Molecular Geometry and Circular Dichroism Spectra of Bicyclo[2.2.1]heptane-2,3-dicarboxylic Anhydrides and Imides[1]

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Several tricyclic anhydrides and imides derived from optically active bicyclo[2.2.1]heptane-2,3-dicarboxylic acids were synthesized, and their circular dichroism spectra are reported. On the basis of MNDO calculations it was estalished that despite rigidity of the norbornane system the five-membered rings of succinic anhydride and imide moieties are slightly twisted. The chromophores are flexible and can be more or less skewed depending on solvent polarity. The chromophore nonplanarity significantly influences magnitude and sign of the first Cotton effect associated with the lowest energy n–π* electronic transition. The sign of the second n–π* Cotton effect is governed by vicinal effect of substituents. The crystal structures of three *N*-(*S*)-1-phenylethylimides were solved to establish the configuration at C-2 of the imide moieties.

Imides and anhydrides are examples of closely related isoelectronic β-dicarbonyl chromophores.[2] Their two lowest energy electronic transitions are both of n–π* character.[3–5] In imides, they can be observed as two low-intensity absorption bands at ca. 250 and 220 nm, whereas in anhydrides analogous transitions are slightly blue shifted and appear as two strongly overlapping bands approximately at 240 and 215 nm. Generally, owing to their related electronic structure, both chromophores show similar chiroptical properties. Because of the opposite symmetry of the excited states involved in the n–π* transitions, two Cotton effects (CEs) of opposite signs are expected in the circular dichroism (CD) spectra.[5,6] A deviation of the chromophore from planarity (C_{2v} symmetry) and conformational equilibria between several forms may complicate the spectra and lead to two CEs of the same sign or more than two CEs in the region of n–π* transitions. Snatzke and co-workers[4] have developed the 12-sector rule for planar and the helicity rule for twisted anhydrides. One of us has proposed a general rule for anhydrides and imides; the antioctant (the sector signs opposite to those known for ketones)[7] for the lowest n–π* excitation and the octant rule for the next n–π* transition.[5] Our recent chiroptical study on substituted succinic anhydrides and imides showed strong substituent and solvent dependence of their CD spectra.[5] Earlier, Sjöberg and Obenius[8] also observed that the CE magnitude and sign of succinic anhydrides are very sensitive to substituent size, solvent, and temperature. These results have been rationalized in terms of conformational equilibrium changes between two skewed conformers of the five-membered ring. Predictions of the CE sign with any sector rule requires differentiation between contributions from the inherent chirality of a chromophore (chiral first sphere according to the Snatzke doctrine of spheres),[9,10] the ring chirality (second sphere), and contributions arising from dissymmetrically placed substituents (third sphere). The estimation of the last type of effect is possible by studying compounds possessing planar five-membered rings and planar chromophores. We have chosen anhydrides and imides of bicyclo[2.2.1]-heptane-2,3-dicarboxylic acids and *cis*-1,2-cyclopropanedicarboxylic acids[11] as potentially good candidates for models meeting these requirements. We have expected that the ring twisting and flexibility of the succinic anhydride and imide moieties will be significantly reduced due to condensation with the rigid norbornane or cyclopropane skeleton. However, contrary to these expectations, the MNDO calculations revealed that the chromophores are slightly distorted from the C_{2v} symmetry which substantially affects the chiroptical spectra.

In this paper, we describe the synthesis and the CD spectra of tricyclic anhydrides and imides **2–7**. For comparison, we also discuss the CD of compounds **8a,b** with the extremely twisted five-membered rings.

Results and Discussion

Synthesis and Stereochemistry. Racemic anhydrides **4a** and **5a** obtained by condensation of cyclopentadiene with citraconic and phenylmaleic anhydride, respectively, were hydrolyzed to the corresponding dicarboxylic acids following the procedure of Alder et al.[12] These acids were resolved to enantiomers with cinchonine. The analogous condensation of mesacoyl chloride with cyclopentadiene, followed by hydrolysis, gave *endo*-2-methyl-*trans*-bicyclo-[2.2.1]hept-5-ene-2,3-dicarboxylic acid, which upon hydrogenation afforded *endo*-2-methyl-substituted acid **9**.[12]

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† Technical University.

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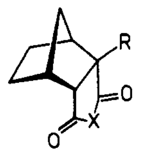
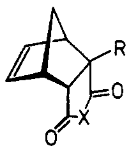
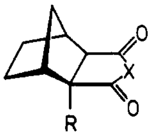


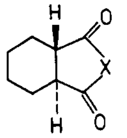
1a R = H, X = O
1b R = H, X = NH
2a R = Me, X = O
2b R = Me, X = NH
2c R = Me, X = NMe
3a R = Ph, X = O
3b R = Ph, X = NH



4a R = Me, X = O
4b R = Me, X = NH
4c R = Me, X = NMe
4d R = Me, X = N-C--H (Me, Ph)
5a R = Ph, X = O
5b R = Ph, X = N-C--H (Me, Ph)

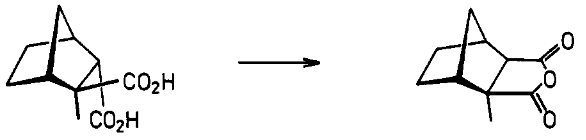


6a R = H, X = O
6b R = H, X = NH
7a R = Me, X = O
7b R = Me, X = NH
7c R = Me, X = N-C--H (Me, Ph)



8a X = O
8b X = NH

It was resolved to enantiomers with cinchonidine. A slow distillation accompanied by thermal isomerization[12] of the optically active acid **9** afforded anhydride **7a** with nearly



9 7a

quantitative yield. To establish the absolute configuration of the synthesized compounds, anhydrides **4a**, **5a**, and **7a** were converted into corresponding imides **4d**, **5b**, and **7c** with (*S*)-1-phenylethylamine. The X-ray crystallographic studies of these compounds allowed us to assign the configuration at C-2 and remaining chiral centers.

