Chiroptical Properties of 1,2-Cyclopropanedicarboxylic Anhydrides and Imides. The Cyclopropane Ring Contribution to the Cotton Effect[1]

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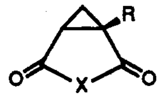
Several optically active 1,2-cyclopropanedicarboxylic anhydrides and imides were prepared and their chiroptical spectra studied. Despite the strained bicyclic skeleton of these compounds, their CD spectra show an unusual solvent dependence. This phenomenon can be explained in terms of the cyclopropane ring contribution to the Cotton effect. A deviation of the skeleton and the anhydride or imide group from the local C_s symmetry, shown by MNDO calculations, causes formation of an inherently chiral chromophore constituted by the three-membered ring and neighboring carbonyls. This kind of chromophore is responsible for the observed strong Cotton effects.

The five-membered ring of substituted succinic anhydrides and imides can be substantially deviated from planarity as it was shown by molecular mechanics calculations,[2,3] X-ray,[4] and electron diffraction studies.[5] The flexibility of the ring is reflected in strong substituent, solvent, and temperature dependence of the circular dichroism (CD) spectra.[2,6,7] The shape of the CD curves depends on the position of equilibrium between two twisted ring conformers. Since the use of conformationally rigid compounds greatly simplifies analysis of the CD spectra, we prepared several bi- and tricyclic anhydrides and imides and studied their chiroptical properties.[8] This paper deals with derivatives of *cis*-1,2-cyclopropanedicarboxylic acids **2–4**. We expected the 3-oxa- and 3-azabicyclo[3.1.0]hexane skeletons to have very little conformational flexibility and the succinic anhydride and imide moieties to be nearly planar due to steric constraints imposed by the cyclopropane ring. The C_s symmetry of these systems precludes contribution of the three-membered ring to the Cotton effect (CE) and thus the substituent at C-1 should be the only dissymmetric perturber. However, the results revealed that dissymmetrically placed substituents together with solvational effects can cause slight distortions of the systems from symmetry, inducing new contributions to the CE. These facts obviously complicate interpretation of the spectra and make careful examintion of molecular geometry extremely important. For this reason we performed MNDO calculations of the optimized molecular geometries and determined crystal structures of two imides.



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 = Pr^i, X = O
3b R = Pr^i, X = NH
3c R = Pr^i, X = NMe
4a R = Ph, X = O
4b R = Ph, X = NH
4c R = Ph, X = NMe

Results and Discussion

Synthesis of Stereochemistry. Anhydrides and imides **2–4** were obtained from corresponding 1-substituted *cis*-1,2-cyclopropanedicarboxylic acids. The racemic acids were prepared according to the McCoy's procedure.[9] The absolute configurations of the optically active 1-isopropyl- and 1-phenyl-substituted acids were already known.[10–12] 1-Methyl-*cis*-1,2-cyclopropanedicarboxylic acid (**5**) was resolved to enantiomers with brucine. Its configuration was established by the chemical correlation with trimethyl 1-methyl-1,2,2-cyclopropanetricarboxylate (−)-**7** of known absolute configuration[13] (Scheme I). Acid (−)-**6** resolved with brucine and esterified with CH_2N_2 gave ester (−)-**7** and upon thermal decarboxylation afforded anhydride (−)-**2a**, which was hydrolyzed to acid (+)-**5**.[14]

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[2] Połoński, T. *J. Chem. Soc., Perkin Trans. 1*, **1988**, 629.

[3] Ivanov, P. M.; Pojarlieff, I. G. *J. Chem. Soc., Perkin Trans 2* **1984**, 245.

[4] Nagao, R.; Marumo, F.; Saito, Y.; Asahara, T. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1971**, *27*, 569. Badour, J. L.; Messager, J. C. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1971**, *27*, 799. (c) Argay, G.; Carstensen-Oeser, E. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1973**, *29*, 1186. Sheldrick, W. S. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1981**, *37*, 299 and 300. Wong, W.; Watkins, S. F. *J. Chem. Soc., Chem. Commun.* **1973**, 888. Karapetyan, H. A.; Andrianov, V. G.; Struchkov, Yu. T. *Cryst. Struct. Commun.* **1980**, *9*, 417. Aubry, A.; Protas, J.; Cung, M. T.; Marraud, M. *Cryst. Struct. Commun.* **1981**, *10*, 839.

[5] Almeningen, Fernholt, A. L.; Rustad, S.; Seip, H. M. *J. Mol. Struct.* **1976**, *30*, 291.

[6] Sjöberg, M.; Obenius, U. *Chem. Scr.* **1982**, *20*, 62.

[7] Gross, M.; Snatzke, G.; Wessling, B. *Justus Liebigs Ann. Chem.* **1979**, 1036.

[8] Połoński, T.; Milewska, M. J.; Gdaniec, M.; Gilski, M. *J. Org. Chem.* **1993**, *58*, 3134–3139.

