Chiroptical Properties of 10,11-Dihydro-5,10-methano-5*H*-dibenzo[*a*,*d*]cycloheptene Derivatives

Sanji HAGISHITA* and Kaoru KURIYAMA

Shionogi Research Laboratories, Shionogi & Co. Ltd., Fukushima-ku, Osaka 553

(Received April 4, 1981)

The titled compounds have been prepared from (+)-(9*R*,10*R*)-dimethyl 11-oxo-9,10-dihydro-9,10-ethanoanthracene-1,5-dicarboxylate. Their absolute configurations were determined by chemical reaction, and by IR and CD spectra. Although the CD spectra of **2** and **3** (R=NH_2) were expected to show an antipodal pattern from analysis of the simple coupling mechanism, they showed approximately the same magnitude of the positive Cotton effect in both regions of the ^1L_b and ^1L_a benzenoid transitions. Their CD spectra were calculated by the point-dipole exciton treatment and by the π-SCF approximation using the dipole velocity procedure with and without the charge transfer transition between the aromatic chromophores. Thus, the electric transition dipole moment should not be treated as a point dipole at any place and the rotational strength should be calculated by the dipole velocity procedure since a local magnetic transition dipole moment was produced perpendicular to the benzene ring in the region of the ^1L_b transition. The charge transfer transition can not be neglected in the calculation of the MO, though it does not cause the alteration of the sequence of the coupling mode.

In our previous report,[1] we pointed out that the chiroptical properties of C_2-symmetrical (+)-2,6-disubstituted 9,10-dihydro-9,10-ethanoanthracene (DEA) **1** should not be analyzed with a dipole-dipole coupling mechanism,[2] but should be calculated with the dipole velocity method using the molecular orbital calculations, which take into consideration an electron exchange effect between the two aromatic chromophores. Mixing of the charge transfer transition may change the sequence of the A- and B-coupling mode of local transitions into the opposite one and thus result in wrong assignment of the configuration.

In order to estimate the limitation of the electron exchange effect in changing the energy sequence, we synthesized optically active 10,11-dihydro-5,10-methano-5*H*-dibenzo[*a*,*d*]cycloheptene (DMDC) derivatives. They have two aromatic chromophores linked with ethylene and methylene chains and are rigid in conformation. Thus they would have a smaller electron exchange effect than DEA.

The skeletons of compounds **2** and **3** are antipodal to each other but they are not antipodes owing to the substituents at the 1,6- and 4,9-positions. But if the substituents are the same in both compounds and the direction of the electric transition dipole moment of the aromatic chromophores does not change, the CD curves of the two compounds can be expected to be quasi mirror images of each other from a simple coupling mechanism. Therefore the deviation from the antipodal pattern of their CD spectra may be a key to clarify the following factors; the contributions of the charge transfer effect, and a local magnetic transition moment produced perpendicular to the plane of the benzene ring, and a treatment of the electric transition dipole moment as a point dipole, and selection of its position (Fig. 1).[1,3]

Synthesis. (+)-Dimethyl 12-oxo-DEA-1,5-dicarboxylate, (+)-**4b**, with an absolute configuration determined by us to be 9*R*,10*R*,**,[4] was reduced with sodium borohydride to give a 1:2 mixture of the diols, (+)-**7b** and (+)-**8b**, with a configuration

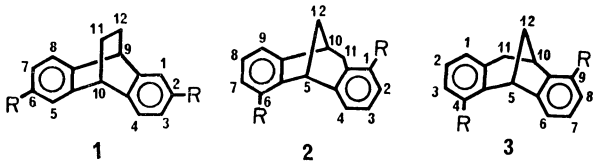
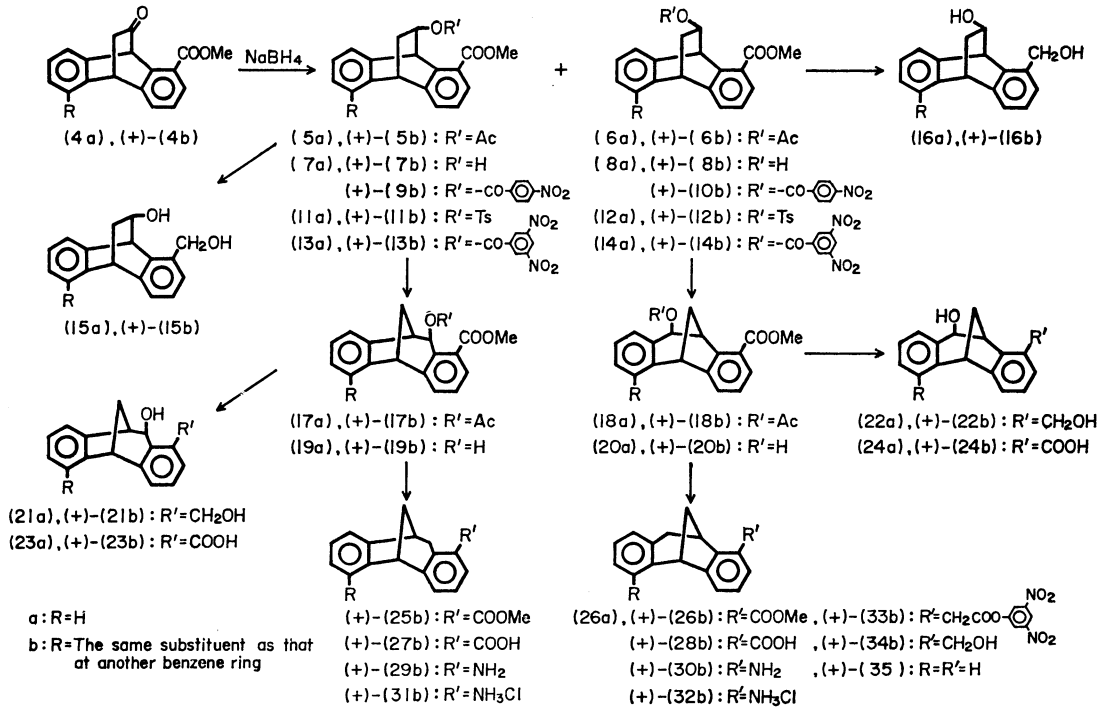


Fig. 1.