Molecular Geometry. The norbornane skeleton is symmetric and fairly rigid with well-defined molecular geometry. The succinic anhydride and imide rings are flexible and their shape depends on substitution.[5] Our primary interest was to learn about the influence of substituents on the symmetry of the succinic anhydride and imide moieties condensed with the norbornane skeletal system. We investigated the structures with the aid of the semiempirical MNDO calculations.[13] All the geometrical parameters were fully optimized at the SCF level by minimizing the energy with the Davidon–Fletcher–Powell algorithm.[14] Table I summarizes selected torsional angles within the five-membered rings. Calculations predict very similar geometries of related anhydrides and imides. Introduction of a methyl group at C-2 causes a CH_3/H eclipsing interaction which can be alleviated by a small torsion angle deformation about the C_2–C_3 bond leading to a twisting of the ring. A further consequence is a slight deviation of the chromophore from planarity.[15] The 2-*endo*-methyl substituent in **7a,b** brings about stronger deformations of the system than the 2-*exo*-one does in **2a,b**. The *N*-methyl group in **2c** enhances nonplanarity of the imide system due to the steric interaction with the neighboring carbonyl oxygens. All calculated deviations of the systems from the symmetry are very small, but in fact, they can be stronger in solution because the MNDO method often underestimates the five-membered ring deformations.[16]

There are several crystal structures of related tricyclic anhydrides known which show small deviations of the anhydride ring from planarity.[17,18] The X-ray structures of N-substituted imides **4d**, **5b**, and **7c** also reveal the ring twisting, direction, and magnitude of which is similar to that calculated by MNDO for structurally related compounds. The imide group appears to be nearly planar in **4d** and **7c**, whereas it is significantly distorted from planarity in both conformers of **5b** present in the crystal state. The strained derivatives of *trans*-1,2-cyclohexanedicarboxylic acid **8a,b** are examples of strongly twisted five-membered rings and chromophores. The calculated geometry of imide **8b** is in good agreement with the structure assigned by the X-ray diffraction.[19]

The calculations show that, despite steric constraints imposed by the tricyclic skeleton in symmetric compounds **6a,b**, the chromophore twisting to ±175° (in terms of the C—O—C═O or C—N—C═O torsional angle) increases the energy of molecule only about 0.5 kcal/mol. Similarly, the increase or decrease of the chromophore twisting in bicyclic compounds **8a,b** by 5° affords only modest enhancements (0.5 kcal/mol) in heat of formation (see supplementary material). Such small energy changes can be indcued by solvational or temperature effects. Bodot and co-workers, on the basis of MNDO calculations, reported also very flat potential energy surfaces around the energy minimum for the anhydride moiety and concluded that deviations from the planar conformation look very easy.[17]

Circular Dichroism. The CD data of the title compounds are given in Table II. Provided the succinic anhydride and imide moieties are planar and because the norbornane skeleton itself is symmetric, the only source of chirality in these molecules is the substituent at C-2. The octant projection shows this group in the upper right (or lower left) sector [cf. **7a,b** (Figure 1a)]. This should lead to a sequence of positive and negative CEs corresponding to the lower and higher energy n–π^* transitions, respectively. Fairly consistent examples of this type of behavior are compounds **3a** and **3b** showing two intense

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[15] The calculations show that the degree of the chromophore twisting depends on the bulkiness of a substituent at C-2; i.e., the dihedral angles O═C—O—C calculated for 2-*tert*-butyl-*endo*,*endo*-bicyclo[2.2.1]heptane-2,3-dicarboxylic anhydride are 174.76 and 176.9°, and for corresponding imide the dihedral angles O═C—N—C are 173.85 and 177.82° (cf. the data for **1a,b** and **2a,b** in Table I).

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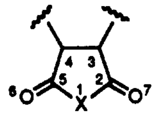
Table I. Selected Torsional Angles and Heats of Formation Calculated by MNDO



compd	(2-3-4-5)	(1-2-3-4)	(1-5-4-3)	(2-1-5-6)	(5-1-2-7)	H_f (kcal/mol)
1a	0.23	−1.50	1.10	179.56	−179.67	−110.71650
1b	−0.13	−1.25	1.47	179.44	−179.58	−73.40557
2a	−4.69	5.47	2.80	178.95	177.44	−109.61911
2b	−4.65	5.42	2.41	179.51	177.18	−71.83236
2c	−4.51	6.08	1.58	−179.41	175.70	−69.81792
6a	0.12	−1.45	1.24	179.07	−178.96	−112.41136
6b	0.24	−1.78	1.38	178.75	−178.51	−74.94187
7a	−6.35	7.00	4.23	179.17	175.67	−110.35132
7b	−6.22	7.15	3.23	179.93	175.09	−72.44125
8a	−29.92	25.76	26.37	171.22	172.15	−127.51306
8b	−29.82	24.65	24.97	172.09	172.55	−90.76817
8b[a]	(−29.70)	(25.59)	(24.32)	(175.02)	(172.89)	

[a] The X-ray structure.[19]