[9] McCoy, L. L. *J. Am. Chem. Soc.* **1958**, *80*, 6568. Bonavent, G.; Causse, M.; Guitardy, M.; Frosu-Julien, R. *Bull. Soc. Chim. Fr.* **1961**, 2462.

[10] Walborsky, H. M.; Sugita, T.; Ohno, M.; Inouye, Y. *J. Am. Chem. Soc.* **1960**, *82*, 5255.

[11] Nishiyama, K.; Oda, J.; Inouye, Y. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 3175.

[12] Epstein, J. W.; Brabander, H. J.; Fanshawe, W. J.; Hofmann, C. M.; McKenzie, T. C.; Safir, S. R.; Osterberg, A. C.; Cosulich, D. B.; Lovell, F. M. *J. Med. Chem.* **1981**, *24*, 481.

[13] Nishiyama, K.; Inouye, Y. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2795.

[14] Compounds **2a–c**, used for chiroptical studies, were obtained from enantiomeric acid (−)-**5**.

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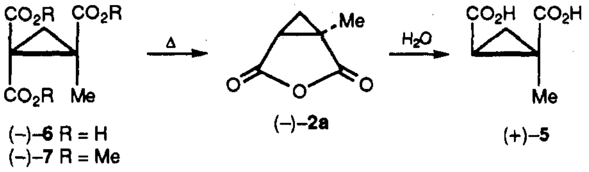
Scheme I



The most notable feature of the ^1H NMR spectra of imides **1b**, **3b**, and **4b** is a long-range coupling between protons at C-1 and the imide nitrogen. The NH signal is too broad to observe the splitting but $^4J_{CHNH}$ measured for protons at C-1 is about 1.5 Hz. A probable reason of this coupling is nearly planar W arrangement of the corresponding bonds in the bicyclic system.

Molecular Geometry. Table I presents selected torsional angles and heats of formation of the title compounds calculated by the MNDO[15] method. The 3-oxa- and 3-azabicyclo[3.1.0]hexane skeletons in **1a** and **1b**, respectively, adopt a kind of sofa conformation (half-boat)[16] with the β-carbon atom out of the plane of the remaining ring atoms (Figure 1). The anhydride and imide groups remain nearly planar. The introduction of a substituent at C-1 causes deviation of the systems from the C_s symmetry, as a result of steric interaction between this substituent and the neighboring carbonyl group; consequently, the carbonyl oxygen shifts out of the chromophore plane (Figure 1, part b). The relative orientation of the carbonyl groups and the three-membered ring, very important for interpretation of the CD spectra, is reflected by the 3-5-6-7 and 5-3-2-8 torsional angles. The calculated geometries are related to the gas-phase structure and the distortions of molecular symmetry are rather small. On the other hand, significant solvent dependence of the chiroptical spectra show that deformations are much stronger in polar media than in nonpolar ones. We believe that the calculations may indicate trends of geometrical changes brought about by solvation.

The X-ray structures of compounds **2b** and **2c**[17] appeared to be similar to that reported by Epstein et al.[12] for the *p*-chloro analogue of imide **4b**; the nitrogen atom remains slightly out of the plane of the five-membered ring, whereas the carbonyl oxygens are shifted in the opposite direction. Despite these small distortions, the C_s symmetry of the skeleton of imide **2b** is retained and only **2c** shows more pronounced skeleton dissymmetry (Table I).

Circular Dichroism Spectra. The CD spectra of the title compounds are presented in Table II. In hydrocarbon solvents imides **2b**–**4b** show a positive CE at about 270 nm and a negative one at ca. 240 nm. Analogous CD bands of anhydrides **2a**–**4a** are shifted to shorter wavelengths, i.e. to 240 and 215 nm, respectively. It has been established that both these bands belong to two n–π* electronic transitions.[2,8] Usually structurally related anhydrides and imides exhibit the same CE signs for two lowest energy excitations. The CD spectra of compounds **2a**,**b**–**4a**,**b** in nonpolar solvents are examples of such a behavior. Their first (long-wavelength) CE sign is governed by the antioctant rule and the second one (at the higher energy part of the spectrum) by the octant rule.[2] The CE sign of compounds with nondistorted bicyclic skeleton (i.e., of the C_s symmetry) is controlled by the substituent at C-1, which makes a positive contribution to the first and a negative one to the second n–π* CE (Figure 1, part a). The strong CD showed by compounds **4a**,**b** (Figure 2) results from homoconjugation of the phenyl group with the anhydride or imide carbonyl and is a characteristic feature of α-substituted succinic anhydrides and imides[2,8] and other β,γ-unsaturated carbonyl compounds.[18,19]

