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X=Y-ZH Compounds as Potential 1,3-Dipoles. Part 43.[1] Metal Ion Catalysed Asymmetric 1,3-Dipolar Cycloaddition Reactions of Imines and Menthyl Acrylate.

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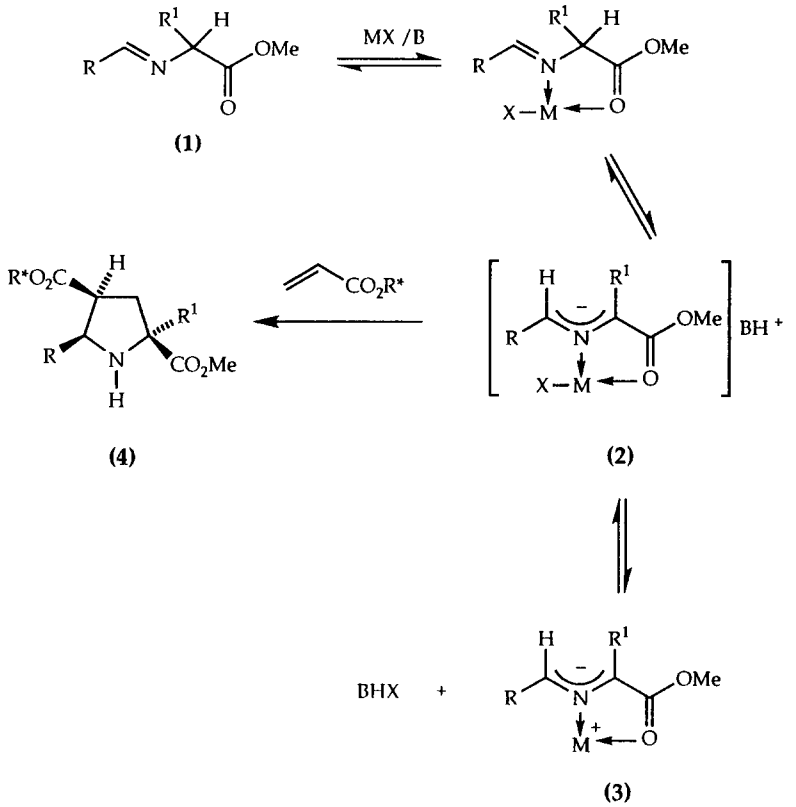
Abstract. *Metallo-azomethine ylides, generated from imines by the action of amine bases in combination with LiBr or AgOAc, undergo cycloaddition with both 1R, 2S, 5R- and 1S, 2R, 5S-menthyl acrylate at room temperature to give homochiral pyrrolidines in excellent yield. The stronger the base the faster the cycloaddition and the greater the yield with: 2-t-butyl-1,1,3,3-tetramethylguanidine > DBU > NEt_3. X-Ray crystal structures of representative cycloadducts establish that the absolute configuration of the newly established pyrrolidine stereocentres is independent of the metal salt and the size of the pyrrolidineC(2)-substituent for a series of aryl and aliphatic imines.*

1,3-Dipolar cycloaddition reactions constitute a core reaction resource in heterocyclic chemistry. The catholic nature of the reaction has led to strong and continuing interest in all aspects of these cycloadditions. A relatively recent development has been efforts to achieve asymmetric 1,3-dipolar cycloaddition reactions. There are three approaches to this problem involving (i) chiral 1,3-dipoles (ii) chiral dipolarophiles and (iii) chiral catalysts. In the case of azomethine ylides there have been numerous reports of high diastereoselectivity using both acyclic and cyclic chiral dipoles.[2] Our own work involving metal ion catalysed regio- and stereo-specific cycloaddition of imines to electronegative olefins at ambient temperature[3] offered an excellent opportunity to evaluate approaches to (ii) and (iii). These metal ion catalysed processes involve intermediate metallo-azomethine ylides. Preliminary publications of our successful achievements in forming homochiral cycloadducts using either a chiral dipolarophile[4,5] or a chiral metal catalyst [Co(II), Mn(II)][6] have appeared. This paper reports full details of our work on cycloaddition reactions of metallo-azomethine ylides with chiral acrylate esters as dipolarophiles. Others have subsequently reported examples of chiral cyclic dipolarophiles[7] and chiral acyclic dipolarophiles[8] in cycloaddition reactions with azomethine ylides whilst we have reported the combination of chiral 1,3-dipolar cycloaddition reactions with palladium catalysed cycloacylpalladation reactions.[9]

Chiral acrylate esters and amides have been widely evaluated in studies of asymmetric Diels-Alder reactions. Menthyl acrylate, even in the presence of Lewis acids and at low temperature, gives only moderate induction (< 62% de) with cyclopentadiene.[10] Substantial improvements in chiral induction were obtained using 8-phenylmenthyl acrylate,[10] or acrylamides incorporating Evans oxazolodinone[11] or Oppolzers sultam[12] chiral auxiliaries. These are but representative examples of a diverse array of acrylate dienophiles all of which rely on coordination (preferably chelation) to Lewis acids to impart the necessary rigidity to the dienophile to ensure high diastereofacial selectivity in the cycloaddition transition state. A further complication in the Diels-Alder

reaction is that the reactions are frequently endo-selective rather than endo-specific. In contrast, our metallo-azomethine ylide cycloadditions exhibit stereospecific formation of the syn- or E, E-dipole [(2) and/or (3), Scheme 1], proceed both regio- and stereo-specifically and are endo-specific.

Menthyl acrylate was selected for evaluation in metallo-azomethine ylide cycloadditions because of the ready availability and low cost of both 1R, 2S, 5R- and 1S, 2R, 5S- menthol. Preliminary studies of cycloadditions of menthyl acrylates with imines using silver acetate-triethylamine as the catalyst system in acetonitrile at room temperature were very encouraging in that single homochiral diastereomers were obtained in each case, as judged by careful examination of the p.m.r. spectra of the reaction mixtures. Thus (1, R=2-naphthyl R^1=H) and (1, R=Ph, R^1=Me) reacted with 1R, 2S, 5R- menthyl acrylate to give (4, R=2-naphthyl, R^1=H) and (4, R=Ph, R^1=Me) in 36 and 33% yield respectively (Scheme 1). [Note that (4) depicts the absolute stereochemistry of cycloadducts derived from 1R, 2S, 5R-menthyl acrylate].

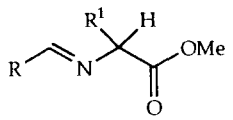


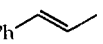
Scheme 1

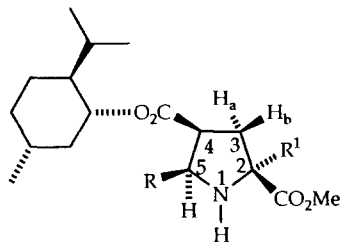
Replacing methyl acrylate by menthyl acrylate led to noticeably slower reactions with arylidene imines of α-amino esters (1-2h for methyl acrylate versus 14-24h for menthyl acrylate) and the slower reactions were associated with significantly lower yields (typically 33-55% for AgOAc catalysed reactions involving menthyl acrylate). It was felt that the slower rate of cycloaddition was responsible for the reduced yields of cycloadducts due to the imine undergoing a slow Lewis acid catalysed hydrolysis by adventitious water. Blank experiments confirmed the slow degradation of imine in the absence of dipolarophile. Previous work had shown that Ag(I) catalysed cycloadditions of imines occur substantially faster in DMSO compared to acetonitrile.[3] Similar rate

enhancements were observed with menthyl acrylate e.g.(1, R=2-naphthyl, R^1=H) undergoes conversion to (4, R=2-naphthyl, R^1=H) in 1h in DMSO using $AgOAc/NEt_3$ as the catalyst system. However (4, R=2-naphthyl, R^1=H) is accompanied by a minor cycloadduct in this case. Although glycine imines are known to be usually sensitive to isomer formation (and hence atypical) it was decided to explore other approaches to increasing the rate of cycloaddition that would function equally well with glycine imines.

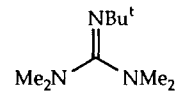
The pka of uncoordinated arylidene imines of α-amino esters is ca. 17.0-19.5[13] and hence use of a stronger base in combination with the metal salt (Scheme 1) would be expected to increase the rate of the cycloaddition reaction, assuming dipole formation is rate determining. Kanemasa et al.[14] had previously shown that DBU accelerated the rate of LiBr catalysed cycloaddition to olefinic dipolarophiles in THF and others subsequently confirmed this.[8,15] We had shown that DBU was also effective with silver salts in toluene as solvent.[15] In our studies in acetonitrile we observe that changing the base from Et_3N to DBU produces a marked rate enhancement and a substantial increase in yield without formation of additional diastereomers. A further noticeable rate enhancement and modest increase in yield was noted when DBU was replaced by 2-t-butyl-1,1,3,3-tetramethylguanidine (5). The trends are illustrated by the reaction times and yields collected in Table 1.



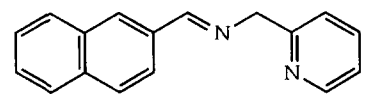
(1) a. R = 2-naphthyl, R^1 = H
b. R = Ph, R^1 = H
c. R = 2-naphthyl, R^1 = Me
d. R = Ph, R^1 = Me
e. R = cyclohexyl, R^1 = Me
f. R = 3-pyridyl, R^1 = CH_2Ph
g. R = 2-naphthyl, R^1 = Ph
h. R = R^1 = Ph
i. R = *p*-$MeOC_6H_4$, R^1 = Ph
j. R = Ph  , R^1 = Ph
k. R = 3-pyridyl, R^1 = Ph
l. R = 3-pyridyl, R^1 = Me



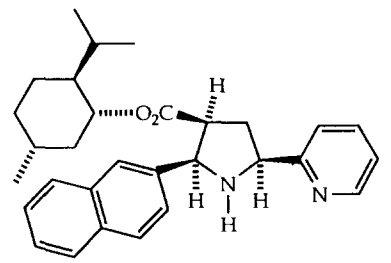
(4)



(5)



(6)



(7)

Table 1. Metal salt/base catalysed cycloaddition reactions of imines (1a-k) and (6) with 1R, 2S, 5R-menthyl acrylate in acetonitrile at 25 °C.

Imine	Metal salt	Base	Time(h)	Product	Yield(%)
1a	AgOAc	NEt_3	8	4a	36
1a	AgOAc	DBU	2	4a	74
1a	AgOAc	5	1	4a	75
1b	AgOAc	NEt_3	26	4b	49
1b	AgOAc	DBU	4	4b	69
1b	AgOAc	5	0.6	4b	72
1c	AgOAc	NEt_3	14	4c	43
1c	AgOAc	DBU	3	4c	72
1c	AgOAc	5	1	4c	75
1d	AgOAc	NEt_3	48	4d	33
1d	AgOAc	DBU	8	4d	63
1d	AgOAc	5	2.5	4d	71
1e	AgOAc	NEt_3	48	4e	0[a]
1e	AgOAc	5	2.5	4e	83[a]
1f	AgOAc	NEt_3	24	4f	51
1f	AgOAc	DBU	6	4f	76
1f	AgOAc	5	0.5	4f	78
1g	LiBr	NEt_3	12	4g	52
1g	LiBr	DBU	3	4g	86
1h	LiBr	NEt_3	9	4h	60
1h	LiBr	DBU	3	4h	84
1h	LiBr	5	1.5	4h	84
1i	LiBr	NEt_3	12	4i	57
1i	LiBr	DBU	3	4i	71
1j	LiBr	NEt_3	14	4j	50
1j	LiBr	DBU	3	4j	64
1j	LiBr	5	1	4j	68
1k	LiBr	NEt_3	11	4k	56
6	LiBr	NEt_3	3	7	83

a. Reaction carried out in toluene as solvent.

