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Crystalline-State Conformational Analysis of MαNP Esters, Powerful Resolution and Chiral ^{1}H NMR Anisotropy Tools

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To compare the crystalline-state conformations of MαNP acid esters with those existing in the solution state, X-ray crystallographic analyses of 22 MαNP esters and two MαNP acids were carried out. It was found that all 27 conformers observed in the solid state have structures in which the 2-CH_3 group and the 2′-H of the naphthyl group are synperiplanar and are almost always located in the same plane. In addition, the CH_3–O7–C2–C1 moiety in all cases has an antiperiplanar structure within the MαNP plane. From further analyses, 22 conformers adopt the so-called *syn* structure, in which the O7–C2–C1–O6 moiety is synperiplanar. On the other hand, the remaining five conformers have the so-called *anti* structure. With regard to the rotational conformation around C1′′–O5, all conformers have structures similar to the synperiplanar conformation. In the so-called *syn* conformers, the interatomic distance *d*(H8′–O6) is distributed between 2.48 Å and 2.96 Å, while the distance *d*(H8′–O7) varies between 2.26 Å and 2.56 Å, indicating the weak bifurcated hydrogen bond between O6–H8′–O7 as the intramolecular stabilizing force. The crystalline-state conformations of MαNP esters are thus similar to those in solution as determined by ^{1}H NMR spectroscopy, implying that the intramolecular forces make a dominant contribution to the conformations of MαNP esters. The X-ray crystallographic analyses of MαNP acids indicated that the O6–H(acid)–O7 bifurcated hydrogen bond also serves as an intermolecular force to stabilize the so-called *syn* conformation. A similar bifurcated hydrogen bond [O6–H(alcohol)–O7] was observed in a MαNP ester containing a tertiary alcohol group. It should be emphasized that despite the existence of the so-called *syn* and *anti* conformations in the crystalline state, the absolute configurations of all MαNP esters determined here by X-ray crystallography all agree with those obtained by the ^{1}H NMR anisotropy method.

Introduction

The MαNP acid (**1**) method (Figure 1) is a powerful tool for enantioresolution of racemic alcohols and simultaneous determination of the absolute configurations of the resolved alcohols by ^{1}H NMR anisotropy.[1–3] In our previous paper[1] we reported on the mechanism of the intramolecular ^{1}H NMR anisotropy effect observed in MαNP acid esters by clarifying the aromatic geometry and solvent effects on $\Delta\delta$ values. To study the mechanism further, we have also carried out crystalline-state conformational analyses of various MαNP acid esters by X-ray crystallography as described below.

We believe that the most reliable method for determining the absolute configuration of a chiral compound is X-ray crystallography of a derivative of it containing an internal reference, the absolute configuration of which is already known.[2–4] From the stereoview of X-ray crystallography, the absolute configuration in question is then automatically determined. It is interesting that we have been able to obtain single crystals of various MαNP acid esters, which were suitable for X-ray diffraction experiments as shown below. This fact indicates that MαNP acid (**1**) has a high probability of yielding single crystals of its esters and that it should therefore be useful as an internal reference for X-ray crystallography.

When determining the absolute configuration of alcohols with the aid of ^{1}H NMR anisotropy reagents, it is important to determine the preferred conformations of derivatives prepared from chiral anisotropy reagents and alcohols. In

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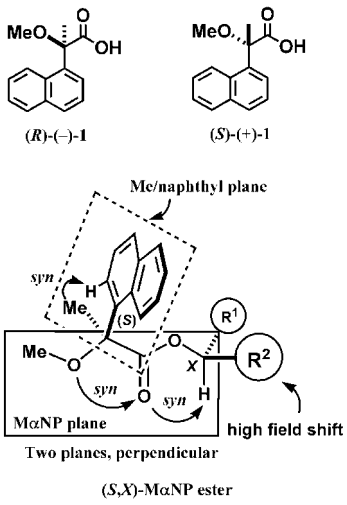

Figure 1. The absolute configurations of MαNP acids **1**, and the preferred conformation of (*S*,*X*)-MαNP acid ester, where *X* denotes the absolute configuration of alcohol to be determined.

most cases their preferred conformations have been proposed on the basis of ^{1}H NMR anisotropy data of compounds with known absolute configurations, while in some cases X-ray crystallographic analyses have been carried out to clarify the preferred conformations. For example, the crystalline-state conformations of MPA esters,[5] MTPA esters,[6–9] and 2NMA esters[10] have been described. To the best of our knowledge, however, no systematic X-ray crystallographic studies of these esters have been reported.

In the MαNP acid method, the *syn*/*syn* conformation (i.e., the so-called *syn* conformation) of a MαNP ester is used as the preferred conformation as shown in Figure 1.[1–3] To clarify the mechanism stabilizing the so-called *syn* conformation, we have carried out X-ray crystallographic analyses of 22 MαNP esters and two MαNP acids as described below, and have compared the crystalline-state conformations with those in the solution state. Such comparisons frequently give rise to comments that crystalline-state conformations are not comparable with those in the solution state because of the so-called packing force in the crystalline state, which is difficult to estimate (Figure 2). In

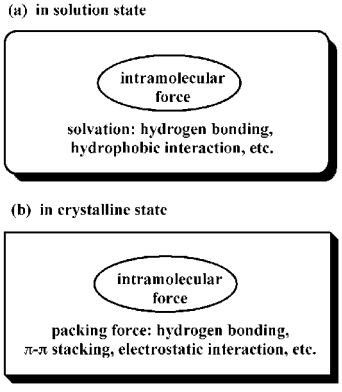

Figure 2. The intramolecular and intermolecular forces governing the conformations of molecules in a) solution and b) crystalline states.

solution, solvation may also change the conformation. We considered, however, that if the intramolecular force for stabilizing the conformation were strong enough and if X-ray crystallographic analyses of many MαNP esters with various substituents were carried out, we should be able to compare the conformations in both states and might find out the mechanism controlling the molecular conformation. As discussed below, it was found that most MαNP esters adopt the so-called *syn* conformation even in the crystalline state, and here we report the details. The *syn* conformation of a MαNP ester is also supported by ab initio MO calculations.[11]

Results and Discussion

Crystallization and X-ray Crystallographic Analyses of MαNP Acids and Esters

In contrast to the CSDP esters,[4] it was rather difficult to obtain single crystals of MαNP acids and esters. However, when these were recrystallized from MeOH, EtOH, or EtOAc as shown in Tables 4–8 we were able to obtain single crystals suitable for X-ray analyses. The single crystals were subjected to X-ray diffraction experiments, their crystal data, as shown in Tables 4–8, were obtained, and the structures were solved by direct methods and successive Fourier syntheses. Full-matrix, least-squares refinement of positional and thermal parameters, including anomalous scattering factors of chlorine, silicon, fluorine, oxygen, and carbon atoms, resulted in the final convergence with *R* values listed in Tables 4–8. The absolute configurations of chiral compounds were determined by using the MαNP acid moiety as the internal reference of absolute configuration. The absolute configurations obtained were also supported by the Flack parameters (χ).

The absolute stereostructures of the chiral MαNP esters (+)-**3b**, (+)-**4b**, (–)-**5a**, (–)-**6a**, (–)-**7b**, (–)-**8b**, (–)-**9a**, (+)-**10**, (–)-**11**, (+)-**12**, (+)-**13b**, (–)-**15b**, (–)-**16b**, (–)-**17a**, (–)-**17b**, and (–)-**18b**, and the relative stereostructure of the racemic MαNP acid methyl ester (±)-**2** are illustrated in Figure 3–Figure 8, with the absolute stereostructure of MαNP ester (+)-**14a**, the X-ray analysis of which was previously reported in a preliminary form.[12] In the case of ester (±)-**2**, methyl moieties of two methoxy groups show disordered structures, while in the case of ester (–)-**8b** an asymmetric unit contained two independent molecules with similar stereostructures, so only the drawing of one molecule is depicted in Figure 5. As can be seen in Figure 5, the *tert*-butyldimethylsilyl (TBDMS) moiety in ester (–)-**9a** has a disordered structure, but the remaining part of the molecule is clearly observed. It should be noted that all compounds shown in Figure 3, Figure 4, Figure 5, Figure 6, Figure 7, and Figure 8 adopt the so-called *syn* conformation, in which two oxygen atoms of the methoxy and ester carbonyl groups are synperiplanar.

On the other hand, Figure 9 and Figure 10 show the absolute stereostructures of MαNP esters (+)-**8a**, (–)-**18a**, (+)-

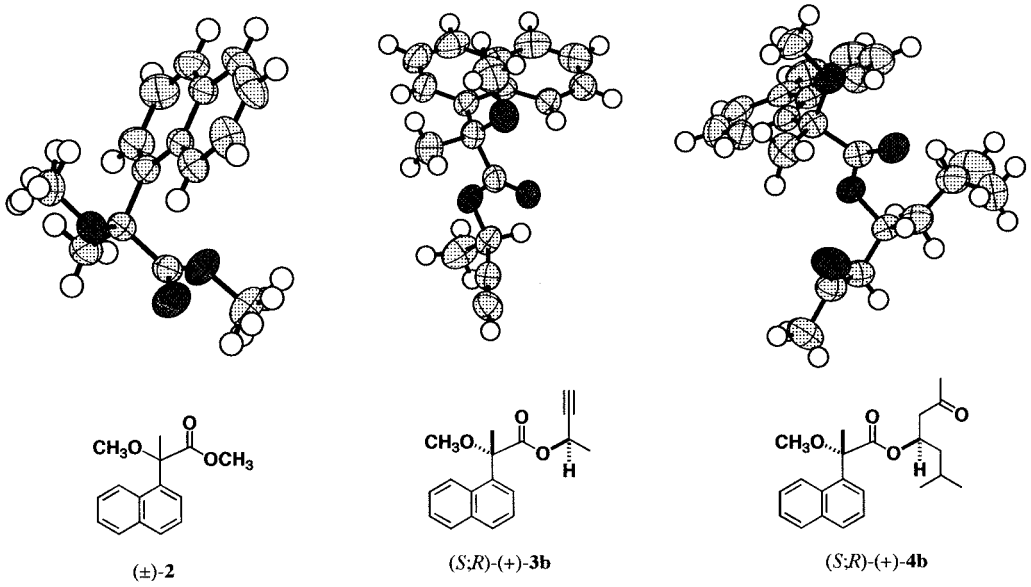

Figure 3. Absolute stereostructures and crystalline-state conformations of MαNP acids esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the synperiplanar (*syn*) relationship. In the case of racemate **2**, the stereostructure shows the relative configuration.