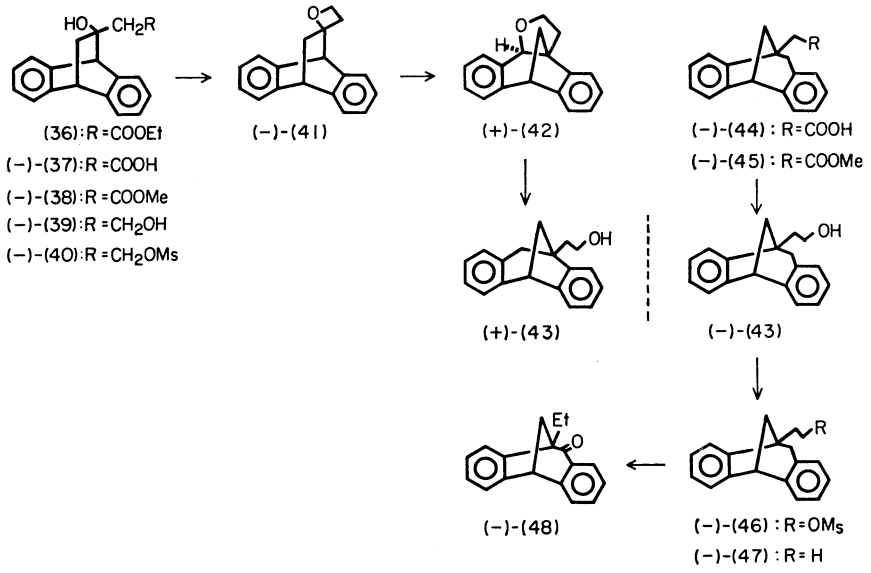
determined by analysis of the NMR spectra of their acetates, (+)-**5b** and (+)-**6b**. The minor product (+)-**7b** was isolated by conversion into the *p*-nitrobenzoyl derivative (+)-**9b** and reduced to the triol (+)-**15b**. Its IR spectrum showed the band attributable to the intramolecular hydrogen bonding at 3483 cm^{-1}, CH_2OH/OH for the dilute chloroform solution, 1.495 mmol/l. Then an *endo*-configuration could be assigned to (+)-**15b** from the model consideration. The solvolysis of the tosylate **11b** took place by Wagner-Meerwein rearrangement giving the rearranged compound, (+)-**17b**, together with less than 5% of other rearranged DMDC, (+)-**18b**. The former could be purified by conversion into the alcohol (+)-**19b**, followed by TLC. The latter was obtained from the crude alcohol (+)-**8b** by the same procedure. The acetate group was assigned the *exo*-configuration in both rearranged products (+)-**17b** and (+)-**18b** by analysis of the NMR spectra.[5] The triol (+)-**21b** obtained from the former acetate showed intramolecular hydrogen bonding at 3439 cm^{-1}, CH_2OH/OH. On the other hand, (+)-**22b** from the latter acetate lacked the corresponding absorption. Thus, from both the NMR and IR spectra, the configurations of the rearranged products (+)-**17b** and (+)-**18b** were assigned as shown in Scheme 1 and coincided with the stereochemical outcome reported by Cristol *et al.*, that is, solvolysis rearrangement brought about migration of the *anti*- to the leaving group.[6] Since the configuration at C-10 of DEA does not change by the rearrangement, the configuration at C-5 of DMDC must possess the (*R*)-configuration. The absolute configurations of (+)-**17b** and (+)-**18b** can therefore be assigned as being (5*R*,10*R*) and (5*R*,10*S*), respectively.

Hydrogenolysis of the hydroxy diesters (+)-**19b** and

** The notation of the absolute configuration of (+)-1,5-disubstituted 11-oxo-DEA in Ref. 4 should be 9*R*,10*R*.



Scheme 1.



Scheme 2.

(+)-**20b** furnished the desired DMDC compounds (+)-**25b** and (+)-**26b** with absolute configurations of 10*S*,5*R* and 10*R*,5*R*, respectively. Other DMDC derivatives (+)-**27b**—**34b** and (+)-**35** could be prepared according to Scheme 1. The same procedure was applied to (±)-methyl 12-oxo-DEA-1-carboxylate **4a**.

11-Hydroxy-DEA-11-acetic acid,*** **37** was resolved with cinchonidine to the (−)-isomer, and (−)-oxetane (−)-**41** was obtained from (−)-**37** as shown in Scheme 2 according to literature[7] cited for the racemate. Rearrangement of the (−)-oxetane (−)-**41** of 94.4% optical purity took place at once with a catalytic amount of *p*-toluenesulfonic acid to give (+)-**42** in quantitative yield. The rearrangement occurred at the asymmetric center. Then in order to determine the optical yield of the reaction, the enantiomer of the hydrogenolyzed alcohol (−)-**43**, was prepared by a different route from optically pure (−)-DMDC-10-acetic acid, (−)-**44** which was obtained from cinchonidine salt. Comparing the optical rotations, $[\alpha]_D$ +180.0° and $[\alpha]_D$ −190.6°, the optical purity of 94.4% was obtained for the alcohol (+)-**43** and was the same as that of the starting carboxylic acid (−)-**37**. Therefore the rearrangement is a completely stereoselective process.

In the NMR spectrum of the rearranged compound

*** This was obtained from the ethyl ester[7] and was very sensitive to acid.

TABLE 1. UV AND CD SPECTRA OF DMDC DERIVATIVES

Compound	UV		CD		Solvent
	λ_{nm}	ε	λ_{nm}	$\Delta\varepsilon$	
(+)-**35**	277	2170	277	+3.80	Cyclohexane
	270	1820	269	+2.85	
	263	1160	262 sh	+1.11	
	256	743	254	+0.676	
	231 sh	6350	231	+12.5	
	222 sh	11800	224	+10.3	
			216 sh	+5.63	
			210	−18.0	
			197 sh	+37.0	
	195!	48900	190	+75.6	
(+)-**30b**	291	3230	293	+9.24	MeOH
	231 sh	19900	238 sh	+29.9	
	213	36000	217	+97.5	
	204	41400	201	−117.	
(+)-**32b**	274	1590	275	−0.755	MeOH-HCl
			272	+1.39	
	266	1540	263	+2.17	
			256 sh	+1.72	
	220 sh	11600	224	+18.8	
	202 sh	36400	197	+60.3	
(+)-**26b**	298	4690	299	+11.6	Cyclohexane
	292	4950	294	+11.6	
			258	−4.73	
			237 sh	+25.6	
	230	20400	217	+91.2	
	210 sh	40500	201	+114.	
	202	54500			
(+)-**28b**	291	4140	295	+10.0	MeOH
			256	−2.90	
	226	20200	214	+90.3	
	210	36800			
	202	42200	197	−83.3	
(+)-**34b**	279	1720	275 sh	+0.991	MeOH
	271	1530	266	+1.92	
	263	1080	259 sh	+1.32	
	235 sh	5490	230	+20.0	
	223 sh	14700	210	+45.8	
	196	47900	195!	0	
(+)-**29b**	289	3340	290	+7.99	MeOH
	231 sh	18100	240	+32.4	
	213 sh	38900	221	−34.3	
	203	44500	201	+17.0	
			195!	0	
(+)-**31b**	274	1630	274	−3.67	MeOH-HCl
	266	1480	268	−1.83	
	260 sh	1190	248	+0.042	
	225 sh	4060	230	−13.0	
	210 sh	24100	211 sh	+30.3	
			202	+41.9	
			196!	0	
(+)-**25b**	299	4630	298	+8.42	Cyclohexane
	292	4580			
	230	18700	237	+32.9	