Table II. CD Data of Anhydrides and Imides

compd	solv[a]	λ, nm ($10^{-3}[\theta]^b$)[c]	compd	solv[a]	λ, nm ($10^{-3}[\theta]^b$)[c]
2a	CD	242 (0.45), 219 (−1.39)	**2b**	CD	251 (−0.92), 230 (−2.58)
	A	239 (0.97), 217 (−1.43)		A	267 (−0.17), 226 (−2.73)
2c	C	255 (−1.88), 231 (−3.07)		M	246sh (−0.44), 228 (−2.57)
	A	252 (−1.16), 229 (−2.98)		H_2O	245sh (−0.50), 226 (−2.49)
	M	251 (−1.07), 228 (−2.86)		HFP	252 (0.41), 224 (−2.62)
	HFP	243sh (−0.57), 225 (−2.95)	**3b**	CD	257 (12.83), 225 (−11.32)
3a	CD	267 (0.26), 239 (15.62), 221 (−15.62)		M	254 (13.54), 226 (−10.00)
	A	267 (0.29), 238 (22.36), 221 (−10.89)		HFP	251 (14.43), 229 (−3.57)
4a	CD	229 (−1.53)	**4b**	CD	256 (−0.59), 230 (−2.40)
	A	243 (0.28)		M	250 (−0.58), 228 (−1.50)
4c	C	255 (−2.83), 230 (−3.03)		HFP	242 (1.91), 218 (−2.11)
	HFP	244 (0.98)	**7b**	CD	257 (−2.36), 229 (−2.02)
5a	CD	268 (0.25), 239 (13.53), 223 (−15.10)		A	256 (−1.71), 228 (−2.29)
7a	CD	233sh (−0.87), 219 (−1.94)		M	254 (−1.48), 227 (−1.92)
	A	255 (−0.09), 233 (0.06), 218 (−2.01)		H_2O	252 (−1.65), 224 (−1.97)
8a[d]	C	245 (2.72), 212 (−1.10)		HFP	248 (−0.59), 217 (−2.73)
	A	242 (2.11), 211 (−1.84)	**8b**[d]	CD	270 (−0.41), 262 (0.03), 232 (−4.61)
				HFP	244 (−3.93), 226 (−4.43)

[a] Key: C, cyclohexane; CD, cyclohexane–dioxane (9:1); A, acetonitrile, M, methanol, HFP, 1,1,1,3,3,3-hexafluoro-2-propanol. [b] Molar ellipticity in deg cm^2/dmol. [c] The highest intensity vibronic band. [d] Data from ref 5.

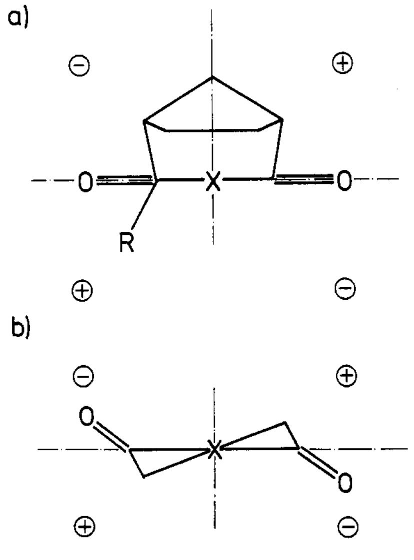


Figure 1. Octant projection of (a) compounds **2** and **3** and (b) the twisted five-membered ring in **8**.

and oppositely signed CEs (Figure 2). The strong magnitude of the CEs results from homoconjugation of the phenyl substituent with the imide and anhydride groups and is characteristic for β,γ-unsaturated carbonyl compounds.[20] The anhydride **3a** (also **5a**) exhibits an additional weak and vibronically structured CD band at 267 nm, which unequivocally can be assigned to the phenyl ^1L_b transition. An analogous band in the imide **3b** spectrum is buried under the much stronger n–π* maximum.

As predicted by the sector rule the methyl-substituted anhydrides and imides **2a,b** and **7a,b** exhibit a negative CE in the region of the second (higher energy) n–π* transition. Its magnitude is largely solvent invariant. Surprisingly, a magnitude of the first CE strongly depends on solvent polarity. Moreover, in some cases the CE sign is negative, i.e., the opposite to that expected. For example, imide **2b** (Figure 3), in spite of a positive contribution from the *exo*-methyl group, shows a weak negative CD at 250 nm in cyclohexane; its intensity gradually decreases in polar solvents and finally reaches a positive value in the strongly polar 1,1,1,3,3,3-hexafluoro-2-propanol (HFP). The long-wavelength CD of *N*-methylimide **2c** is much stronger than that in **2b** and remains negative even in the HFP solution. An analogous trend is found in the CD spectra of **7b**.

The sign reversal of the first CE in **2b,c** and **7a,b** is probably caused by an additional contribution to the CE, which overweighs that of the 2-methyl substituent. According to the MNDO calculations the succinic anhydride and imide molecular fragments are not planar; the five-

