Pergamon

Tetrahedron 55 (1999) 569–584

TETRAHEDRON

9-Anthrylmethoxyacetic Acid Esterification Shifts-Correlation with the Absolute Stereochemistry of Secondary Alcohols

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Received 11 September 1998; revised 22 October 1998; accepted 5 November 1998

Abstract

Assignment of the absolute configuration of a secondary alcohol can be carried out by comparison of its proton NMR spectra with that of its ester with 9-anthrylmethoxyacetic acid [*(R)* or *(S)*-9AMA]. The esterification shifts observed for the two substituents L_1/L_2 of the alcohol depend on their spatial location with respect to the anthryl group. Identification of the substituent that results strongly shielded and of the one not shielded leads to the absolute configuration of the alcohol. Several open and cyclic alcohols of known absolute stereochemistry have been tested and the scope and limitations of the method discussed.

Keywords. *Alcohols; Configuration; NMR; Stereochemistry*

In the last few years, we and others have shown that the absolute configuration of secondary alcohols, [1,2] α-chiral primary amines,[3,4] β-chiral primary alcohols[5] and α-chiral carboxylic acids[6, 7, 8] can be effectively determined by ^{1}H-NMR spectroscopy. The procedure consists of derivatization of the substrate with *(R)*- and *(S)*-enantiomers of the chiral reagent [methoxyphenylacetic acid (MPA), 9-anthrylmethoxyacetic acid (9AMA), ethyl 2-(9-anthryl)-2-hydroxyacetate (AHA)] and comparison of the NMR spectra of the resulting two diastereomeric derivatives. The method is based on the shielding produced in each

0040-4020/99/$ - see front matter
PII: S0040-4020(98)01055-2

derivative by the aryl ring of the auxiliary reagent on that substituent L_1/L_2 of the alcohol part (substrate) located besides the aryl ring in the main conformer (Figure 1a-b). In this way, the *R/S* configuration of the reagent is linked to that of the alcohol by the NMR spectrum and comparison of the chemical shifts of L_1/L_2 in the *(R)* and the *(S)*-derivatives allows assignment of absolute configuration.

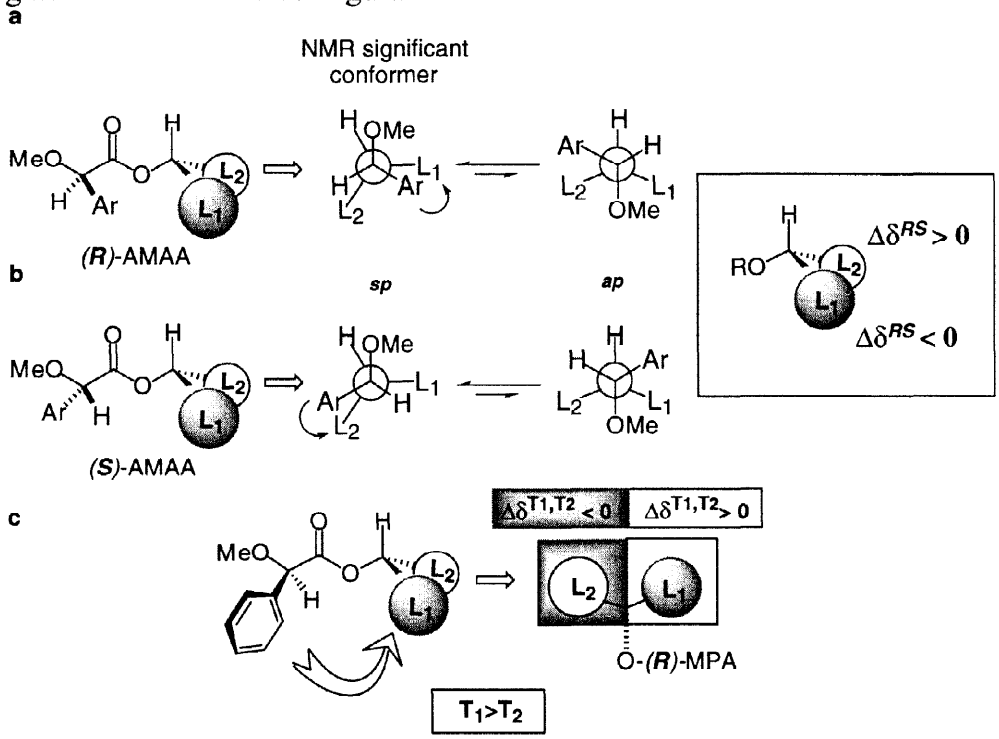
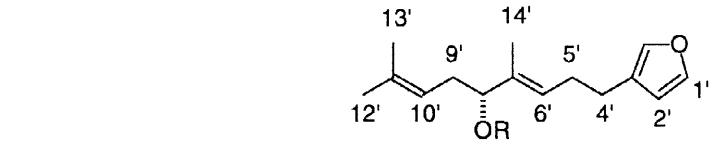


Figure 1.

In an effort to simplify this procedure, we have recently shown that the absolute configuration of secondary alcohols devoid of anisotropic groups in the vicinity of the OH group can in fact be assigned using only one derivative, the *(R)* or the *(S)*-MPA ester, if two NMR spectra are taken at two sufficiently separated temperatures[9] and the sign of $\Delta\delta^{T1T2}$, instead of that of $\Delta\delta^{RS}$, is considered (Figure 1c). Still, new efforts would be welcome if additional simplifications are incorporated to further simplify the procedure. The best conceivable method should involve the preparation of only one derivative, room temperature NMR experiments and assignment of the fewest and most observable signals with complete confidence. With this objective in mind, we have explored some new approaches for establishment of absolute stereochemistry.

In this paper we wish to communicate that the absolute configuration of secondary alcohols can be determined using a single derivative, without resorting to low temperature NMR spectroscopy, by direct comparison of the NMR spectra of the alcohol with that of an ester with 9AMA.