Compound	UV		CD		Solvent
	λ_{nm}	ε	λ_{nm}	$\Delta\varepsilon$	
	209 sh	10100	218	−36.1	
	202	13100	209	+53.9	
			200	−18.7	
(+)-**27b**	294	3130	297	+5.56	MeOH
	228 sh	13100	235	+16.7	
			218	−25.8	
	201	34500	209	+34.5	
			198	−21.1	
(+)-**22b**	280	1310	280	+4.76	MeOH
	272	1150	273	+2.49	
			232 sh	+15.7	
	211	27400	211	+49.2	
	196	47600	195!	−54.1	
(+)-**19b**	293	3860	294	+4.76	CH_3CN
			279	+7.91	
	227 sh	20100	236	+16.9	
			221	−18.6	
	207 sh	37000	211	+32.4	
	200	54000			
(+)-**21b**	279	1010	280	−8.03	MeOH
	270	1060	274	−3.64	
			266	+0.855	
			259	+0.670	
			241	−0.893	
	214 sh	26200	215	+22.6	
	195!	40500	193!	−37.7	
(+)-**42**	276	1900	276	+5.74	Hexane
	269	1630	269	+3.17	
	263	1120	256	−0.114	
	255 sh	649	230	+14.4	
	211 sh	26900	211	−18.2	
	204.5sh	32800	190	+57.1	
(−)-**43**	276	2110	276	−3.58	MeOH
	269	1810	269	−2.81	
	263	1190	263 sh	−1.56	
	256 sh	753	254 sh	−0.836	
	229 sh	7230	231	−13.9	
	221 sh	12000	224	−10.3	
	203	37500	217	−8.09	
			211	+6.72	
			195!	−39.1	
(−)-**44**	276	4020	275	−2.77	MeOH
	268.5	3490	268	−2.36	
	262	2350	262 sh	−1.28	
	256 sh	1570	253 sh	−0.074	
	230 sh	13900	229	−13.1	
	221 sh	23700	223 sh	−10.4	
	194	92700	216	−10.1	
(−)-**45**	276	4070	275	−2.91	Hexane
	269	3480	268	−2.42	
	262	2230	262 sh	−1.44	
	229 sh	15900	229	−12.9	
	221 sh	24800	222 sh	−9.15	

Table 1. (continued)

Compound	UV λ_{nm}	UV ε	CD λ_{nm}	CD $\Delta\varepsilon$	Solvent
	202 sh	75300	214	−12.4	
			209	+9.72	
	195 sh	98500	196	−33.6	
(−)-**46**	276	4070	275	−2.92	Hexane
	269	3480	268	−2.42	
	262	2230	262 sh	−1.44	
	256 sh	1390			
	229 sh	15900	229	−12.9	
	221 sh	24800	222 sh	−9.15	
	202 sh	75300	214	+9.72	
	195 sh	98500	196	−33.6	
(−)-**47**	276	2170	276	−3.79	Hexane
	269	1830	269	−2.88	
	263	1150	262 sh	−1.40	
	256 sh	674			
	230 sh	7000	229	−13.2	
	221 sh	12100	223 sh	−10.8	
	203 sh	36700	215	−10.3	
			210	+12.0	
			197 sh	−30.9	
			189	−72.1	
(−)-**48**	377	184	375	−3.06	Hexane
	358	395	357.5	−6.18	
	342.5	389	341	−5.76	
	328	251	326	−3.09	
	303	987	314	−1.18	
	293.5	1000	300 sh	+3.48	
	275.5	2090	293	+4.97	
	266 sh	2580	275	−8.61	
	257 sh	4140	267	−12.0	
	247 sh	7970	258	−13.5	
	239	12900	244 sh	+7.55	
	233	13800	238 sh	+33.9	
	217 sh	23400	232	+38.2	
	211	26200	212	−31.8	
			201	+57.6	
			187	−38.8	

sh; Shoulder, !; lowest recorded value, not a maximum.

(+)-**42** in benzene-d_6, the signal at the C-11 proton appeared in lower field than other methylene and bridgehead protons and exhibited W-letter long-range coupling, J=1.0 Hz, with the C-12 *exo*-proton. This led us to decide upon an α-configuration for the hydrogen at C-11.

(−)-10-Ethyl-DMDC (−)-**47** was prepared from the (−)-alcohol, (−)-**43**, and showed an almost antipodal CD spectrum to (+)-**35**, (Fig. 2). Since the ethyl group at the bridgehead did not have a significant effect on the CD spectrum, the absolute configuration of (−)-**47** assigned was 5*R*,10*S*. This assignment was also supported by the negative Cotton effect attributable to the n-π^* transition of (−)-**48** (Table 1), since Tatemitsu *et al.*[8] have reported that in the structurally similar compound (+)-**49**, the contribution of β,γ-unsaturation is predominant and that of α,β-unsaturation is negligibly small in this region of the CD spectrum (Fig. 3).

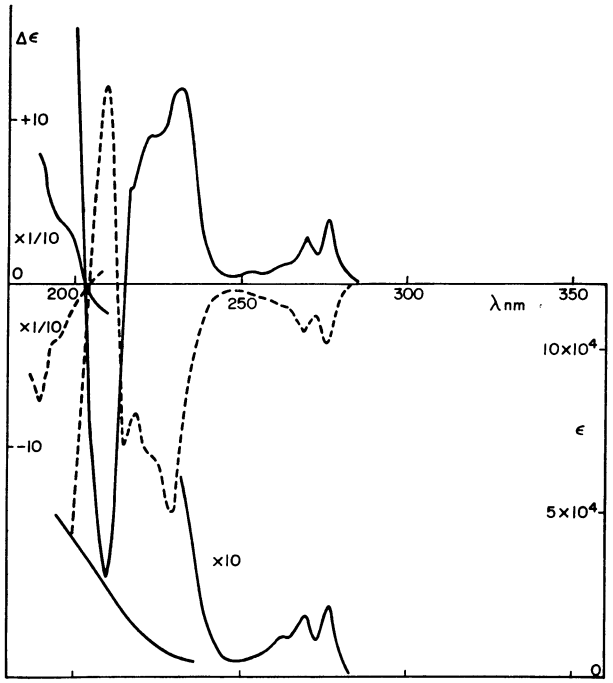
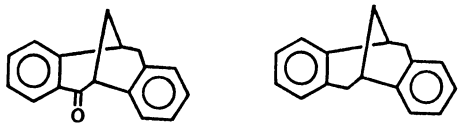


Fig. 2. UV and CD spectra of (+)-**35**, (——), and CD spectrum of (−)-**47**, (- - -).



(+)-**49** (+)-**50**

Fig. 3.

Results and Discussion

Figure 4 shows temperature-dependent CD spectra of (−)-**47** in M.I.† Though the vibrational structure became fine for the ^1L_b transition with a decrease in temperature, the rotational strengths, -5.18×10^{-40} cgs at 25 °C, -5.08×10^{-40} cgs at −68 °C, and -5.16×10^{-40} cgs at −190 °C, were invariable within the experimental error. The DMDC skeleton proved to be rigid in conformation, as was expected from the model consideration.

Table 1 shows the UV and CD spectra. (+)-DMDC, (+)-**35**, did not exhibit the couplet pattern but did show a positive Cotton effect with fine structure in the region of the ^1L_b transition. We tried to apply the sector rule[9] to (+)-**35**, assuming the presence of two chromophores with CD spectra that were merely additive. Figure 5 shows two projections along the C_2-axis of the A and B benzene chromophores. In projection A, the rule predicts a negative CD within the ^1L_b band, while projection B predicts that contributions from the second benzene ring should be strongly positive. As they have op-

† Methylcyclohexane isopentane, 4:1,

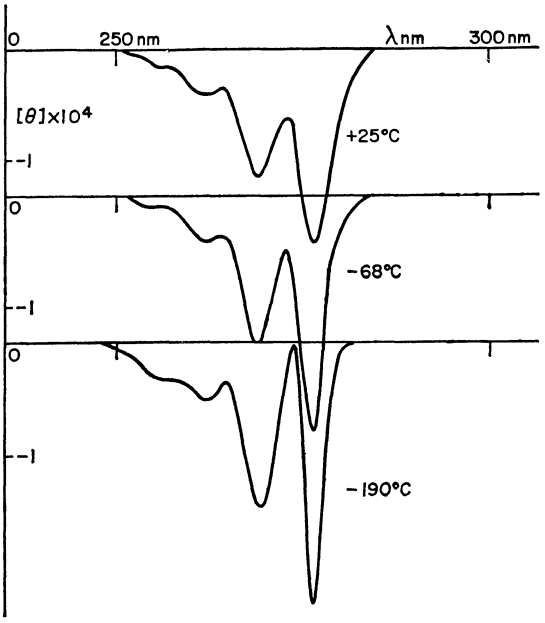


Fig. 4. Temperature-dependent CD spectra of (−)-**47**.

posite signs, a small positive value is expected and this agrees with the measurements.