An additional weak CD band at 268 nm with a pronounced fine structure in anhydride **4a** corresponds to the ^1L_b benzene transition. The analogous band in imide **4b** is completely masked by the much stronger n–π* CE. An interesting feature of this compound is a very strong CE at 221 nm overlapping with the second n–π* band appearing as a shoulder. It can be attributed neither to the ^1L_a aromatic transition nor to the imide π–π* excitation, since it is enormously shifted to the red in comparison with the normal positions of these bands (i.e., about 200 nm).[2,20] The CD spectra of related α-phenyl-substituted succinic,[2] glutaric,[21] and norbornanedicarboxylic anhydrides and imides[8] do not show any analogous band, so it seems reasonable to attribute it to the presence of the cyclopropane ring. Snatzke reported that the vinylcyclopropane system, encountered in some terpenoids, exhibits strong CEs and should be treated as an inherently chiral chromophore, the helicity of which determines the CE sign.[22] Similarly the phenyl group "conjugated" with the three-membered ring[23] constitutes the inherently chiral chromophore responsible for the above strong CE in **4b**. We believe that the intense CD at 215 nm in anhydride **4a** is of the same origin.

A striking feature of the CD of imides **2b**,**c**–**4b**,**c** is their extreme sensitivity to solvent changes. For example, the very weak first CE of **2b** (Figure 3) gradually decreases in polar solvents and finally disappears in strongly hydrogen bonding 1,1,1,3,3,3-hexafluoro-2-propanol (HFP). On the contrary the higher energy CE shows an opposite trend and significantly increases in highly polar media. Similarly, the positive CE of **3b** and **4b** decreases and the negative one increases on going from cyclohexane to HFP. In some solvents the long-wavelength CE has bisignate character (e.g., **3b** in MeOH and **4b** in HFP solution). Such strong solvent effects are rather unexpected for molecules with strained bicyclic skeletons. There are two possible explanations: (i) so-called asymmetric solvation, which influences the CD spectra, or (ii) the molecules studied are, in fact, not rigid and therefore solvation can induce their conformational changes. The first explanation was formulated as early as in 1966 to rationalize the CE sign reversal of some bicyclic ketones caused by solvents.[24] Severn and Kosower criticized that explanation because asymmetric induction brought about by solvent

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[15] Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899. Thiel, W. *QCPE* No. 353.

[16] Cremer, D.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 1364.

[17] The authors have deposited atomic coordinates for these structures 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 1EZ, UK.

[18] Hagishita, S.; Kuriyama, K. *J. Chem. Soc., Perkin. Trans. 2* **1977**, 1937 and refs therein.

[19] Snatzke, G.; Snatzke, F. *Fundamental Aspects and Recent Developments in Optical Rotatory Dispersion and Circular Dichroism*; Ciardelli, F.; Salvadori, P., Eds.; Heyden: London, 1973; Chapter 3.2.

[20] Jaffe, H. H.; Orchin, M. *Theory and Applications of Ultraviolet Spectroscopy*; Wiley: New York, 1962; Chapter 12.

[21] Połoński, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 639.

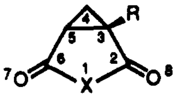
[22] Snatzke, G. *Pure Appl. Chem.* **1979**, *51*, 769.

[23] Jorgensen, W. L.; Salem, L. *The Organic Chemists Book of Orbitals*; Academic Press: New York, 1973.

[24] Coulombeau, C.; Rassat, A. *Bull. Soc. Chim. Fr.* **1966**, 3752.

[25] Severn, D. J.; Kosower, E. M. *J. Am. Chem. Soc.* **1969**, *91*, 1710.

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



compound	2-3-5-6	1-2-3-5	1-6-5-3	5-3-2-8	3-5-6-7	6-1-2-8	2-1-6-7	H_f (kcal/mol)
1a	−0.06	1.00	−0.91	−179.95	−179.76	179.14	−179.35	−89.41860
1b	−0.29	1.33	−0.85	−179.57	−179.99	178.79	−178.96	−53.16814
2a	−2.81	3.96	0.89	−176.24	−177.97	176.50	179.27	−96.03829
2b	−1.85	3.19	−0.13	−176.92	−179.09	176.51	−178.60	−59.39506
2b[a]	(0.42)	(3.15)	(−3.86)	(−176.23)	(176.57)	(173.40)	(−174.17)	
2c	−2.56	4.76	−0.50	−174.98	−179.88	174.34	−176.88	−57.71664
2c[a]	(1.6)	(1.8)	(−4.4)	(−178.6)	(176.2)	(175.5)	(−174.7)	
3a	−3.99	5.12	1.79	−177.26	−177.26	174.92	−179.28	−100.21213
3b	−4.26	5.87	1.15	−173.33	−178.00	173.62	−177.94	−63.38156
4a	−1.97	3.16	0.23	−177.06	−178.90	176.94	−178.86	−62.46789
4b	−2.32	3.48	0.34	−176.63	−178.80	176.52	−178.73	−25.76396

[a] X-ray structure.