The relative stereochemistries of the cycloadducts (4a-k) was established by n.O.e. studies (see experimental section) whilst the absolute stereochemistry was established by single crystal X-ray structures of three representative cycloadducts: (4a) (figure 1), (4f) (figure 2) and (7) (figure 3). These structures encompass a small C(2)-substituent (R^1=H, 4a), a large C(2)-substituent (R^1=CH_2Ph, 4f) and replacement of the C(2)-ester moiety by the 2-pyridyl group (7). In all cases the absolute stereochemistry at C(2), C(4) and C(5) of the pyrrolidine was the same. Most of the cycloadducts in our work were prepared from 1R, 2S, 5R- menthyl acrylate but several adducts of 1S, 2R, 5S-menthyl acrylate were also prepared (see below and experimental section).

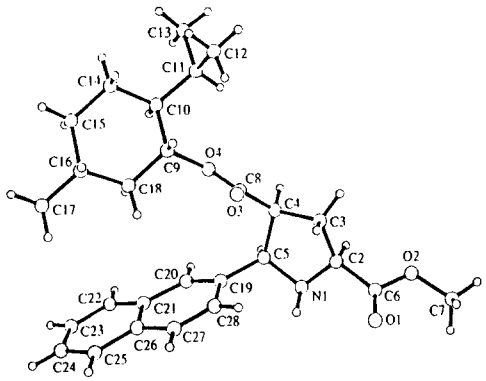


Figure 1. The molecular structure of compound 4a.

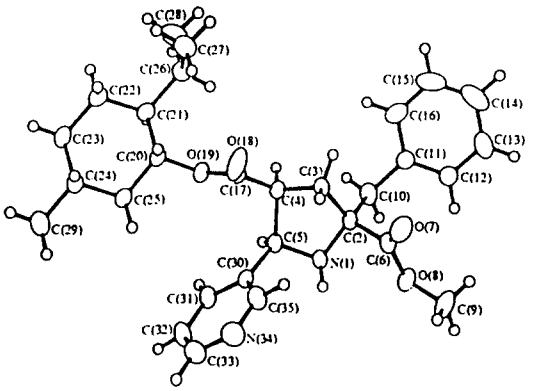


Figure 2. The molecular structure of compound 4f. Ellipses are shown at the 50% probability level with hydrogen atoms drawn with an arbitrary small radius.

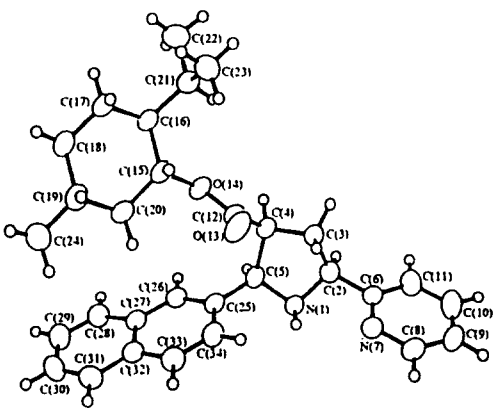
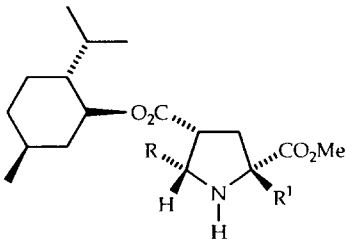
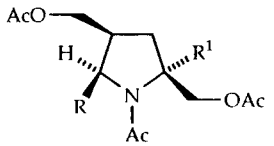


Figure 3. The molecular structure of compound 7. Probability levels are the same as for Figure 2.

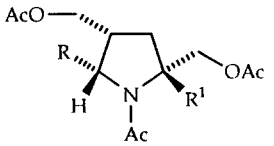
The homochiral integrity of the cycloadducts was established by several methods. Initial ^{13}C and ^{1}H n.m.r. examination of the crude reactions mixtures indicated the presence of a single diestereomer and this was further supported by $LiAlH_4$ reduction and acetylation of two pairs of enantiomers (4a)/(8a) and (4d)/(8b). The ^{1}H n.m.r. spectra of the enantiomeric triacetates (9a)/(10a) and (9b)/(10b) were then compared with those of the racemic triacetates prepared from racemic cycloadducts (11a,b) via the racemic diols. In each case the spectra were determined in the presence of a mixture of the (+)-Pirkle reagent (12) and $Eu(hfc)_3$ which resolved the signals of the acetyl methyl groups in the racemic samples and confirmed the homochiral integrity of the acetates derived from (4a)/(8a) and (4d)/(8b).



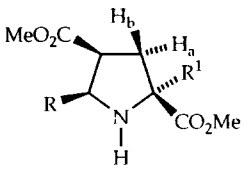
(8) a. R = 2-naphthyl, R^1 = H
b. R = Ph, R^1 = Me



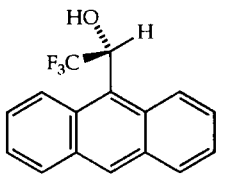
(9) a. R = 2-naphthyl, R^1 = H
b. R = Ph, R^1 = Me



(10) a. R = 2-naphthyl, R^1 = H
b. R = Ph, R^1 = Me



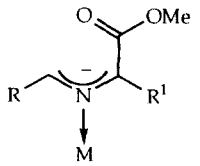
(11) a. R = 2-naphthyl, R^1 = H
b. R = Ph, R^1 = Me
c. R = 3-pyridyl, R^1 = Ph
d. R = 3-pyridyl, R^1 = Me



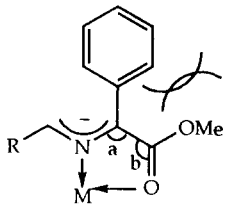
(12)

In the later stages of these studies chiral HPLC became available and this provided further support for the homochiral integrity of the menthyl acrylate cycloadducts. Good separation was achieved on a Chiralcel OD column eluting with 15% isopropanol in hexane.

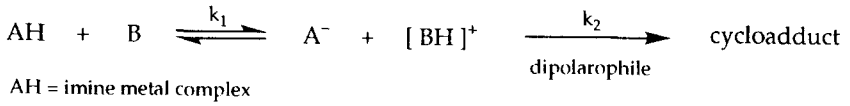
Mechanism. The results collected in Table 1 indicated that both aryl, heteroaryl and aliphatic (1e) aldimines are good substrates for the chiral cycloaddition. In the latter case it is necessary to employ toluene as the reaction solvent since use of acetonitrile results in formation of an additional (minor) cycloadduct arising from the E, Z- or anti-metallo dipole (13).[15] The formation of a homochiral cycloadduct from imine (6) demonstrates that other electron withdrawing substituents can replace the ester moiety. We have previously shown that a range of such substituents furnish racemic cycloadducts in excellent yield.[19]



(13)



(14) a. M = Ag(I)
b. M = Li(I)



Scheme 2

The results collected in Table 1 accord with Scheme 2 in which k_2 is rate limiting. The concentration of the dipole obviously depends on the base strength [NEt_3, pka 10.8; DBU, pka 12; guanidine (5), pka 14.3][16] whilst the sensitivity of the rate to the structure of the dipolarophile (methyl acrylate substantially faster than menthyl acrylate) also accords with cycloaddition (k_2) as the rate limiting step. Comparing Scheme 1 and 2 it becomes apparent that the reactive metallodipole could be either (2) or (3) (Scheme 1). At present we have no definitive evidence on this point although use of chiral tertiary amine bases cinchonidine and sparteine, in combination with silver acetate, for the cycloaddition of imines (1) and methyl acetate results in cycloadducts exhibiting low enantiomeric excess (13 - 18%)[17].

Although silver salts are, in general, much more efficient and selective catalysts than lithium salts[3] there are some cases where lithium salts are the catalysts of choice. Thus bulky substituents on the imine sp^3 centre [R^1 in (1)] impede metallodipole formation from silver salt catalysts. Conversely such bulky substituents impede Michael addition of the corresponding lithio metallodipole to the dipolarophile. This latter process often severely limits the usefulness of lithium salt catalysts. Thus LiBr is the catalyst of choice for cycloaddition of (1g - k) to menthyl acrylate (Table 1). This switch in effectiveness of the metal salt catalysts is ascribed to steric factors arising in formation of the metal coordinated azomethine ylides. The silver cation (ionic radius 1.26 Å) is considerably larger than the lithium cation (ionic radius 0.68Å) and when chelated (14a) causes the angles a and b to increase resulting in increased steric compression between the phenyl and methoxy moieties which is relieved by twisting of the phenyl group out of plane of the azomethine ylide. This would both disrupt conjugation [effect on the pka of chelated imine (Scheme 1)] and sterically hinder the cycloaddition. The much smaller lithium cation allows the steric compression between the phenyl and methoxy moieties in (14b) to be accommodated by a decrease in the angles a and b. A wide range of other metal ions [e.g. Tl(I), Zn(II), Mg(II), Co(II), Mn(II), Ti(IV)][3] catalyse imine cycloadditions but, apart from Ti(IV)[4], have not yet been evaluated with menthyl acrylate as dipolarophile. Titanium (IV) catalysts are particularly valuable in that they reverse the regiochemistry of the cycloaddition whilst retaining the stereospecificity.[18] Homochiral cycloadducts have been obtained with Ti(IV) catalysts[4] and will be reported in detail in a subsequent publication.

The successful cycloaddition (6) → (7) indicated that the ester moiety on the imine can be replaced by another electronegative group[19] with no diminution in the % de.

Cycloaddition Transition States. In Lewis acid catalysed Diels-Alder reactions it is the dienophile (2π-component) that is coordinated to the catalyst whilst in metallodipole cycloaddition reactions the azomethine ylide (4π-component) is coordinated to the catalyst. Studies of the s-cis/s-trans conformational equilibrium in non-chelating Lewis acid complexed, acrylate esters have shown that various Lewis acids predominately coordinate to the carbonyl oxygen in an anti-orientation to the OR group.[20] This coordination effectively suppresses the s-cis conformation (15b) and the Lewis acid catalysed reactions proceed via the s-trans conformer (15a).[21] Additionally Oppolzer has concluded, based on X-ray data[22] and other considerations, that for acrylate esters of secondary alcohols the conformer with a syn-periphaner relationship between H_A/C=O (15a) is favoured.