In the 210—231 nm region, four Cotton effects were detected, three positive CD band followed by one negative CD band at shorter wavelength, with the last two CD bands looking like a couplet. Compound (−)-**50**, with two benzene rings linked with two ethylene chains, has been reported to have four Cotton effects in the 214—226 nm region.[8] Presumably, the couplet centered around 224 nm of (−)-**50** corresponds to the couplet at about 213 nm of (+)-**35** by the nature of the transition, owing to the similarity of the couplet pattern. In this region, besides the ^1L_a transition, the charge transfer transition between two aromatic chromophores are predicted to play an important role, and the positive CD bands at 231 and 224 nm of (+)-**35** and the negative CD bands at 218 and 214 nm of (−)-**50** seem to be assignable to the charge transfer transition by nature. The energy sequences seem likely to displace each other in (+)-**35** and (−)-**50** by their geometrical change.

In the ^1B transition region, two positive Cotton effects were observed but not the couplet pattern.

Compounds (−)-**43**—(−)-**47** have the opposite configuration in the DMDC skeleton to (+)-**35** and showed almost antipodal CD spectra to that of (+)-**35**, though their couplet was clearer in the region of 222—210 nm. Thus the substituent at the bridgehead has only a minor effect on the CD spectrum of DMDC.

Compound (+)-**42** showed a larger magnitude of the positive Cotton effect in the ^1L_b transition than (+)-**35** and only two Cotton effects were observed in the region of 221—230 nm, unlike the case of (+)-**35**. The tetrahydrofuran ring seems to produce little strain on the DMDC skeleton from model inspection. From another point of view, one of the aromatic chromophores is perturbed by oxygen of the ring or

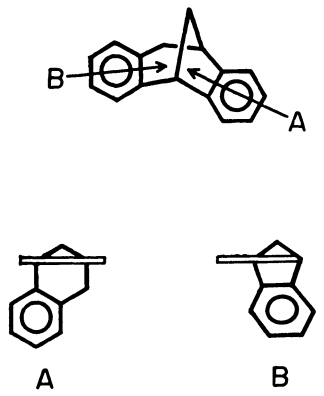


Fig. 5. Stereoformula of (+)-**35** and projection diagrams in the directions A and B.

the ring itself, though the sector rule[9] could not predict their contributions because the oxygen is situated in the negative sector while the ring is in the positive one. The contribution of the hydroxyl group at C-11 to the ^1L_b band CD was found to be positive from comparison of the CD spectra of (+)-**22b** with that of (+)-**34b**. Though this disagrees with the sector rule, it may suggest the predominance of the effect of the oxygen rather than the tetrahydrofuran ring in (+)-**42**.

Compounds (+)-**29b** and (+)-**31b** are antipodal to compounds (+)-**30b** and (+)-**32b** in the skeleton itself, respectively. The substituents, NH_2 or NH_3Cl do not change the direction of electric transition dipole moment of the aromatic chromophores. We would expect from the simple exciton coupling mechanism that they show CD spectra antipodal to each other. In fact, compounds (+)-**29b** and (+)-**30b** showed oppositely signed CD spectra in the wavelength region shorter than 230 nm. However, they showed almost the same magnitude of the positive Cotton effects in the region of the ^1L_b and ^1L_a transition. On the other hand, compounds (+)-**31b** and (+)-**32b** showed antipodal CD spectra in the region of the ^1L_b and ^1L_a transitions but the same signed Cotton effects in the shorter wavelength region.

Compounds (+)-**31b** and (+)-**32b** are not suitable for detailed treatments of the chiroptical properties, because of the uncertainty of the molecular orbitals of the chromophores or the direction of the transition dipoles. Therefore we will later describe the results of theoretical treatments of the optical activity of (+)-**29b** and (+)-**30b**.

In spite of the (+)-DMDC skeleton being rigid in conformation as previously described, the CD spectra of (+)-**25b** and (+)-**26b** were found to vary with temperature as shown in Table 2. For (+)-**25b**, assuming the equilibrium between two conformers, we estimated the free energy difference (ΔG^0) and the $\Delta\varepsilon$ values of two conformers by a simple method described by Moscowitz *et al.*[10]: $\Delta G^0 = 1.0$ kcal/mol; 298 nm ($\Delta\varepsilon$, +11.9 and −7.64); 235 nm ($\Delta\varepsilon$, +31.3 and −6.15).

With compound (+)-**26b**, the magnitude also increased for positive Cotton effects at 295—298 nm and at 230 nm and the negative Cotton effect at 254—

Table 2. Temperature dependent CD spectra of (+)-**25b** and (+)-**26b**

25 °C		−68 °C		−190 °C	
λ_{nm}	$\Delta\varepsilon$	λ_{nm}	$\Delta\varepsilon$	λ_{nm}	$\Delta\varepsilon$
(+)-**25b** in E. P. A.					
297	+8.94	298	+10.4	299	+11.8
260.5	+1.02	260.5	+0.40	260	−0.58
235	+25.7	235.5	+28.4	236	+31.2
227	0	227	0	227	0
(+)-**26b** in E. P. A.					
296.5	+7.97	295	+13.3	298	+13.8
257	−1.90	255	−5.06	254	−9.79
230 sh	+87.3	230	−87.9	230	+90.9
215	+136.	215.5	+135.	216	+138.

E. P. A. = Ether-isopentane-ethanol 5:5:2.

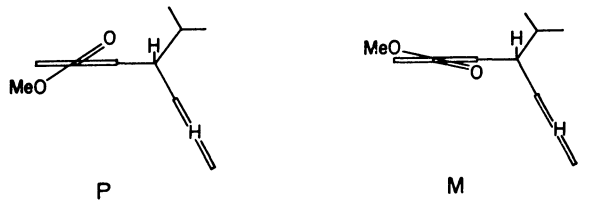


Fig. 6. Projective diagram of the rotamers P and M from the methoxycarbonyl group.

257 nm with the decrease in temperature. But the change could not be analyzed by assuming it to be an equilibrium between two kinds of species.

The methoxycarbonyl group at C-6 of (+)-**25b** and those at C-4 and C-19 of (+)-**26b** are not coplanar with the benzene ring judging from the steric interaction with the bridgehead proton (Fig. 6). But that at C-1 of (+)-**25b** can be coplanar with the benzene ring. Therefore, we deduced that (+)-**25b** had two rotamers. On the other hand, (+)-**26b** had more than two rotamers and showed complex temperature-dependent CD spectra.

The sign of the Cotton effect of the conjugation band in the 270 nm region is correlated with chirality of the conjugated system in some lactonic aromatic compounds, the absolute configurations of which have been determined. The P (right-handed) and M (left-handed) helicity produced positive and negative Cotton effects, respectively, as found with lycorenine alkaloids[11] (Table 3), ochracin derivatives[12] and dihydroisocoumarin compounds.[13]

This empirical rule predicts that the rotamer P will show a positive Cotton effect and the rotamer M, a negative one. Rotamer P would be more stable than rotamer M owing to an additional steric interaction of the methoxycarbonyl group with the proton at C-4. The experimental results of (+)-**25b** support the preference of the rotamer P.