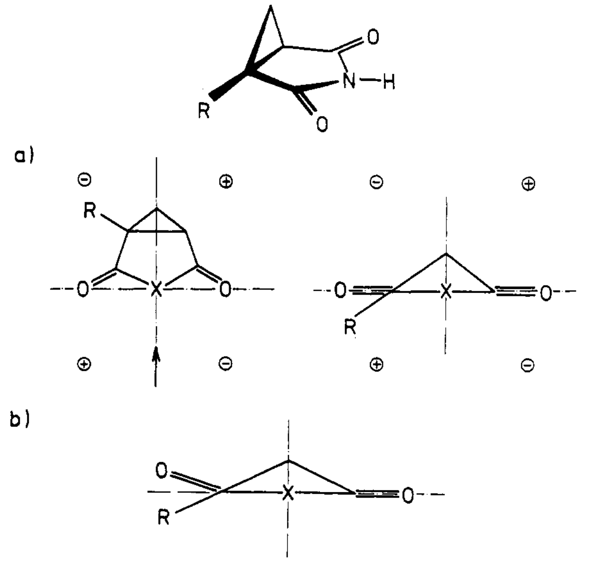


Figure 1. The octant projection of title compounds with (a) undistorted (C_s) and (b) distorted skeleton.

molecules is simply to small to change the CD sign. Also more recent quantum mechanical calculations showed that hydrogen bonding effects are very weak and ambiguous in sign.[26] Therefore we favor the second explanation, which is supported by our MNDO calculations[8] revealing that despite the rigid molecular skeletons the imide and anhydride functions are flexible. Moreover, the bisignate CEs corresponding to the first n–π* transition points to a contribution from two species in solution having opposite CD signs. The first one is probably unsolvated, with the undistorted and thus nearly symmetric (C_s) framework. According to the sector rule it is responsible for a weak positive long-wavelength CE and a negative one at the higher energy part of the spectrum. The concentration of this form diminishes in polar media, which results in decrease of the positive CE. The second form, distorted due to solvation, is probably responsible for the first negative CE. Obviously in polar solvents the solvated form dominates and thus the magnitude of the negative CE increases. Solvent molecules coordinated by hydrogen bonds to the carbonyl enhance its steric repulsion with the neighboring C-1 substituent and thus the carbonyl oxygen moves out of the chromophore plane (Figure 1, part b). This type of chromophore distortion is suggested by the MNDO calculations described in the preceding section. The N-methylation also increases steric interactions within the imide group and then facilitates its distortion. This is reflected in the CD of *N*-methylimides **2c**–**4c**; the first positive CE in **2c** disappears completely (Figure 3) or diminishes significantly in **3c** and **4c**, whereas, the negative CE of **2c** and **3c** reaches extremely high magnitudes in polar solvents. Such strong CEs are rather unusual for alkyl-substituted imides. In the case of **4b** and **4c** in HFP solution the twisted chromophore effect even prevails over a strong contribution from the phenyl group.

In our opinion, the above observations point to the important role of the cyclopropane ring in generation of the rotatory power; as the C_s symmetry of the system is disturbed, the three-membered ring atoms are no longer symmetrically disposed in respect to the sector nodal plane and they begin to contribute to the CE. This contribution must be substantial because the cyclopropane ring, as a π-electronic system,[23] is "conjugated" with the neighboring carbonyls and they constitute together the inherently chiral chromophore (chiral first sphere[27]). There is a close analogy to the cyclopropyl ketones, where the three-membered ring makes a strong and opposite contribution to that made by alkyl substituents so the simple octant rule fails.[19,28]

Anhydrides **2a**–**4a** show the positive CE near 240 nm, as predicted by the octant rule, whereas the 12-sector rule proposed by Snatzke and co-workers[7] predicts the opposite CE signs to those observed for the above compounds. The CE magnitude reaches relatively high value and increases slightly on going from hydrocarbon to acetonitrile solution. It seems that the anhydride chromophore is less flexible than the imide one or that the anhydride CD spectra are less influenced by small geometry changes than those of related imides.[8]

Concluding, the results presented here demonstrate that even small distortions of the molecular skeleton strongly influence the chiroptical spectra of anhydrides and imides. This extreme sensitivity of the CD spectroscopy to molecular geometry may be very useful because it allows detection of even minute conformational effects, which cannot be observed with other spectroscopic techniques.

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(26) Ruiz-Lopez, M. F.; Rinaldi, D.; Rivail, J. L. *Chem. Phys.* **1986**, *110*, 403.

(27) Snatzke, G. *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 363.

(28) Djerassi, C.; Klyne, W.; Norin, T.; Ohloff, G.; Klein, E. *Tetrahedron* **1965**, *21*, 163. Lightner, D. A.; Beavers, W. A. *J. Am. Chem. Soc.* **1971**, *93*, 2677. Lightner, D. A.; Jackman, D. E. *Tetrahedron Lett.* **1975**, 3051.