1, R= H; **1a**, R= *(R)*-9AMA; **1b**, R= *(S)*-9AMA

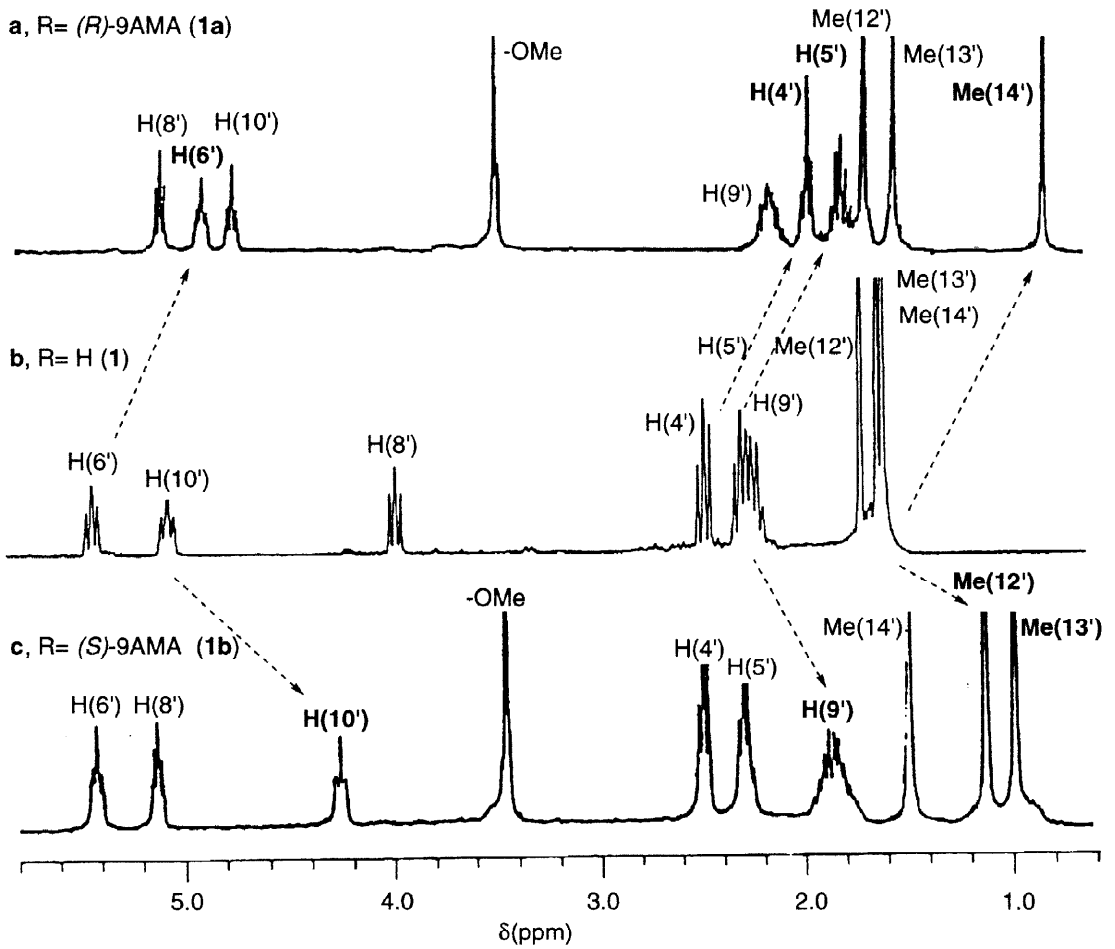


Figure 2.

A good starting point for this research was provided by furan alcohol **1** (Figure 2b), a recently isolated marine metabolite.[10] Figure 2b shows the 300 MHz ^{1}H NMR spectra of the free alcohol **1** and Figures 2a and 2c those of its *(R)*- and *(S)*-9-anthrylmethoxyacetic acid esters (**1a** and **1b**, respectively).

When one compares these spectra, two groups of signals can be distinguished. One group is formed by those protons that in the esters move upfield with respect to the free alcohol and the other group is formed by those signals that resonate at practically the same field in both the 9AMA esters and in the free alcohol. Thus, in the *(R)*-9AMA ester (Figure 2a), H(6'), H(5'), and H(4') are intensely shielded with respect to the free alcohol (Figure 2b), while H(9'), H(10'), Me(12') and Me(13') resonate at practically identical chemical shifts in the ester and in the free alcohol. Analogously in the *(S)*-9AMA ester (Figure 2c), protons H(9'), H(10'), Me(12') and Me(13') are now shielded with respect to those of the free alcohol while H(6'), H(5') and H(4') resonate approximately at the same shifts in the ester and the alcohol.

When alcohol **1** is esterified with other arylmethoxyacetic acids such as MPA, the protons of the substrate are again distributed in two groups depending on the magnitude of the shielding produced upon esterification.

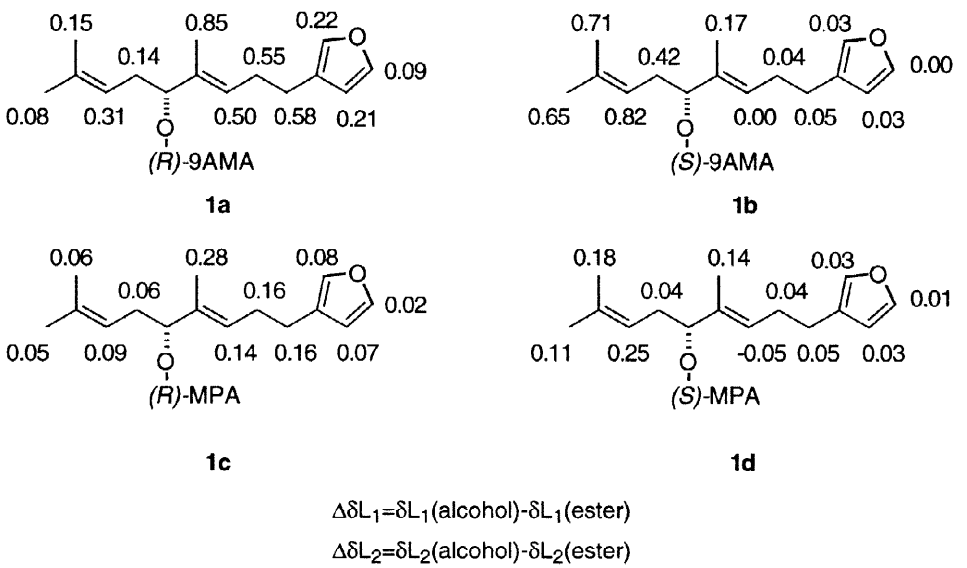


Figure 3.

This esterification shift can be quantitatively expressed for each individual proton as the difference between the chemical shift in the free alcohol and that in the ester. As we can use the two enantiomers of the reagent, two different magnitudes can be measured: $\Delta\delta^{AR}$ for the ester made with *(R)*-AMAA and $\Delta\delta^{AS}$ for the *(S)*-AMAA ester.

Figure 3 shows the esterification shifts obtained for the furan alcohol **1** with 9AMA (**1a** and **1b**) and MPA (**1c** and **1d**). The values are far superior to the experimental error and indicate that 9AMA produce esterification shifts far greater than MPA.

