J* 8.5, 6-H), 7.16 (2 H, d, *J* 8.3, ArH) and 7.20 (2 H, d, *J* 8.3, ArH); *m/z* 277 (M^+) (Found: C, 65.0; H, 6.9; N, 5.05. $C_{15}H_{19}NO_4$ requires C, 64.96; H, 6.91; N, 5.05%).

Ethyl 6-(4-*methoxyphenyl*)-3-*methyl*-2-*oxo*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **7c** was an oil; ν_{max}(neat)/cm^{-1} 1720 and 1705 (CO); δ_H($CDCl_3$) 1.06 (3 H, t, *J* 7.3, CO_2CH_2-*Me*), 3.05 (3 H, s, NMe), 3.14 (1 H, ddd, *J* 10.0, 9.0 and 6.0, 5-H), 3.39 (1 H, dd, *J* 12.0 and 6.0, 4-H), 3.70 (1 H, dd, *J* 12.0 and 10.0, 4-H), 3.80 (3 H, s, OMe), 4.03 (2 H, q, *J* 7.3, CO_2CH_2Me), 5.36 (1 H, d, *J* 9.0, 6-H), 6.88 (2 H, d, *J* 8.5, ArH) and 7.26 (2 H, d, *J* 8.5, ArH) (Found: M^+, 293.1262. $C_{15}H_{19}NO_5$ requires M, 293.1264).

Ethyl 3-*methyl*-6-(3,4-*methylenedioxyphenyl*)-2-*oxo*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **7d** had m.p. 104–107 °C (from benzene–light petroleum; ν_{max}(Nujol)/cm^{-1} 1720 and 1705 (CO); δ_H($CDCl_3$) 1.10 (3 H, t, *J* 7.3, CO_2CH_2*Me*), 3.05 (3 H, s, NMe), 3.10 (1 H, ddd, *J* 9.8, 9.0, and 6.0, 5-H), 3.40 (1 H, dd, *J* 12.0 and 6.0, 4-H), 3.70 (1 H, dd, *J* 12.0 and 9.8, 4-H), 4.05 (2 H, q, *J* 7.3, CO_2CH_2Me), 5.32 (1 H, d, *J* 9.0, 6-H), 5.97 (2 H, s, OCH_2O), 6.77 (2 H, s, ArH) and 6.84 (1 H, s, ArH); *m/z* 307 (M^+) (Found: C, 58.6; H, 5.5; N, 4.6. $C_{15}H_{17}NO_6$ requires C, 58.63; H, 5.58; N, 4.56%).

Ethyl 6-(4-*chlorophenyl*)-3-*methyl*-2-*oxo*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **7e** was an oil; ν_{max}(neat)/cm^{-1} 1720 and 1700 (CO); δ_H($CDCl_3$) 1.08 (3 H, t, *J* 7.0, CO_2-CH_2*Me*), 3.06 (3 H, s, NMe), 3.12 (1 H, ddd, *J* 9.2 8.6, and 6.8, 5-H), 3.39 (1 H, dd, *J* 12.2 and 6.8, 4-H), 3.71 (1 H, dd, *J* 12.2 and 9.2, 4-H), 4.04 (2 H, q, *J* 7.0, CO_2CH_2Me), 5.41 (1 H, d, *J* 8.6, 6-H), 7.28 (2 H, d, *J* 8.5, ArH) and 7.36 (2 H, d, *J* 8.5, ArH) (Found: M^+, 297.0770. $C_{14}H_{16}ClNO_4$ requires M, 297.0769).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-(4-*chlorophenyl*)-3-(*methylsulphonyloxy*)*propionate* **8e** had m.p. 75–77 °C (from benzene–light petroleum); ν_{max}(Nujol)/cm^{-1} 1725 and 1695 (CO), and 1365 and 1170 (SO_2); δ_H($CDCl_3$) 1.03 (3 H, t, *J* 7.3, CO_2CH_2*Me*), 1.44 (9 H, s, Bu^t), 2.71 (3 H, s, NMe), 2.85 [3 H, s, $S(O)_2Me$], 3.34 (1 H, m, CHCO), 3.64 (1 H, dd, *J* 13.8 and 9.9, C*H*H_2), 3.80 (1 H, dd, *J* 13.8 and 4.4, CH*H*), 3.94 (2 H, q, *J* 7.3, CO_2CH_2Me), 5.62 (1 H, m, ArC*H*) and 7.37 (4 H, br s, ArH); *m/z* 449 (M^+) (Found: C, 50.6; H, 6.2; N, 3.0. $C_{19}H_{28}ClNO_7S$ requires C, 50.72; H, 6.27; N, 3.11%).