Table II. CD Data of 1,2-Cyclopropanedicarboxylic Anhydrides and Imides

compd	solvent[a]	λ, nm ($10^{-3}[\Theta]^{b}$)[c]	compd	solvent[a]	λ, nm ($10^{-3}[\Theta]^{b}$)[c]
2a	CD	241 (3.15), 215 (−0.90)	**2b**	CD	270 (0.21), 239 (−1.60)
	A	239 (3.30), 210 (−1.40)		A	267 (0.41), 238 (−1.88)
				M	272 (0.08), 240 (−1.67)
2c	C	252 (−3.13)		H_2O	269 (0.08), 243 (−3.24)
	A	252 (−4.75)		HFP	237 (−3.49)
	M	251 (−4.84)			
	H_2O	250 (−7.03), 215 (13.80)			
	HFP	248 (−7.20)			
3a	CD	239 (3.97)	**3b**	CD	268 (1.91), 241 (−0.50)
	A	238 (5.33)		A	266 (1.05), 233 (−0.63)
				M	274 (−0.07), 268 (0.07), 240 (−0.88)
3c	C	270 (0.28), 244 (−1.31)		H_2O	262 (0.24), 234 (−2.60)
	M	271 (−0.03), 242 (−3.01)		HFP	266 (0.34), 231 (−2.66)
	HFP	244 (−6.81)			
4a	CD	268 (−0.21), 243 (13.92), 215 (−33.03)	**4b**	CD	260 (7.98), 235 sh (−7.33), 221 (−37.13)
	A	269 (−0.22), 243 (12.78), 215 (−28.20)		M	260 (6.23), 234 sh (−10.86), 220 (−34.00)
				H_2O	260 (3.16), 232 (−11.92), 221 (−27.11)
4c	C	261 (6.76), 238 sh (−13.15), 225 (−32.87)		HFP	268 (−0.53), 259 (1.34), 233 sh (−11.00), 221 (−31.60)
	M	261 (3.14), 231 sh (−14.03), 225 (−19.26)			
	HFP	262 (−2.96), 235 (−12.24)			

[a] 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.

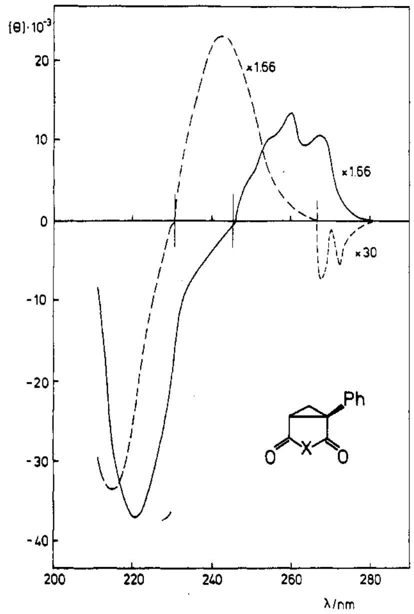

Figure 2. CD spectra of anhydride **4a** (broken line) and imide **4b** (solid line) in cyclohexane–dioxane (9:1) solution.

However, sometimes it may cause difficulties in application of this technique as a diagnostic tool for configurational predictions. Therefore a careful examination of the CD in several solvents together with molecular modeling is always desirable.

Experimental Section

All spectroscopic measurements were carried out as described previously.[8] ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ unless otherwise indicated.

(1*S*,2*R*)-1-Methyl-1,2-cyclopropanedicarboxylic Acid (5). The racemic acid **5**[9] (8.2 g, 57 mmol) and brucine (21.5 g, 57 mmol) were dissolved in hot water (450 mL). The resulting monosalt was recrystallized two times from water to obtain 10.4 g of the material with mp 140–142 °C; $[\alpha]^{22}_{D}$ −16.3° (*c* 1, acetone). The regenerated laevorotatory acid had mp 148–150 °C (from toluene) (lit.[9] racemate mp 139–141 °C); $[\alpha]^{22}_{D}$ −77.8° (*c* 1, acetone).

(1*S*,2*R*)-1-Methyl-1,2-cyclopropanedicarboxylic Anhydride (2a). The above acid (1.45 g) was refluxed with acetyl chloride (5 mL) for 0.5 h, after which the mixture was evaporated to dryness and the residue was crystallized from toluene–hexane to obtain **2a** (1.25 g): mp 66 °C (lit.[9] racemate mp 45–47 °C); $[\alpha]^{23}_{D}$ +7.9° (*c* 5, C_6H_6); IR (CCl_4) 1865, 1850, 1790 cm^{-1}; ^{1}H NMR δ 2.54 (dd, *J* = 3.4 and 8.3 Hz, 1 H, 2-H), 1.70 (dd, *J* = 3.4 and 4.9 Hz, 1 H, 3-H), 1.52 (s, 3 H, Me), 1.49 (dd, *J* = 4.9 and 8.3 Hz, 1 H, 3-H); ^{13}C NMR δ 170.72 (CO), 167.90 (CO), 29.04 (C-1), 26.48, 23.74, 12.22 (Me).