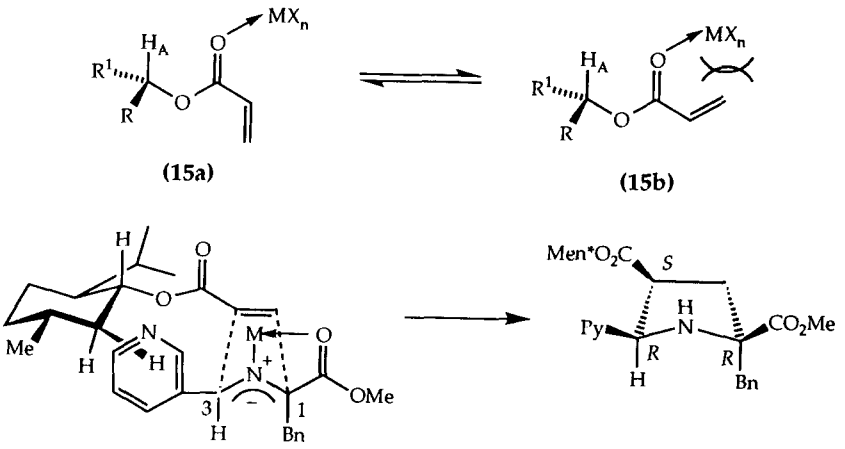
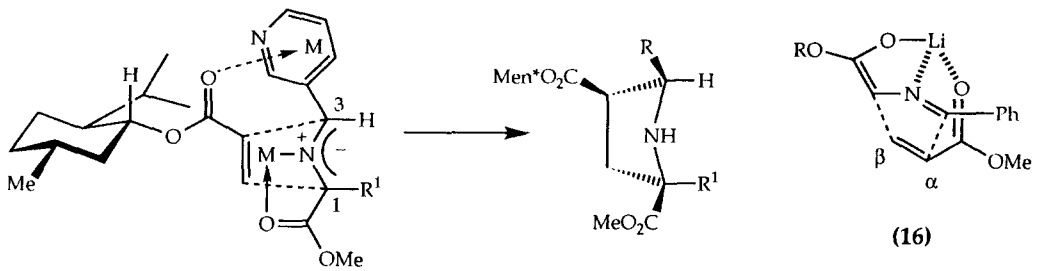


Figure 4

The regio- and endo-specificity of the cycloaddition together with the established absolute configuration of the cycloadducts and the facial shielding effect of the menthyl isopropyl moiety are accommodated in the transition state shown in figure 4 for formation of (4f). This involves addition of the 1-si, 3-re-face of the dipole to the re-face of the s-cis acrylate. The menthyl isopropyl group effectively shields the si-face in the s-cis acrylate. In this transition state the C(6) equational hydrogen atom of the menthyl moiety infringes slightly on the π-cloud of any C(3)-aryl substituent on the dipole.

Addition of the metallodipole to the s-trans acrylate (15a) (or the non-Lewis acid coordinated species) would require attack of the 1-re, 3-si face of the E,E- dipole on the acrylate si-face due to steric blockade of the re-face by the menthyl isopropyl group. This transition state (figure 5) would lead to the opposite enantiomer to that observed i.e. would produce the 2S, 4R, 5S- cycloadduct.



(16)

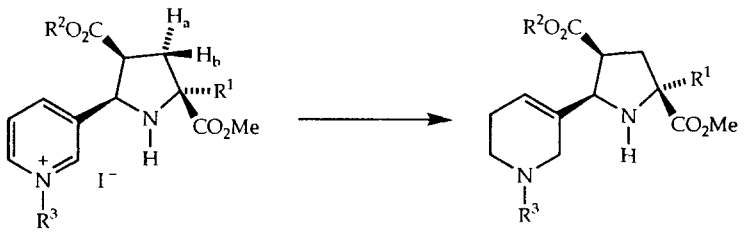
Figure 5

The results in Table 1 and figures 1-3 show that both Ag(I) and Li(I) catalysed reactions give rise to cycloadducts with the same absolute stereochemistry even though these metal ions have different coordination numbers/geometry and donor atom preferences and substantially different ionic radii (vide infra). Moreover, particularly with lithium salts, polymeric species[23] may be involved so that transition state representations such as (16) (below) must be treated with due caution. Furthermore substantial amounts of silver acetate remain undissolved in acetonitrile whilst lithium bromide is completely soluble. Several authors have reported results of LiBr catalysed cycloadditions with non-chiral acrylates and enones in which both dipole and dipolarophile are considered to be coordinated to the same Li(I) cation and which are postulated to involve the Li(I)-complexed s-cis dipolarophile (e.g. 16).[24]

A number of conceptional problems arise with such transition states: (i) for dipolarophiles lacking β-substituents [cf (16)] coordination to a metal ion via a carbonyl oxygen lone pair should result in steric exclusion of the s-cis conformed (15b) (ii) the carbonyl oxygen lone pair electrons in the dipolarophile have the wrong geometry for coordination to the Li(I) ion in the manner depicted in (16). However, coordination of Li(I) to carbonyl groups may have substantial ion-dipole character which effectively relaxes geometrical constraints [23,26] (iii) the transition state for the cycloaddition is expected, by analogy with the Diels-Alder reaction, to be asynchronous and to have an "open-jaw" geometry[25] in which the four centres involved in bond formation comprise the narrow end of the "open-jaw". In this situation the dipolarophile carbonyl group is at too great a distance from the Li(I) ion to be coordinated unless it rotates out of the plane of the dipolarophile π-bond thereby deactivating the dipolarophile. Thus the postulated transition states for metalloazomethine ylide cycloadditions reactions offer an expedient interpretation rather than an accurate one.

The stereospecificity observed in the metallo-azomethine ylide-menthyl acrylate cycloaddition reactions contrasts with the moderate diastereomeric excesses observed for the Diels-Alder reactions of Lewis acid complexed menthyl acrylate. This is believed to be due to the accentuated steric interactions in the 5- versus 6-membered transition states.

Further Reactions of the 5-(3′-Pyridyl)pyrrolidines. The chiral 5-(3′-pyridyl)pyrrolidines (4f), (4k) together with the racemic pyrrolidines (11c) and (11d) were converted to the pyridinium salts (17a-c) and (17d) in good yield by heating with n-propyl iodide or methyl iodide respectively in boiling acetonitrile. The salts (17a-d) were then reduced with sodium borohydride in methanol at -10 °C to afford the 5-(1′,2′,5′,6′-tetrahydropyridyl)pyrrolidines (18a-d) which were of interest as potential antipsychotic compounds.[27]



(17) (18)

a. $R^1 = CH_2Ph$, R^2 = 1*R*, 2*S*, 5*R* – menthyl, $R^3 = n\text{-}C_3H_7$

b. $R^1 = Ph$, R^2 = 1*R*, 2*S*, 5*R* – menthyl, $R^3 = n\text{-}C_3H_7$

c. $R^1 = Ph$, $R^2 = Me$, $R^3 = n\text{-}C_3H_7$

d. $R^1 = R^2 = R^3 = Me$

The menthyl series of compounds (17a,b)/(18a,b) proved resistant to crystallisation and were obtained as gums whilst the racemic dimethyl esters (17c,d)/(18c,d) were obtained as low melting solids.

Experimental. General experimental details were as previously described.[28] The aldimines, most of which are all known compounds[3], were prepared by the general method noted below. Optical rotations were determined on an Optical Activity Ltd., AA1000 polarimeter, and chiral h.p.l.c. was performed on a Chiralcel OD column (Daicel) eluting with 15% isopropanol in hexane and a flow rate of 1ml/min.

General Procedure for Aldimines. A mixture of the methyl ester of the appropriate amino acid as its hydrochloride salt, triethylamine (1eq) and anhydrous magnesium sulphate (excess) was stirred in dry dichloromethane for 1h before the addition of the aldehyde (1eq). The suspension was stirred at room temperature for a further 11h, filtered, the filtrate washed with brine (2x), dried (magnesium sulphate) and the solvent evaporated under vacuum. The residual gum was triturated with ether and the resulting solid crystallised from an appropriate solvent.

Methyl N-(3-pyridylidene)phenylglycinate(1k). The **product** (80%) crystallised from ether-petroleum ether as colourless prisms, m.p. 70-71 °C (Found: C, 70.55; H, 5.65; N, 10.95. $C_{15}H_{14}N_2O_2$ requires C, 70.85; H, 5.55; N, 11.0%); m/z (%) 255 (M+1, 2), 196(21), 195(100), 168(11), 167(10), 91(7) and 59(23); δ 8.89 and 8.68 (2xdd, 2x1H, pyridine-H), 8.34 (s, 1H, CH=N), 8.34 (tt, 1H, pyridine-H), 7.50-7.26 (m, 6H, pyridine-H and ArH), 5.23 (s, 1H, CHN) and 3.75 (s, 3H, OMe).

Methyl N-(3-pyridylidene)alaninate(1j). The **product** (60%) was obtained as a colourless oil, b.p. 98-100 °C/0.1mmHg (Found: C, 62.6; H, 6.35; N, 14.4. $C_{10}H_{12}N_2O_2$ requires C, 62.5; H, 6.3; N, 14.6%); m/z(%) 192(M^+,1) 133(100), 177(11), 134(8), 106(14), 105(6) and 88(5); δ 8.89 (dd, 1H, pyridine-H), 8.60 (s, 1H, pyridine-H), 8.51 (dd, 1H, pyridine-H), 8.41 (s, 1H, CH=N), 7.3(dd, 1H, pyridine-H), 4.2(q, 1H, C<u>H</u>Me), 3.71(s, 3H, OMe), and 1.45 (d, 3H, Me).

General Procedure for Cycloaddition Reactions. A mixture of the imine (1eq), base [triethylamine DBU or (5)] (1eq), menthyl acrylate (2eq) and metal salt (AgOAc or LiBr) (1.5eq) in acetonitrile or toluene was stirred at room temperature for the time shown in Table 1. The reaction was quenched by the addition of saturated aqueous ammonium chloride, and extracted with ether (2x). The combined ether extracts were washed with brine (2x), dried ($MgSO_4$), filtered and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography (silica) eluting with ether-petroleum ether. Yields are collected in Table 1.