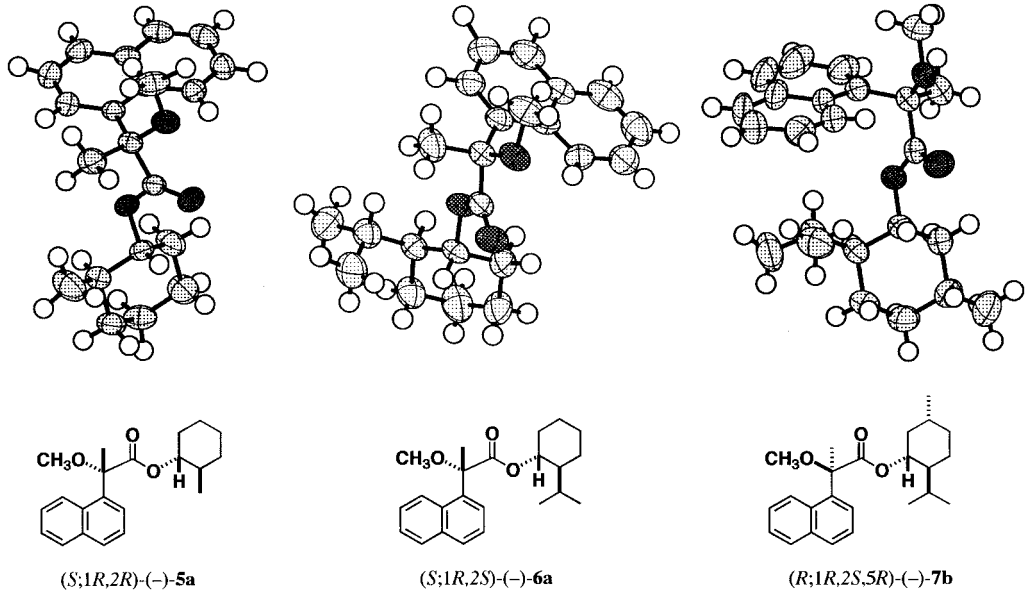

Figure 4. Absolute stereostructures and crystalline-state conformations of MαNP acids esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the synperiplanar (*syn*) relationship.

19a, (–)-**20a**, and (–)-**21**, indicating that these compounds adopt the so-called *anti* conformation, in which the two oxygen atoms of the methoxy and ester carbonyl groups are antiperiplanar in the crystalline state.

To check the dependence of conformation on the molecular packing in crystals, the chiral and racemic forms of MαNP acid **1** were also subjected to X-ray crystallography. The absolute stereostructure of MαNP acid (+)-**1** and the relative stereostructure of the racemic acid (±)-**1**, in which the acid protons could be clearly determined by difference Fourier syntheses, are illustrated in Figure 11. It is interesting that despite the difference in molecular packing, the two MαNP acids have similar conformations (i.e., so-called *syn* conformations) in the crystalline state. Figure 11 also shows the absolute stereostructure of the M9PP acid menthyl ester (–)-**22a**, an X-ray crystallographic analysis of which was previously reported.[13] The M9PP ester also takes the *syn* conformation, as shown.

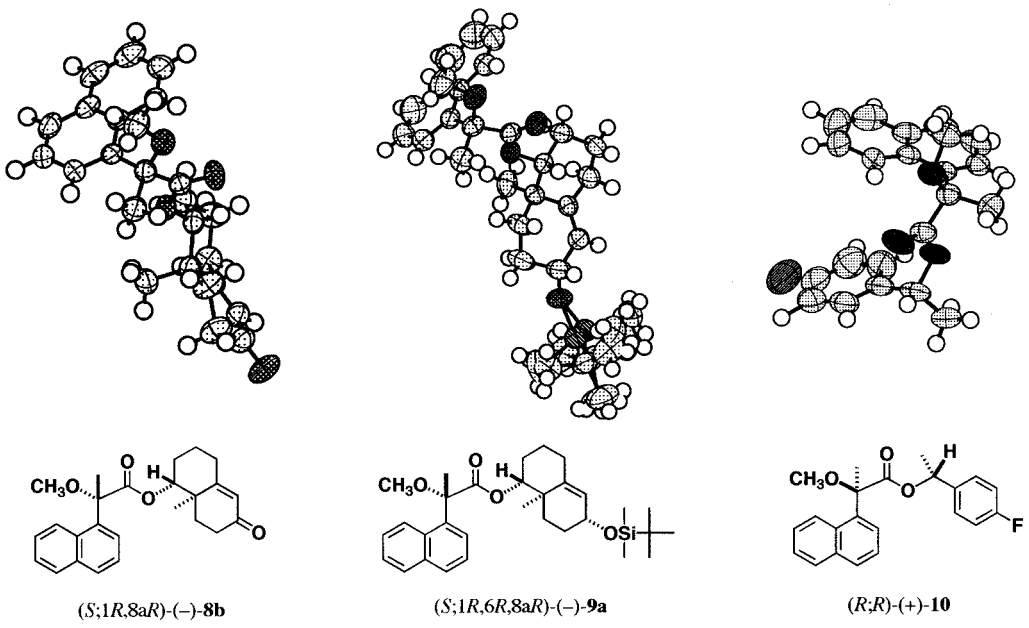

Figure 5. Absolute stereostructures and crystalline-state conformations of MαNP acids esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the synperiplanar (*syn*) relationship.

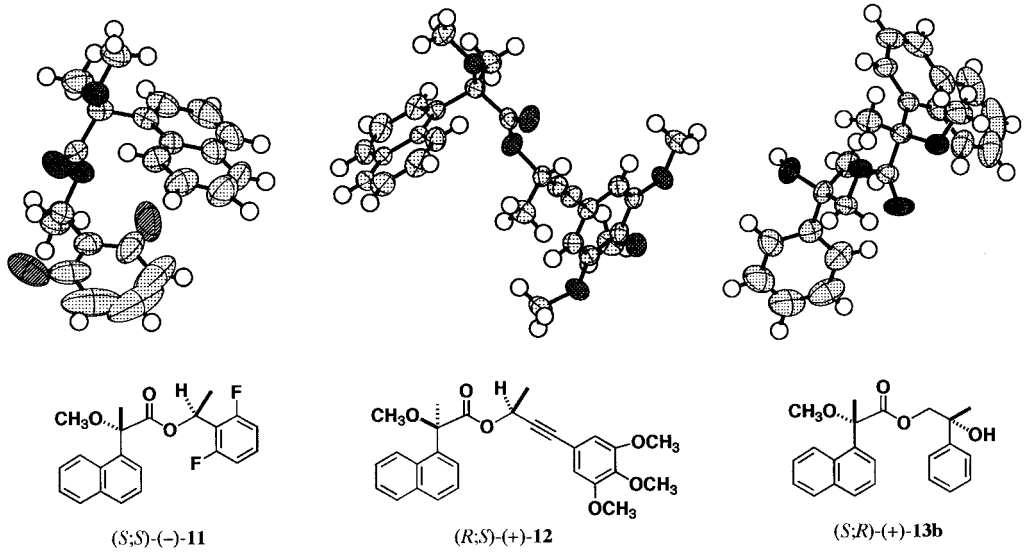

Figure 6. Absolute stereostructures and crystalline-state conformations of MαNP acids esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the synperiplanar (*syn*) relationship.

Crystalline-State Conformational Analyses of MαNP Acids, MαNP Esters, and M9PP Ester

To analyze the crystalline-state conformations in detail, the dihedral angles around some specific bonds were next examined. The *syn*/*syn* (so-called *syn*) and *anti*/*syn* (so-called *anti*) conformations of MαNP esters are shown together with the atomic numbering in Figure 12. The first rotational conformation checked was around the C1′–C2 bond connecting the naphthyl group and the propionic acid moiety, and the dihedral angles ϕ(C2′–C1′–C2–C3) of compounds adopting the *syn*/*syn* conformation are listed in Table 1, while the dihedral angles ϕ(C2′–C1′–C2–C3) of MαNP esters taking the *anti*/*syn* conformation are listed in Table 2. In all cases of MαNP esters, and also including MαNP acids (+)-**1** and (±)-**1**, the dihedral angles ϕ(C2′–C1′–C2–C3) are less than 10° (hereafter only the absolute values of dihedral angles are used for discussion unless the signs of the dihedral angles are essential for analyses). In the case of the M9PP ester (–)-**22a**, the corresponding dihedral angle ϕ(C10′–C9′–C2–C3) of 3.5° is listed in Table 1. The distribution pattern of the dihedral angles ϕ(C2′–C1′–C2–C3) is illustrated in Figure 13 and shows that the dihedral angles ϕ(C2′–C1′–C2–C3) fall in a very narrow range: 22 conformers, ϕ(C2′–C1′–C2–C3) $\leq$ 5°; 5 conformers, 5° $<$ ϕ(C2′–C1′–C2–C3) $\leq$ 10°. These results clearly indicate