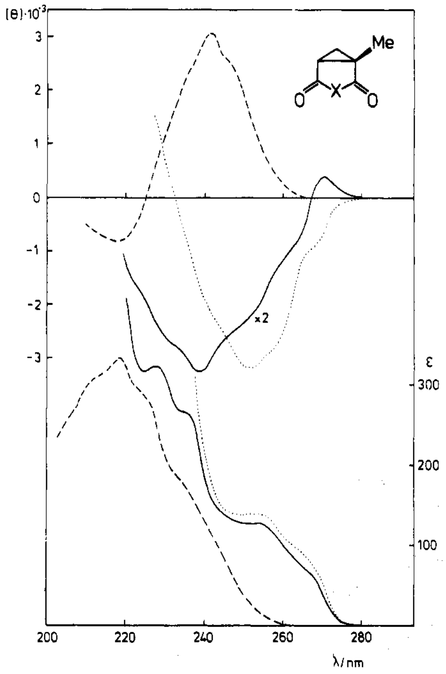

Figure 3. CD and UV spectra of anhydride **2a** and imides **2b** and **2c** (broken, solid, and dotted lines, respectively) in cyclohexane–dioxane (9:1) solution.

(1*S*,2*R*)-1-Methyl-1,2-cyclopropanedicarboximide (2b). Gaseous ammonia was passed over a solution of the anhydride **2a** (1.27 g) in benzene (20 mL), after which the solvent was evaporated and the residue was heated at 200 °C for 10 min. The crude product was dissolved in chloroform, decolorized with silica gel, evaporated to dryness and crystallized from toluene–hexane to obtain **2b** (0.92 g): mp 109–110 °C; $[\alpha]^{20}_{D}$ −9.8° (*c* 2, C_6H_6); IR (CCl_4) 3420, 3200 br, 1780, 1725 cm^{-1}; ^{1}H NMR δ 8.55 (br s, 1 H, NH), 2.29 (dd, *J* = 3.4 and 8.1 Hz, 1 H, 2-H), 1.65 (dd, *J* = 3.4 and 4.6 Hz, 1 H, 3-H), 1.48 (s, 3 H, Me), 1.40 (dd, *J* = 4.6 and 8.1 Hz, 1 H, 3-H); ^{13}C NMR δ 177.46 (CO), 175.26 (CO), 28.31 (C-1), 27.22, 27.10, 12.46 (Me). Anal. Calcd for $C_6H_7NO_2$ (125): C, 57.59; H, 5.64; N, 11.19. Found: C, 57.51; H, 5.70; N, 11.07.

(1*S*,2*R*)-*N*-Methyl-1-methyl-1,2-cyclopropanedicarboximide (2c). The anhydride **2a** (0.5 g) was treated with 33% ethanolic solution of methylamine (1.4 mL), after which the ethanol was evaporated at reduced pressure and the residue was heated at 200 °C for 20 min. The product was dissolved in carbon tetrachloride, decolorized with silica gel, evaporated to dryness and crystallized from ethyl ether–pentane to obtain **2c** (0.47 g): mp 58 °C; $[\alpha]^{20}_{D}$ −34.9° (*c* 0.7, CCl_4); IR (CCl_4) 1770, 1710 cm^{-1}; ^1H NMR δ 2.77 (s, 3 H, NMe), 2.21 (dd, J = 3.3 and 8.2 Hz, 1 H, 2-H), 1.43 (s, 3 H, Me), 1.42 (m, 1 H, 3-H), 1.29 (dd, J = 4.7 and 8.1 Hz, 1 H, 3-H); ^{13}C NMR δ 177.33 (CO), 175.24 (CO), 27.55, 26.76 (C-1), 25.75, 24.15 (NMe), 12.54 (Me). Anal. Calcd for $C_7H_9NO_2$ (139): C, 60.42; H, 6.52; N, 10.07. Found: C, 60.30; H, 6.49; N, 10.20.

(1*R*,2*R*)-1-Isopropyl-1,2-cyclopropanedicarboxylic anhydride (3a) was obtained from (1*R*,2*R*)-1-isopropyl-1,2-cyclopropanedicarboxylic acid[29] in a similar manner to the compound **2a** and had mp 32–33 °C (from toluene–hexane); $[\alpha]^{20}_{546}$ −6.8° (*c* 4, C_6H_6); $[\alpha]^{20}_{578}$ −6.3° (*c* 4, C_6H_6); IR (CCl_4) 1885, 1810 cm^{-1}; ^1H NMR δ 2.49 (dd, J = 3.6 and 8.3 Hz, 1 H, 2-H), 2.08 (sep, J = 6.9 Hz, 1 H, $CHMe_2$), 1.63–1.51 (m, 2 H, 3-H_2), 1.08 (d, J = 6.9 Hz, 3 H, $CHMe_2$), 1.02 (d, J = 6.9 Hz, 3 H $CHMe_2$); ^{13}C NMR δ 169.50 (CO), 167.93 (CO), 38.99 (C-1), 26.08, 24.30, 20.94, 19.44, 18.88. Anal. Calcd for $C_8H_{10}O_3$ (154): C, 62.33; H, 6.54. Found: C, 62.12; H, 6.65.