If these results were general for secondary alcohols, the identification of the intensely shielded substituent and the substituent that is only slightly shielded (L_1/L_2), along with consideration of the absolute configuration of the auxiliary reagent [*(R)*- or *(S)*-AMAA], should allow the assigment of the absolute configuration of the alcohol.

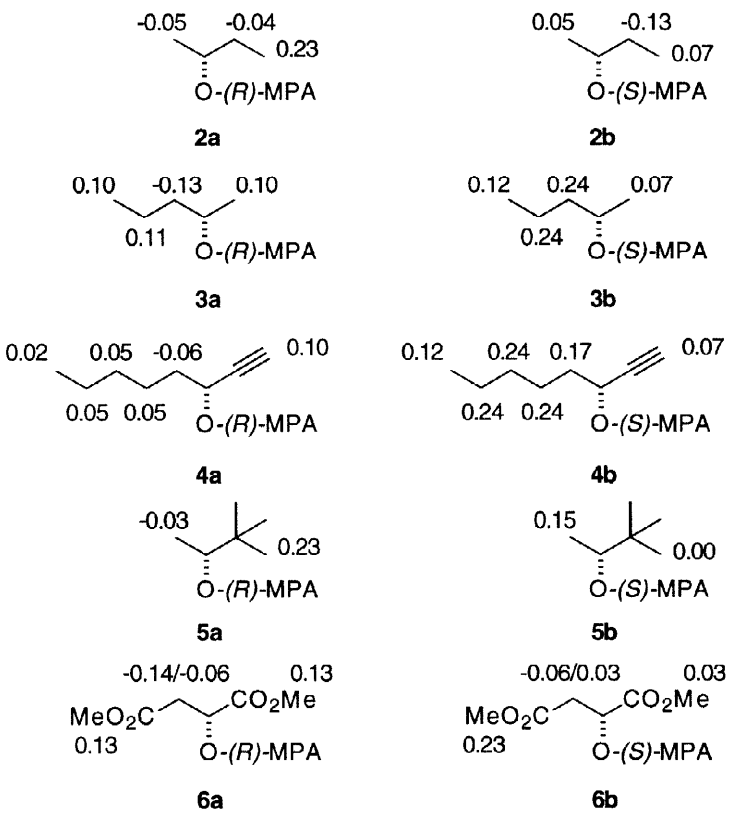


Figure 4.

In order to test the generality of this approach and to select the best auxiliary reagent, several secondary alcohols of known absolute stereochemistry were esterified with *(R)*- and *(S)*-MPA and *(R)*- and *(S)*-9AMA, and the NMR spectra of the esters compared with those of the free alcohols. The results obtained with *(R)*- and *(S)*-MPA are shown in Figure 4 and indicate that MPA produces small esterification shifts, and even negative values for some protons, that not always allow a clear identification of the shielded and non-shielded protons with substituents L_1 or L_2 (see e.g. compounds **2** and **6**). As a consequence, the method

cannot be safely used to assign the absolute configuration of the alcohol and we therefore discarded MPA as a reagent and continued the studies with 9AMA.

The esterification shifts obtained for several linear secondary alcohols with 9AMA are shown in Figure 5. These data are fully coherent and confirm the results advanced from the study of furan **1**, i. e. (a) two groups of signals are clearly distinguished according to the magnitude of the esterification shift (those heavily shielded and those that are practically non-shielded) and (b) a correlation exists between the intensity of the esterification shift ($\Delta\delta^{AR}$ or $\Delta\delta^{AS}$) of a given proton, its spatial location around the asymmetric centre of the alcohol and the configuration of the 9AMA.

Thus, in the *(R)*-9AMA ester represented in Figure 5, the most intensely shielded protons are all located in the right hand substituent (L_1) while those that are only slightly shielded are located in the left hand substituent (L_2): $\Delta\delta^{AR}$ L_1>>$\Delta\delta^{AR}$ L_2 and the reverse occurs in the *(S)*-9AMA esters where $\Delta\delta^{AS}L_1$<<$\Delta\delta^{AS}L_2$.

In this way, the configuration of a secondary alcohol such as *sec*-butanol **2** is *R* (as indicated in Figure 5) if the more intensely shielded protons in the *(R)*-9AMA ester are in the right hand side of the projection (i.e. the ethyl substituent) and those that are only very slightly shielded are on the left hand side (i.e. the methyl substituent). This results in $\Delta\delta^{AR}L_1$>>$\Delta\delta^{AR}L_2$. The reverse ($\Delta\delta^{AS}L_1$<<$\Delta\delta^{AS}L_2$) is observed when we use the enantiomeric reagent *(S)*-9AMA and also when the configuration of the *sec*-butanol alcohol is *S* (the opposite to that shown in the Figure).[11]

In many cases it is not necessary to analyze all the resonances in L_1 and L_2, and comparison of the $\Delta\delta$ values of just a couple of protons located at both sides of the asymmetric carbon (one in L_1 and other in L_2) that are approximately the same distance from the asymmetric centre is sufficient to assign the configuration of the alcohol. This is exemplified in Figure 5 where the pairs of protons selected are indicated by dashed arrows. Nevertheless, a more rigorous approach should consider the effect of the anthryl group on all the protons in L_1 and in L_2 and not just a few. To this end we have measured the mean value of the esterification shifts of all protons in substituent L_1 and those of substituent L_2 and used them in the form $\Delta\delta_mL_1$ and $\Delta\delta_mL_2$.

The plot shown in Figure 6a represents the intensity of the mean values $\Delta\delta_mL_1$ and $\Delta\delta_mL_2$ produced by 9AMA, on the alcohols **1**-**6**, and illustrates perfectly the potential of this method

to distinguish between L_1 and L_2. Thus, $\Delta\delta_m L_1$ is very much larger than $\Delta\delta_m L_2$ in the *(R)*-9AMA esters and $\Delta\delta_m L_1$ is clearly smaller than $\Delta\delta_m L_2$ in the esters formed with the enantiomeric reagent *(S)*-9AMA.