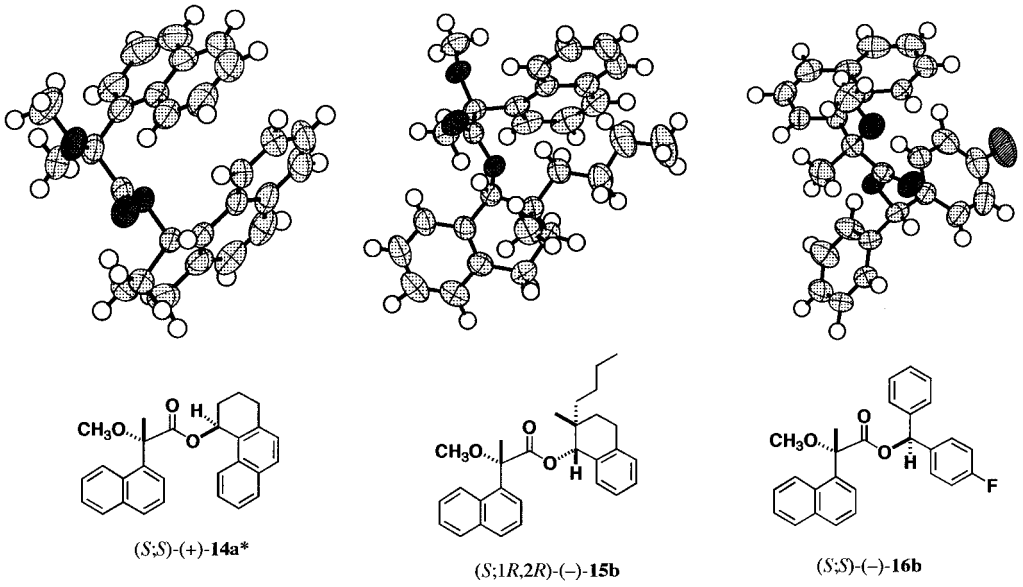

Figure 7. Absolute stereostructures and crystalline-state conformations of MαNP acids esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the synperiplanar (*syn*) relationship. The drawing of (*S*,*S*)-(+)-**14a** was adapted from ref.[12]

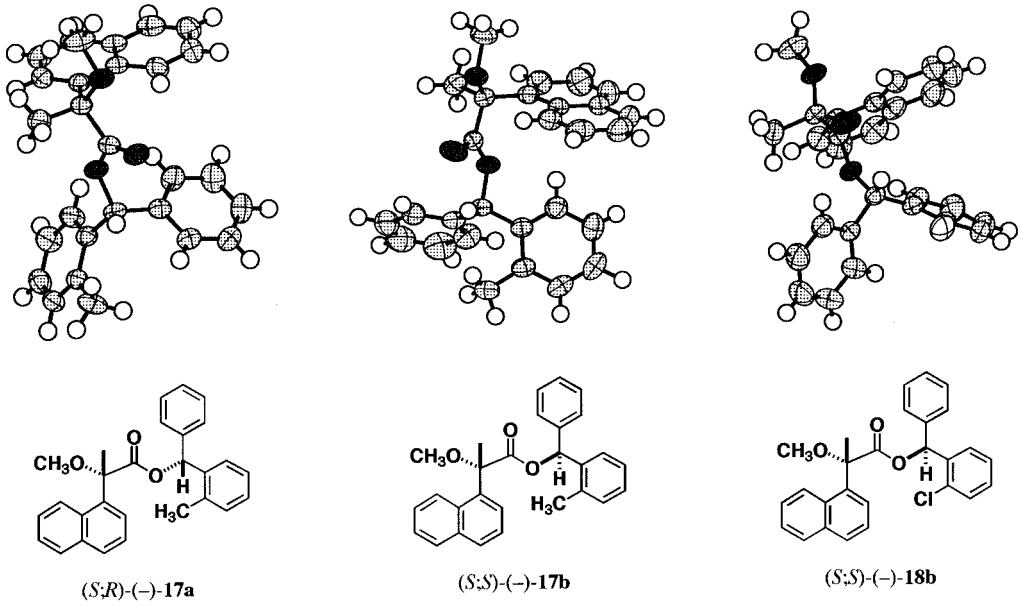

Figure 8. Absolute stereostructures and crystalline-state conformations of MαNP acids esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the synperiplanar (*syn*) relationship.

that the 2-CH_3 group and 2′-H of the naphthyl group are of *s-cis* geometry and are almost always located in the same plane (Me/naphthyl plane). Namely the rotational conformation around C1′–C2 is fixed as shown in Figure 12.

The second rotational conformation studied is concerned with the dihedral angle C1–C2–O7–C4 [i.e., rotation around the C2–O7 bond (Figure 12)]. As listed in Table 1 and Table 2, the angle ranges from 169.9° to 179.9°, indicating the *s-trans* geometry of this moiety in all cases, and its distribution pattern is shown in Figure 13: 1 conformer, 165° $< \phi$(C1–C2–O7–C4) $\leq$ 170°; 7 conformers, 170° $< \phi$(C1–C2–O7–C4) $\leq$ 175°; 19 conformers, 175° $< \phi$(C1–C2–O7–C4) $\leq$ 180°. These results indicate that the C4–O7–C2–C1 moiety lies on the same plane (i.e., the MαNP plane shown in Figure 12). The *s-trans* geometry of this moiety is significant for the weak bifurcated hydrogen bond between O6–H8′–O7, which is discussed below in detail. The lone-pair orbitals of the methoxy oxygen atom O7 are always oriented towards H8′, forming the bifurcated relationship.

The third and fourth rotational conformations are those of the ester moiety. The dihedral angle C1′′–O5–C1–C2 ranges from 168.9° to 179.2° as listed in Table 1 and

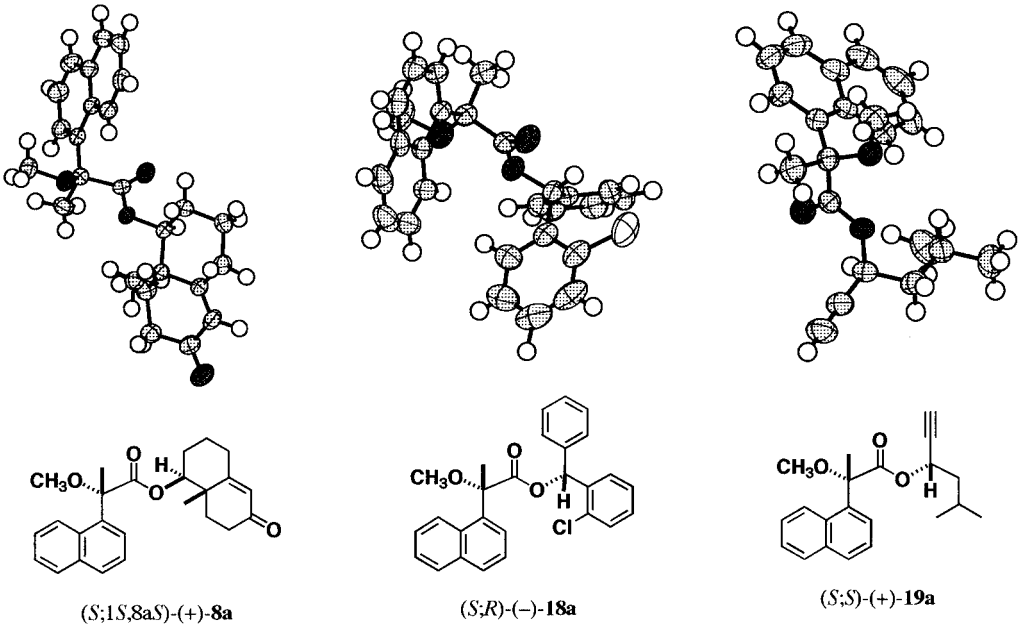

Figure 9. Absolute stereostructures and crystalline-state conformations of MαNP acids esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the antiperiplanar (*anti*) relationship.

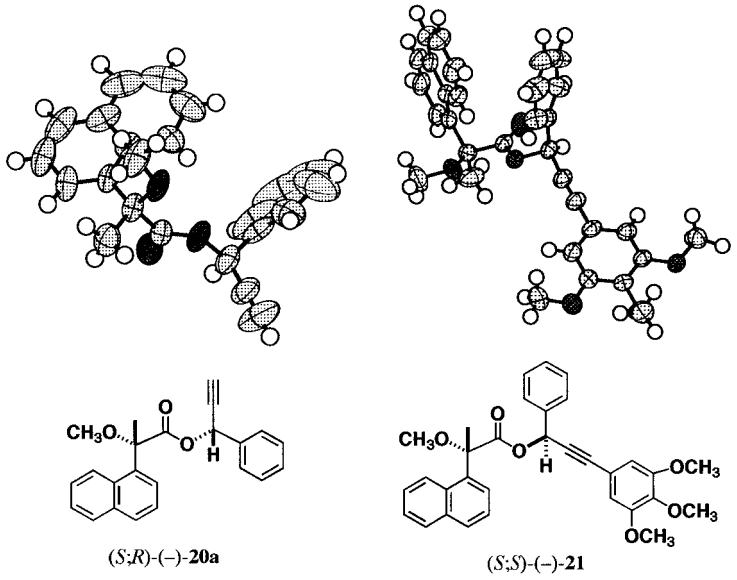

Figure 10. Absolute stereostructures and crystalline-state conformations of MαNP acids esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the antiperiplanar (*anti*) relationship.