1'R, 2'S, 5'R-Menthyl r-2R-methoxycarbonyl-c-5R-(2'-naphthyl)pyrrolidine-c-4S-carboxylate(4a). The **product** crystallised from ether-petroleum ether as colourless needles, m.p. 124-126 °C (Found: C, 74.25; H, 8.2; N, 3.1. $C_{27}H_{35}NO_4$ requires C, 74.1; H, 8.05; N, 3.2%); $\alpha]_D$ 31.6 ° (c. 0.05g/ml, $CHCl_3$); ν_{max} (KBr) 2953, 1736, 1697, 1204, and 1168cm^{-1} m/z(%) 437(M^+, 59), 378(32), 298(42), 240(38), 227(100), and 167(71); δ 7.81-7.76 (m, 4H, ArH), 7.47-7.42(m, 3H, ArH), 4.66(d, 1H, J 7.5Hz, 5-H), 4.24(m, 1H, OCH), 4.04(t, 1H, J 8.2Hz, 2-H), 3.85(s, 3H, OMe), 3.41(m, 1H, 4-H), 2.53-2.43 (m, 2H, 3-Ha and 3-Hb), 1.47-1.39 (m, 3H, menthyl-H), 1.03 and 0.69 (2xm, 2xH, menthyl-H), 0.68(d, 3H, J 7.0Hz, CH<u>M</u>e_2), 0.52(m, 1H, menthyl-H), 0.42 (d, 3H, J 6.9Hz, CH<u>M</u>e_2), 0.28 (d, 3H, J 6.5Hz, Me), and -0.11 (q, 1H, menthyl-H); n.O.e. (%): irradiation of 2-H effected enhancement of 5-H(8); irradiation of 4-H effected enhancement of 3-Ha(5) and 5-(13). The **enantiomer** prepared from 1S, 2R, 5S-menthyl acrylate had m.p. 123-125 °C. $\alpha]_D$+30.8 ° (c.0.004g/ml,

$CHCl_3$).

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-c-5R-phenylpyrolidine-c-4S-carboxylate(4b). The **product** crystallised from ether as colourless needles, m.p. 110 °C (>99% de, HPLC) (Found: C, 70.9; H, 8.55; N, 3.4. $C_{23}H_{33}NO_4$ requires C, 71.2; H, 8.6; N, 3.6%); $\alpha]_D$-10.4 ° (c.1.0g/100ml, CH_2Cl_2); m/z(%) 387(M^+, 15), 328(64), 248(52), 190(95), 177(100), 144(57) and 117(75); δ 7.38 - 7.22 (m, 5H, phenyl-H), 4.51(d, 1H, J 7.4Hz, 5-H), 4.40 - 4.31(m, 1H, OCH), 3.99(t, 1H, J 8.2Hz, 2-H), 3.83(s, 3H, OMe), 3.35(m, 1H, 4-H), 2.52(m, 1H, 3-Ha), 2.47(m, 1H, 3-Hb), 1.57 and 1.27(2xm, 2x3H, menthyl-H), 0.90(m, 2H, menthyl-H), 0.79 and 0.74(2xd, 2x3H, J 6.5Hz, $CH\underline{Me}_2$), 0.57(d, 3H, J 6.8Hz, Me) and 0.28(q, 1H, menthyl-H); n.O.e.(%): irradiation of 2-H effected enhancement of 3-Ha(5) and 4-H(1); irradiation of 4-H effected enhancement of 3-Ha(4) and 5-H(4).

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-2-methyl-c-5R-(2′-naphthyl)pyrrolidine-c-4S-carboxylate(4c). The **product** crystallised as colourless needles from ether-petroleum ether; m.p. 96-98 °C (>99%) d.e., HPLC) (Found C, 74.4; H, 8.4; N, 3.05. $C_{28}H_{37}NO_4$ requires C, 74.45; H, 8.25; N, 3.1%); $\alpha]_D$ -16.6 °(c.2.8g/100ml, $CHCl_3$); m/z (%) 451(M^+,22), 392(90) 312(27), 241(77) and 181(73); δ 7.81 - 7.31(m, 7H, ArH), 4.72(d, 1H, J 7.0Hz, 5-H), 4.20(m, 1H, OCH), 3.78 (s, 3H, OMe), 3.41(m, 1H, 4-H), 2.72(dd, 1H, J 4.4 and 13.7Hz, 3-Hb), 2.02(dd, 1H, J7.7 and 13.6Hz, 3-Ha), 1.52(s, 3H, Me), 1.42(m, 3H, menthyl-H), 1.32(m, 2H, menthyl-H), 1.01(m, 3H, menthyl-H) 0.82 and 0.62(2xd, 2x3H, J 6.4Hz, $CH\underline{Me}_2$), 0.41(d, 3H, J 6.4 Hz, Me) and -0.10(q, 1H, menthyl-H).

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-2-methyl-c-5R-phenylpyrrolidine-c-4S-carboxylate(4d). The **product** crystallised as colourless needles, m.p. 68-70 °C, from petroleum ether at -10 °C (Found: C, 71.55; H, 8.75; H, 8.75; N, 3.4. $C_{24}H_{35}NO_4$ requires C, 71.8; H, 8.8; N, 3.5%); $\alpha]_D$-16.9 °C(c. 0.61g/100ml, $CHCl_3$) ν_{max} (KBr) 3457, 2945, 1743, 1713, and 1386 cm^{-1}; m/z (%) 401 (M^+,3), 342(100), 262(4), 204(36), and 191(47); δ 7.34-7.21(m, 5H, ArH), 4.62(d, 1H, J 7.3Hz, 5-H), 4.33(m, 1H, OCH), 3.81(s, 3H, OMe), 3.37(m, 1H, 4-H), 2.68(dd, 1H, J 5.0 and 13.6Hz, 3-Hb), 2.10(dd, 1H, J 7.6 and 13.5Hz, 3-Ha), 1.55(m, 3H, menthyl-H), 1.51(s, 3H, 2-Me), 1.16-1.03(m, 3H, menthyl-H), 0.88(m, 1H, menthyl-H), 0.79(d, 3H, J 7.0Hz, $CH\underline{Me}_2$) 0.74(m, 1H, menthyl-H), 0.71(d, 3H, J 6.6Hz, Me), 0.55(d, 3H, J 6.9Hz, $CH\underline{Me}_2$), and 0.18(m, 1H, menthyl-H). The **enantiomer** prepared from 1S, 2R, 5S-menthol had m.p. 68-70 °C, $\alpha]_D$ + 15.8 ° (c. 0.73g/100ml, $CHCl_3$).

1′R,2′S,5′R-Menthyl r-2R-methoxycarbonyl-2-methyl-c-5R-cyclohexylpyrrolidine-c-4S-carboxylate(4e). Work up followed by column chromatography eluting with 1:1 v/v ether-petroleum ether gave the **product** as a colourless viscous gum (> 99% de, HPLC). (Found: C, 71.1; H, 9.8; N, 3.4. $C_{24}H_{41}NO_4$ requires C, 70.9; H, 9.9; N, 3.45%); $\alpha]_D$-17.4 °C (c. 0.9g/100ml, $CHCl_3$); m/z(%) 406(M-1, 6), 347(20) and 224(100); δ 4.64(m, 1H, OCH), 3.85(dd, 1H, J 5.6 and 10.4Hz, 5-H), 3.20(m, 1H, 4-H), 2.91(dd, 1H, J 7.2 and 14.4Hz, 3-Hb), 2.60(dd, 1H, J 14.4 and 9.1Hz, 3Ha), 1.90 - 1.81(m, 1H, cyclohexyl-H), 1.74(s, 3H, 2-Me), 1.76 - 1.60(m, 4H, cyclohexyl-H), 1.58(m, 2H, menthyl-H), 1.54(m, 1H, HCCHN), 1.31 and 1.24 (2xm, 2x1H, menthyl-H), 1.20 - 1.15(m, 4H, cyclohexyl-H), 1.10 and 1.03 (2xm, 2x1H, cyclohexyl-H), 0.90, 0.88 and 0.79(3xm, 3x1H, menthyl-H), 0.74 and 0.72(2xd, 2x3H, J 6.6Hz $CH\underline{Me}_2$), 0.66(d, 3H, J 6.9Hz, NCMe), 0.60(m, 1H, menthyl-H) and 0.58(d, 3H, J 7.0Hz, menthyl-H).

1'R, 2'S, 5'R-Menthyl r-2R-methoxycarbonyl-2-benzyl-c-5R-(3'-pyridyl)pyrrolidine-c-4S-carboxylate (4f). Work up followed by column chromatography, eluting with 9:1 v/v ether-petroleum ether, gave the **product** which crystallied as colourless cubes from ether, m.p. 115-116 °C (>99% d.e., HPLC) (Found: C, 72.75; H, 8.25; N, 5.9. $C_{29}H_{38}N_2O_4$ requires: C, 72.75; H, 8.0; N, 5.85%); $\alpha]_D$-18.3 ° (c.1.4g/100ml, $CHCl_3$); m/z (%) 479(M+1, 57), 419(25), 387(83), 281(27), 249(100) and 203(17); δ 8.54 - 7.23(m, 9H, phenyl-H), 4.52(d, 1H, J 7.6Hz, 5-H), 4.36(m, 1H, OCH), 3.73(s, 3H, OMe), 3.31(m, 1H, 4-H), 3.14 and 2.94(2xd, 2x1H, J 13.2Hz, C$\underline{H}_2$Ph), 2.75(dd, 1H, J 5.4 and 13.7Hz, 3-Hb), 2.27(dd, 1H, J 7.7 and 13.7Hz, 3-Ha), 1.58 - 1.51(m, 3H, menthyl-H), 1.16 and 1.10 (2xm, 2x2H, menthyl-H), 0.81(m, 1H, menthyl-H), 0.79(d, 3H, J 7Hz, Me), 0.72(d, 3H, J 6.5Hz, Me), 0.57(d, 3H, J 7.0Hz, Me) and 0.19(q, 1H, menthyl-H); n.O.e.(%): irradiation of 3-Ha effected enhancement of 3-Hb(7), 4-H(3) and 5-H(2); irradiation of 4-H effected enhancement of 3-Ha(3) and 5-H(12).

1'R, 2'S, 5'R-Menthyl r-2R-methoxycarbonyl-2-phenyl-c-5R-(2'-naphthyl)pyrrolidine-c-4S-carboxylate(4g). Work up followed by column chromatography, eluting with 1:4 v/v ether-petroleum ether gave the **product** which separated as a colourless amorphous powder from ether-petroleum ether, m.p. 116-117 °C (>98% d.e., HPLC) (Found: C, 77.1; H, 7.75; N, 2.7. $C_{33}H_{39}NO_4$ requires C, 77.15; H, 7.65; N, 2.75%); $\alpha]_D$-14.0 ° (c. 1.3g/100ml, $CHCl_3$); m/z % 513(M^+, 17), 454(100), 316(92), 303(47) and 243(77); δ 7.88 - 7.29(m, 12H, ArH), 4.68(d, 1H, J 7.3Hz, 5-H), 4.29(m, 1H, OCH), 3.78(s, 3H, OMe), 3.36(m, 1H, 4-H), 3.26(dd, 1H, J 5.2 and 13.3Hz, 3-Hb), 2.76(dd, 1H, J 7.2 and 13.2Hz, 3-Ha), 1.46(m, 3H, menthyl-H), 1.23(m, 2H, menthyl-H), 0.9(m, 3H, menthyl-H), 0.73 and 0.49(2xd, 2x3H, J 7.1Hz, CH$\underline{Me}_2$), 0.30(d, 3H, J 7.0Hz, Me) and -0.14(q, 1H, menthyl-H); n.O.e. (%): irradiation of 3-Ha effected enhancement of 3Hb(27) and 4-H(12); irradiation of 4-H effected enhancement of 3-Ha(4) and 5-H(12).