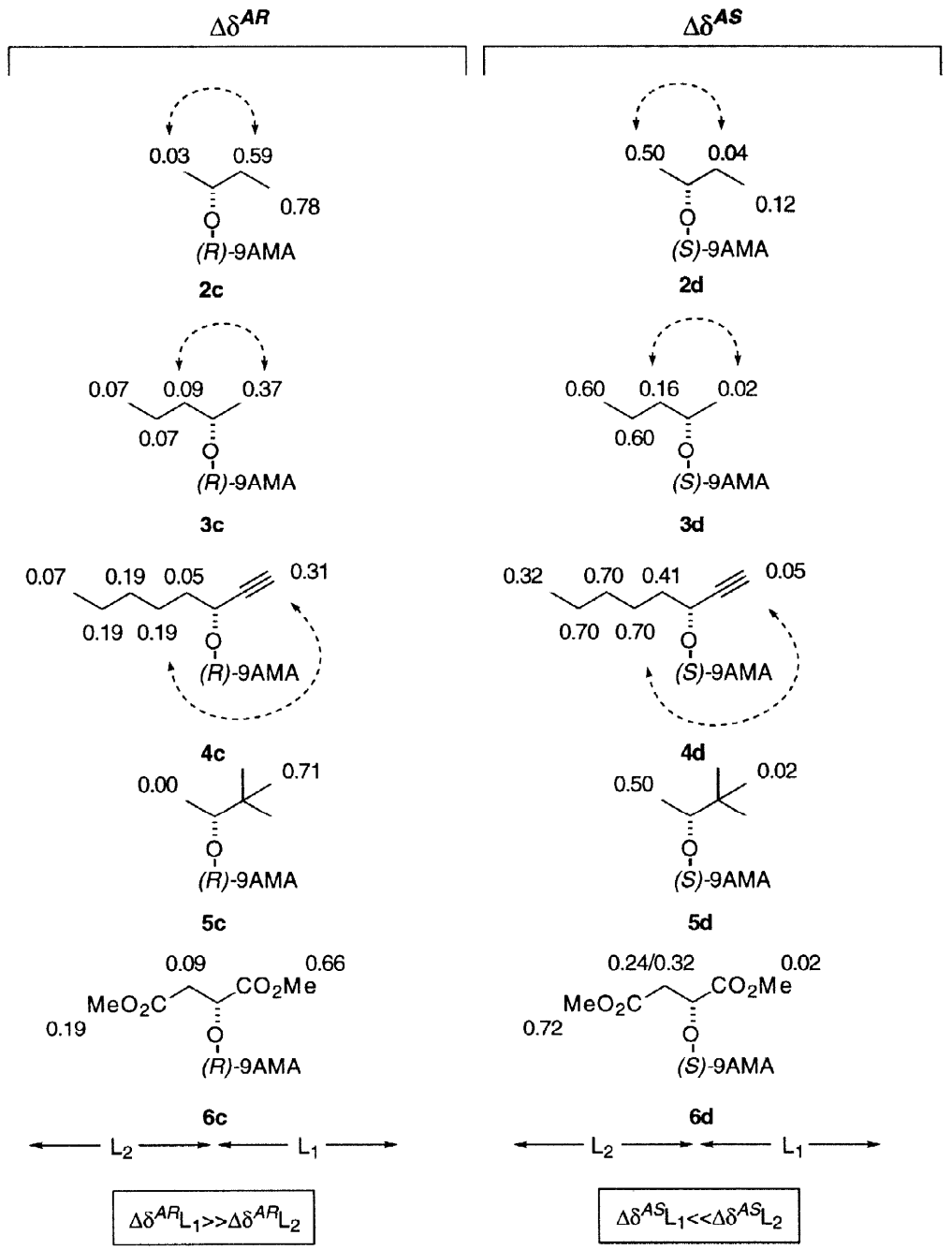


Figure 5. $\Delta\delta^{AR}$ and $\Delta\delta^{AS}$ values for *(R)* and *(S)*-9AMA esters of alcohols **2-6**. Dashed arrows showing possible comparison proton to proton.

Quantitatively, compounds **2** and **5** present the highest difference in esterification shifts (i.e. 0.03 vs. 0.68 ppm in **2**) in the *(R)*-9AMA esters, and compound **4** the smallest (0.13 vs. 0.31 ppm). The ratio $\Delta\delta_m L_2/\Delta\delta_m L_1$ is a good measure of the capacity to discriminate the shielded from the non-shielded substituents and, in that series, rises from 1/20 to 1/3. In the *(S)*-9AMA esters the results are even more favorable and the ratio $\Delta\delta_m L_1/\Delta\delta_m L_2$ changes from 1/25 in compound **5** to 1/6 in compound **2**.

Although the zone of maximum shielding effect is located up to 3-4 carbon bonds from the chiral centre, [1] and consequently the protons at those distances are the best candidates, when protons outside that zone are considered the $\Delta\delta_m$ values still allow a definitive discrimination between L_1 and L_2. Figure 6b shows the magnitudes obtained for compound **1a** considering either all the protons (ranging from 1 to 7 bonds away; Entry 1) or just the ones located in the maximum shielding zone (Entry 2). In both cases, the same correct conclusion about the absolute stereochemistry is reached.

In summary, the differences observed for the shielded and the non-shielded substituents are quantitatively so important that no mistake can be expected in the application of this method to the assignment of absolute configuration.

In order to extend our studies to cover the widest variety of substrates, cyclic alcohols **7-11** were also investigated. The results shown in Figure 7 show once again demonstrate that two groups of protons can be distinguished in every alcohol depending on the intensity of the esterification shift. However, in contrast to the linear alcohols **1-6**, use of just two protons, one at each side of the asymmetric centre and at approximately the same distance, for comparison of $\Delta\delta$ values is not sufficient to identify the shielded and the non-shielded substituent. This is so because, in many cases, the geometry of the molecule influences quite different orientations of those two protons with respect to the anthryl ring. This means that although the protons are separated from the asymmetric centre by the same number of bonds, equivalent aromatic shielding effects are not acting in each case.

This phenomenon is quite apparent when the hydroxyl group is axial as in *cis*-androsterone (**11**), where the α–protons at C-2 and C-4 show very different $\Delta\delta$ values depending on their axial or equatorial orientation. In this case, comparison of stereochemical mixed protons [i.e. H(2'eq) vs H(4'ax) leads to erroneous conclusions $\Delta\delta^{AR}$H(2'eq) vs. $\Delta\delta^{AR}$H(4'ax): 0.70 vs. 0.47 ppm indicates that C-2 is the shielded substituent and C-4 the non-shielded one]; selection

of protons with the same axial orientation leads to the correct assignment, [$\Delta\delta^{AR}$H(2'ax) vs. $\Delta\delta^{AR}$H(4'ax): 0.27 vs. 0.47 ppm; C-2 non-shielded and C-4 shielded] while comparison of the equatorial ones [$\Delta\delta^{AR}$H(2'eq) vs. $\Delta\delta^{AR}$H(4'eq): 0.70 vs. 0.72] does not afford a definitive answer in this case.