Table 2, and its distribution pattern is shown in Figure 14: 1 conformer, 165° < ϕ(C1′′–O5–C1–C2) ≤ 170°; 5 conformers, 170° < ϕ(C1′′–O5–C1–C2) ≤ 175°; 19 conformers, 175° < ϕ(C1′′–O5–C1–C2) ≤ 180°. These data clearly indicate that the C1′′–O5–C1–C2 moiety has the *s-trans* geometry. Another dihedral angle C1′′–O5–C1–O6 ranges from 0.0° to 6.8°, and its distribution pattern is also shown in Figure 14: 21 conformers, 0° < ϕ(C1′′–O5–C1–O6) ≤ 5°; 4 conformers, 5° < ϕ(C1′′–O5–C1–O6) ≤ 10°. The data indicate the *s-cis* geometry for the C1′′–O5–C1–O6 moiety. Those geometries are characteristic of esters.

The fifth rotational conformation is defined by the dihedral angle O6–C1–C2–O7. In the MαNP esters with the so-called *syn* conformation, the dihedral angle O6–C1–C2–O7 ranges from 2.4° to 25.6° as listed in Table 1, and its distribution pattern is illustrated in Figure 15: 3 conformers, 0° < ϕ(O6–C1–C2–O7) ≤ 5°; 4 conformers, 5° < ϕ(O6–C1–C2–O7) ≤ 10°; 6 conformers, 10° < ϕ(O6–C1–C2–O7) ≤ 15°; 5 conformers, 15° < ϕ(O6–C1–C2–O7) ≤ 20°; 3 conformers, 20° < ϕ(O6–C1–C2–O7) ≤ 25°; 1 conformer, 25° < ϕ(O6–C1–C2–O7) ≤ 30°; total, 22 conformers. The distribution pattern is broader than those of the dihedral

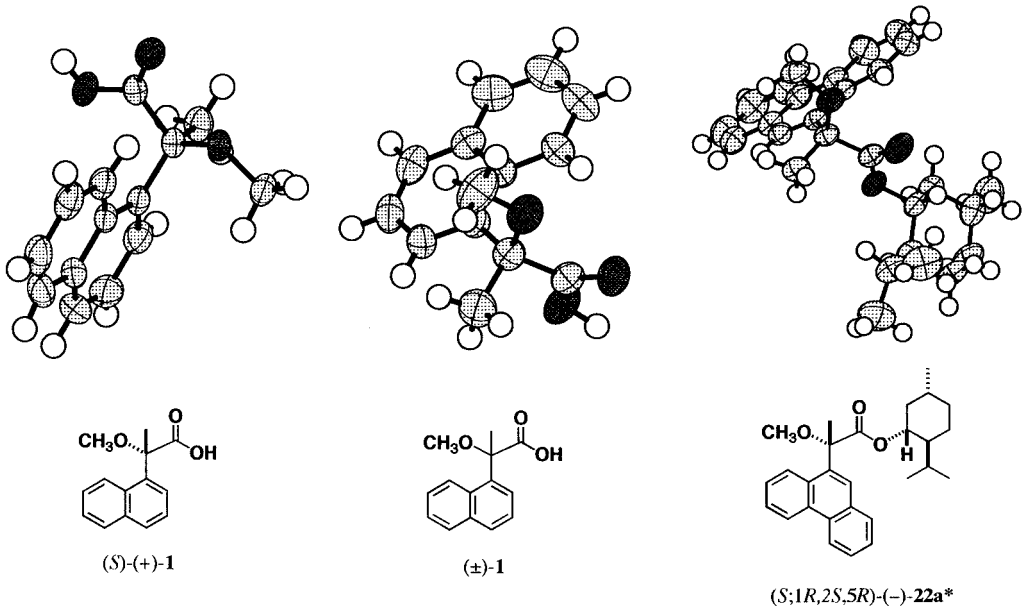

Figure 11. Absolute stereostructures and crystalline-state conformations of chiral and racemic MαNP acids and M9PP acid esters, as determined by X-ray crystallography, in which methoxy oxygen and ester carbonyl oxygen atoms are in the synperiplanar (*syn*) relationship. In the case of racemic acid (±)-**1** the stereostructure shows the relative configuration. The drawing of (*S*;1*R*,2*S*,5*R*)-(–)-**22a** was adapted from ref.[13]

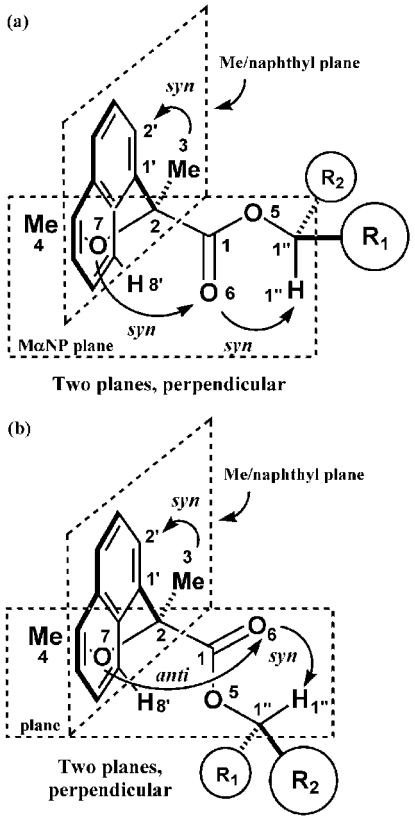

Figure 12. The conformations of MαNP esters and atomic numbering: a) *syn*/*syn* conformation, b) *anti*/*syn* conformation. In both conformations Me/naphthyl and MαNP planes are perpendicular to each other.

angles discussed above, implying an increase in the flexibility of rotation around C1–C2. The dihedral angles determined fall in the category of synperiplanar, and it should be noted that those 22 conformers adopt the synperiplanar (the so-called *syn*) conformation.

In the MαNP esters listed in Table 2, the dihedral angle O6–C1–C2–O7 ranges from 147.6° to 167.7°, and its distribution pattern is illustrated in Figure 15: 1 conformer, 145° $< \phi$(O6–C1–C2–O7) $\leq$ 150°; 1 conformer, 160° $< \phi$(O6–C1–C2–O7) $\leq$ 165°; 3 conformers, 165° $< \phi$(O6–C1–C2–O7) $\leq$ 170°; total, 5 conformers. The distribution pattern is similarly broad, indicating the flexibility of rotation around the C1–C2 bond. These five conformers are classified as the so-called *anti* conformation. The number of *anti* conformers is thus smaller than that of *syn* conformers: namely, we have observed 27 crystalline-state conformers of MαNP esters, among which 22 conformers have the so-called *syn* conformation, while only five conformers show the so-called *anti* conformation.

The last conformation analyzed relates to the rotation around the C1′′–O5 bond (Figure 12). The H1′′–C1′′–O5–C1 dihedral angle ranges from 4° to 49° (Table 1 and Table 2), and its distribution pattern is illustrated in Figure 16: 1 conformer, 0° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 5°; 6 conformers, 5° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 10°; 1 conformer, 15° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 20°; 3 conformers, 20° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 25°; 3 conformers, 25° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 30°; 2 conformers, 30° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 35°; 3 conformers, 35° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 40°; 3 conformers, 40° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 45°; 1 conformer, 45° $< \phi$(H1′′–C1′′–O5–C1) $\leq$ 50°; total, 23 conformers. The distribution pattern is broad, indicating that the rotational conformation around C1′′–O5 is more flexible, but the maximum value is less than 50°. Therefore, it is approximated that the methine hydrogen H1′′ is synperiplanar to the ester carbonyl oxygen O6 in all cases.

Table 1. Crystalline-state *syn*/*syn* conformation and intramolecular bifurcated hydrogen bond of MαNP acids and esters.[a]

Compound	(+)-**1**	(±)-**1**	(±)-**2**	(+)-**3b**	(+)-**4b**	(–)-**5a**	(–)-**6a**	(–)-**7b**	(–)-**8b**[b]	(–)-**8b**[b]	(–)-**9a**
Dihedral angle [°]											
C2′–C1′–C2–C3	+9.8	+1.1	–1.5	+3.6	+1.6	–5.9	–1.0	–5.2	+1.6	+0.7	–0.1
C1–C2–O7–C4	–176.5	–172.8	+174.8	–178.7	+175.7	–175.0	+172.6	–175.2	+178.6	–179.9	+171.9
C1′′–O5–C1–C2	–	–	–177.2	+177.7	–168.9	–171.8	–177.4	+175.0	+177.4	+176.9	–177.4
C1′′–O5–C1–O6	–	–	+1.2	–4.1	+6.8	+4.6	–2.1	–0.3	–4.6	–4.9	0.0
O6–C1–C2–O7	+14.2	+18.6	+9.2	+5.7	+25.6	+10.4	+21.0	–16.3	+9.5	+13.6	+20.9
H1′′–C1′′–O5–C1	–	–	–	–49	+10	+28	+40	+25	+10	+7	43
Interatomic distance [Å]											
C8′–H8′	0.99	0.96	0.96	1.00	0.96	0.88	1.02	0.96	0.96	0.93	0.83
H8′···O6 (= d_1)	2.48	2.70	2.65	2.52	2.89	2.85	2.92	2.72	2.65	2.73	2.96
H8′···O7 (= d_2)	2.55	2.45	2.40	2.44	2.44	2.52	2.25	2.40	2.37	2.41	2.45
Interatomic angle [°]											
C8′–H8′···O6 (= θ_1)	140.6	141.4	135.6	136.2	136.8	139.3	125.0	131.3	130.0	140.8	132.3
C8′–H8′···O7 (= θ_2)	114.7	116.5	119.1	114.9	118.5	109.2	124.7	123.4	121.2	123.0	124.1
O6···H8′···O7 (= θ_3)	62.4	61.2	62.5	63.3	58.9	57.5	59.3	61.1	62.8	60.5	58.1
Compound	(+)-**10**	(–)-**11**	(+)-**12**	(+)-**13b**	(+)-**14a**[c]	(–)-**15b**	(–)-**16b**	(–)-**17a**	(–)-**17b**	(–)-**18b**	(–)-**22a**[d,e]
Dihedral angle [°]											
C2′–C1′–C2–C3	+3.4	–6.6	+1.6	–2.9	+0.9	+0.4	+1.5	–0.7	–2.3	–2.7	+3.5
C1–C2–O7–C4	–172.3	+179.2	–177.2	+177.2	+177.5	–179.6	+176.5	–175.1	–179.7	+179.8	+169.9
C1′′–O5–C1–C2	+177.4	+176.4	–177.2	+177.9	–177.8	–170.2	–173.3	–171.4	+178.6	+178.1	+175.2
C1′′–O5–C1–O6	–0.7	–5.8	+4.0	–3.8	–0.2	+6.3	+3.6	+4.7	–4.0	–4.9	–6.7
O6–C1–C2–O7	–4.8	+5.3	–3.5	+16.6	+2.4	+14.7	+23.8	+12.2	+16.7	+17.4	+12.0
H1′′–C1′′–O5–C1	–33	+40	–29	–	–42	–16	+22	+42	–4	–6	+7
Interatomic distance [Å]											
C8′–H8′	1.04	0.99	0.95	1.11	1.00	1.03	0.91	0.90	0.95	0.90	0.88
H8′···O6 (= d_1)	2.48	2.59	2.58	2.66	2.48	2.70	2.89	2.68	2.72	2.77	2.68
H8′···O7 (= d_2)	2.30	2.27	2.37	2.26	2.35	2.34	2.47	2.45	2.38	2.42	2.41
Interatomic angle [°]											
C8′–H8′···O6 (= θ_1)	140.4	133.1	135.2	133.1	132.3	133.5	136.2	145.9	136.1	136.8	133.4
C8′–H8′···O7 (= θ_2)	117.0	121.0	119.6	118.8	120.8	117.6	115.7	114.5	118.4	118.4	125.5
O6···H8′···O7 (= θ_3)	66.3	64.8	63.5	62.7	64.7	61.7	58.8	62.1	61.5	60.5	61.8