1'R, 2'S, 5'R-Menthyl r-2R-methoxycarbonyl-2, c-5R-diphenylpyrrolidine-c-4S-carboxylate(4h). Work up followed by column chromatography, eluting with 3:7 v/v ether-petroleum ether gave the **product** as a colourless viscous oil, dec. 200 °C/0.03mmHg (>99% de., HPLC); (Found: C, 75.3; H, 8.1; N, 3.0. $C_{29}H_{37}NO_4$ requires C, 75.1; H, 8.05; N, 3.0%); $\alpha]_D$-6.9 ° (c. 1.2g/100ml, $CHCl_3$); m/z% 464(M+1, 1), 404(100), 266(93), 220(30), 193(50), 115(25), 104(30) and 55(35); δ 7.79 - 7.77(m, 4H, ArH), 7.40 - 7.25(m, 6H, ArH), 4.51(d, 1H, J 7.4Hz, 5-H), 4.41(m, 1H, OCH), 3.75(s, 3H, OMe), 3.26(m, 1H, 4-H), 3.16(dd, 1H, J 5.6 and 13.4Hz, 3-Hb), 2.68(dd, 1H, J 7.3 and 13.4Hz, 3-Ha), 1.56 and 1.25(2xm, 2x3H, menthyl-H), 0.95 - 0.83(m, 2H, menthyl-H), 0.81(d, 3H, J 7.0Hz, Me), 0.74(d, 3H, J 6.5Hz, Me), 0.59(d, 3H, J 6.9Hz, Me) and 0.25(q, 1H, menthyl-H). The **enantiomer** prepared from 1S, 2R, 5S-menthol had $\alpha]_D$ 7.1 ° (c.2.92g/100ml, $CHCl_3$).

1'R, 2'S, 5'R-Menthyl r-2R-methoxycarbonyl-2-phenyl-c-5R-(4'-methoxyphenyl)pyrrolidine-c-4S-carboxylate(4i). Work up followed by column chromatography eluting with 3:2 v/v ether-petroleum ether gave the **product** as a colourless amorphous solid from ether-petroleum ether, m.p. 109-111 °C (>99% d.e., HPLC) (Found: C, 72.75; H, 7.95; N, 2.85. $C_{30}H_{39}NO_5$ requires C, 72.95; H, 7.95; N, 2.85%); $\alpha]_D$ -22.2 ° (c.0.6g/100ml, $CHCl_3$); m/z% 494(M+1,7), 434(100), 283(51) and 223(81); δ 7.75 - 6.82(m, 9H, ArH), 4.44(d, 1H, J 7.6Hz, 5-H), 4.37(m, 1H, OCH), 3.77 and 3.73 (2xs, 2x3H, OMe), 3.22(m, 1H, 4-H), 3.12(dd, 1H, J 5.1 and 13.3Hz,3-Hb), 2.60(dd, 1H, J 13.3 and 6.9Hz, 3-Ha), 1.61(m, 2H, menthyl-H), 1.20, 1.11, 0.90, 0.87 and 0.81(5xm, 5x1H, menthyl-H), 0.74 and 0.68(2xd, 2x3H, J 6.9Hz, CH$\underline{Me}_2$), 0.65(m, 1H, menthyl-H), 0.6(d, 3H, J 7.1Hz, Me) and 0.30(m, 1H, menthyl-H).

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-2-phenyl-c-5R-styrylpyrrolidine-c-4S-carboxylate(4j). Work up followed by flash chromatography eluting with 7:3 v/v ether-petroleum ether gave the **product** which crystallised as colourless fine needles from ether, m.p. 97-98 °C (>99% d.e., HPLC). (Found: C, 76.3; H, 8.1; N, 2.7. $C_{31}H_{39}NO_4$ requires C, 76.05; H, 8.05; N, 2.85%); $\alpha]_D$-40.0 ° (c. 0.54g/100ml, CH_2Cl_2), m/z% 489(M^+,1), 444(1), 430(1), 292(15), 279(6), 246(7), 219(5) and 160(100); δ 7.71(m, 2H, ArH), 7.38-7.21 (m, 8H, ArH), 6.60(d, 1H, J 15.9Hz, PhCH), 6.17(dd, 1H, J 15.8 and 7.6Hz, PhC=CH), 4.65-459(m, 1H, OCH), 4.12-407(m, 1H, 5-H), 3.73(s, 3H, OMe), 3.11-3.09(m, 1H, 4-H), 3.08-3.03(m, 1H, 3-Hb), 2.61-2.55(dd, 1H, J 5.1 and 11.1Hz, 3-Ha), 1.84-1.70(m, 3H, menthyl-H), 1.68-1.54, 1.33-1.23, and 0.98-0.62(3xm, 3x2H, menthyl-H), 0.83(d, 3H, J 6.9Hz, Me), 0.67(d, 3H, J 6.6Hz, Me), and 0.59(d, 3H, J 6.4Hz, Me).

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-2-phenyl-c-5R-(3′-pyrridyl)pyrrolidine-c-4S-carboxylate(4k). Work up followed by flash chromatography eluting with 7:3 v/v ether-petroleum ether gave the product as a colourless viscous gum (Found: C, 72.3; H, 7.9; N, 5.95. $C_{28}H_{36}N_2O_4$ requires C, 72.4; H, 7.8; N, 6.0%); $\alpha]_D$ -14.03 ° (c. 1.3g/100ml, $CHCl_3$); m/z(%) 465(M + 1, 10), 405(100), 267(95), 254(10), 221(35), 194(43) and 104(27); δ 8.59 and 8.5(2xm, 2x1H, ArH), 7.77-7.70(m, 3H, ArH), 7.39-7.35 and 7.31-7.25(2xm, 2x2H, ArH), 4.53(d, 1H, J 7.7Hz, 5-H), 4.38-4.32(m, 1H, OCH), 3.74(s, 3H, OMe), 3.31-3.25(m, 1H, 4-H), 3.15-3.10(dd, 1H, J 6.3 and 13.5Hz, 3-Hb), 2.71-2.66(dd, 1H, J 7.4 and 13.5Hz, 3-Ha), 1.60-1.53(m, 3H, menthyl-H), 1.25-1.10(m, 2H, menthyl-H), 0.98-0.64(m, 3H, menthyl-H), 0.80(d, 3H, J 7.0Hz, Me), 0.73(d, 3H, J 6.5Hz, Me), 0.59(d, 3H, J 6.9Hz, Me) and 0.24-0.19(q, 1H, menthyl-H); n.O.e.(%): irradiation of 3-Ha effected enhancement of 3-Hb(27) and 4-H(12); irradiation of 4-H effected enhancement of 3-Ha(4) and 5-H(12).

1′R, 2′S, 5′R-Menthyl r-2R-(2′-pyridyl)-c-5R-(2′-naphthyl)pyrrolidine-c-4S-carboxylate(7). Work up followed by flash chromatography, eluting with 2:8 v/v ether-petroleum ether gave the **product** which crystallised as colourless plates from ether-petroleum ether; m.p. 139-141 °C (Found: C, 78.8; H, 8.1; N, 6.1. $C_{30}H_{36}N_2O_2$ requires C, 78.9; H, 7.9; N, 6.15%); $\alpha]_D$-39.5 ° (c. 1g/100ml, $CHCl_3$); m/z(%) 456(M^+,19), 301(23), 246(73) and 230(100); δ 8.62-7.23(m, 11H, ArH), 4.84(d, 1H, J 7.4Hz, 5-H), 4.51(t, 1H, J 8.1Hz, 2-H), 4.24(m, 1H, OCH), 3.57(m, 1H, 4-H), 2.62(m, 1H, 3-Hb), 2.44(m, 1H, 3-Ha), 1.59-1.39(m, 5H, menthyl-H), 1.21-0.92(m, 3H, menthyl-H), 0.79(d, 3H, J 7.0Hz, $CHMe_2$), 0.58(d, 3H, J 6.5Hz, $CHMe_2$), 0.25(d, 3H, J 6.8Hz, Me) and -0.03(q, 1H, menthyl-H).

Dimethyl 2-methyl-c-5-(3′-pyridyl)pyrrolidine-r-2, c-4-dicarboxylate(11c). Work up followed by flash chromatography eluting with 95:5 v/v methylene chloride-methanol afforded the **product** (76%) as a colourless oil b.p. 200 °C/0.5mmHg. (Found: C, 60.4; H, 6.6; N, 10.1. $C_{14}H_{18}N_2O_4$ requires C, 60.4; H, 6.5, N, 10.1%); ν_{max} (film) 3400, 2950, 1730, 1590, 1400, and 200cm^{-1}; m/z(%) 278(M^+, 1), 219(100), 192(13), and 159(33); δ 8.51(m, 2H, ArH), 7.70 and 7.25(2xm, 2x1H, ArH), 4.71(d, 1H, J 7.6Hz, 5-H), 3.83(s,3H, OMe), 3.43(m, 1H, 4-H), 3.25(s, 3H, OMe), 2.91(br s, NH), 2.73(dd, 1H, J 5.8 and 12.7Hz, 3b-H), 2.08(dd, 1H, J 7.5, 13.6Hz, 3a-H) and 1.51(s, 3H, Me); n.O.e.(%): irradiation of 3-Ha effected enhancement of 3-Hb(20), 4-H(10), 5-H(13) and 2-Me(5).

Dimethyl 2-phenyl-c-5-(3′-pyridyl)pyrrolidine-r-2, c-4-dicarboxylate(11d). Work up afforded a pale yellow oil which solidified on storage at -4 °C for one week. Crystallisation from methanol afforded the **product** (83%) as colourless cubes, m.p. 87 °C (Found: C, 66.8; H, 5.8; N, 8.4. $C_{19}H_{20}N_2O_4$ requires: C, 67.0; H, 5.9; N, 8.2%); ν_{max} (KBr) 3367, 2999, 1735, 1375, and 1250cm^{-1}; m/z(%) 341(M+1, 3), 309(8), 281(100), and

221(19); δ 8.53(m, 2H, ArH), 7.75-7.66(m, 3H, ArH), 7.40-7.25(m, 4H, ArH), 4.59(d, 1H, J 7.8Hz, 5-H), 3.76(s, 3H,OMe), 3.28(m, 1H, 4-H), 3.26(s, 3H, OMe), 3.14(dd, 1H, J 6.4, and 13.3Hz, 3-H) and 2.64(dd, 1H, J 7.2, and 13.4Hz, 3-H).