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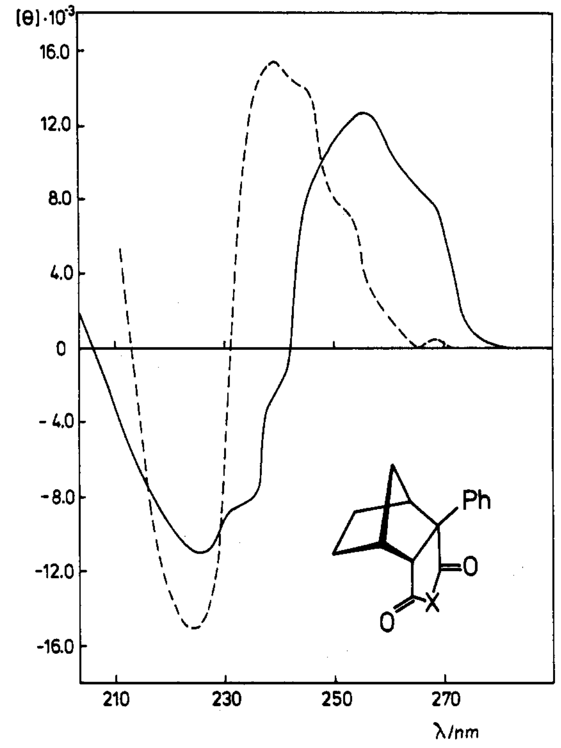

Figure 2. CD spectra of anhydride **3a** and imide **3b** (broken and solid line, respectively) in cyclohexane–dioxane (9:1).

membered rings are slightly twisted, and also the chromophores show small distorsions from planarity. However, the ring twisting alone cannot be responsible for the negative CD since it contributes with the same sign as the C-2 substituent does. Therefore, a contribution from the nonplanar and thus inherently chiral chromophore must be the source of observed anomalies. A perfect model of imide with the twisted chromophore the CD of which, we believe, helps in understanding of the above effect is **8b**. Its geometry is well established,[19] and one of us reported its CD earlier but without offering a complete explanation.[5] The CD curve of the imide **8b** has an appearance similar to those of compounds **2b** and **7b**; i.e., it consists of two overlapping CEs with the negative signs. A contribution from the extremely twisted five-membered ring (Figure 2b) should lead to a sequence of positive and negative CEs at longer and shorter wavelengths, respectively (cf., anhydride **8a**). However, the observed long-wavelength CE sign reversal must be caused by the chiral imide group, the effect of which prevails over the oppositely signed ring contribution. Based solely on the experiment we may conclude that the chromophore twisted in the P-sense (as in **8b**) contributes with a negative sign to the lowest energy n–π* CE. Thus, we can associate the anomalies observed in the CD spectra of imides **2b** and **7b** with a distorsion of the imide group from planarity. In both cases MNDO predicts P-chirality of the chromophore, which contributes with a negative sign and overweighs a weak positive contribution from the methyl substituent. As a result, we observe double-humped CD curves instead of bisignate ones. Solvation may influence the degree of the chromophore twisting, and this is reflected in significant solvent dependence of the long-wavelength CE. In polar solvents with high dielectric constants the chromophore is nearly planar due to decreased dipole–dipole interaction within the imide or anhydride group, and thus the CD signs are determined by vicinal effects of the substituents. On the contrary, N-methylation of the imide group increases the degree of twisting and thus enhances the negative CE (cf. **2c**). Vicinal effects of strong perturbers, like the phenyl group in compounds **3a,b**, overweigh a relatively weak effect of the slightly twisted chromophore causing observed strong and consignate[21] CEs.

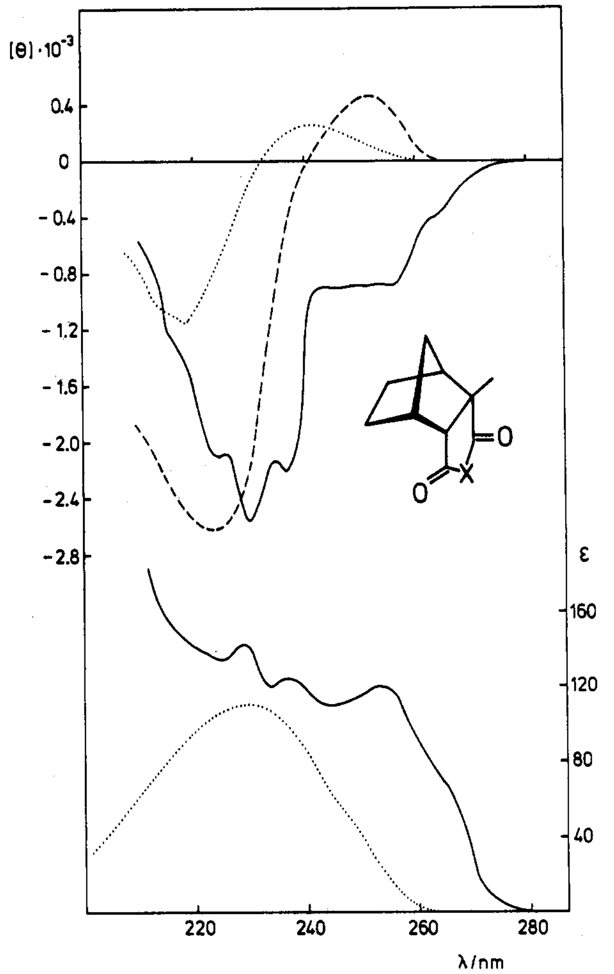

Figure 3. CD and UV spectra of anhydride **2a** and imide **2b** in cyclohexane–dioxane (9:1) and **2b** in HFP (dotted, solid, and broken line, respectively).

There are some unusual solvent and temperature effects reported for methyl-substituted adamantanones[22a,b] and adamantanethiones,[22c] which were difficult to explain considering the rigidity of the adamantanone skeleton. These results may be related in some respect to ours; we believe that also in these compounds small geometry changes are possible and they may be responsible for solvent and temperature dependence of the CD, especially in the case of weak CEs. This, in fact, has been suggested earlier by Djerassi and co-workers.[23]

It is noteworthy that chiroptical methods are extremely sensitive to small geometry changes, which cannot be detected by other spectroscopic techniques. For instance, comparison of the $^{13}C{=}O$ chemical shifts for **1a** and **8a** and similarly for **1b** and **8b** (supplementary material) shows only very small differences (ca. 2 ppm) despite

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significant structural differences (i.e., the planar and strongly twisted chromophores).