[a] For the definition of parameters, see Figure 12 (a) and Figure 17 (a). [b] One asymmetrical unit of (–)-**8b** contains two independent molecules, the conformational data of which are listed. [c] The data were taken from ref.[12] [d] The data were taken from ref.[13] [e] For M9PP acid ester (–)-**22a**, the dihedral angle, interatomic distance, and interatomic angle corresponding to those of MαNP ester are listed.

Table 2. Crystalline-state *anti*/*syn* conformation and intramolecular bifurcated hydrogen bond of MαNP acid esters.[a]

Compound	(+)-**8a**	(–)-**18a**	(+)-**19a**	(–)-**20a**	(–)-**21**
Dihedral angle [°]					
C2′–C1′–C2–C3	–0.6	–0.5	+5.2	–3.3	+1.7
C1–C2–O7–C4	+172.4	+175.8	–173.6	+175.5	+177.2
C1′′–O5–C1–C2	+176.8	+172.6	+175.9	–179.2	–178.3
C1′′–O5–C1–O6	+1.6	–3.3	–0.4	+4.1	+4.4
O6–C1–C2–O7	–147.6	–165.4	–164.0	–167.3	–167.7
H1′′–C1′′–O5–C1	–34	–24	27	–10	–38
Interatomic distance [Å]					
C8′–H8′	0.87	0.92	0.92	0.93	0.96
H8′···O5 (= d_1)	3.18	2.76	2.76	2.67	2.69
H8′···O7 (= d_2)	2.41	2.43	2.51	2.42	2.48
Interatomic angle [°]					
C8′–H8′···O5 (= θ_1)	136.0	148.7	139.2	145.4	132.3
C8′–H8′···O7 (= θ_2)	121.7	119.0	116.1	114.9	114.5
O5···H8′···O7 (= θ_3)	52.4	57.7	56.6	58.7	58.3

[a] For the definition of parameters, see Figure 12 (b) and Figure 17 (b).

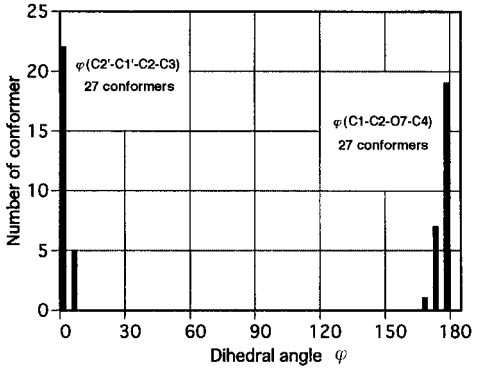

Figure 13. The distribution of conformers against dihedral angles ϕ(C2′–C1′–C2–C3) and ϕ(C1–C2–O7–C4), with use of the absolute values of dihedral angles.

From the crystalline-state conformational analyses described above, two planes can be defined: the MαNP plane contains the Me(4)–O7–C2–C1–O6 and C1–O5–C1′′–H1′′ moieties, while the Me/naphthyl plane contains the Me(3)–C2-naphthalene plane (Figure 12). It should be emphasized that these two planes are perpendicular to each other, and the *syn*/*syn* conformation depicted in Figure 12 (a) is consistent with that used in the ^{1}H NMR anisotropy method.[1–3]

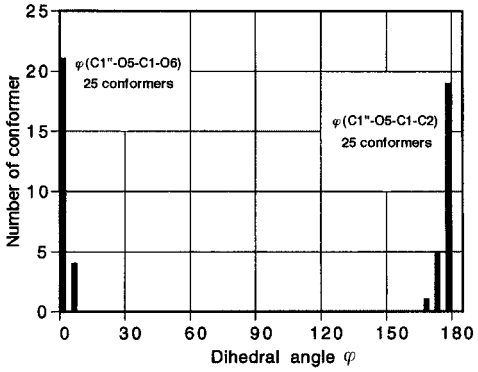

Figure 14. The distribution of conformers against dihedral angles ϕ(C1′′–O5–C1–O6) and ϕ(C1′′–O5–C1–C2), with use of the absolute values of dihedral angles.

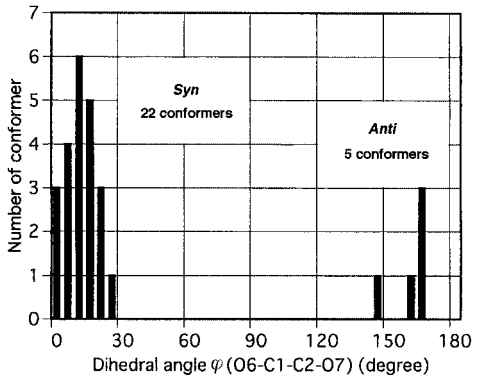

Figure 15. The distribution of conformers against dihedral angle ϕ(O6–C1–C2–O7), with use of the absolute values of dihedral angles.

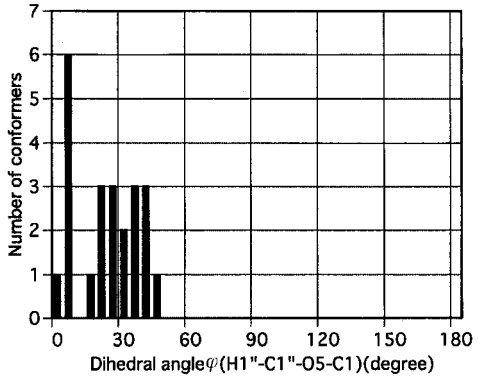

Figure 16. The distribution of conformers against dihedral angle ϕ(H1′′–C1′′–O5–C1), with use of the absolute values of dihedral angles.

Weak Bifurcated Intramolecular Hydrogen Bond Between O6–H8′–O7 with a Triangular Shape

With respect to the intramolecular force stabilizing the so-called *syn* conformation, we have proposed the weak bifurcated hydrogen bond of triangular shape between O6–H8′–O7 (Figure 17) in both experimental[1] and theoretical calculation[11] results. To check the weak bifurcated hydrogen bond[14,15] in the crystalline state, the interatomic distances d(H8′–O6) = d_1 and d(H8′–O7) = d_2 in MαNP acids and esters with the *syn*/*syn* conformation were determined as listed in Table 1.

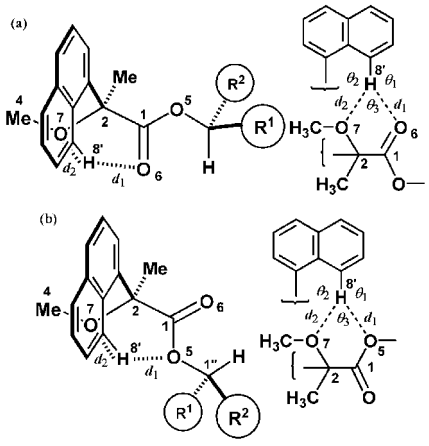

Figure 17. The weak bifurcated hydrogen bond and definition of geometrical parameters: a) *syn*/*syn* conformation; b) *anti*/*syn* conformation.

The distance d(H8′–O6) ranges from 2.48 Å to 2.96 Å: 15 conformers, d(H8′–O6) ≤ 2.70 Å; 7 conformers, d(H8′–O6) > 2.70 Å. It has been reported that if the O–H distance is shorter than 3.0 Å, a hydrogen bond between oxygen atom and C–H proton is possible.[14–16] Furthermore, as the sum of the van der Waals radii of oxygen and hydrogen atoms is calculated to be 2.7 Å, these distances also indicate that a hydrogen bond would be possible. On the other hand, the d(H8′–O7) distance ranges from 2.26 Å to 2.56 Å, indicative of the weak hydrogen bond. Figure 18 illustrates the distribution of conformers with respect to d(H8′–O6) and d(H8′–O7), which falls in a very narrow area. The weak bifurcated hydrogen bond between O6–H8′–O7, stabilizing the so-called *syn* conformation, was thus observed in the crystalline-state conformations.