A methoxycarbonyl group will change the direction of the electric transition dipole moment of the benzenoid chromophore, if it is fixed. But the CD spectra of (+)-**25b** and (+)-**26b** are quite similar to those of (+)-**29b** and (+)-**30b**, respectively. This may indicate that the CD spectra of DMDC are not altered very much by the minor change of direction of the local electric transition dipole moment.

Theoretical Consideration. For insight into the contribution of various factors to the chiroptical properties of (+)-**29b** and (+)-**30b**, we tried the following calculations.

1) The rotational strength was obtained by a coupling theory[14] using a point dipole approximation located at the center of the benzene ring. The local transition energy and intensity were taken from the experimental value of the four transitions of 5-aminotetralin.[††,4] Structural parameters required for the calculation were derived from idealized geometry as follows: aromatic C-alkyl C bond length=1.52 Å, aromatic C–C=1.40 Å, alkyl C–C=1.54 Å, C–N=1.38 Å, C_{11}–C_{1a}–C_{4a} and C_{1a}–C_{4a}–C_5 bond angles=122°, C_5–C_{5a}–C_9 and C_{5a}–C_{9a}–C_{10}=110°, and atoms C_5, C_{4a}, C_{1a}, C_{11}, and C_{10} in a plane.

2) The point dipole moment was displaced from the center of the benzene ring according to the calculation by the dipole velocity procedure[15] as follows: ^1L_b, −0.098 Å; ^1L_a, 0.375 Å; ^1B_b, −0.050 Å and ^1B_a, −0.038 Å toward the nitrogen atom.

3) The calculation of the molecular orbital and the rotational strength was as described in Ref. 1. The resonance energies between the two aromatic chromophores were evaluated by proportion to the overlap integrals.

4) All of the charge transfer (c.t.) transitions were neglected in calculating the rotational strength in the above treatment, though the MO contained the c.t. transition.

5) All of the c.t. transitions were neglected in obtaining the MO, and the rotational strength was calculated as in method 3.

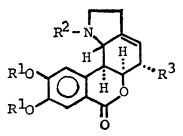
Figure 7 shows the results of the calculations by methods 1—5. The CD spectra calculated by method 1 are completely antipodal to each other for (+)-**29b** and (+)-**30b**. The displacement of the point dipole moment does not seem to improve the rotational strength. Thus the disagreement between the calculated and the observed CD spectra may be caused by the assumption of the local electric transition dipole moment as a point dipole and the neglect of the c.t. transition. The results calculated by method 3 reproduce the qualitative features of the CD spectra quite well, with the exception of the transition energy (Figs. 7 and 8). The shift, *ca.* 10 nm, is mainly caused by the direct use of the value of the π-SCF-MO of aniline as a local transition energy. Even if the contribution of the c.t. transition is neglected in calculating the rotational strength by the same MO in method 4, the difference from the results by method 3 is not very large. This similarity indicates that the rotational strength is mainly produced by the coupling of the local transition dipole moments and not very much by the c.t. transition.

When the c.t. transition is completely neglected in obtaining the MO, by method 5, the calculated CD spectra do not reproduce the experimental one. Though the couplet pattern around 230 nm in method

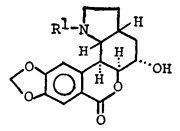
†† The unit should be corrected to 10^{19} cgs in Ref. 4.

TABLE 3. UV AND CD SPECTRA OF LYCORENINE ALKALOIDS

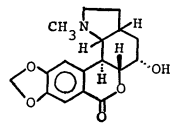
Compound	UV		CD		Solvent	Chirality
	λ_{nm}	ε	λ_{nm}	$\Delta\varepsilon$		
51	307	7040	275	−4.67	MeOH	M
	269	6050	254	+0.97		
	227	28700	232	−16.8		
51 HCl	306	4720	275	−4.79	MeOH	M
	269	4270	252	+4.21		
	227	20400	230	−6.67		
52	307	5330	275	−5.30	MeOH	M
	270	4050	252	+1.62		
	227.5	21400	232	−11.5		
52 HCl	305	6190	275	−4.21	MeOH	M
	270	5790	255	+3.67		
	227	27000	232	−9.58		
53	302	5230	310	−0.91	MeOH	M
	268	8650	273	−6.93		
	277	18300	250	+4.96		
			230	−9.82		
54	307	4550	311	−2.52	MeOH	M
	269	4100	272.5	−4.12		
	227	16800	250	+2.20		
			236	−1.12		
55	306	5150	310	−2.29	MeOH	M
	268	4920	273	−3.24		
	226	21100				
56	306	5420	305	−1.16	MeOH	P
	268	5450	271.5	+4.52		
	225.5	19500	245	−2.63		
			229.5	+6.97		



51: R^1=-CH_2-, R^2=CH_3, R^3=OH
52: R^1=-CH_2-, R^2=CH_3, R^3=OAc
53: R^1=CH_3, R^2=CH_3, R^3=H



54: R^1=CN
55: R^1=CH_3



56

5 is shared by six transitions in method 3, the sequence of the coupling mode does not change and method 3 gives good agreement with the experimental results in this region. Thus the c.t. transition must be taken into consideration in the calculation of the MO.

In method 5, the local electric transition dipole moment is not assumed to be a point dipole and the rotational strength is calculated by the dipole velocity method.

Also, in method 5 a local magnetic transition dipole moment is produced perpendicular to the benzene ring,[16] which distinguishes this method from methods 1 and 2. The result from method 5 agrees better with the experimental one than those from methods 1 and 2, especially in the region of the ^1L_b transition. This indicates that the induced magnetic transition dipole moment can not be neglected in the transition of small rotational strength.

In summary, the electric transition dipole moment should not treated as a point dipole at any place and the rotational strength should be calculated with a dipole velocity method. The c.t. transition continues

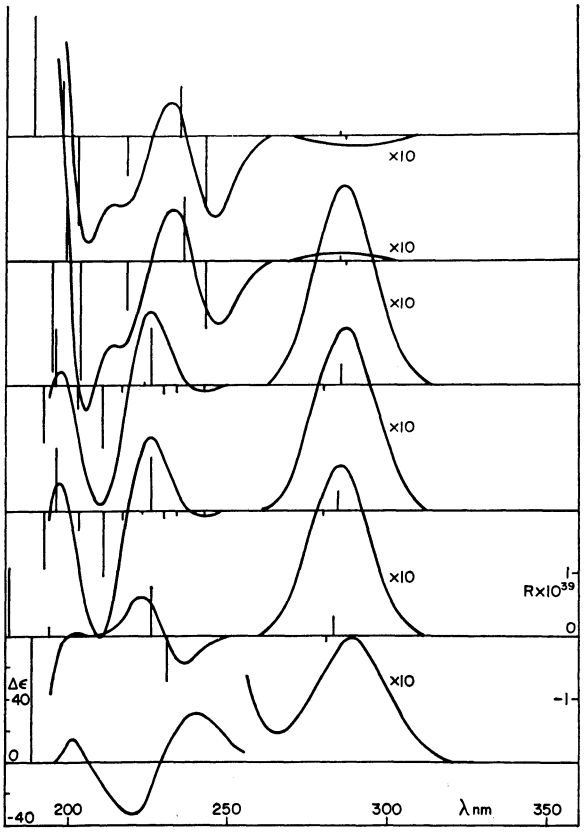


Fig. 7. CD spectra of (+)-**29b**. The theoretical spectra refer to calculations by methods 1 to 5 from the top. The experimental spectrum in cyclohexane is at the bottom.