In contrast to imides, there are fewer anomalies among the anhydride spectra; their CD seems to be less influenced by the chromophore nonplanarity (e.g., **2a** and **8a**). However, due to the relative chromophore flexibility their CE magnitudes are affected by solvent polarity.

The contribution of the chromophore chirality to the second, higher energy $n-\pi^*$ transition of imides and anhydrides is rather negligible; the CE intensity is almost independent of solvent polarity and does not change upon N-methylation of the imide group. The CE sign is, first of all, governed by vicinal effects of substituents, and then it can be considered as diagnostic for configurational predictions.

In conclusion, the title imides and anhydrides, despite their tricyclic structure, are not completely rigid. The most flexible part of the molecules appears to be the chromophore. Its nonplanarity, though minute, cannot be ignored since it often significantly affects the magnitude and sign of the CE associated with the lowest energy $n-\pi^*$ transition.

Experimental Section

CD spectra were recorded on a JASCO J-20 spectropolarimeter. UV measurements were performed on a Beckman 3600 spectrophotometer. ^{1}H and ^{13}C NMR spectra were determined with a Bruker MSL-300 spectrometer operating at 300 and 50 MHz, respectively, in $CDCl_3$ unless otherwise indicated. IR absorptions were taken with a Zeiss UR-10 spectrophotometer in CCl_4. Compounds **1a,b** were obtained according to the literature methods,[24] and the preparation of compounds **8a,b** was described earlier.[5] The optical purity of anhydrides **4a**, **5a**, and **7a** was determined from the ^{1}H NMR studies of corresponding *N*-(*S*)-1-phenylethylimides **4d**, **5b**, and **7c**. The derivatives prepared from racemic anhydrides showed two singlets corresponding to the 2-Me group (compounds **4d** and **7c**) and two doublets corresponding to the methyl from the 1-phenylethyl residue (imide **5b**), whereas the imides obtained from the optically active anhydrides exhibited one singlet and one doublet, respectively. The spectra were measured for crude compounds, prior to crystallization. These results mean that the anhydrides **4a**, **5a**, and **7a**, being key intermediates for preparation of other optically active compounds, were nearly optically pure.

(1*R*)-2-Methyl-*endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic Acid. The resolution of the racemic acid[12] with cinchonidine (two crystallizations of monosalt from 85% EtOH) gave levorotatory acid: mp 140–141 °C (from $CHCl_3$–hexane) [lit.[12] mp 139 °C (racemate)]; $[\alpha]^{22}_{578}$ −11° (*c* 3, $CHCl_3$); ^{1}H NMR (acetone-d_6) δ 9.67 (br s, 2 H, CO_2H), 6.39 and 6.28 (m, 2 H, $CH{=}CH$), 3.12 (m, 1 H), 2.94 (d, J = 3.0 Hz, 1 H, 3-*H*), 2.91 (m, 1 H), 1.79 (m, 1 H), 1.77 (s, 3 H, Me), 1.54 (m, 1 H).

(1*R*)-1-Methyl-*endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic Anhydride (4a). The above acid (0.45 g) was refluxed with acetyl chloride (5 mL) for 0.5 h, after which the mixture was evaporated to dryness and the residue crystallized upon addition of hexane to give the title product: mp 139 °C [lit.[25] mp 143–144 °C (racemate)]; $[\alpha]^{22}_{546}$ +3.4° (*c* 5, C_6H_6); $[\alpha]^{22}_{578}$ +2.9° (*c* 5 in C_6H_6); IR ν 1850, 1780 cm^{-1}; ^{1}H NMR δ 6.36, 6.27 (m, 2 H, $CH{=}CH$), 3.44 (m, 1 H), 3.10 (d, J = 2.1 Hz, 1 H, 3-*H*), 3.01 (m, 1 H), 1.81 (m, 2 H, 7-H_2), 1.60 (s, 3 H, Me); ^{13}C NMR δ 174.85 (CO), 170.86 (CO), 137.29, 135.25, 53.79 (C-2), 53.47 (C-3), 52.01, 50.67, 46.69 (C-7), 21.35 (Me).

(1*R*)-2-Methyl-*endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide (4b). Gaseous ammonia was passed over a solution of the anhydride **4a** (1.0 g) dissolved in benzene (10 mL), after which the solvent was evaporated and the residue was heated at 180 °C until it became liquid (ca. 10 min). The crude product was dissolved in carbon tetrachloride, decolorized with silica gel, evaporated to dryness, and crystallized from toluene–hexane to give **4b** (0.65 g): mp 191 °C; $[\alpha]^{22}_{D}$ −48.3° (*c* 3, $CHCl_3$); IR 3410, 3210 br, 1775, 1735, 1720, 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.65 (br s, 1 H, NH), 6.24 and 6.13 (m, 2 H, $CH{=}CH$), 3.35 (m, 1 H), 2.87 (m, 1 H), 2.83 (d, J = 4.5 Hz, 1 H, 3-*H*), 1.74 (m, 2 H, 7-H_2), 1.49 (s, 3 H, Me); ^{13}C NMR δ 181.74 (CO), 177.97 (CO), 136.55, 134.20, 54.22 (C-3), 53.01 (C-2), 50.63, 50.20, 45.48 (C-7), 21.08 (Me).