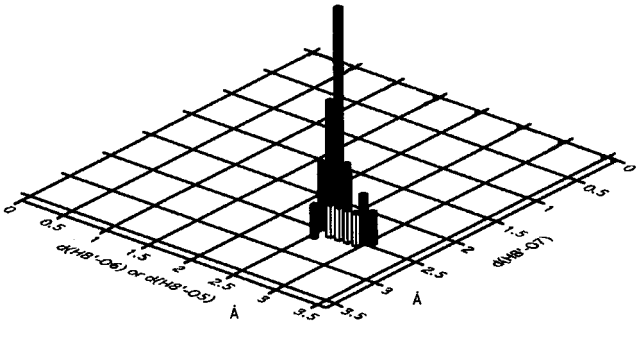

Figure 18. The distribution of conformers against interatomic distances d(H8′–O6) or d(H8′–O5) and d(H8′–O7).

For the MαNP esters possessing the *anti*/*syn* conformation, the interatomic distances d(H8′–O5) and d(H8′–O7) were similarly determined (Table 2). Except in the case of

ester (+)-**8a**, the *d*(H8′–O5) distances range from 2.69 Å to 2.76 Å, so a weak bifurcated hydrogen bond between the ether oxygen atom O5 of the ester group and the aromatic H8′ proton is possible. A similar interaction between ether oxygen atom O7 and proton H8′ is possible for all esters listed in Table 2, because the *d*(H8′–O7) distance ranges from 2.4 Å to 2.51 Å. The so-called *anti* conformation is thus stabilized by the intramolecular bifurcated hydrogen bond. The data for MαNP esters possessing the *anti*/*syn* conformation are also contained in Figure 18.

To confirm the bifurcated hydrogen bond, the interatomic angles θ_1, θ_2, and θ_3 defined in Figure 17 were determined as listed in Table 1 and Table 2. In the cases of MαNP acids and esters with the *syn*/*syn* conformation, the angle θ(C8′–H8′–O6) = θ_1 of the C–H···O=C–O moiety ranges from 125.0° to 145.9°: average value, 135.8° (Table 1). In cases of MαNP esters with the *anti*/*syn* conformation, the angle θ(C8′–H8′–O5) = θ_1 of the C–H···O–C=O moiety ranges from 114.5° to 121.7°: average value, 131.5° (Table 2). The correlation between angle θ and distance *d* is plotted with black circles in Figure 19; these symbols reasonably distribute in the area of typical weak hydrogen bond C–H···O.[15]

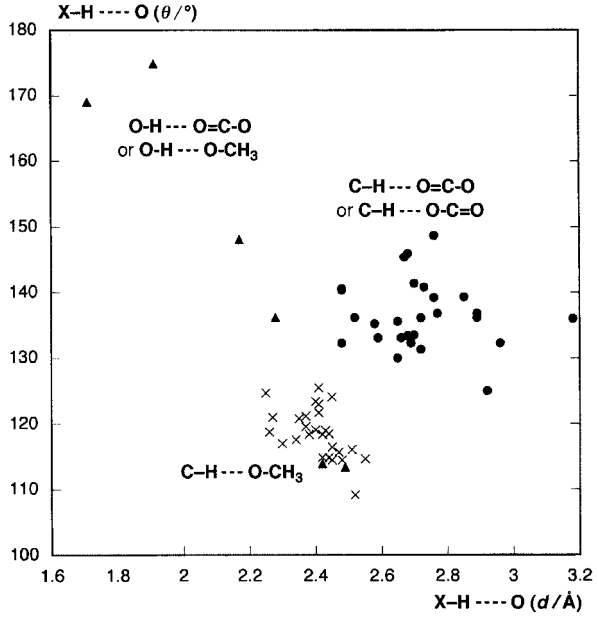

Figure 19. The correlation between distance X–H···O (*d* [Å]) and angle X–H···O (θ [°]) in the strong and weak bifurcated hydrogen bonds of MαNP acids and esters. Filled triangles: the correlation *d* vs. θ in the strong hydrogen bond O–H···O. Filled circles: the correlation d_1 vs. θ_1 in the weak hydrogen bond C–H···O. Crosses: the correlation d_2 vs. θ_2 in the weak hydrogen bond C–H···OCH_3. See Figure 17 and Figure 21 for the definition of geometrical parameters.

On the other hand, the angle θ(C8′–H8′–O7) = θ_2 of the C–H···O–CH_3 moiety was determined for all MαNP acids and esters (Table 1 and Table 2): the angle θ_2 ranges from 109.2° to 125.5°: average value, 118.6°. The correlation between angle θ and distance *d* is plotted with × in Figure 19; the symbols × appear in a narrower range than the circles filled with black, indicating that the conformation of the C–H···O–CH_3 moiety is more tightly fixed. The distribution area of × deviates slightly from that of a typical C–H···O weak hydrogen bond;[15] namely both d_2 and θ_2 are smaller than typical values. These results imply that the so-called *syn* conformations of MαNP esters are stabilized by the intramolecular bifurcated hydrogen bond as illustrated in Figure 17.

Intermolecular Bifurcated Hydrogen Bond of Triangular Shape Between O6–H(Acid or Alcohol)–O7

In the crystal structures of MαNP acids (+)-**1** and (±)-**1** we have found an interesting intermolecular bifurcated hydrogen bond stabilizing the so-called *syn* conformation. It is well known that carboxylic acids usually form dimeric structures through hydrogen bonds, as shown in Figure 20. These dimeric structures have often been observed in the crystalline state. In the case of MαNP acid (+)-**1**, however, the acid proton H5′′ of a neighboring molecule makes a hydrogen bond with the ester carbonyl oxygen atom O6 and also with the oxygen atom O7 of the methoxy group as illustrated in Figure 21: interatomic distance, *d*(H5′′–O6) = d_1 = 2.49 Å, *d*(H5′′–O7) = d_2 = 1.91 Å (Table 3). The so-called *syn* conformation of MαNP acid is thus stabilized by an intermolecular bifurcated hydrogen bond. The same intermolecular bifurcated hydrogen bond was also observed in the racemic form of the MαNP acid (±)-**1**: interatomic distance, *d*(H5′′–O6) = d_1 = 1.71 Å, *d*(H5′′–O7) = d_2 = 2.42 Å. The interatomic angles θ_1 and θ_2 of the bifurcated hydrogen bond were also determined as listed in Table 3. In the case of MαNP acid (+)-**1**, the angles are θ(O5′′–H5′′–O6) = θ_1 = 113.4° and θ(O5′′–H5′′–O7) = θ_2 = 174.9°. On the other hand, in the racemic acid (±)-**1**, the angles are θ_1 = 169.0° and θ_2 = 113.9°. The distance and angle of the bifurcated hydrogen bond are thus different in chiral and racemic MαNP acids, reflecting the differences in the crystal systems.

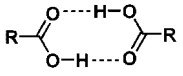

Figure 20. The general dimeric structure of carboxylic acids formed by hydrogen bonds.

Table 3. Geometries of intermolecular bifurcated hydrogen bonds in MαNP acids and ester.[a]

Compound	(+)-**1**	(±)-**1**	(+)-**13b**
Interatomic distance [Å]			
O–H	0.85	0.96	0.91
H···O= (= d_1)	2.49	1.71	2.17
H···O– (= d_2)	1.91	2.42	2.28
Interatomic angle [°]			
O–H···O= (= θ_1)	113.4	169.0	148.1
O–H···O– (= θ_2)	174.9	113.9	136.2
O···H···O (= θ_3)	71.5	76.9	–

[a] For the definition of parameters see Figure 21.

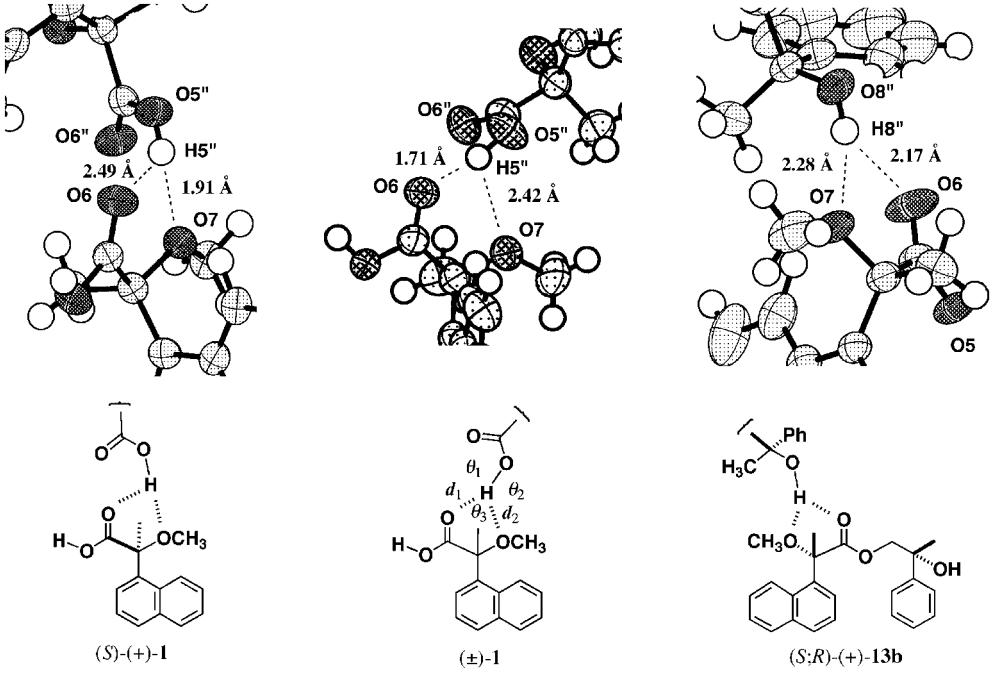

Figure 21. Intermolecular bifurcated hydrogen bonds of MαNP acids and esters identified by X-ray crystallography.