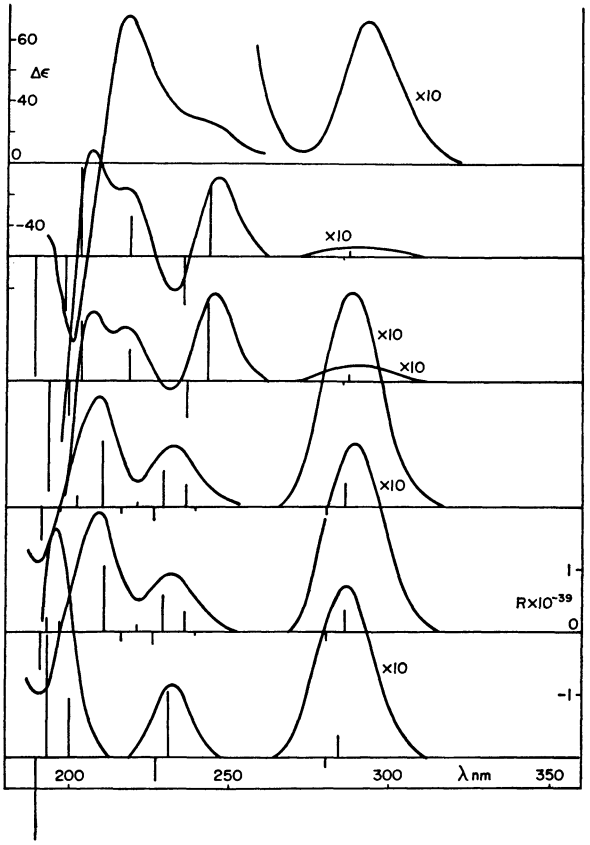


Fig. 8. CD spectra of (+)-**30b**. The experimental spectrum in cyclohexane is at the top. The theoretical spectra refer to calculations by methods 1—5 from the upper part.

to function in the chiroptical properties of the DMDC compounds and can not be neglected in the calculation of the MO, though it does not cause alteration of the coupling mode sequence. The rotational strength is mainly produced by the coupling of the local electric transition dipole moments without much contribution from the c.t. transition.

Experimental

IR spectra were recorded on a JASCO-DS-402G grating spectrophotometer. Optical rotations were determined with a Perkin-Elmer Model 141 polarimeter using a 1-dm microcell. Circular dichroism curves were obtained using a JASCO Model J-40C spectropolarimeter. ^{1}H NMR spectra were measured with a Varian A56/60 D spectrometer using tetramethylsilane as an internal standard. UV spectra were obtained with a Hitachi Model 323 spectrometer.

*Methyl 12-Hydroxy-DEA-1-carboxylate (**7a**) and (**8a**).* $NaBH_4$ (0.42 g) was added in small portions to a solution of methyl 12-oxo-DEA-1-carboxylate (**4a**) (1.03 g) in dry diglyme (20 ml) with ice cooling. The mixture was stirred for 3 h and dilute HCl was added dropwise at 0 °C. The mixture was extracted with ether. The solution was washed with water, dried (Na_2SO_4) and concentrated *in vacuo* to 1.05 g.

A small portion of the residue (53 mg) treated with acetic anhydride and pyridine gave the acetate. Its NMR showed it to be a 1:2 mixture of the epimers.

*(+)-Dimethyl 12-Hydroxy-DEA-1,5-dicarboxylate [(+)-(**7b**) and (+)-(**8b**)].* Dimethyl 12-oxo-DEA-1,5-dicarboxylate [(+)-(**4b**)] (10.1 g) was reduced as above to obtain the desired mixture, 11.0 g.

*Methyl 12-(3,5-Dinitrobenzoyloxy)-DEA-1-carboxylate (**13a**).* 3,5-Dinitrobenzoyl chloride (3.0 g) was added to a solution of a mixture of the alcohols **7a** and **8a** (1.0 g) in pyridine (15 ml) with ice cooling. The mixture was stirred for 1 h and allowed to stand overnight, poured into water and allowed to stand for 1 h. The mixture was extracted with chloroform. The solution was washed with dilute HCl, water, aqueous Na_2CO_3, and water, then dried (Na_2SO_4) and concentrated *in vacuo*. The oily residue was crystallized from benzene–ether and recrystallized twice from the same solvent, giving a colorless powder (113 mg): mp 216—217 °C; IR (Nujol) 1735, 1713, 1340 cm^{-1}; NMR ($CDCl_3$) δ 1.72 (1H, ddd, J=3, 3, 14 Hz), 2.59 (1H, ddd, J=3, 8, 14 Hz), 3.88 (3H, s), 4.45 (1H, t, J=3 Hz), 5.49 (1H, m), 6.02 (1H, d, J=2 Hz), 7.1—7.9 (7H, m), 8.90 (2H, d, J=2 Hz), 9.13 (1H, t, J=2 Hz). Found: C, 63.65; H, 3.75; N, 5.78%. Calcd for $C_{25}H_{18}N_2O_8$: C, 63.29; H, 3.82; N, 5.90%.

The epimer could not be isolated in pure form.

*(+)- and (±)-Dimethyl 11-(3,5-Dinitrobenzoyloxy)-DEA-1,5-dicarboxylate [(+)- and (±)-(**13a**) and (**13b**)].* The (+)- and (±)-alcohols (+)- and (±)-**7b** and **8b** were treated as above but both of the products could not be crystallized. The NMR spectrum showed a mixture of *ca.* 1:2 of the epimers.

*(+)-Dimethyl 11-(4-Nitrobenzoyloxy)-DEA-1,5-dicarboxylate [(+)-(**9b**)].* The (+)-alcohol (+)-**7b** and (+)-**8b**

(11.0 g) was treated with *p*-nitrobenzoyl chloride in the same manner as above. The residue was crystallized and recrystallized from ether, giving colorless prisms (1.5 g): mp 189—191 °C (racemic mp 189—190 °C) $[\alpha]_D^{21}$ +246.3°± 3.5° (*c* 0.709, $CHCl_3$); $\Delta\varepsilon$ +0.065 (333 nm), −0.036 (312), +7.12 (290), +15.9$_{sh}$ (235), +20.9$_{sh}$ (219), +26.6 (208); IR (Nujol) 1715, 1526, 1280 cm^{-1}; NMR ($CDCl_3$) δ 1.72 (1H, ddd, J=3, 3, 13 Hz), 2.52 (1H, ddd, J=13, 9, 3 Hz), 3.78 (3H, s), 4.96 (3H, s), 5.46 (1H, ddd, J=10, 3, 3 Hz), 5.78 (1H, t, J=3 Hz), 6.02 (1H, d, J=3 Hz), 7.0—8.4 (10H, m). Found: C, 66.27; H, 4.31; N, 2.81%. Calcd for $C_{27}H_{21}NO_8$: C, 66.53; H, 4.34; N, 2.87%.

The epimer could not be purified.

(+)-Dimethyl endo-*11-hydroxy-DEA-1,5-dicarboxylate* [*(+)-(**7b**)*]. A suspension of the (+)-ester (+)-**9b** (1.5 g) in a solution of sodium methoxide in methanol [Na metal (0.05 g) and methanol (25 mg)] was heated under reflux for 18 h and concentrated *in vacuo*. Water was added. The mixture was extracted with ethyl acetate. The solution was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was chromatographed on thick silica gel plate [Merck, pre-coated plate; benzene–ethyl acetate (3:1)]. The residue (0.7 g) could not be crystallized (racemic mp 142—145 °C).