Anal. Calcd for $C_{10}H_{11}NO_2$ (177): C, 67.78; H, 6.26; N, 7.90. Found: C, 67.55; H, 6.38; N, 7.77.

(1*R*)-*N*-Methyl-2-methyl-*endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide (4c). The anhydride **4a** (0.5 g) was dissolved in a 10% ethanolic solution of methylamine (5 mL), and then the ethanol was evaporated and the procedure continued as for compound **4b** to obtain imide **4c**: mp 120 °C (from hexane); $[\alpha]^{23}_{D}$ −36.7° (*c* 1, MeOH); IR ν 1770, 1705 cm^{-1}; ^{1}H NMR δ 6.12 and 6.02 (m, 2 H, $CH{=}CH$), 3.29 (m, 1 H), 2.86 (m, 1 H), 2.79 (d, 1 H, 3-*H*), 2.77 (s, 3 H, NMe), 1.72 (m, 2 H, 7-H_2), 1.46 (s, 3 H, Me); ^{13}C NMR δ 180.85 (CO), 177.23 (CO), 136.37, 133.97, 52.96 (C-3), 51.50 (C-2), 50.50, 50.08, 45.40 (C-7), 24.06 (NMe), 21.13 (Me).

Anal. Calcd for $C_{11}H_{13}NO_2$ (191): C, 69.09; H, 6.85; N, 7.32. Found: C, 69.17; H, 6.85; N, 7.34.

(1*R*)-*N*-[(*S*)-1-Phenylethyl]-2-methyl-*endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide (4d). The anhydride **3a** (0.4 g) and (*S*)-1-phenylethylamine (0.6 mL) were refluxed in benzene (5 mL) for 12 h. The reaction mixture was washed with diluted hydrochloric acid, dried ($MgSO_4$), and evaporated to dryness. The residue was refluxed with acetyl chloride (3 mL) for 2 h, evaporated, dissolved in benzene, and washed with aqueous $NaHCO_3$. The organic layer was dried ($MgSO_4$) and evaporated to dryness, and the resulting oil was crystallized from hexane to give **4d**: mp 103 °C; $[\alpha]^{22}_{D}$ −44.3° (*c* 1.9, C_6H_6); IR ν 1765, 1700 cm^{-1}; ^{1}H NMR δ 7.37–7.23 (m, 5 H, Ph), 6.08 and 5.76 (m, 2 H, $CH{=}CH$), 5.24 (q, J = 7.3 Hz, 1 H, C*H*CH_3), 3.28 (m, 1 H), 2.88 (m, 1 H), 2.74 (d, J = 4.5 Hz, 1 H, 3-*H*), 1.70 (d, J = 7.3 Hz, 3 H, CHC*H*$_3$), 1.76–1.65 (m, 2 H), 1.45 (s, 3 H, Me).

Anal. Calcd for $C_{18}H_{19}NO_2$ (281): C, 76.84; H, 6.81; N, 4.98. Found: C, 76.59; H, 6.78; N, 4.89.

(1*S*)-2-Methyl-*endo,endo*-bicyclo[2.2.1]heptane-2,3-dicarboxylic Anhydride (2a). The anhydride **4a** (1.0 g) was hydrogenated in ethyl acetate (20 mL) in the presence of 10% palladium on charcoal (0.1 g). The product was crystallized from toluene–hexane and had mp 132 °C [lit.[25] mp 133 °C (racemate)]; $[\alpha]^{22}_{D}$ +33.4° (*c* 2, C_6H_6); IR ν 1850, 1780 cm^{-1}; ^{1}H NMR δ 2.91 (dd, J = 1.2 and 5.4 Hz, 1 H, 3-*H*), 2.79 (m, 1 H), 2.39 (m, 1 H), 1.82–1.35 (complex m, 6 H), 1.39 (s, 3 H, Me); ^{13}C NMR δ 175.71 (CO), 171.64 (CO), 56.20 (C-3), 55.34 (C-2), 46.54 (C-7), 40.78, 39.90, 25.47, 24.18, 22.35 (Me).

(1*S*)-2-Methyl-*endo,endo*-bicyclo[2.2.1]heptane-2,3-dicarboximide (2b) was obtained by hydrogenation of imide **4b** in ethyl acetate in the presence of 10% palladium on charcoal and had mp 182–183 °C (from toluene–hexane): $[\alpha]^{22}_{546}$ −20.6° (*c* 4, $CHCl_3$); $[\alpha]^{22}_{578}$ −18.0° (*c* 4, $CHCl_3$); IR ν 3415, 3200 br, 1775, 1725, 1710 cm^{-1}; ^{1}H NMR δ 9.19 (br s, 1 H, NH), 2.65 (m, 1 H), 2.60 (dd, J = 1.3 and 5.3 Hz, 1 H, 3-*H*), 2.25 (m, 1 H), 1.75–1.0 (complex m, 6 H), 1.26 (s, 3 H, Me); ^{13}C NMR δ 182.65 (CO), 178.84 (CO), 56.90 (C-3), 54.54 (C-2), 45.19 (C-7), 39.64, 39.55, 25.27, 23.79, 22.04 (Me).

Anal. Calcd for $C_{10}H_{13}NO_2$ (179): C, 67.02; H, 7.31; N, 7.82. Found: C, 67.08; H, 7.56; N, 7.71.