Of course, the intermolecular hydrogen bonds observed in MαNP acids are not effective for the stabilization of the so-called *syn* conformation in MαNP esters. However, these data indicate that the two oxygen atoms of methoxy and ester carbonyl groups can form a bifurcated hydrogen bond, provided that a pertinent hydrogen atom is nearby.

The X-ray crystallographic data for the MαNP ester (+)-**13b** with a tertiary alcohol moiety in the molecule provide a striking example of such an intermolecular bifurcated hydrogen bond (O6–H(alcohol)–O7, as illustrated in Figure 21). The alcoholic hydrogen atom of the neighboring molecule hydrogen bonds with the two oxygen atoms of the methoxy and ester carbonyl groups: interatomic distance, d(H8′′–O6) = d_1 = 2.17 Å, d(H8′′–O7) = d_2 = 2.28 Å; interatomic angle, θ(O8′′–H8′′–O6) = θ_1 = 148.1° and θ(O8′′–H8′′–O7) = θ_2 = 136.2° (Table 3). The correlation between angles θ and distances d listed in Table 3 is plotted with filled triangles in Figure 19; the black triangles are distributed over a wider range than in the cases of the intramolecular bifurcated hydrogen bonds C–H···O. However, the distribution of the triangles agrees reasonably well with that of a typical hydrogen bond O–H···O,[15] confirming the intermolecular bifurcated hydrogen bond. It is thus obvious that the so-called *syn* conformation of the MαNP ester (+)-**13b** is stabilized by the intermolecular bifurcated hydrogen bonds. In our previous paper[1] we proposed the intermolecular hydrogen bonding mechanism for stabilizing *syn* conformations of MαNP esters dissolved in protic solvents. The crystal structure of MαNP ester (+)-**13b** thus strongly supports this mechanism.

Comparison of the Absolute Configurations of MαNP Esters Determined by the ^{1}H NMR Anisotropy and X-ray Crystallographic Methods

In this paper we have described the X-ray crystallographic structure determination of various MαNP esters with use of the MαNP acid moiety as the internal reference of absolute configuration. It should be emphasized that in all cases, including those of the MαNP esters possessing the so-called *anti* conformation in the crystalline state,[17–19,21] the absolute configurations determined by X-ray crystallography agree with those assigned by ^{1}H NMR spectroscopy. These results clearly indicate that MαNP esters that adopt the *anti* conformation in the crystalline state have *syn* conformations in solution. For example, although MαNP esters **8a** and **8b** in the crystalline state have the *anti* and *syn* conformations, respectively, this ester pair shows normal $\Delta\delta$ values,[17] so it can be concluded that ester **8a** has the *syn* conformation in solution. The X-ray crystallographic data thus validate the reliability of the ^{1}H NMR anisotropy method with MαNP esters.

Conclusions

X-ray crystallographic analyses of 22 MαNP esters and two MαNP acids were carried out in order to compare their conformations in crystalline and solution states. From these data it was shown that 22 conformers have the so-called *syn* structure, while five conformers have the so-called *anti* structure. In *syn* conformers, the weak bifurcated hydrogen

bond between O6–H8′–O7 was proposed as the intramolecular force stabilizing the so-called *syn* conformation. The crystalline-state conformations of MαNP esters are thus similar to those in solution as determined by ^{1}H NMR spectroscopy. X-ray crystallographic analyses of MαNP acids and of an ester indicated the presence of intermolecular bifurcated hydrogen bonds between O6–H(acid or alcohol)–O7 as another mechanism giving rise to the *syn* conformation. These mechanisms should also govern the solution conformations of MαNP esters as well.

Experimental Section

Compounds Used for X-ray Crystallography: The preparation of MαNP acid and some MαNP esters has already been reported as follows: chiral MαNP acid (+)-**1**,[18] racemic MαNP acid (±)-**1**,[18] MαNP esters (±)-**2**,[18] (–)-**5a**,[18] (–)-**6a**,[18] (–)-**7b**,[18] (+)-**8a**,[17] (–)-**8b**,[17] (–)-**9a**,[17] (+)-**12**,[19] (–)-**16b**,[20] (–)-**17a**,[18] (–)-**17b**,[18] (–)-**18a**,[18] (–)-**18b**,[18] and (–)-**21**.[19] Some MαNP esters – (+)-**3b**,[21] (+)-**4b**,[21] (+)-**10**,[22] (–)-**11**,[22] (+)-**13b**,[23] (–)-**15b**,[24] (+)-**19a**,[21] and (–)-**20a**[21] – were synthesized by us, and their preparation procedures and physical data will be published elsewhere. Single crys-

Table 4. X-ray crystallographic data for 2-methoxy-2-(1-naphthyl)propionic (MαNP) acids (+)-**1**, (±)-**1** and esters (±)-**2**, (+)-**3b**, (+)-**4b**.

Compound	(+)-**1**	(±)-**1**	(±)-**2**	(+)-**3b**	(+)-**4b**
Formula	$C_{14}H_{14}O_3$	$C_{14}H_{14}O_3$	$C_{15}H_{16}O_3$	$C_{18}H_{18}O_3$	$C_{22}H_{28}O_4$
Formula weight [amu]	230.26	230.26	244.29	282.34	356.46
Solvent	EtOAc	EtOH	EtOAc	MeOH	MeOH
Crystal dimension [mm]	0.47 × 0.42 × 0.20	0.41 × 0.30 × 0.23	0.25 × 0.20 × 0.19	0.45 × 0.40 × 0.30	0.46 × 0.25 × 0.25
Crystal system	orthorhombic	rhombohedral	monoclinic	orthorhombic	monoclinic
Space group	$P2_12_12_1$ (#19)	*R*–3 (#148)	$P2_1/c$ (#14)	$P2_12_12_1$ (#19)	$P2_1$ (#4)
a [Å]	11.171(2)	28.113(3)	8.569(1)	12.530(3)	9.499(2)
b [Å]	12.653(2)	28.113(3)	22.585(4)	12.613(3)	13.715(2)
c [Å]	8.443(2)	8.108(1)	6.961(1)	10.093(2)	8.426(2)
β [°]	–	–	104.65(1)	–	111.33(1)
V [Å^3]	1193.4(4)	5550(1)	1303.3(3)	1595.0(6)	1022.5(3)
Z	4	18	4	4	2
$D_{calcd.}$ [g cm^{-3}]	1.282	1.240	1.245	1.176	1.159
D_{obsd} [g cm^{-3}]	1.283	1.237	1.237	1.173	1.148
No. of independent reflections, $F_o > 2.0\sigma(F_o)$	1187	2097	2214	1558	1814
No. of variables	210	210	253	262	314
Goodness of fit *S*	1.20	1.14	1.053	1.096	1.107
Absolute configuration	*S*	–	–	(*S*;*R*)	(*S*;*R*)
R and R_w	0.0455 (0.1091)	0.0441 (0.1138)	0.0455 (0.1094)	0.0430 (0.1012)	0.0403 (0.0944)
Flack *χ*	–0.1(3)	–	–	–	0.0(2)

Table 5. X-ray crystallographic data for 2-methoxy-2-(1-naphthyl)propionic (MαNP) acid esters (–)-**5a**, (–)-**6a**, (–)-**7b**, (+)-**8a**, (–)-**8b**.

Compound	(–)-**5a**	(–)-**6a**	(–)-**7b**[a]	(+)-**8a**	(–)-**8b**
Formula	$C_{21}H_{26}O_3$	$C_{23}H_{30}O_3$	$C_{24}H_{32}O_3$	$C_{25}H_{28}O_4$	$C_{25}H_{28}O_4$
Formula weight [amu]	326.44	354.49	368.52	392.49	392.49
Solvent	EtOAc	MeOH	ether/MeOH	EtOH	MeOH
Crystal dimension [mm]	0.34 × 0.32 × 0.32	0.32 × 0.25 × 0.23	0.45 × 0.26 × 0.19	0.40 × 0.22 × 0.19	0.40 × 0.33 × 0.15
Crystal system	orthorhombic	orthorhombic	triclinic	orthorhombic	orthorhombic
Space group	$P2_12_12_1$ (#19)	$P2_12_12_1$ (#19)	*P*1 (#1)	$P2_12_12_1$ (#19)	$P2_12_12_1$ (#19)
a [Å]	12.362(4)	11.803(6)	10.627(5)	13.065(3)	22.810(4)
b [Å]	20.238(7)	20.959(9)	8.590(2)	21.644(5)	24.049(5)
c [Å]	7.341(2)	8.316(4)	6.336(4)	7.370(1)	7.872(2)
β [°]	–	–	86.71(4)	–	–
V [Å^3]	1837(1)	2057(2)	538.4(4)	2084.3(7)	4318(2)
Z	4	4	1	4	8
$D_{calcd.}$ [g cm^{-3}]	1.181	1.145	1.137	1.251	1.207
D_{obsd} [g cm^{-3}]	1.173	1.152	1.138	1.249	1.202
No. of independent reflections, $F_o > 2.0\sigma(F_o)$	1824	2018	2012	2054	4160
No. of variables	317	309	293	374	728
Goodness of fit *S*	1.208	1.087	1.134	1.157	1.060
Absolute configuration	(*S*;1*R*,2*R*)	(*S*;1*R*,2*S*)	(*R*;1*R*,3*R*,4*S*)	(*S*;1*S*,8a*S*)	(*S*;1*R*,8a*R*)
R and R_w	0.0594 (0.1288)	0.0988 (0.1715)	0.0723 (0.1692)	0.0436 (0.1012)	0.0429 (0.0991)
Flack *χ*	–0.2(3)	–0.1(8)	–0.1(3)	0.1(3)	0.2(2)

[a] For the triclinic of (–)-**7b**, *α* [°] = 82.33(3), *γ* [°] = 109.14(3).

tals were prepared by recrystallization from the solvents listed in Tables 4, 5, 6, 7, and 8.