(+)-Dimethyl exo-*11-hydroxy-DEA-1,5-dicarboxylate* [*(+)-(**8b**)*]. The crude ester (+)-**10b**, obtained from the mother liquor, was treated as above and gave the crude product (5.5 g).

Methyl endo-*12-hydroxy-DEA-1-carboxylate (**7a**)*. The ester **13a** was treated as above and gave an oily product.

Methyl exo-*12-hydroxy-DEA-1-carboxylate (**8a**)*. *1)* The crude ester **14a**, obtained from the mother liquor was treated as above and gave an oily product. *2)* A mixture of the ester **14a** (657 mg), obtained from the mother liquor, in a solution of 5% KOH in methanol (12 ml) was heated under reflux for 2 h, poured into water, acidified with dilute HCl and extracted with ether. The solution was washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The crystalline residue could not be fractionally recrystallized and was heated under reflux in methanol (20 ml) and concentrated H_2SO_4 (1 ml) for 15 h. The mixture was poured into water and extracted with ether. The solution was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was chromatographed on alumina (23 g, Merck, grade *2)* in benzene to obtain methyl 3,5-dinitrobenzoate and in ethyl acetate to obtain the oily product **8a** (402 mg).

(±)- and (+)-Dimethyl 11-Acetoxy-DMDC-1,6-dicarboxylate [*(±) (**17b**) and (+)-(**17b**)*]. A solution of *p*-toluenesulfonyl chloride (0.9 g) in pyridine (8 ml) was added dropwise to a solution of the alcohol (±) **7b** (0.45 g) in pyridine (15 ml) at −5——7 °C over a period of 1.5 h. The mixture was allowed to stand at 4 °C for 40 h, poured into ice water and extracted with ether. The solution was washed with dilute HCl and water, dried (Na_2SO_4), and concentrated *in vacuo*.

A solution of the crude tosylate (0.423 g) in a solution of anhydrous sodium acetate (0.5 g) in glacial acetic acid (20 ml) was heated at 105 °C for 3 d, concentrated *in vacuo* and dissolved in a mixture of ether and aqueous $NaHCO_3$. The organic phases were washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The NMR spectrum of the crude product was contaminated with less than 5% of dimethyl 11-acetoxy-DMDC-4,9-dicarboxylate (**18b**). The residue was crystallized from hexane and recrystallized from ether, giving a powder (152 mg): mp 173—175 °C; IR (Nujol) 1743, 1722 cm^{-1}; NMR ($CDCl_3$) δ 2.06 (3H, s), 2.40 (2H, m), 3.63 (2H, m), 3.75 (3H, m), 3.89 (3H, m), 4.90 (1H, m), 6.29 (1H, d, J=2 Hz), 7.0—7.4 (2H, m), 7.6—7.9 (4H, m). Found: C, 69.29; H, 5.29%. Calcd for $C_{22}H_{20}O_6$: C, 69.46; H, 5.30%.

The (+)-isomer (+)-**17b** could not be crystallized.

(+)-Dimethyl 11-Acetoxy-DMDC-4,9-dicarboxylate [*(+)-(**18b**)*]. The alcohol (+)-**8b** (5.5 g) was treated as above and gave an oily product (4.1 g).

*Methyl 11-Acetoxy-DMDC-1-carboxylate (**17a**)*. The alcohol **7a** (0.3 g) gave an oily product **17a** by the same treatment.

*Methyl 11-Acetoxy-DMDC-9-carboxylate (**18a**)*. The alcohol **8a** (0.402 g) gave the rearranged compound **18a** (0.286 g).

(+)-Dimethyl 11-Hydroxy-DMDC-1,6-dicarboxylate [*(+)-(**19b**)*]. The crude acetate (+)-**17b** obtained above was treated as in the solvolysis of **9b** and gave the crude product, which was chromatographed on thin silica gel plate [Merck, pre-coated; benzene–ethyl acetate (2:1)] and gave an oily material: $[\alpha]_D^{26}$ +310.4°±5.5° (*c* 0.714, $CHCl_3$); IR ($CHCl_3$) 3465, 1714 cm^{-1}; NMR ($CDCl_3$) δ 2.2—2.9 (2H, m), 3.68 (1H, broad s), 3.83 (3H, s), 3.90 (3H, s), 4.88 (1H, broad s), 4.91 (1H, d, J=4 Hz), 6.9—7.9 (6H, m).

(+)-Dimethyl 11-Hydroxy-DMDC-4,9-dicarboxylate [*(+)-(**20b**)*]. Oil, $[\alpha]_D^{22}$ +433.5°±9.9° (*c* 0.480, MeOH); IR ($CHCl_3$) 3610, 1717 cm^{-1}; NMR ($CDCl_3$) δ 2.43 (2H, m), 3.90 (3H, s), 3.95 (3H, s), 4.16 (1H, broad s), 4.85 (1H, d, J=2 Hz), 4.98 (1H, broad s), 6.9—7.9 (6H, m); (racemic compound, mp 152—153 °C).

*Methyl 11-Hydroxy-DMDC-1-carboxylate (**19a**)*. Oil; IR (film) 3480, 1700 cm^{-1}; NMR ($CDCl_3$) δ 2.2—2.8 (2H, m), 3.65 (1H, m), 3.78 (1H, s), 3.94 (1H, m), 4.88 (1H, d, J=3 Hz), 6.9—7.5 (1H, m), 7.71 (1H, dd, J=7, 2 Hz).

*Methyl 11-Hydroxy-DMDC-9-carboxylate (**20a**)*. Mp 159—161 °C; IR (Nujol) 3503, 1698, 1024, 1012 cm^{-1}; NMR ($CDCl_3$) δ 2.40 (2H, m), 3.89 (3H, s), 3.90 (1H, s), 4.17 (1H, m), 4.82 (1H, d, J=2 Hz), 6.9—7.5 (6H, m), 7.72 (1H, dd, J=7.2 Hz). Found: C, 76.77; H, 5.64%. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75%.

1-Hydroxymethyl-endo-*12-hydroxy-DEA and 1-Hydroxymethyl*-exo-*1-hydroxy-DEA* [*(**15a**) and (**16a**)*]. A solution of the keto ester **4a** (193 mg) in dry tetrahydrofuran (5 ml) was added to a slurry of $LiAlH_4$ (100 mg) in tetrahydrofuran (5 ml) with ice cooling. This mixture was heated under reflux for 2 h. Excess $LiAlH_4$ was decomposed with a solution of methanol in ether then dilute HCl with ice cooling. The organic phase was separated and the aqueous phase was extracted with ether. The combined organic phases were washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The oily residue was chromatographed on thin silica gel plate [Merck, pre-coated; benzene–ethyl acetate (1:3)].

Fraction 1, 54.3 mg, was recrystallized from benzene: mp 169—170 °C; IR ($CHCl_3$) 3611, 3482 cm^{-1} (8.565×10^{-3} M/l); NMR ($CDCl_3$) δ 1.36 (1H, ddd, J=3, 3, 13 Hz), 2.28 (1H, ddd, J=3, 9, 13 Hz), 4.30 (1H, t, J=3 Hz), 4.30 (1H, m), 4.52 (1H, d, J=12 Hz), 4.80 (1H, d, J=3 Hz), 5.01 (1H, d, J=11 Hz), 7.0—7.5 (7H, m), Found: C, 80.45; H, 6.30%. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39%.