Ethyl 3-*methyl*-6-(4-*nitrophenyl*)-2-*oxo*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **7f** was an oil; ν_{max}(neat)/cm^{-1} 1730 and 1710 (CO); δ_H($CDCl_3$) 1.10 (3 H, t, *J* 7.0, CO_2-CH_2*Me*), 3.08 (3 H, s, NMe), 3.15 (1 H, ddd, *J* 9.4, 9.0, and 5.6, 5-H), 3.42 (1 H, dd, *J* 12.0 and 5.6, 4-H), 3.75 (1 H, dd, *J* 12.0 and 9.4, 4-H), 4.06 (2 H, q, *J* 7.0, CO_2CH_2Me), 5.55 (1 H, d, *J* 9.0, 6-H), 7.56 (2 H, d, *J* 8.6, ArH) and 8.25 (2 H, d, *J* 8.6, ArH) (Found: M^+, 308.1007. $C_{14}H_{16}N_2O_6$ requires M, 308.1009).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-(*methylsulphonyloxy*)-3-(4-*nitrophenyl*)*propionate* **8f** had m.p. 116–119 °C (from benzene–light petroleum); ν_{max}(Nujol)/cm^{-1} 1730 and 1690 (CO), 1575 and 1320 (NO_2), and 1365 and 1170 (SO_2); δ_H($CDCl_3$) 1.08 (3 H, t, *J* 7.4, CO_2CH_2*Me*), 1.43 (9 H, s, Bu^t), 2.84 and 2.90 (each 3 H, each s, $MeSO_2$ and NMe), 3.97 (2 H, q, *J* 7.4, CO_2CH_2Me), 5.80 (1 H, br s, $CHOSO_2$), 7.62 (2 H, d, *J* 7.8, ArH) and 8.25 (2 H, d, *J* 7.8, ArH); *m/z* 460 (M^+) (Found: C, 49.3; H, 6.0; N, 5.7. $C_{19}H_{28}N_2O_9S$ requires C, 49.56; H, 6.13; N, 6.08%).

Ethyl 3-*methyl*-2-*oxo*-6-*vinyl*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **17** was an oil; ν_{max}(neat)/cm^{-1} 1730 and 1700 (CO); δ_H($CDCl_3$) 1.28 (3 H, t, *J* 6.8, CO_2CH_2*Me*), 2.88 (1 H, td, *J* 7.0 and 5.2, 5-H), 3.0 (3 H, s, NMe), 3.41 (1 H, dd, *J* 12.0 and 5.2, 4-H), 3.63 (1 H, dd, *J* 12.0 and 7.0, 4-H), 4.20 (2 H, q, *J* 6.8, CO_2CH_2Me), 4.98 (1 H, dd, *J* 7.0 and 5.2, 6-H), 5.34 (1 H, dd, *J* 11.0 and 1.2, CH=C*H*^{c}H),* 5.43 (1 H, dd, *J* 17.0 and 1.2, CH=C*H*^{t}H) and 5.86 (1 H, ddd, *J* 17.0, 11.0, and 5.2, CH=) (Found: M^+, 213.100. $C_{10}H_{15}NO_4$ requires M, 213.1002).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-(*methylsulphonyloxy*)*pent*-4-*enoate* **18** was an oil; ν_{max}(neat)/cm^{-1} 1730 and 1690 (CO), and 1365 and 1170 (SO_2); δ_H($CDCl_3$) 1.20 (3 H, t, *J* 7.4, CO_2CH_2*Me*), 2.79 (3 H, s, NMe), 2.95 [3 H, s, $S(O)_2Me$], 3.0–3.65 (3 H, m, CHCO and NCH_2), 4.10 (2 H, q, *J* 7.4, CO_2CH_2Me), 5.16 (1 H, br s, $CHOSO_2$), 5.35 (1 H, d, *J* 11.0, CH=C*H*^{c}H), 5.42 (1 H, d, *J* 17.4, CH=C*H*^{t}H) and 5.90 (1 H, m, CH=); *m/z* 366 (M^+ + 1) [Found: (M^+ + 1), 366.1580. $C_{15}H_{20}NO_7S$ requires *m/z*, 366.1585].