Racemic r-2, c-4-di(hydroxymethyl)-c-5-(2′naphthyl)pyrolidine. Racemic pyrrolidine (11a) (1.1g, 3.5mmol) in dry ether (30ml) was added dropwise over 5 min. to a stirred solution of $LiAlH_4$ (0.33g, 8.7mmol) in dry ether (50ml). The resulting yellow suspension was stirred at room temperature for 2.5h when water (0.05ml) was added, followed by aqueous sodium hydroxide (0.05ml, 15% solution), and water (0.2ml). The grey precipitate was filtered off, crushed, stirred with ether (50ml) for 10 min. and filtered. The combined filtrates were dried ($MgSO_4$) and evaporated. The residue was crystallised from methylene chloride-ether to afford the **product** (0.9g, 89%) as pale yellow plates m.p. 124-126 °C. (Found: C, 74.6; H, 7.55; N, 5.2. $C_{16}H_{19}NO_2$ requires C, 74.7; H, 7.45; N, 5.45%); ν_{max} (KBr) 3306, 2929, and 1074cm^{-1}; m/z(%) 257 (M^+,2), 226(100) and 191(3); δ 7.88-7.77(m, 4H, ArH), 7.48-7.41(m, 3H, ArH), 4.56(d, 1H, J 6.8Hz, 5-H), 3.85 and 3.73(2xm, 2x1H, 2-CH_2OH), 3.54(m, 1H, 2-H), 3.27(m, 2H, 4-CH_2OH), 2.69(br s, NH, OH) 2.51, (m, 1H, 4-H), 2.20(m, 1H, 3-H), and 1.75(m, 1H, 3-H).

Chiral diols were prepared from (4a) and (8a) in an analogous manner but were acetylated without purification because of problems of separating them from the menthol by-products.

Racemic N-acetyl-r-2, c-4-di(acetoxymethyl)-c-5-(2′naphthyl)pyrrolidine. Racemic diol (above) (0.15g, 0.58mmol) was dissolved in a mixture of dry pyridine (30ml) and acetic anhydride (1ml) and the solution stirred at room temperature for 16h. The pyridine was then removed by azeotropic distillation with toluene. The residue was diluted with water (10ml), and the mixture extracted with methylene chloride (3 x 30ml). The combined organic extracts were washed with aqueous sodium carbonate (2 x 30ml), dried ($MgSO_4$), and the solvent removed to leave a colourless oil which was purified by flash chromatography, eluting with ethyl acetate, to give the **product** as a colourless oil (0.18g, 81%). (Found: C, 69.1; H, 6.8; N, 3.75. $C_{22}H_{25}NO_5$ requires C, 68.9; H, 6.5; N, 3.65%); ν_{max} (film) 3454, 2950, 1722, 1656, 1389, 1250, and 1050cm^{-1}; m/z(%) 383(M^+,10), 240(21), 285(16), 268(20), 242(50) and 141(100); δ 7.85-7.81(m, 4H, ArH), 7.54-7.47(m, 3H, ArH), 5.17(d, 1H, J 3.3Hz, 5-H), 4.84-4.70(m, 2H, 2-CH_2OAc), 4.29(m, 1H, 2-H), 3.63(m, 2H, 4-CH_2OAc), 2.86(m, 1H, 4-H), 2.24-2.15(m, 1H, 3-H), 2.21 and 1.99(2xs,2x3H, Me), 1.92-1.84(m, 1H, 3-H), and 1.88(s, 3H, Me).

N-Acetyl-r-2R, c-4S-di(acetoxymethyl)-c-5R-(2′-naphthyl)pyrrolidine(9a). Prepared from the chiral diol derived from (4a) in an analogous manner to that described above. The **product** $\alpha]_D$-102.5 ° (c. 0.35g/100ml, $CHCl_3$), had identical spectral data to that of the racemic material above.

N-Acetyl r-2S, c-4R-di(acetoxymethyl)-c-5S-(2′-naphthyl)pyrrolidine(10a). Prepared from the chiral diol derived from (8a) in an analogous manner to that described above. The **product,** $\alpha]_D$ + 101.2 ° (c.0.36g/100ml, $CHCl_3$), had identical spectral data to that of the racemic material above.

Racemic r-2, c-4-di(hydroxymethyl)-2-methyl-c-5-phenylpyrrolidine. Racemic pyrolidine (11b) was reduced to the diol in a manner analogous to that described above for (11a). The product was a pale yellow oil (94%), which decomposed on attempted distillation (130-140 °c/0.01mm Hg), and could not be purified further. m/z (%) 221 (M^+,1), 190(100), 134(49), and 91(87); δ 7.41-7.23(m, 5H, ArH), 4.67(d, 1H, J 7.4Hz, 5-H), 3.50 and

3.44(2xd, 2x1H, J 10.6Hz, MeCC$\underline{H}_2$O), 3.31-3.20(m, 2H, CHC$\underline{H}_2$O), 2.59(m, 1H, 4-H), 1.94(br s, OH, NH), 1.90(dd, 1H, J 5.0 and 13.3Hz, 3-H), 1.81(dd, 1H, J 8.7 and 13.3Hz, 3-H), and 1.25(s, 3H, Me).

The corresponding chiral diols were prepared from (4d) and (8b) in an analogous manner and were acetylated (below) without further purification.

Racemic N-acetyl-r-2, c-4-di(acetoxymethyl)-2-methyl-c-5-phenylpyrrolidine. Prepared from the corresponding racemic diol by the method described above. Work up after 16h afforded a colourless oil which was purified by flash chromatography eluting with 1:1 v/v ethyl acetate-petroleum ether to give the **product** (67%) as a colourless oil. (Found: C, 65.45; H, 7.3; N, 3.9. $C_{19}H_{25}NO_5$ requires C, 65.7; H, 7.25; N, 4.05%); ν_{max} (film) 3441, 2930, 1737, 1648, and 1434cm^{-1}; m/z (%) 347 (M^+,2), 304(3), 288(4), 274(87), 232(100), and 206(26); δ 7.44-7.27(m, 5H, ArH), 5.01(d, 1H, J 8.6Hz, 5-H), 4.93 and 4.59(2xd, 2x1H, J 11.1Hz, 2-CH_2O) 3.58(m, 2H, 4-CH_2O), 3.01(m, 1H, 4-H), 2.18(s, 3H, Me), 2.00(m, 4H, Me and 3-H), 1.75(s, 3H, Me), 1.72(dd, 1H, J 6.0 and 12.5Hz, 3-H), and 1.51(s, 3H, Me).

N-Acetyl-r-2R, c-4S-di(acetoxymethyl)-2-methyl-c-5R-phenylpyrrolidine(9b). Prepared from the chiral diol derived from (4d) in an analogous manner to that described above. The **product**, $\alpha]_D$-36.7° (c.0.32g/100ml, $CHCl_3$), had identical spectral data to that of the racemic material above.

N-Acetyl-r-2S, c-4R-di(acetoxymethyl)-2-methyl-c-5S-phenylpyrrolidine(10b). Prepared from the chiral diol derived from (8b) in an analogous manner to that described above. The **product**, $\alpha]_D$ + 38.9° (c.1.05g/100ml, $CHCl_3$), had identical spectral data to that of the racemic material above.

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-2-benzyl-c-5R-(1′-propyl pyridinium-3′-yl)pyrrolidine -c-4S-carboxylate iodide(17a). A solution of the pyrrolidine (4f) (1.33, 2.78mmol) and 1-iodopropane (1.08ml, 11.1mmol) in acetonitrile (70ml) was boiled under reflux for 4h. The solvent was then evaporated under reduced pressure and the residue dissolved in methanol and precipitation induced by ether to give the **product** as a colourless sticky solid (1.44g, 80%) (Found: C, 58.9; H, 7.15; N, 4.25. $C_{32}H_{45}IN_2O_4$ requires C, 59.2; H, 7.0; N, 4.3%); m/z(%) 648(M^+,1), 521(1), 508(1), 491(1), 142(50) and 91(50); δ 9.36(s, 1H, pyridyl-H), 9.25(d, 1H, J 5Hz, pyridyl-H), 8.51(d, 1H, J 8Hz, pyridyl-H), 7.95(t, 1H, pyridyl-H), 7.31-7.21(m, 5H, ArH), 5.27(d, 1H, J 8.3Hz, 5-H), 4.81-4.67(m, 2H, NCH_2), 4.34(m, 1H, OCH), 3.75(s, 3H, OMe), 3.67-3.56(m, 1H, 4-H), 3.25 and 3.05(2xd, 2x1H, J 13.4Hz, C$\underline{H}_2$Ph), 2.70(dd, 1H, J 6.1 and 13.5Hz, 3-Hb), 2.37(dd, 1H, J 8.0 and 13.6Hz, 3-Ha), 2.12-2.05(m, 2H, $\underline{CH}_2$Me), 1.58 and 1.20 (2xm, 2x2H, menthyl-H), 1.04(t, 3H, J 7Hz, $CH_2\underline{Me}$), 0.96(m, 3H, menthyl-H), 0.90-0.64(m, 2H, menthyl-H), 0.84(d, 3H, J 6.8Hz, Me), 0.79(d, 3H, J 6.4Hz, Me), and 0.58(d, 3H, J 6.8Hz, Me); n.O.e. (%): irradiation of 3-Ha effected enhancement of 3-Hb (7), 4-H (5) and $\underline{CH}_2$Ph (1); irradiation of 5-H effected enhancement of 4-H (6).

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-2-phenyl-c-5R-(1′-propylpyridinium-3′-yl)pyrrolidine-c-4S-carboxylate iodide(17b). Prepared from pyrrolidine (4k) in an analogous manner to that described above. The **product** (81%) was a colourless gum. (Found: C, 58.55; H, 6.7; N, 4.25. $C_{31}H_{43}IN_2O_4$ requires C, 58.65; H, 6.85; N, 4.4%); m/z (%) 634(M^+,1), 506(60), 447(62), 418(67), 405(63), 267(100) and 160(77); δ 9.33(s, 1H, pyridyl-H), 9.09(d, 1H, J 5.9Hz, pyridyl-H), 8.53(d, 1H, J 7.9Hz, pyridyl-H), 7.96(t, 1H, pyridyl-H), 7.60-7.24(m, 5H, PhH), 5.2(d, 1H, J 9Hz, 5-H), 4.85-4.67(m, 2H, NCH_2), 4.35(m, 1H, OCH), 3.70(s, 3H, OMe), 3.69-3.43(m, 1H, 4-H), 3.12(dd, 1H, J 13.2 and 8.3Hz, 3-Hb), 2.69(dd, 1H, J 13.2 and 7.5Hz, 3-Ha), 2.16-

2.09(m, 2H, $\underline{CH_2}Me$), 1.60(m, 2H, menthyl-H), 1.29-1.12(m, 3H, menthyl-H), 1.08(t, 3H, J 7.2Hz, $CH_2\underline{Me}$), 0.92-0.43(m, 4H, menthyl-H), 0.83(d, 3H, J 6.9Hz, Me), 0.78(d, 3H, J 6.5Hz, Me), and 0.57(d, 3H, J 6.9Hz, Me).