(1*S*)-*N*-Methyl-2-methyl-*endo,endo*-bicyclo[2.2.1]heptane-2,3-dicarboximide (2c). Hydrogenation of imide **4c** following the procedure for compound **2b** gave imide **2c**: mp 104–105 °C (from hexane); $[\alpha]^{23}_{D}$ +19.8° (*c* 2.4, C_6H_6); IR ν 1770, 1705 cm^{-1}; ^{1}H NMR 2.90 (s, 3 H, NMe), 2.69 (m, 1 H), 2.59 (dd, J = 1.4 and 5.2 Hz, 1 H, 3-*H*), 2.29 (m, 1 H), 1.8–1.0 (complex m, 6 H), 1.26 (s, 3 H, Me); ^{13}C NMR δ 181.51 (CO), 177.84 (CO), 55.86 (C-3), 53.26 (C-2), 45.15 (C-7), 39.65, 39.55, 25.26, 24.09 (NMe), 23.78, 22.17 (Me).

Anal. Calcd for $C_{11}H_{15}NO_2$ (193): C, 68.37; H, 7.82; N, 7.25. Found: C, 68.30; H, 7.85; N, 7.43.

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Resolution of 2-Phenyl-*endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic Acid. The resolution of racemic acid[12,26] with cinchonine (two crystallizations of the monosalt from acetone) gave the levorotatory acid: mp 166–167 °C [lit.[12] mp 172–174 °C (racemate)]; $[\alpha]^{22}_{D}$ −87.4° (*c* 0.5, acetone); ^{1}H NMR (acetone-d_6) δ 7.90 and 7.40 (m, 5 H, Ph), 6.53 and 6.26 (m, 2 H, CH=CH), 3.80 (m, 1 H), 3.30 (d, 1 H, 3-*H*), 3.08 (m, 1 H), 1.42 (m, 2 H, 7-H_2). The crude dextrorotatory acid isolated from the mother liquor from the above crystallization. It was purified by crystallization of its quinine monosalt from acetone to obtain the (+)-enantiomer: mp 166–167 °C; $[\alpha]^{22}_{D}$ +86.0° (*c* 0.5, acetone).

(1*R*)-2-Phenyl-*endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride (5a) was obtained from the above (+)-acid in a manner similar to compound **2a** and had mp 68 °C (from toluene–hexane): $[\alpha]^{22}_{D}$ +156° (*c* 0.4, C_6H_6); IR ν 1860, 1780 cm^{-1}; ^{1}H NMR δ 7.6–7.3 (m, 5 H, Ph), 6.46 and 6.39 (m, 2 H, CH=CH), 3.88 (d, *J* = 4.8 Hz, 1 H, 3-*H*), 3.61 (m, 1 H), 3.55 (m, 1 H), 1.80–1.68 (m, 2 H, 7-H_2); ^{13}C NMR δ 172.60 (CO), 170.70 (CO), 137.28, 136.94, 136.35, 129.19, 128.42, 126.93, 62.62 (C-2), 53.46, 52.62, 50.96, 46.92 (C-7).

Anal. Calcd for $C_{15}H_{12}O_3$ (240): C, 74.99; H, 5.03. Found: C, 74.85; H, 4.94.

(1*R*)-*N*-[(*S*)-1-Phenylethyl]-2-phenyl-*endo,endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide (5b) was obtained in a manner similar to compound **4d** and had mp 103 °C (from hexane): $[\alpha]^{20}_{D}$ +19.4° (*c* 1.36, CCl_4); IR ν 1765, 1700 cm^{-1}; ^{1}H NMR δ 7.47–7.22 (m, 10 H, Ph), 6.20 and 5.91 (m, 2 H, CH=CH), 5.28 (q, 1 H, *J* = 7.3 Hz, C*H*CH$_3$), 3.59 (m, 1 H), 3.49 (d, *J* = 4.7 Hz, 1 H, 3-*H*), 3.40 (m, 1 H), 1.74 (d, 3 H, *J* = 7.3 Hz, CHC*H*$_3$), 1.70–1.65 (m, 2 H, 7-H_2).

Anal. Calcd for $C_{23}H_{21}NO_2$ (343): C, 80.44; H, 6.16; N, 4.08. Found: C, 80.36; H, 5.99; N, 3.89.

(1*S*)-2-Phenyl-*endo,endo*-bicyclo[2.2.1]heptane-2,3-dicarboxylic anhydride (3a) was obtained by hydrogenation of compound **5a** in ethyl acetate in the presence of 10% palladium on charcoal and had mp 69 °C (from toluene–hexane): $[\alpha]^{20}_{D}$ +162.5° (*c* 0.3, C_6H_6); IR ν 1855, 1780 cm^{-1}; ^{1}H NMR δ 7.45–7.32 (m, 5 H, Ph), 3.76 (dd, *J* = 1.3 and 5.6 Hz, 1 H, 3-*H*), 3.07 (m, 1 H), 2.96 (m, 1 H), 1.9–1.5 (m, 6 H); ^{13}C NMR δ 173.39 (CO), 171.41 (CO), 137.23, 129.02, 128.16, 126.24, 63.50 (C-2), 54.81 (C-3), 47.59 (C-7), 41.06, 40.15, 25.55, 24.84.

Anal. Calcd for $C_{15}H_{14}O_3$ (242): C, 74.36; H, 5.82. Found: C, 74.02; H, 6.10.