(1*R*,2*R*)-1-Isopropyl-1,2-cyclopropanedicarboximide (3b) was obtained in a similar manner to compound **2b** and had mp 106 °C (from toluene–hexane); $[\alpha]^{20}_{D}$ −78° (*c* 3, $CHCl_3$); IR (CCl_4) 3430, 3220 br, 1780, 1735 cm^{-1}; ^1H NMR δ 8.17 (br s, 1 H, NH), 2.21 (ddd, J = 1.4, 3.4, and 8.2 Hz, 1 H, 2-H), 2.12 (sep, J = 6.9 Hz, 1 H $CHMe_2$), 1.52 (dd, J = 3.4 and 4.9 Hz, 1 H, 3-H), 1.44 (dd, J = 4.9 and 8.2 Hz, 1 H, 3-H), 1.08 (d, J = 6.9 Hz, 3 H, $CHMe_2$), 0.98 (d, J = 6.9 Hz, 3 H, $CHMe_2$); ^{13}C NMR δ 177.20 (CO), 175.86 (CO), 38.14 (C-1), 25.78, 24.29, 19.87, 18.87. Anal. Calcd for $C_8H_{11}NO_2$ (153): C, 62.73; H, 7.24; N, 9.14. Found: C, 62.71; H, 7.62; N, 8.89.

(1*R*,2*R*)-*N*-Methyl-1-isopropyl-1,2-cyclopropanedicarboximide (3c) was obtained in a similar manner to **2c** and had mp 68 °C (from hexane); $[\alpha]^{22}_{D}$ −56.3° (*c* 2, CCl_4); IR (CCl_4) 1775, 1710 cm^{-1}; ^1H NMR δ 2.83 (s, 3 H, NMe), 2.23 (dd, J = 3.6 and 8.0 Hz, 1 H, 2-H), 2.15 (sep, 1 H, $CHMe_2$), 1.44–1.36 (m, 2 H, 3-H_2), 1.08 (d, J = 6.9 Hz, 3 H, $CHMe_2$), 0.99 (d, J = 6.9 Hz, 3 H, $CHMe_2$); ^{13}C NMR δ 176.76 (CO), 175.52 (CO), 36.87 (C-1), 26.06, 24.79, 24.19 (NMe), 23.25, 20.02, 19.00. Anal. Calcd for $C_9H_{13}NO_2$ (167): C, 67.65; H, 7.84; N, 8.38. Found: C, 64.43; H, 7.86; N, 8.26.

(1*S*,2*R*)-1-Phenyl-1,2-cyclopropanedicarboxylic anhydride (4a) was obtained from (1*S*,2*R*)-1-phenyl-1,2-cyclopropanedicarboxylic acid[11] in a similar manner to compound **2a** and had mp 58 °C (from toluene–hexane); $[\alpha]^{22}_{D}$ −26.0° (*c* 2.3, C_6H_6); IR (CCl_4) 1885, 1815 cm^{-1}; ^1H NMR δ 7.36 (s, 5 H, Ph), 2.96 (dd, J = 3.8 and 8.5 Hz, 1 H, 2-H), 2.05 (dd, J = 3.8 and 5.0 Hz, 1 H, 3-H), 1.95 (dd, J = 5.0 and 8.5 Hz, 1 H, 3-H); ^{13}C NMR δ 168.65 (CO), 167.24 (CO), 129.61, 129.07, 128.71, 37.28 (C-1), 27.42 (C-3), 24.08 (C-2). Anal. Calcd for $C_{11}H_8O_3$ (187): C, 70.21; H, 4.29. Found: C, 70.08; H, 4.34.

(1*S*,2*R*)-1-Phenyl-1,2-cyclopropanedicarboximide (4b) was obtained in a similar manner to **2b** and had mp 140–141 °C (from toluene): $[\alpha]^{18}_{D}$ −74.6° (*c* 1, $CHCl_3$) [lit.[12] mp 137.5–138.5 °C; $[\alpha]^{25}_{D}$ −75° (MeOH)]; IR (CCl_4) 3425, 3230 br, 1785, 1740, 1720 cm^{-1}; ^1H NMR δ 8.19 (br s, 1 H, NH), 7.38 (m, 5 H, Ph), 2.71 (ddd, J = 1.8, 3.6 and 8.3 Hz, 1 H, 2-H), 1.99 (dd, J = 4.7 and 8.3 Hz, 1 H, 3-H), 1.87 (dd, J = 4.7 and 8.3 Hz, 1 H, 3-H); ^{13}C NMR δ 175.84 (CO), 175.01 (CO), 131.47, 128.89, 128.66, 128.30, 36.66 (C-1), 27.76 (C-3), 27.25 (C-2).