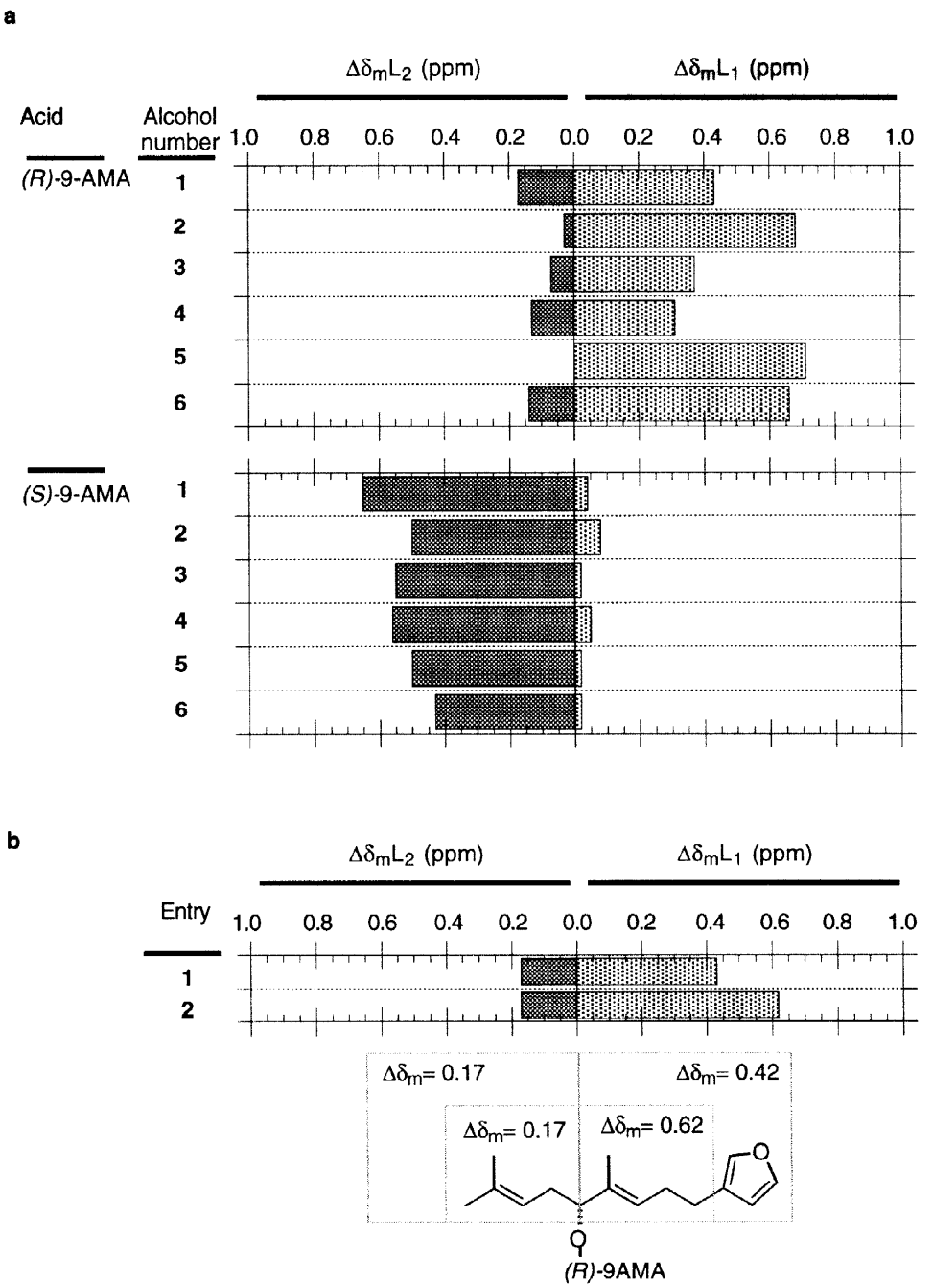


Figure 6. Esterification shifts (mean values ($\Delta\delta_m$ L_1 and $\Delta\delta_m L_2$) for the *(R)* and *(S)*-9AMA esters of alcohols **1-6** expressed as mean values ($\Delta\delta_m$ L_1 and $\Delta\delta_m L_2$, 6a) and as a function of the distance to the asymmetric center (6b).