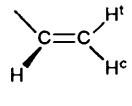
Ethyl 6-(1,1-*Dimethyl*-1H-*inden*-3-*yl*)-3-*methyl*-2-*oxo*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **20** was an oil; ν_{max}-(neat)/cm^{-1} 1720 and 1700 (CO); δ_H($CDCl_3$) 1.16 (3 H, t, *J* 7.0, CO_2CH_2*Me*), 1.31 (6 H, s, 2 × Me), 3.05 (3 H, s, NMe), 3.27 (1 H, td, *J* 6.0 and 5.5, 5-H), 3.39 (1 H, dd, *J* 11.0 and 5.5, 4-H), 3.68 (1 H, dd, *J* 11.0 and 6.0, 4-H), 4.13 (2 H, q, *J* 7.0, CO_2CH_2Me), 5.65 (1 H, br d, *J* 6.0, 6-H), 6.36 (1 H, d, *J* 1.0, CH=) and 7.20–7.36 (4 H, m, ArH) (Found: M^+, 329.1625. $C_{19}H_{23}NO_4$ requires M, 329.1628).

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*}-3-(1,1-*dimethyl*-1H-*inden*-3-*yl*)-3-(*methylsulphonyloxy*)*propionate* **21** was an oil, which was identical with an authentic sample by comparison of their IR and ^{1}H NMR spectra.[8]

Ethyl 2-{[(t-*butoxycarbonyl*(*methyl*)*amino*]*methyl*]-3-*cyclohexyl*-3-(*methylsulphonyloxy*)*propionate* **23** was an oil; ν_{max}-(neat)/cm^{-1} 1725 and 1680 (CO), and 1370 and 1170 (SO_2); δ_H($CDCl_3$) *inter alia* 1.27 (3 H, t, *J* 7.0, CO_2CH_2*Me*), 1.46 (9 H, s, Bu^t), 2.83, 2.84, 2.98, and 3.08 [total 6 H, each s, NMe and $S(O)_2Me$], 3.10–3.60 (3 H, m, CH_2CH), 4.13 and 4.15 (total 2 H, each q, *J* 7.0, CO_2CH_2Me), 4.67 and 4.75 (total 1 H, each m, $CHOSO_2$) (Found: M^+, 421.2130. $C_{19}H_{35}NO_7S$ requires M, 421.2132).

threo- *and* erythro-*Ethyl* 2-{[(t-*Butoxycarbonyl*(*methyl*)-*amino*]*methyl*}-3-*hydroxy*-2-*methylpent*-4-*enoates* **25** *and* **26**.—By a similar procedure to that (Method A) described for the preparation of compound **6a**, the crude product which was obtained from compound **24** (2.20 g, 9 mmol) and 90% acrylaldehyde (622 mg, 10 mmol) in the presence of LDA (10 mmol) was chromatographed to give compound **26** (1.04 g, 40%) from the first fraction and compound **25** (1.23 g, 47%) from the second fraction.

* Throughout this section, NMR data for the vinyl terminal hydrogens are given as follows:



Compound **25** was an oil; ν_{max}(neat)/cm^{-1} 3450 (OH), 1720 and 1680 (CO); δ_H($CDCl_3$) 1.18 (3 H, s, Me), 1.28 (3 H, t, *J* 7.4, CO_2CH_2*Me*), 1.45 (9 H, s, Bu^t), 2.86 (3 H, s, NMe), 3.39–3.84 (2 H, m, CH_2), 4.08 (1 H, br s, $CHOSO_2$), 4.18 (2 H, q, *J* 7.4, CO_2CH_2Me), 5.19 (1 H, m, CH=C*H*^{c}H), 5.31 (1 H, d, *J* 17.3, CH=C*H*^{t}H) and 5.88 (1 H, m, CH=) (Found: M$^+$, 301.1880. $C_{15}H_{27}NO_5$ requires M, 301.1890).