(1*S*,2*R*)-*N*-Methyl-1-phenyl-1,2-cyclopropanedicarboximide (4c) was obtained in a similar manner to **2c** and had mp 66–67 °C (from toluene–hexane); $[\alpha]^{20}_{D}$ −39.6° (*c* 0.5, C_6H_6); IR (CCl_4) 1775, 1710 cm^{-1}; ^1H NMR δ 7.36 (m, 5 H, Ph), 2.90 (s, 3 H, NMe), 2.70 (dd, J 5.0 and 7.0 Hz, 1 H, 2-H), 1.82 (m, 2 H, 3-H_2); ^{13}C NMR δ 175.18 (CO), 174.48 (CO), 131.87, 128.73, 128.61, 128.16, 35.29 (C-1), 27.70, 26.62, 24.46 (NMe). Anal. Calcd for $C_{12}H_{11}NO_2$ (201): C, 71.63; H, 5.51; N, 6.96. Found: C, 71.74; H, 5.27; N, 7.21.

(*R*)-1-Methyl-1,2,2-cyclopropanetricarboxylic Acid (−)-(6). To the suspension of sodium hydride (4.8 g, 0.2 mol) in benzene (50 mL) the mixture of diethyl monochloromalonate (39.0 g, 0.2 mol) and methyl methacrylate (40.0 g, 0.4 mol) was added dropwise with stirring and maintaining temperature at ca. 15 °C. After standing overnight at room temperature the reaction mixture was diluted with benzene (50 mL), washed with water, and dried ($MgSO_4$). The benzene was evaporated at reduced pressure, and the residue was distilled, collecting the fraction boiling in 168–172 °C at 16 mmHg. The resulted crude triester (18.4 g) was refluxed with 20% aqueous NaOH (50 mL) until desappearence of organic layer (ca. 1 h). After cooling the solution was extracted with ethyl ester, water phase was concentrated to a small volume, acidified with concd hydrochloric acid, and extracted five times with ethyl ether. The combined extracts were dried ($MgSO_4$) and evaporated to dryness, and the residue was recrystallized from ethyl acetate–toluene to obtain the racemic acid **6**: mp 121–125 °C; ^1H NMR (D_2O) δ 1.98 (d, 1 H, J = 5.3 Hz), 1.63 (d, 1 H, J = 5.3 Hz), 1.28 (s, 3 H). The above acid (18.8 g, 0.1 mol) and brucine (79.0 g, 0.2 mol) were dissolved in hot water (2 L) and left to stand overnight at room temperature. The precipitated salt was recrystallized twice from boiling water to obtain material (36.5 g) with $[\alpha]^{22}_{D}$ −34.7° (*c* 1, MeOH). The regenerated levorotatory tricarboxylic acid (−)-**6** had mp 124–126 °C, $[\alpha]^{22}_{D}$ −47.5° (*c* 0.5, H_2O). Anal. Calcd for $C_7H_8O_6$ (188): C, 47.69; H, 4.29. Found: C, 47.49; H, 4.38.

Trimethyl (*R*)-1-methyl-1,2,2-cyclopropanetricarboxylate (−)-(7) was obtained by esterification of acid (−)-**6** with diazomethane: oil, $[\alpha]^{22}_{D}$ −64.9° (*c* 1, MeOH) (ee 83%) {lit.[13] $[\alpha]^{25}_{D}$ −77.78° (*c* 2.05, MeOH) calculated for ee 100%}; ^1H NMR δ 3.67 (s, 3 H), 3.61 (s, 3 H), 3.60 (s, 3 H), 1.99 (d, J = 5.2 Hz, 1 H), 1.55 (d, J = 5.2 Hz, 1 H), 1.34 (s, 3 H).

Decarboxylation of (−)-6. The levorotatory acid (−)-**6** (1.89 g, 10 mmol) was heated in 180–190 °C for 1 h. The product was dissolved in benzene (20 mL) and washed with aqueous $NaHCO_3$. The organic layer was dried ($MgSO_4$), decolorized with silica gel, and evaporated to dryness. The residue was refluxed with water (1 mL). The resulting dextrorotatory acid **5** was crystallized from ethyl acetate–hexane to obtain the material, which had mp 143–144 °C; $[\alpha]^{22}_{D}$ +64.8° (*c* 0.34, acetone) (ee 83%, i.e., the same as for acid (−)-**6**).

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[29] Rydon, H. N. *J. Chem. Soc.* **1936**, 829.