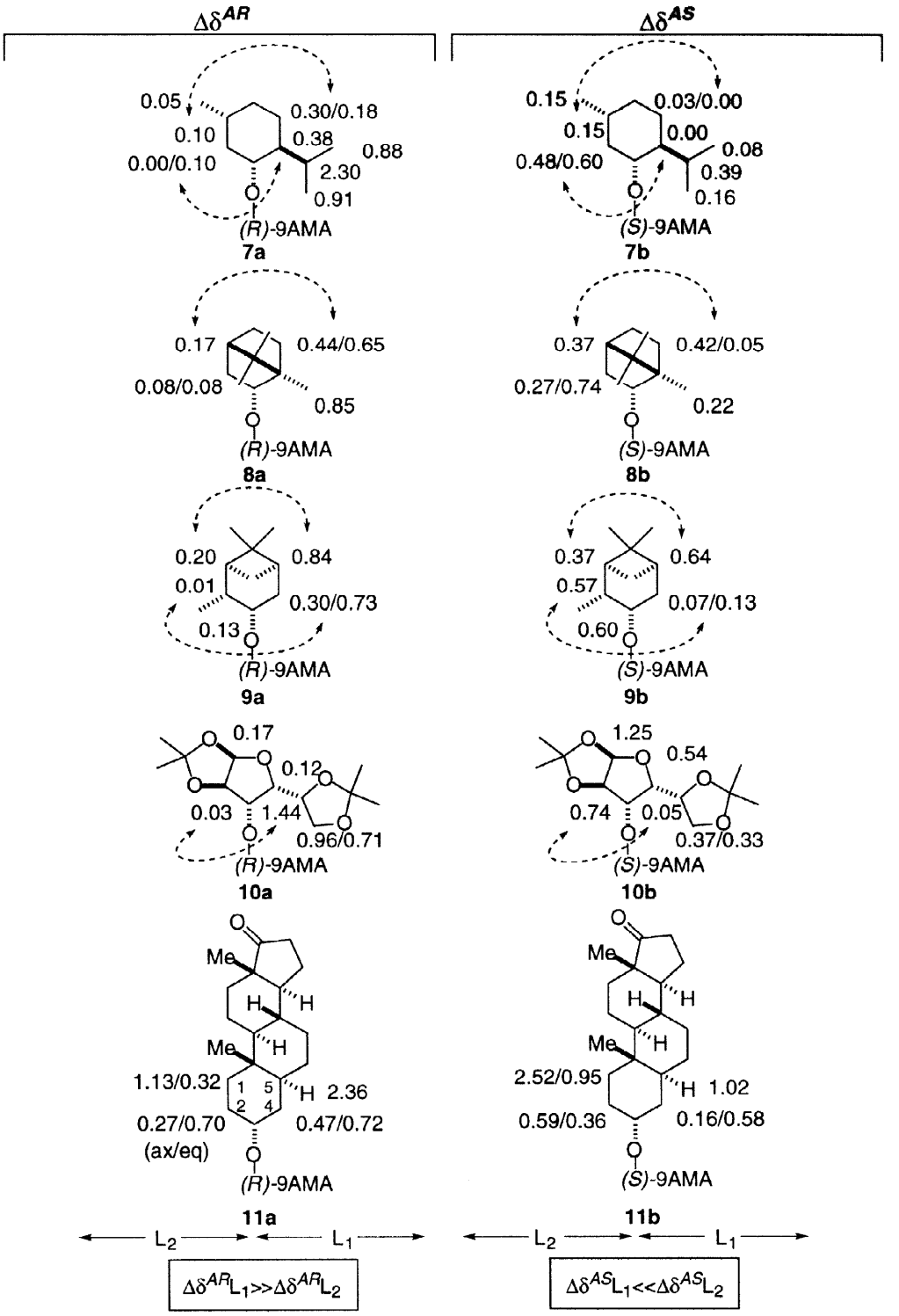


Figure 7. $\Delta\delta^{AR}$ and $\Delta\delta^{AS}$ values for *(R)* and *(S)*-9AMA esters of alcohols **7**-**11**.

If the hydroxyl group is equatorial, the proton to proton comparison can apparently be safely used to identify the shielded and non-shielded parts of the molecule provided that the selected protons are attached to carbon atoms at symmetric positions with respect to the chiral center. Such protons are marked with dashed arrows in Figure 7.On the basis of these results, the use of the mean values $\Delta\delta_m L_2$ and $\Delta\delta_m L_1$ (Figure 8) instead of single protons becomes of utmost importance for safe assignments of absolute configuration of cyclic alcohols. Thus, in the *(R)*-9AMA esters of alcohols **7-11** the mean values of $\Delta\delta_m L_1$ are, in all cases, much greater than $\Delta\delta_m L_2$ while the reverse occurs in the corresponding *(S)*-9AMA esters. The $\Delta\delta_m$ values observed for the shielded and non-shielded substituents are different enough to allow a clear distinction between L_1 and L_2 and therefore to assure a correct application of this method to the assignment of absolute configuration.

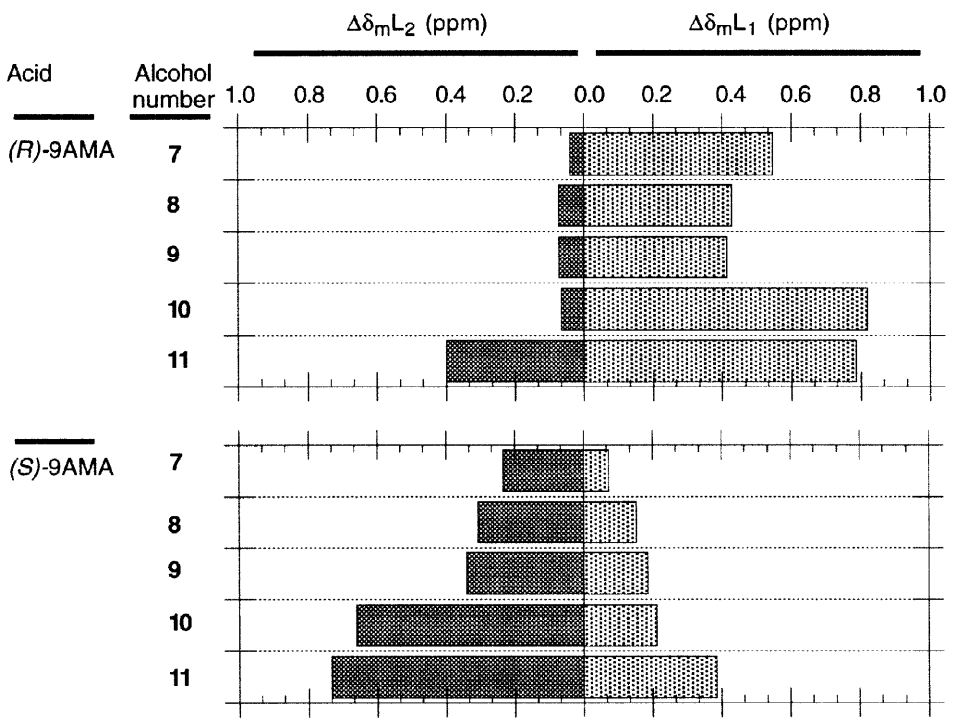


Figure 8. Distribution of $\Delta\delta_m$ (L_1/L_2) values for the *(R)* and *(S)*-9AMA esters of alcohols **7-11**.

From a theoretical point of view, the different esterification shifts observed for the shielded and non-shielded substituents can be explained on the basis of the conformational composition and structure of the 9AMA esters. In a *(R)*-9AMA ester, substituent L_1 is located near the anthryl ring of the reagent in conformer *sp* (OMe synperiplanar to CH) and is

therefore shielded, while in conformer *ap* (OMe antiperiplanar to CH) it is not shielded (Figure 1a). The reverse holds for L_2 (shielded in the minor conformer *ap* and non affected in *sp*). As a result, when one compares the spectrum of an alcohol with the configuration shown in Figure 9a with that of its *(R)*-9AMA derivative, substituent L_1 is shifted much more than L_2 (Figure 9b).

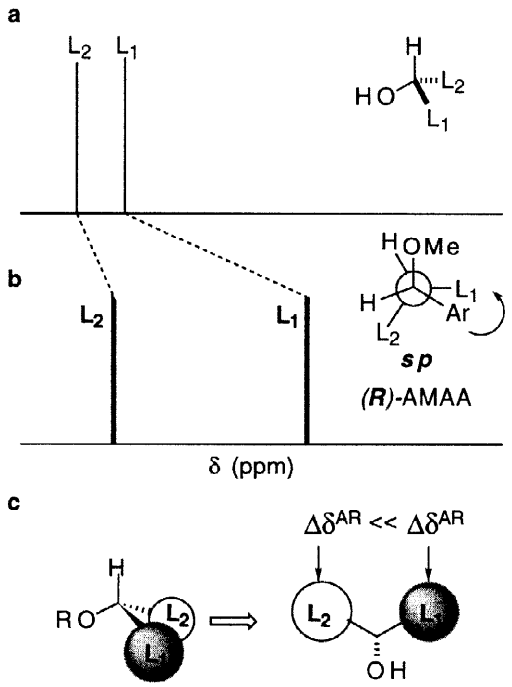


Figure 9.