Compound **26** was an oil; ν_{max}(neat)/cm^{-1} 3420 (OH), 1720 and 1680 (CO); δ_H($CDCl_3$) 1.04 (3 H, s, Me), 1.29 (3 H, t, *J* 7.3, CO_2CH_2*Me*), 1.47 (9 H, s, Bu^t), 2.77 (3 H, s, NMe), 3.0 and 3.90 (each 1 H, each d, *J* 15.0, CH_2), 4.15 (2 H, q, *J* 7.3, CO_2CH_2Me), 4.49 (1 H, br s, OH), 4.97 (1 H, t, *J* 1.3, C*H*OH), 5.19 (1 H, d, *J* 11.0, CH=C*H*^{c}H), 5.41 (1 H, d, *J* 17.2, CH=C*H*^{t}H) and 5.84 (1 H, ddd, *J* 17.2. 11.0 and 1.3, CH=) (Found: M$^+$, 301.1882).

trans- *and* cis-t-*Butyl* N-[(2,2,5-*trimethyl*-4-*vinyl*-1,3-*dioxan*-5-*yl*)*methyl*]-N-*methylcarbamate* **27** *and* **28**.—By a similar procedure to that described for the preparation of compound **11**, the alcohol **25** (or **26**) (426 mg, 1.4 mmol) was reduced with $LiBH_4$–methanol. Work-up as described for the preparation of compound **9** gave the corresponding diol in 35–40% yield. The diol (100 mg, 0.4 mmol) was condensed with 2,2-dimethoxypropane (3.0 cm^3, 24 mmol) and TsOH (69 mg, 0.4 mmol). Work-up gave an oil, which was purified by column chromatography [benzene–EtOAc (8:1)] to give the dioxane **27** (93 mg, 77%) or **28** (95 mg, 80%).

Compound **27** was an oil; ν_{max}(neat)/cm^{-1} 1685 (CO); δ_H($CDCl_3$) 1.09 (3 H, s, 5-Me), 1.43 (3 H, s, 2-Me), 1.62 (12 H, s, Bu^t and 2-Me), 2.88 (3 H, s, NMe), 2.94–3.33 (2 H, m, CH_2-NBoc), 3.48 and 3.94 (each 1 H, each m, 6-H_2), 4.16 (1 H, br s, 4-H), 5.26 (1 H, d, *J* 8.5, CH=C*H*^{c}H), 5.32 (1 H, d, *J* 16.8, CH=C*H*^{t}H) and 5.80 (1 H, m, CH=); *m*/*z* 300 (M$^+$ + 1) [Found: M$^+$ + 1), 300.2173. $C_{16}H_{30}NO_4$ requires (M + 1), 300.2098].

Compound **28** was an oil; ν_{max}(neat)/cm^{-1} 1685 (CO); δ_H($CDCl_3$) 0.78 (3 H, s, 5-Me), 1.45 (9 H, s, Bu^t), 1.46 (6 H, s, 2 × Me), 3.24–3.48 (2 H, m, CH_2NBoc), 3.50 and 3.62 (each 1 H, each d, *J* 12.0, 6-H_2), 4.14 (1 H, d, *J* 5.8, 4-H), 5.25 (1 H, d, *J* 8.5, CH=C*H*^{c}H), 5.27 (1 H, d, *J* 16.8, CH=C*H*^{t}H) and 5.81 (1 H, m, CH=) (Found: M$^+$, 299.2094. $C_{16}H_{29}NO_4$ requires M, 299.2098).