Dimethyl 2-phenyl-c-5-(1′-propylpyridinium-3′-yl)pyrrolidine-r-2,c-4-dicarboxylate iodide(17c). Prepared in analogous manner to the corresponding menthyl ester but with a reaction time of 4h. The acetonitrile solution of the product was concentrated and set aside to crystallise at 0 °C. The **product** (74%) crystallised as pale orange needles, m.p. 171-172 °C (Found: C, 51.65; H, 5.05; N, 5.55. $C_{22}H_{27}IN_2O_4$ requires C, 51.75; H, 5.35; N, 5.5%); ν_{max} (KBr) 3237, 2970, 1735, 1722 and 1252cm^{-1}; m/z(%) 383(3), 323(21), 281(39) and 142(100); δ 9.36(m, 2H, PyH), 8.57(d, 1H, J 8.1Hz, PyH), 8.03(dd, 1H, J 7.0, and 7.8Hz, PyH), 7.59-7.32(m, 5H, PhH), 5.25(d, 1H, J 8.8Hz, 5-H), 4.81-4.71(m, 2H, NCH_2), 3.72(s, 3H, OMe), 3.58(m, 1H, 4-H), 3.32(s, 3H, OMe), 3.14 and 2.66(2xdd, 2x1H, J 7.4, and 13.2Hz, 2x3-H), 2.11(m, 2H, $C\underline{H_2}Me$) and 1.02(t, 3H, J 7.3Hz, $CH_2\underline{Me}$).

Dimethyl 2-methyl-c-5-(1′-methylpyridinium-3′-yl)pyrrolidine-r-2, c-4-dicaboxylate iodide(17d). Prepared from pyrrolidine (11d) and methyl iodide in a manner analogous to that described above but with a reaction time of 1h. Work up afforded a brown oil which gave the **product** as a yellow solid on trituration with ether-methanol (0.45g, 75%) which crystallised from ethanol-ether as pale yellow prisms, m.p. 155-156 °C (Found: C, 42.75; H, 5.0; N, 6.45. $C_{15}H_{21}INO_4$ requires: C, 42.85, H, 5.05; N, 6.65%); ν_{max} (KBr) 3450, 3300, 2975, 1750, 1450, and 1100cm^{-1}; δ 9.36(s, 1H, PyH), 9.25(d, 1H, J 5.9Hz, PyH), 8.56(d, 1H, J 8.1Hz, PyH), 8.02(dd, 1H, J 6.1, and 8.0Hz, PyH), 5.55(d, 1H, J 8.2Hz, 5-H), 4.60(s, 3H, NMe), 3.78(s, 3H, OMe), 3.74(m, 1H, 4-H), 3.38(s, 3H, OMe), 2.77(dd, 1H, J 6.2, and 13.5Hz, 3-H), 2.16(dd, 1H, J 7.7, and 13.5Hz, 3-H), and 1.57(s, 3H, Me).

General Procedure for the Reduction of Pyridinium Salts (17a-d). The pyridinium salt was dissolved in methanol and stirred and cooled to -10 °C. Sodium borohydride (4mol) was added portionwise over ca. 10 min. and the resulting mixture was stirred and allowed to warn to room temperature over 1 -2 h. The solution was then neutralised with glacial acetic acid and the solvent removed *in vacuo*. The residue was taken up in water, basified with aqueous ammonia and extracted with ethyl acetate (3 x). The combined extracts were washed with water (2 x), dried ($MgSO_4$), and the solvent evaporated to leave a yellow gum. The residue was purified by flash chromatography or crystallisation as noted below.

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-2-benzyl-c-5R-(1′,2′,5′,6′-tetrahydropyrid-3′-yl)pyrrolidine-c-4S-carboxylate(18a). Work up followed by flash chromatography eluting with 2:1 v/v ether-methanol afforded the product (65%) as a colourless gum. Accurate mass: found 524.3625. $C_{32}H_{48}N_2O_4$ requires 524.3614. m/z(%) 525(M + 1, 1), 465(1), 387(10), 314(35), 254(10), 186(52) and 91(100); δ 7.29-7.16(m, 5H, ArH), 5.69(m, 1H, HC=C), 4.58(m, 1H, OCH), 3.68(s, 3H, OMe), 3.65(d, 1H, J 9.2Hz, 5-H), 3.02 and 2.99 (2xd, 2x1H, J 13.1Hz, $NC\underline{H_2}C$=), 3.00 (d, 1H, J 15Hz, $C\underline{H_2}Ph$), 2.97-2.88(m, 1H, 4-H), 2.85(d, 1H, J 15Hz, $C\underline{H_2}Ph$), 2.62-2.57(m, 3H, 3-Hb and NCH_2C=), 2.46-2.35(m, 2H, $NC\underline{H_2}Et$), 2.19-2.10(m, 3H, 3-Ha), 1.85-1.80(m, 2H, $C\underline{H_2}HC$=), 1.63(m, 2H, menthyl-H), 1.55(m, 2H, $NCH_2C\underline{H_2}Me$), 1.43(m, 2H, menthyl-H), 1.29-0.94(m, 3H, menthyl-H), 0.92(d, 3H, J 7.3Hz, $NCH_2CH_2\underline{Me}$, 0.89(m, 1H, menthyl-H), 0.86 and 0.85 (2xd, 2x3H, J 6.9Hz, $CHMe_2$), 0.84-0.71(m, 1H, menthyl-H), and 0.69(d, 3H, J 6.9Hz, Me).

1′R, 2′S, 5′R-Menthyl r-2R-methoxycarbonyl-2-phenyl-c-5r-(1′-propyl-1′,2′,5′,6′-tetrahydropyrid-3′-yl)pyrrolidine-c-4S-carboxylate(18b). Work up followed by flash chromatography eluting with 2:1 v/v ether-methanol afforded the **product** (62%) as a colourless gum. Accurate Mass: found 510.3477. $C_{31}H_{46}N_2O_4$ requires 510.3458; m/z(%) 511(M + 1, 22), 451(10), 371(12), 327(15), 300(100), 240(63), 142(27) ad 115(15); δ 7.71-7.22(m, 5H, PhH), 5.80(m, 1H, HC=), 4.64(m, 1H, OCH), 3.71(s, 3H, OMe), 3.69(d, 1H, J 6.9Hz, 5-H), 3.1(m, 1H, 3-Ha), 3.02(m, 2H, NCH_2C=), 2.86(m, 1H, 4-H), 2.54(m, 2H, H_2CN), 2.44(dd, 1H, J 13.6 and 7.3Hz, 3-Hb), 2.38(m, 2H, Et$\underline{CH_2}$N, 2.19(m, 2H, $\underline{H_2}CCH_2HC$=), 1.98-1.83(m, 2H, menthyl-H), 1.65(m, 2H, menthyl-H), 1.54(m, 2H, $C\underline{H_2}$Me), 1.45-1.22(m, 3H, menthyl-H), 1.0-0.76(m, 2H, menthyl-H), 0.90(d, 3H, J 7.4Hz, Me), 0.89 and 0.88(2xd, 2x3H, J 6.7Hz, $CH\underline{Me_2}$) and 0.69(d, 3H, J 6.9Hz, Me).

Dimethyl 2-phenyl-c-5-(1′-propyl-1′, 2′, 5′, 6′-tetrahydropyrid-3′-yl)pyrrolidine-r-2, c-4-dicarboxylate(18c). Work up afforded a yellow gum which on storing under petroleum ether at -4° for two weeks afforded the **product** (79%) as colourless needles, m.p. 58-59°C. Microanalytical data were obtained for the oxalate salt, m.p. 92-95°C (Found: C, 60.4; H, 6.85; N, 5.75. $C_{24}H_{32}N_2O_8$ requires C, 60.5; H, 6.75; N, 5.9%). Spectroscopic data refer to the free base: ν_{max} (KBr) 2955, 1735, 1433, 1055, and 700cm^{-1}; m/z(%) 386(M^+, 4), 327(12), 300(100), 240(51), and 222(50); δ 7.67(m, 2H, ArH), 7.27(m, 3H, ArH), 5.79(m, 1H, C=CH), 3.71(s, 3H, OMe), 3.69(m, 1H, 5-H, coupled to NH), 3.60(s, 3H, OMe), 3.29(d, 1H, NH), 3.09(dd, 1H, J 3.7 and 18.4Hz, 3-H), 3.06(, 1H, 4-H), 2.98 and 2.84(2xd, 2x1H, J 16.7Hz, $NC\underline{H_2}C$=C), 2.55(m, 1H, NCH_2), 2.48-2.41(m, 2H, 3-H and NCH_2), 2.35(m, 2H, $NC\underline{H_2}Et$), 2.20(m, 2H, C=CHC$\underline{H_2}$), 1.79(m, 2H, $NCH_2C\underline{H_2}Me$), ad 0.92(t, 3H, J 7.31Hz, Me).

Dimethyl 2-methyl-c-5-(1′methyl-1′,2′5′,6′-tetrahydropyrid-3′-yl)pyrrolidine-r-2, c-4-dicarboxylate (18d). Work up followed by flash chromatography eluting with 2:1 v/v ether-methanol afforded a colourless oil which solidified on keeping. Crystallisation from pentane-ether afforded the **product** (68%) as colourless prisms, m.p. 48-50°C (Found: C, 60.95; H, 8.3; N, 9.4. $C_{15}H_{24}N_2O_4$ requires C, 60.8; H, 8.15; N, 9.45%); ν_{max} (KBr) 2962, 1736, 1436, and 1138cm^{-1}; m/z(%) 296(M^+, 2), 237(21), 235(17), 210(61), 194(66) and 150(100); δ5.71(M, 1H, CH=C), 3.79(m, 4H, OMe and 5-H), 3.58(s, 3H, OMe), 3.11(m, 1H, 4-H), 3.09-2.78(m, 2H, $N\underline{CH_2}CH$=C), 2.64(dd, 1H, J 3.0 and 13.9Hz, 3-H), 2.45(m, 2H, $N\underline{CH_2}CH_2$), 2.34(s, 3H, N-Me), 2.18(m, 2H, $NCH_2C\underline{H_2}$), 1.94(dd, 1H, J 7.44 and 13.8Hz, 3-H), and 1.43(s, 3H, Me).

Crystal Data for (4a): $C_{27}H_{35}NO_4$. M = 437.6, orthorhombic, space group $P2_12_12_1$, a = 5.887(4), b = 14.135(8), c = 29.976(19) Å, U = 2495(3)Å^3, μ(Mo-Kα) = 0.77cm^{-1}, F(000) = 944. Z = 4, D_c = 1.17g cm^{-3}, Siemens P3/V2000 diffractometer, $\theta/2\theta$ scan, scan range $3 < 2\theta < 40°$, 1409 unique reflections measured, direct methods solution (SHELXS-86), full matrix least squares refinement on F^2 (SHELXL-93), non-hydrogen atoms anisotropic, hydrogen atoms added at geometrically calculated positions, with each of the possible positions for the hydrogen on the pyramidal N being tested independently; the 705 data with $F > 4\sigma(F)$ gave R1 = .072, wR2 = .156, GoF = 1.034. A projection of the molecule is shown in Figure 1.