Thus, the signals that are shifted upfield upon esterification with *(R)*-9AMA correspond to the protons that are shielded by the aryl group in conformer *sp* and are located in the right hand side of the asymmetric center in the projection (L_1 shielded, Figure 9c), while those that resonate at the same chemical shift are due to protons not affected by the aryl group in that conformer and correspond to those in the left hand side (L_2, Figure 9c). The reverse holds for the *(S)*-AMA esters and also when the configuration of the alcohol is the opposite.[11]

Conclusions

We have shown that when a secondary alcohol $L_1L_2C(H)OH$ is esterified of with 9AMA, the resonances of the ester are distributed in two sets of signals easily distinguishable in the NMR spectrum. The signals due to one of the substituents (L_1 or L_2) are heavily shielded with respect to the alcohol and those of the other substituent are only very slightly shielded or remain unaffected. Consideration of the aromatic shielding effect of the anthryl group indicates that the shielded substituent is the one located near the anthryl group in the major

conformer *sp* and, therefore, the absolute configuration of the alcohol (spatial location of L_1 /L_2) can be correlated with that of the auxiliary reagent 9AMA (known) by NMR identification of L_1/L_2 as the shielded/non-shielded substituents.Assignment of the absolute configuration of the alcohol can then be performed in the following way: (1) comparison of the NMR spectra of the alcohol with that of one 9AMA ester (*R* or *S*), (2) evaluation of the esterification shifts ($\Delta\delta^{AR}L_1/\Delta\delta^{AR}L_2$ or $\Delta\delta^{AS}L_1/\Delta\delta^{AS}L_2$ or $\Delta\delta mL_1/\Delta\delta mL_2$,) and identification of the shifted and the non-shifted substituents and (3) application of the model represented in Figure 10.

In the simpler structures, configuration can be assigned comparing the esterification shifts of only one proton in L_1 and another in L_2, located at symmetric positions with respect to the asymmetric center [i.e. $\Delta\delta^{AR}L_1/\Delta\delta^{AR}L_2$ (or $\Delta\delta^{AS}L_1/\Delta\delta^{AS}L_2$)]. Comparison of the $\Delta\delta mL_1$ and $\Delta\delta mL_2$ mean values (mean of the $\Delta\delta$ values for each substituent) is in general a much more rigorous and safer approach.

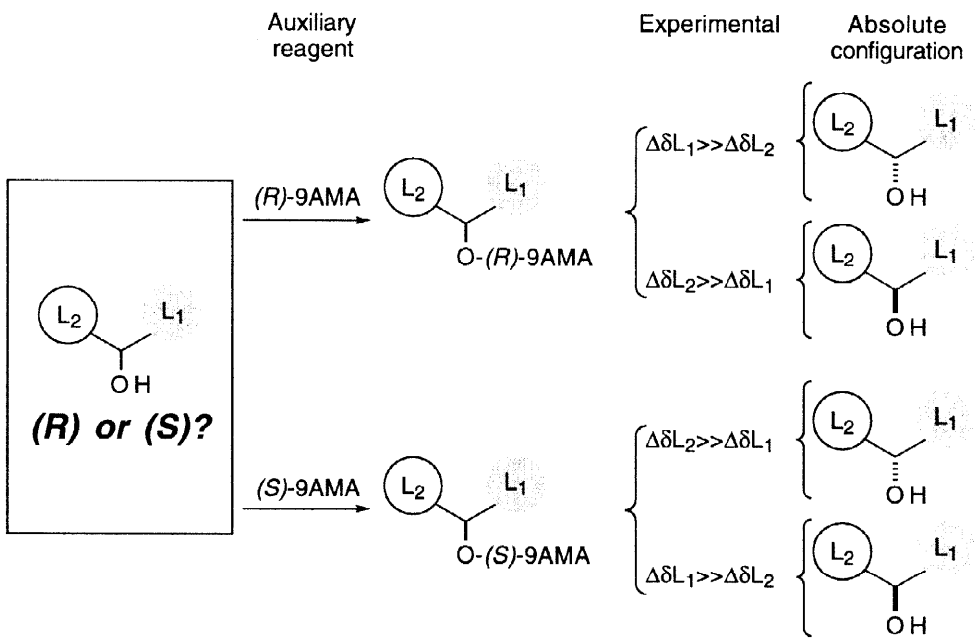


Figure 10.

Experimental Section

NMR Spectroscopy. ^{1}H-NMR spectra of samples in $CDCl_3$ (4 mg in 0.5 mL) were recorded at 300 MHz. Chemical shifts (ppm) are internally referenced to the TMS signal (0 ppm) in all cases. For 1D ^{1}H-NMR spectra, size 32 K, pulse length 2.8 ms (30°), 16 acquisitions were used.

General. Preparations of diastereomeric esters from the alcohol and O-methylmandelic acid or 9AMA were carried out by standard procedures with DCC-DMAP in practically quantitative yields (see reference 1). The reaction mixtures were filtered to remove the dicyclohexylurea and the esters purified by flash chromatography on silica gel eluting with dichloromethane. Further purification was accomplished by HPLC (Spherisorb S5W, 10 mm x 250 mm, hexane-ethyl acetate). For experimental data on compounds **1a-d** see reference 10, **2a-b** see reference 1, **3a-b** and **4a-b** see reference 5, **2c-d**, **5c-d**, **7a-b**, **8a-b**, **9a-b** and **11a-b** see reference 1.

(S)-Pentan-2-yl (R)-α-methoxy-α-(9-anthryl) acetate (**3c**): Oil; HPLC: t_R= 42.3 min (hexane: ethyl acetate, 96:4, 2 mL/min); $[\alpha]_D$= -79.8 (c= 0.033; $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.80 (d, J= 6.3 Hz, 3H), 0.81 (t, J= 7.2 Hz, 3H), 1.10-1.50 (m, 4H), 3.41 (s, 3H), 4.91-5.02 (m, 1H), 6.25 (s, 1H), 7.54-8.61 (m, 9H); MS (EI) *m/z* 336 (M^+).

Anal. Calcd. for $C_{22}H_{24}O_3$: C, 78.54; H, 7.19. Found: C, 78.52; H, 7.21.