trans-*Ethyl* 3,5-*Dimethyl*-2-*oxo*-6-*vinyl*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **29**.—By a similar procedure to that described for the reaction of compound **6a** with MsCl–Et_3N, the crude product which was obtained from the alcohol **25** (387 mg, 1.28 mmol), Et_3N (0.54 cm^3, 3.84 mmol) and MsCl (0.15 cm^3, 1.92 mmol) was purified by column chromatography [benzene–EtOAc (1:1)] to give the *title compound* **29** (251 mg, 86%) as an oil; ν_{max}(neat)/cm^{-1} 1720 and 1700 (CO); δ_H($CDCl_3$) 1.22 (3 H, s, 5-Me), 1.29 (3 H, t, *J* 7.3, CO_2CH_2*Me*), 3.0 (3 H, s, NMe), 3.08 (1 H, d, *J* 12.0, 4-H), 3.69 (1 H, dd, *J* 12.0 and 1.5, 4-H), 4.22 (2 H, q, *J* 7.3, CO_2CH_2Me), 5.02 (1 H, dq, *J* 6.0 and 1.5, 6-H), 5.40 (1 H, dt, *J* 10.5 and 1.5, CH=C*H*^{c}H), 5.45 (1 H, dt, *J* 17.1 and 1.5, CH=C*H*^{t}H) and 5.81 (1 H, ddd, *J* 17.1, 10.5 and 6.0, CH=); *m*/*z* 228 (M$^+$ + 1) [Found: (M$^+$ + 1), 228.1235. $C_{11}H_{18}NO_4$ requires *m*/*z*, 228.1234].

Ethyl 2-{[(t-*Butoxycarbonyl*(*methyl*)*amino*]*methyl*}-2-*methyl*-3-(*methylsulphonyloxy*)*pent*-4-*enoate* **30**.—By a similar procedure to that described for the preparation of compound **7** with MsCl–Et_3N, the crude product which was obtained from compound **26** (387 mg, 1.28 mmol), Et_3N (0.54 cm^3, 3.84 (mmol), and MsCl (0.15 cm^3, 1.92 mmol) was purified by column chromatography to give the *mesate* **30** (418 mg, 79%) as an oil; ν_{max}(neat)/cm^{-1} 1730 and 1690 (CO), and 1365 and 1170 (SO_2); δ_H($CDCl_3$) 1.29 (3 H, t, *J* 7.4, CO_2CH_2Me), 1.27 (9 H, s, Bu^t), 1.39 (3 H, s, Me), 2.81 (3 H, s, Me), 2.95–3.25 (2 H, m, CH_2NBoc), 3.0 [3 H, s, $S(O)_2$Me], 4.20 (2 H, q, *J* 7.4, CO_2CH_2Me), 4.66 (1 H, m, $CHOSO_2$), 5.12 (1 H, d, *J* CH=C*H*^{c}H), 5.35 (1 H, d, *J* 16.8, CH=C*H*^{t}H) and 5.84 (1 H, m, CH=) (Found: M$^+$, 379.1661. $C_{16}H_{29}NO_7S$ requires M, 379.1663).

cis-*Ethyl* 3,5-*Dimethyl*-2-*oxo*-6-*vinyl*-3,4,5,6-*tetrahydro*-2H-1,3-*oxazine*-5-*carboxylate* **31**.—After the mesate **30** (418 mg, 1.1 mmol) was stored for 3 days, the oily material was purified by column chromatography [benzene–EtOAc (1:1)] to give the *title compound* **31** (186 mg, 82%) as an oil; ν_{max}(neat)/cm^{-1} 1730 and 1710 (CO); δ_H($CDCl_3$) 1.28 (3 H, t, *J* 7.3, CO_2CH_2*Me*), 1.39 (3 H, s, 5-Me), 3.0 (3 H, s, NMe), 3.06 (1 H, d, *J* 12.0, 4-H), 3.62 (1 H, d, *J* 12.0, 4-H), 4.20 (2 H, q, *J* 7.3, CO_2CH_2Me), 4.66 (1 H, dt, *J* 6.0 and 1.4, 6-H), 5.36 (1 H, dd, *J* 10.5 and 1.4, CH=C*H*^{c}H), 5.39 (1 H, dd, *J* 17.0 and 1.4, CH=C*H*^{t}H) and 5.85 (1 H, ddd, *J* 17.0, 10.5 and 6.0, CH=) (Found: M$^+$, 227.1168. $C_{11}H_{17}NO_4$ requires M, 227.1158).

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