Single crystal X-ray diffraction analysis of (4f) and (7) - All crystallographic measurements were carried out at 200K on a Stoe STADI4 diffractometer operating in the ω-θ scan mode using graphite monochromated molybdenum-K_a X-radiation (λ = 0.71069Å) and an on-line profile fitting method.[29] The data-sets were corrected for Lorentz and polarisation factors but not for absorption. Both structures were solved by direct methods using SHELXS-86[30] and refined by full-matrix least-squares (based on F^2) using SHELXL-93.[31]

Refinement was essentially the same for both compounds in that all non-hydrogen atoms were refined with anisotropic displacement parameters. For both structures all hydrogen atoms were constrained to calculated positions (C-H = 0.95, 0.98, 1.00, 0.99 and 0.88Å for phenyl, methyl, methine, methylene and amino respectively) and were assigned fixed isotropic thermal parameters of $n(U_{eq})$ of the parent non-hydrogen atom, where n was 1.5 for methyl hydrogen atoms and 1.2 for all others. The weighting scheme $w = [\sigma^2(F_o) + (xP)^2 + yP]^{-1}$ was used. The absolute structure of both compounds was based on the known configuration of the (-) menthyl substituent. ORTEP[32] representations of compounds **4f** and **7** are given in Figures 2 and 3 respectively.

Crystal data for compound **4f** - $C_{29}H_{38}N_2O_4$, 0.70 x 0.60 x 0.35 mm, M = 478.61, triclinic, space group $P1$, a = 6.1085(5), b = 7.8999(8), c = 13.955(4) Å, α = 90.128(10), β =93.312(9), γ = 97.596(11)°, V = 666.38(11) Å^3, Z = 1, D_{calc} = 1.193 Mg m^{-3}, μ = 0.079 mm^{-1}, $F(000)$ = 258.

Data collection - $4.0 < 2\theta < 50.0°$, each scan divided into 30 steps, scan widths and step sizes calculated from a learned profile; scan speeds 0.4 - 1.3 seconds per step. Total number of data collected = 4931; number of unique data, n = 4706; number of data with $F_o > 4.0\ \sigma(F_o)$ = 4626; R_{sig} {= $\Sigma[\sigma F_o^2]/\Sigma[F_o]$} = 0.0095.

Structure refinement - Number of parameters, p = 320; R_1 {= $\Sigma||F_o|-|F_c|| / \Sigma|F_o|$} = 0.0312, wR_2 {= ($\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma [w(F_o^2)^2]$)$^{1/2}$ } = 0.0829, weighting parameters x and y (see above) = 0.0556, 0.0835; goodness of fit, s {= [$\Sigma[w(F_o^2 - F_c^2)^2] / (n-p)$]$^{1/2}$ } = 1.050; max. Δ/σ = 0.002 [in *tors* of H(28a)], mean Δ/σ = 0.000.

Crystal data for compound **7** - $C_{30}H_{36}N_2O_2$, 0.75 x 0.40 x 0.20 mm, M = 456.61, orthorhombic, space group $P2_12_12_1$, a = 6.6973(9), b = 14.1236(12), c = 26.621(4) Å, V = 2518.1(6) Å^3, Z = 4, D_{calc} = 1.204 Mg m^{-3}, μ = 0.075 mm^{-1}, $F(000)$ = 984.

Data collection - As for compound **4f** with the following differences: total number of data collected = 5152; number of unique data, n = 4412; number of data with $F_o > 4.0\ \sigma(F_o)$ = 4112; R_{sig} = 0.0171.

Structure refinement - Number of parameters = 312, R_1 = 0.0289, wR_2 = 0.0764; weighting parameters x and y = 0.0366, 0.3442, goodness of fit = 1.053, max. Δ/σ = 0.001 [in the overall scale factor], mean Δ/σ = 0.000.

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Table 2. Selected bond lengths (Å) and angles (°) for compound **4a** with e.s.d.'s in parentheses.

O(1)-C(6)	1.15(2)	O(2)-C(6)	1.24(2)
O(2)-C(7)	1.41(2)	O(3)-C(8)	1.17(2)
O(4)-C(8)	1.36(2)	O(4)-C(9)	1.45(2)
N(1)-C(2)	1.37(2)	N(1)-C(5)	1.46(2)
C(2)-C(6)	1.46(2)	C(2)-C(3)	1.51(2)
C(3)-C(4)	1.55(2)	C(4)-C(8)	1.51(2)
C(4)-C(5)	1.58(2)	C(5)-C(19)	1.55(2)
C(9)-C(18)	1.50(2)	C(9)-C(10)	1.55(2)
C(10)-C(11)	1.54(2)	C(10)-C(14)	1.55(2)
C(11)-C(12)	1.52(2)	C(11)-C(13)	1.56(2)
C(14)-C(15)	1.49(2)	C(15)-C(16)	1.57(2)
C(16)-C(17)	1.52(2)	C(16)-C(18)	1.52(2)
C(19)-C(20)	1.38(2)	C(19)-C(2)	1.41(2)
C(20)-C(21)	1.44(2)	C(21)-C(22)	1.39(2)
C(21)-C(26)	1.40(2)	C(22)-C(23)	1.34(2)
C(23)-C(24)	1.35(2)	C(24)-C(25)	1.39(2)
C(25)-C(26)	1.40(2)	C(26)-C(27)	1.42(2)
C(27)-C(28)	1.32(2)		

C(6)-O(2)-C(7)	117(2)	C(8)-O(4)-C(9)	117.9(11)
C(2)-N(1)-C(5)	108.9(12)	N(1)-C(2)-C(6)	113.8(14)
N(1)-C(2)-C(3)	109.1(13)	C(6)-C(2)-C(3)	120(2)
C(4)-C(3)-C(2)	102.8(12)	C(3)-C(4)-C(8)	113.5(14)
C(3)-C(4)-C(5)	102.4(10)	C(8)-C(4)-C(5)	117.4(13)
N(1)-C(5)-C(19)	114.4(12)	N(1)-C(5)-C(4)	106.9(11)
C(19)-C(5)-C(4)	114.3(12)	O(1)-C(6)-O(2)	119(2)
O(1)-C(6)-C(2)	123(2)	O(2)-C(6)-C(2)	115(2)
O(3)-C(8)-O(4)	124(2)	O(3)-C(8)-C(4)	126.5(14)
O(4)-C(8)-C(4)	109(2)	O(4)-C(9)-C(18)	110.3(11)
O(4)-C(9)-C(10)	109.1(12)	C(18)-C(9)-C(10)	111.8(12)

Table 3. Selected bond lengths (Å) and angles (°) for compound **4f** with e.s.d.'s in parentheses.

N(1)-C(2)	1.468(2)	N(1)-C(5)	1.470(2)
C(2)-C(6)	1.524(2)	C(2)-C(3)	1.533(2)
C(2)-C(10)	1.558(2)	C(3)-C(4)	1.521(2)
C(4)-C(17)	1.507(2)	C(4)-C(5)	1.564(2)
C(5)-C(30)	1.521(2)	C(6)-O(7)	1.196(2)
C(6)-O(8)	1.340(2)	O(8)-C(9)	1.442(2)
C(10)-C(11)	1.507(2)	C(17)-O(18)	1.200(2)
C(17)-O(19)	1.337(2)	O(19)-C(20)	1.459(2)
C(30)-C(31)	1.384(2)	C(30)-C(35)	1.392(2)
C(31)-C(32)	1.388(2)	C(32)-C(33)	1.378(2)
C(33)-N(34)	1.339(2)	N(34)-C(35)	1.334(2)

C(2)-N(1)-C(5)	111.77(10)	N(1)-C(2)-C(6)	108.48(11)
N(1)-C(2)-C(3)	102.67(10)	C(6)-C(2)-C(3)	110.40(11)
N(1)-C(2)-C(10)	112.43(11)	C(6)-C(2)-C(10)	109.29(11)
C(3)-C(2)-C(10)	113.35(11)	C(4)-C(3)-C(2)	103.24(11)
C(17)-C(4)-C(3)	114.25(11)	C(17)-C(4)-C(5)	114.14(11)
C(3)-C(4)-C(5)	104.25(11)	N(1)-C(5)-C(30)	109.86(11)
N(1)-C(5)-C(4)	103.79(10)	C(30)-C(5)-C(4)	116.22(11)
O(7)-C(6)-O(8)	123.06(13)	O(7)-C(6)-C(2)	125.33(13)
O(8)-C(6)-C(2)	111.60(11)	C(6)-O(8)-C(9)	115.00(12)
C(11)-C(10)-C(2)	113.85(11)	O(18)-C(17)-O(19)	124.27(13)
O(18)-C(17)-C(4)	125.38(12)	O(19)-C(17)-C(4)	110.35(11)
C(17)-O(19)-C(20)	118.57(10)	O(19)-C(20)-C(25)	107.42(10)
C(31)-C(30)-C(35)	116.92(13)	C(31)-C(30)-C(5)	121.03(12)
C(35)-C(30)-C(5)	121.90(12)	C(30)-C(31)-C(32)	119.28(13)
C(33)-C(32)-C(31)	119.07(14)	N(34)-C(33)-C(32)	122.98(14)
C(35)-N(34)-C(33)	116.92(13)	N(34)-C(35)-C(30)	124.79(14)

Table 4. Selected bond lengths (Å) and angles (°) for compound **7** with e.s.d.'s in parentheses.

N(1)-C(2)	1.464(2)	N(1)-C(5)	1.472(2)
C(2)-C(6)	1.502(2)	C(2)-C(3)	1.532(2)
C(3)-C(4)	1.523(2)	C(4)-C(12)	1.507(2)
C(4)-C(5)	1.601(2)	C(5)-C(25)	1.513(2)
C(6)-N(7)	1.341(2)	C(6)-C(11)	1.383(2)
N(7)-C(8)	1.337(2)	C(8)-C(9)	1.368(3)
C(9)-C(10)	1.373(3)	C(10)-C(11)	1.387(3)
C(12)-O(13)	1.206(2)	C(12)-O(14)	1.341(2)
O(14)-C(15)	1.463(2)		
C(2)-N(1)-C(5)	105.40(10)	N(1)-C(2)-C(6)	112.81(11)
N(1)-C(2)-C(3)	103.94(11)	C(6)-C(2)-C(3)	113.63(12)
C(4)-C(3)-C(2)	103.02(11)	C(12)-C(4)-C(3)	114.19(12)
C(12)-C(4)-C(5)	113.99(12)	C(3)-C(4)-C(5)	103.38(10)
N(1)-C(5)-C(25)	113.54(11)	N(1)-C(5)-C(4)	106.02(11)
C(25)-C(5)-C(4)	116.22(11)	N(7)-C(6)-C(11)	122.89(14)
N(7)-C(6)-C(2)	115.65(13)	C(11)-C(6)-C(2)	121.39(14)
C(8)-N(7)-C(6)	116.9(2)	N(7)-C(8)-C(9)	124.4(2)
C(8)-C(9)-C(10)	118.1(2)	C(9)-C(10)-C(11)	119.3(2)
C(6)-C(11)-C(10)	118.4(2)	O(13)-C(12)-O(14)	124.41(13)
O(13)-C(12)-C(4)	125.87(12)	O(14)-C(12)-C(4)	109.72(12)
C(12)-O(14)-C(15)	118.73(11)		

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