(S)-Pentan-2-yl (S)-α-methoxy-α-(9-anthryl) acetate (**3d**): Oil; HPLC: t_R= 42.5 min (hexane: ethyl acetate, 96:4, 2 mL/min); $[\alpha]_D$= +127.091 (c= 0.022; $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.32 (t, J= 6.9 Hz, 3H), 0.47-0.51 (m, 2H), 1.02-1.45 (m, 2H), 1.15 (d, J= 6.3 Hz, 3H), 3.44 (s, 3H), 4.85-4.93 (m, 1H), 6.24 (s, 1H), 7.54-8.58 (m, 9H); MS (EI) *m/z* 336(M^+).

Anal. Calcd. for $C_{22}H_{24}O_3$: C, 78.54 ; H, 7.19. Found: C, 78.54; H, 7.22.

(R)-Oct-1-yn-3-yl (R)-α-methoxy-α-(9-anthryl) acetate (**4c**): Oil; $[\alpha]_D$= -93.1 (c= 0.043; $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.82 (t, J= 6.7 Hz, 3H), 1.16-1.31 (m, 6H), 1.64-1.69 (m, 2H), 2.15 (d, J= 2.2 Hz, 1H), 3.43 (s, 3H), 5.36 (ddd, J= J'= 6.6, J"= 2.1 Hz, 1H), 6.30 (s, 1H), 7.54-8.59 (m, 9H); MS (EI) m/z 374 (M^+).

Anal. Calcd. for $C_{25}H_{26}O_3$: C, 80.18; H, 7.00. Found: C, 80.13; H, 7.05.

(R)-Oct-1-yn-3-yl (S)-α-methoxy-α-(9-anthryl) acetate (**4d**): Oil; $[\alpha]_D$= +83.5 (c= 0.022; $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.57 (t, J= 6.6 Hz, 3H), 0.60-0.79 (m, 6H),

1.30 (m, 2H), 2.41 (d, J= 2.1 Hz, 1H), 3.47 (s, 3H), 5.34 (ddd, J= J'= 6.3, J"= 2.2 Hz, 1H), 6.30 (s, 1H), 7.54-8.37 (m, 9H); MS (EI) *m/z* 374 (M^+).

Anal. Calcd. for $C_{25}H_{26}O_3$: C, 80.18; H, 7.00. Found: C, 80.14; H, 7.02.

Dimethyl-2-O-((R)-α-methoxy-α-(9-anthryl) acetyl)-D-malate (**6c**): Oil; HPLC: t_R= 31.1 min (hexane: ethyl acetate, 80:20, 2 mL/min); $[\alpha]_D$= -42.8 (c= 0.030; $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.66 (dd, J= 16.6, J'= 7.9 Hz, 1H), 2.84 (dd, J= 16.6, J'= 4.47 Hz, 1H), 3.10 (s, 3H), 3.46 (s, 3H), 3.48 (s, 3H), 5.55 (dd, J= 7.9, J'= 4.47 Hz, 1H), 6.35 (s, 1H), 7.45-8.57 (m, 9H); MS (EI) *m/z* 410 (M^+).

Anal. Calcd. for $C_{23}H_{22}O_7$: C, 67.31; H, 5.40. Found: C, 67.28; H, 5.42.

Dimethyl-2-O-((S)-α-methoxy-α-(9-anthryl) acetyl)-D-malate (**6d**): Oil; HPLC: t_R= 31.4 min (hexane: ethyl acetate, 80:20, 2 mL/min); $[\alpha]_D$= +75.6 (c= 0.038; $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.51 (d, J= 6.3 Hz, 2H), 2.95 (s, 3H), 3.46 (s, 3H), 3.74 (s, 3H), 5.41 (t, J= 6.2 Hz, 1H), 6.38 (s, 1H), 7.45-8.57 (m, 9H); MS (EI) *m/z* 410 (M^+).

Anal. Calcd. for $C_{23}H_{22}O_7$: C, 67.31; H, 5.40. Found: C, 67.21; H, 5.40.

Diacetone-3-O-((R)-α-methoxy-α-(9-anthryl) acetyl)-D-glucose (**10a**): Oil; HPLC: t_R= 20.5 min. (hexane: ethyl acetate, 80:20, 2 mL/min); $[\alpha]_D$= -66.1 (c= 0.029; $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 0.57 (s, 3H), 1.08 (s, 3H), 1.26 (s, 3H), 1.44 (s, 3H), 2.97-3.03 (m, 1H), 3.07-3.43 (m, 1H), 3.44-3.56 (m, 1H), 3.45 (s, 3H), 3.95 (dd, J= 7.4, J'= 3.2 Hz, 1H), 4.51 (d, J= 3.7 Hz, 1H), 5.21 (d, J= 3.1 Hz, 1H), 5.78 (d, J= 3.5 Hz, 1H), 6.31 (s, 1H), 7.45-8.62 (m, 9H); MS (EI) *m/z* 508 (M^+).

Anal. Calcd. for $C_{29}H_{32}O_8$: C, 68.49; H, 6.34. Found: C, 68.44; H, 6.32.

Diacetone-3-O-((S)-α-methoxy-(9-anthryl) acetyl)-D-glucose (**10b**): Oil; HPLC: t_R= 23 min. (hexane: ethyl acetate, 80:20, 2 mL/min); $[\alpha]_D$= +38.2 (c= 0.009; $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 1.07 (s, 3H), 1.31 (s, 3H), 1.37 (s, 6H), 3.46 (s, 3H), 3.64-3.68 (m, 1H), 3.76-3.85 (m, 3H), 4.02 (dd, J= 6.6, J'= 3.1 Hz, 1H), 4.70 (d, J= 3.6 Hz, 1H), 5.21(d, J= 3.1 Hz, 1H), 6.30 (s, 1H), 7.47-8.51 (m, 9H); MS (EI) *m/z* 508 (M^+).

Anal. Calcd. for $C_{29}H_{32}O_8$: C, 68.49; H, 6.34. Found: C, 68.47; H, 6.34.

Acknowledgment. This work was financially supported by grants from CICYT (MAR95-1-33-CO2-O2 and PM95-0135) and the *Xunta de Galicia* (XUGA-20908B97 and XUGA-20910B96). J. M. Seco thanks the Universidad de Santiago de Compostela for a postdoctoral research grant.

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[11] To ensure that the esterification shifts reported in this study are not due to associations in solution, we checked the absence of concentration effects and the symmetry of the chemical shifts for enantiomeric pairs. Thus, the NMR spectra of *(R)*- and *(S)*-9AMA esters of *(S)*-2-pentanol and (-)-menthol (in $CDCl_3$, T=300 K) were repeated at concentrations ranging from 1 to 8 mg/mL and found to be practically identical. For its part, the ^1H NMR spectra of *(R)*- and *(S)*-9AMA esters of (R)-2-pentanol and (+)-menthol were taken and found to be identical to those of their enantiomeric pairs.