X-ray Crystallography: In each case a single crystal was selected for data collection and mounted on a Mac Science MXC18 automated four-circle diffractometer: radiation, Cu-K_α (1.54178 Å); monochromator, graphite crystal. The crystal system, space group, unit cell parameters, and orientation matrix were determined. Data collection was carried out with a 2θ-θ scan: temperature, 20 °C; scan speed, 14° min^{-1}; scan range, 1.29–2.92° + 0.2° tan θ; 2θ scan limits, 2°–136°; standard reflections, 3 per 100 reflections; crystal stability, no indication of standard reflection decay during data collection. The densities of crystals were measured by flotation in CCl_4/hexane or aqueous KBr.

The structures were solved by direct methods and successive Fourier syntheses. Some hydrogen atoms were placed at the calculated positions. Full-matrix, least-squares refinement of positional and thermal parameters, including anomalous scattering factors of chlorine, silicon, fluorine, oxygen, and carbon atoms, resulted in the final convergence with R values listed in Tables 4–8. The absolute configurations of chiral compounds were determined by use of the MαNP acid moiety as the internal reference of absolute configuration. The absolute configurations obtained were also supported by the Flack parameters.

The crystallographic data for the compounds were deposited with the Cambridge Crystallographic Data Centre. CCDC-621126 for (+)-**1**, -621127 for (±)-**1**, -621128 for (±)-**2**, -621129 for (+)-**3b**, -621130 for (+)-**4b**, -621131 for (–)-**5a**, -621132 for (–)-**6a**, -621133 for (–)-**7b**, -621134 for (+)-**8a**, -621135 for (–)-**8b**, -621136 for (–)-**9a**, -621137 for (+)-**10**, -621138 for (–)-**11**, -621139 for (+)-**12**, -621140 for (+)-**13b**, -621141 for (–)-**15b**, -621142 for (–)-**16b**, -621143 for

Table 6. X-ray crystallographic data for 2-methoxy-2-(1-naphthyl)propionic (MαNP) acid esters (–)-**9a**, (+)-**10**, (–)-**11**, (+)-**12**, and (+)-**13b**.

Compound	(–)-**9a**	(+)-**10**	(–)-**11**	(+)-**12**	(+)-**13b**
Formula	$C_{31}H_{44}O_4Si$	$C_{22}H_{21}FO_3$	$C_{22}H_{20}F_2O_3$	$C_{27}H_{28}O_6$	$C_{23}H_{24}O_4$
Formula weight [amu]	508.76	352.41	370.40	448.52	364.43
Solvent	EtOH	EtOH	EtOH	MeOH	EtOH
Crystal dimension [mm]	0.34 × 0.33 × 0.32	0.33 × 0.32 × 0.30	0.35 × 0.30 × 0.22	0.27 × 0.25 × 0.10	0.30 × 0.28 × 0.24
Crystal system	orthorhombic	orthorhombic	orthorhombic	monoclinic	orthorhombic
space group	$P2_12_12_1$ (#19)	$P2_12_12_1$ (#19)	$P2_12_12_1$ (#19)	$P2_1$ (#4)	$P2_12_12_1$ (#19)
a [Å]	16.041(3)	11.408(2)	13.331(3)	18.587(3)	10.144(2)
b [Å]	22.932(4)	17.979(3)	16.957(4)	7.382(1)	26.217(6)
c [Å]	8.155(1)	9.282(2)	8.383(2)	8.612(2)	7.673(1)
β [°]	–	–	–	96.59(2)	–
V [Å^3]	2999.7(9)	1903.8(7)	1894.9(7)	1173.7(4)	2040.5(7)
Z	4	4	4	2	4
$D_{calcd.}$ [g cm^{-3}]	1.127	1.230	1.298	1.269	1.186
D_{obsd} [g cm^{-3}]	1.132	1.225	1.299	1.264	1.182
No. of independent reflections, $F_o > 2.0\sigma(F_o)$	291	1866	1856	2161	2144
No. of variables	438	319	312	410	302
Goodness of fit S	1.079	1.099	1.064	1.068	1.102
Absolute configuration	(S;1R,6R,8aR)	(R;R)	(S;S)	(R;S)	(S;R)
R and R_w	0.0616 (0.1457)	0.0606 (0.1312)	0.0606 (0.1477)	0.0323 (0.0801)	0.0541 (0.1292)
Flack χ	–0.09(6)	–0.5(3)	0.4(4)	0.3(2)	0.0(3)

Table 7. X-ray crystallographic data for 2-methoxy-2-(1-naphthyl)propionic (MαNP) acid esters (–)-**15b**, (–)-**16b**, (–)-**17a**, (–)-**17b**, (–)-**18a**.

Compound	(–)-**15b**	(–)-**16b**	(–)-**17a**	(–)-**17b**	(–)-**18a**
Formula	$C_{29}H_{34}O_3$	$C_{27}H_{23}FO_3$	$C_{28}H_{26}O_3$	$C_{28}H_{26}O_3$	$C_{27}H_{23}ClO_3$
Formula weight [amu]	430.59	414.47	410.51	410.51	430.93
Solvent	hexane/EtOAc	MeOH	EtOH	hexane/EtOAc	EtOH
Crystal dimension [mm]	0.24 × 0.21 × 0.14	0.45 × 0.39 × 0.30	0.27 × 0.22 × 0.14	0.30 × 0.25 × 0.17	0.33 × 0.24 × 0.15
Crystal system	monoclinic	orthorhombic	monoclinic	monoclinic	monoclinic
Space group	$C2$ (#5)	$P2_12_12_1$ (#19)	$P2_1$ (#4)	$P2_1$ (#4)	$P2_1$ (#4)
a [Å]	26.622(5)	10.799(2)	16.174(4)	10.177(2)	11.923(2)
b [Å]	9.255(2)	19.854(3)	8.017(2)	14.431(3)	8.539(2)
c [Å]	10.124(2)	10.236(2)	8.417(2)	8.245(1)	11.406(2)
β [°]	90.83(1)	–	92.89(2)	111.78(1)	109.05(1)
V [Å^3]	2494.0(8)	2194.5(6)	1089.9(4)	1124.5(3)	1097.7(4)
Z	4	4	2	2	2
$D_{calcd.}$ [g cm^{-3}]	1.147	1.255	1.251	1.212	1.304
D_{obsd} [g cm^{-3}]	1.144	1.258	1.246	1.217	1.302
No. of independent reflections, $F_o > 2.0\sigma(F_o)$	2278	2138	1988	1995	2007
No. of variables	414	337	384	384	372
Goodness of fit S	1.089	1.152	1.105	1.080	1.068
Absolute configuration	(S;1R,2R)	(S;S)	(S;R)	(S;S)	(S;R)
R and R_w	0.0436 (0.1023)	0.0635 (0.1383)	0.0407 (0.0853)	0.0361 (0.0843)	0.0389 (0.0990)
Flack χ	0.0(3)	–0.4(4)	–0.3(3)	0.0(2)	–0.03(2)

Table 8. X-ray crystallographic data for 2-methoxy-2-(1-naphthyl)propionic (MαNP) acid esters (–)-**18b**, (+)-**19a**, (–)-**20a**, and (–)-**21**.

Compound	(–)-**18b**	(+)-**19a**	(–)-**20a**	(–)-**21**
Formula	$C_{27}H_{23}ClO_3$	$C_{21}H_{24}O_3$	$C_{23}H_{20}O_3$	$C_{32}H_{30}O_6$
Formula weight [amu]	430.93	324.42	344.41	510.59
Solvent	EtOH	MeOH	MeOH	MeOH
Crystal dimension [mm]	$0.25 \times 0.25 \times 0.22$	$0.40 \times 0.34 \times 0.24$	$0.38 \times 0.35 \times 0.34$	$0.40 \times 0.29 \times 0.24$
Crystal system	monoclinic	orthorhombic	orthorhombic	orthorhombic
Space group	$P2_1$ (#4)	$P2_12_12_1$ (#19)	$P2_12_12_1$ (#19)	$P2_12_12_1$ (#19)
a [Å]	10.088(2)	11.376(2)	9.195(1)	12.533(2)
b [Å]	14.515(3)	18.829(4)	27.261(5)	30.675(7)
c [Å]	8.224(2)	8.640(1)	7.670(2)	7.156(1)
β [°]	111.81(1)	–	–	–
V [Å^3]	1118.1(4)	1850.8(6)	1922.7(6)	2751.2(9)
Z	2	4	4	4
$D_{calcd.}$ [g cm^{-3}]	1.280	1.164	1.190	1.233
D_{obsd} [g cm^{-3}]	1.277	1.163	1.183	1.229
No. of independent reflections, $F_o > 2.0\sigma(F_o)$	1982	1822	1895	2706
No. of variables	372	298	248	419
Goodness of fit S	1.094	1.165	1.103	1.137
Absolute configuration	(*S*;*S*)	(*S*;*S*)	(*S*;*R*)	(*S*;*S*)
R and R_w	0.0306 (0.0742)	0.0562 (0.1211)	0.0816 (0.1979)	0.0503 (0.1134)
Flack χ	–0.02(2)	–0.6(3)	–0.4(6)	–0.1(3)

(–)-**17a**, -621144 for (–)-**17b**, -621145 for (–)-**18a**, -621146 for (–)-**18b**, -621147 for (+)-**19a**, -621148 for (–)-**20a**, and -621149 for (–)-**21** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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