(1*S*)-2-Phenyl-*endo,endo*-bicyclo[2.2.1]heptane-2,3-dicarboximide (3b) was obtained in a manner similar to compound **2b** and had mp 124–126 °C (from toluene–hexane): $[\alpha]^{25}_{D}$ +180° (*c* 0.2, $CHCl_3$); IR ν 3420, 1770, 1730 cm^{-1}; ^{1}H NMR δ 8.59 (br s, 1 H, NH), 7.48–7.24 (m, 5 H, Ph), 3.50 (dd, *J* = 1.2 and 5.6 Hz, 1 H, 3-*H*), 3.06 (m, 1 H), 2.87 (m, 1 H), 1.82–1.47 (m, 6 H); ^{13}C NMR δ 179.73 (CO), 178.22 (CO), 138.22, 128.83, 127.63, 126.41, 62.96 (C-2), 55.98 (C-3), 45.65 (C-7), 40.22, 40.00, 25.47, 24.67.

Anal. Calcd for $C_{15}H_{15}NO_2$ (241): C, 74.67; H, 6.27; N, 5.80. Found: C, 74.39; H, 6.18; N, 5.66.

(1*R*)-2-Methyl-*exo,exo*-bicyclo[2.2.1]heptane-2,3-dicarboxylic Anhydride (7a). The resolution of racemic *endo*-2-methyl-*exo,endo*-2,3-bicyclo[2.2.1]heptanedicarboxylic acid, obtained according to the procedure of Alder et al.[12] and purified by crystallization from ethyl acetate, was resolved with cinchonidine (three crystallizations of monosalt from 90% ethanol) to give dextrorotatory acid: mp 212–214 °C (from ethyl acetate) (lit.[12] racemate mp 191–192 °C); $[\alpha]^{22}_{D}$ +62.3° (*c* 3, acetone); ^{1}H NMR (acetone-d_6) δ 3.66 (dd, *J* = 1.5 and 6.1 Hz, 1 H, 3-H), 2.65 (m, 2 H), 2.07 (m, 1 H), 1.86 (m, 1 H), 1.65–1.40 (complex m, 4 H), 1.47 (s, 3 H, Me). A slow dry distillation of the above acid (1.3 g) gave crude anhydride **7a** (1.21 g), which was purified by crystallization from toluene–hexane to obtain pure **7a** (0.82 g): mp 115–117 °C (lit.[12] racemate mp 140 °C); $[\alpha]^{22}_{546}$ +28.8 ° (*c* 4, C_6H_6); $[\alpha]^{22}_{578}$ +25.3° (*c* 4, C_6H_6); IR ν 1850, 1780 cm^{-1}; ^{1}H NMR δ 2.77 (d, *J* = 4.4 Hz, 1 H), 2.59 (d, *J* = 4.0 Hz, 1 H), 2.38 (s, 1 H, 3-*H*), 1.82–1.25 (complex m, 6 H), 1.41 (s, 3 H, Me); ^{13}C NMR δ 177.15 (CO), 172.51 (CO), 55.06 (C-3), 51.89 (C-2), 44.75, 42.29, 36.16 (C-7), 27.04, 22.23, 17.71 (Me).

Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.63; H, 7.07.

(1*R*)-2-Methyl-*exo,exo*-bicyclo[2.2.1]heptane-2,3-dicarboximide (7b) was obtained in a similar manner to compound **4b** and had mp 123–125 °C (from toluene–hexane); $[\alpha]^{22}_{546}$ −20.8° (*c* 4, MeOH); $[\alpha]^{22}_{578}$ −17.8° (*c* 4, MeOH); IR ν 3415, 3200 br, 1775, 1725, 1710 cm^{-1}; ^{1}H NMR δ 8.87 (br, 1 H, NH), 2.67 (d, *J* = 4.0 Hz, 1 H), 2.44 (d, *J* = 3.9 Hz, 1 H), 2.11 (s, 1 H, 3-*H*), 1.78–1.25 (m, 6 H), 1.29 (s, 3 H, Me); ^{13}C NMR δ 183.68 (CO), 179.22 (CO), 54.74 (C-3), 51.84 (C-2), 43.32, 41.10, 35.41 (C-7), 27.59, 22.72, 17.75 (Me).

Anal. Calcd for $C_{10}H_{13}NO_2$ (179): C, 67.02; H, 7.31; N, 7.82. Found: C, 67.10; H, 7.22; N, 7.98.

(1*S*)-*N*-[(*S*)-1-Phenylethyl]-2-methyl-*exo,exo*-bicyclo[2.2.1]heptane-2,3-dicarboximide (7c) was obtained in a similar manner to compound **4d** and had mp 63 °C (from hexane): $[\alpha]^{20}_{D}$ −67.3° (*c* 0.6, CCl_4); IR ν 1765, 1700 cm^{-1}; ^{1}H NMR δ 7.43–7.24 (m, 10 H, Ph), 2.16 (q, *J* = 7.3 Hz, 1 H, CHCH$_3$), 2.54 (d, *J* = 4.1 Hz, 1 H), 2.41 (d, *J* = 3.7 Hz, 1 H), 2.02 (s, 1 H, 3-*H*), 1.79 (d, *J* = 7.3 Hz, 3 H, CHC*H*$_3$), 1.7–1.0 (complex m, 6 H), 1.20 (m, 3 H, Me).

Anal. Calcd for $C_{18}H_{21}NO_2$ (283): C, 76.30; H, 7.47; N, 4.94. Found: C, 76.55; H, 7.45; N, 4.87.

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Supplementary Material Available: PLUTO drawings of the X-ray structures of **4b**, **5b**, and **7c**, ^{1}H and ^{13}C NMR data of **1a,b** and **8a,b**, and torsional angle dependence of heats of formation for **6a,b** and **8a,b** (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information. The authors have deposited atomic coordinates of **4b**, **5b**, and **7c** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1E2, UK.

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