Fraction 2, 76.1 mg, was recrystallized from benzene: mp 142—143 °C; IR ($CHCl_3$) 3606, 3576 cm^{-1} (7.525×10^{-3} M/l); NMR ($CDCl_3$) δ 1.30 (1H, ddd, J=3, 3, 13 Hz), 2.21 (1H, ddd, J=3, 9, 13 Hz), 4.10 (1H, m), 4.20 (1H, t, J=3 Hz), 4.66 (3H, d, J=3 Hz), 6.9—7.4 (7H, m). Found: C, 81.89; H, 6.47%. Calcd for $C_{17}H_{16}O_2\cdot1/2C_6H_6$: C, 82.44; H, 6.57%.

Reduction of the diesters **5a** and **6a** gave the same product.

(+)-11-Hydroxy-1,6-bis(hydroxymethyl)-DMDC [*(+)-(**21b**)*]. The ester (+)-**19b** (80 mg) was reduced as described above and recrystallized from ethyl acetate: mp 194—196 °C, (31.6 mg), $[\alpha]_D^{22}$ +47.9°±1.6° (*c* 0.553, MeOH); IR ($CHCl_3$) 3595, 3439 cm^{-1} (a supernatant of 3.09 mg/5 ml); NMR (CD_3OD) δ 2.1—2.8 (2H, m), 3.47 (1H, broad s), 4.78 (1H, m), 4.44 (1H, d, J=13 Hz), 4.60 (2H, s), 4.78 (1H, d, J=13 Hz), 4.82 (s), 6.9—7.4 (6H, m). Found: C, 76.04; H, 6.44%. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43%.

(+)-11-Hydroxy-4,9-bis(hydroxymethyl)-DMDC [*(+)-(**22b**)*]. The ester (+)-**20b** (101 mg) was reduced as described above to give a powder (24.5 mg): mp 155—156 °C, $[\alpha]_D^{22}$ +357.8°±7.0° (*c* 0.573, MeOH); IR ($CHCl_3$) 3603 cm^{-1} (supernatant of 3.26 mg/5 ml); NMR (CD_3OD) δ 2.42 (2H, m), 3.62 (1H, broad s), 4.35 (1H, broad s), 4.65 (2H, s), 6.8—7.4 (6H, m). Found: C, 76.34; H, 6.53%. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43%.

11-Hydroxy-1-hydroxymethyl-DMDC (***21a***). The ester **19a** (87 mg) was reduced in the same manner to give a powder (48 mg): mp 155 °C; IR ($CHCl_3$) 3590, 3440 cm^{-1} (8.52×10^{-3} M/l); NMR ($CDCl_3$) δ 2.2—2.7 (2H, m), 3.52 (1H, broad s), 3.93 (1H, m), 4.23 (1H, d, J=12 Hz), 4.64 (1H, d, J=12 Hz), 4.80 (1H, d, J=2 Hz), 6.9—7.5 (7H, m). Found: C, 80.65; H, 6.51%. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39%.

11-Hydroxy-9-hydroxymethyl-DMDC (***22a***). The ester **20a** (24 mg) was reduced as described above to give a powder (6.5 mg): mp 129—130 °C; IR ($CHCl_3$) 3604 cm^{-1} (8.53×10^{-3} M/l); NMR ($CDCl_3$) δ 2.40 (2H, m), 3.63 (1H, m), 3.87 (1H, t, J=2 Hz), 4.62 (2H, s), 4.72 (1H, d, J=2 Hz), 6.9—7.3 (7H, m). Found: C, 80.78; H, 6.34%. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39%.

(+)-Dimethyl DMDC-4,9-dicarboxylate [*(+)-(**26b**)*]. A mixture of the hydroxy ester (+)-**20b** (2.8 g), 30% palladium charcoal (0.9 g) and a few drops of 70% perchloric acid in methanol (130 ml) was stirred in a hydrogen atmosphere for 6 d. The catalyst was filtered then washed with methanol. The filtrate was concentrated *in vacuo*. The residue was dissolved in dichloromethane, washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was distilled at 220 °C (bath temperature) at 0.05 mmHg through a short-path distillation apparatus and gave a viscous oil (2.4 g).

A solution of the (+)-diester (2.25 g) in a solution of 5% KOH in methanol (60 ml) was heated under reflux for 2 h and concentrated to the half volume *in vacuo*. Ice-cold dilute HCl was added. The crystals were collected by filtration, washed with water and dissolved in ethyl acetate. The solution was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was recrystallized from acetone, ethyl acetate then methanol and gave (+)-**28b**: mp 258—262 °C, $[\alpha]_D^{21}$ +575.4°±9.4° (*c* 0.349, MeOH); IR (Nujol) 1692 cm^{-1}; NMR (CD_3OD) δ 2.00 (1H, d, J=11 Hz), 2.42 (1H, ddd, J=11, 6, 1 Hz), 2.84 (1H, dd, J=4 Hz), 3.33 (1H, dd, J=18, 6 Hz), 4.18 (1H, broad t, J=4 Hz), 4.98 (1H, d, J=4 Hz), 6.9—7.8 (6H, m). Found: C, 73.37; H, 4.91%. Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.79%.

The (+)-dicarboxylic acid (55.3 mg) was esterified with excess diazomethane to give the diester (60 mg), which was crystallized from hexane: mp 92.5—93.5 °C; $[\alpha]_D^{21}$ +547.4°±9.6° (*c* 0.327, $CHCl_3$); IR ($CHCl_3$) 1716 cm^{-1}; NMR ($CDCl_3$) δ 2.04 (1H, d, J=13 Hz), 2.46 (1H, ddd, J=10, 6, 1 Hz), 2.92 (1H, dd, J=16, 1 Hz), 3.38 (1H, dd, J=16, 5 Hz), 3.88 (3H, s), 3.93 (3H, s), 4.15 (1H, broad t, J=4 Hz), 4.91 (1H, d, 5 Hz), 6.9—7.8 (6H, m), Found: C, 73.84; H, 5.49%. Calcd for $C_{20}H_{18}O_4$: C, 74.51; H, 5.63%.

(+)-Dimethyl DMDC-1,6-dicarboxylate [*(+)-(**25b**)*]. The same hydrogenolysis was carried out on the alcohol (+)-**19b** (110 mg) giving the desired product (44 mg): mp 113 °C; $[\alpha]_D^{22}$ +315.3°±2.0° (*c* 0.275, $CHCl_3$); IR (film) 1719 cm^{-1}; NMR ($CDCl_3$) δ 1.9—2.8 (2H, m), 2.9—3.3 (1H, m), 3.3—3.7 (2H, m), 3.77 (3H, s), 3.90 (3H, s), 4.82 (1H, d, J=5 Hz), 6.9—7.9 (6H, m). Found: C, 74.65; H, 5.57%. Calcd for $C_{20}H_{18}O_4$: C, 74.51; H, 5.63%.

Methyl DMDC-9-carboxylate (***26a***). The acetate **20a** (238 mg) was hydrogenolyzed according to the procedure cited above and gave prisms (53.3 mg): mp 80—81 °C; IR 1713 cm^{-1}; NMR ($CDCl_3$) δ 2.12 (1H, d, J=13 Hz), 2.47 (1H, broad dd, J=13, 6 Hz), 2.85 (1H, d, J=16 Hz), 3.32 (1H, dd, J=16, 6 Hz), 6.8—7.3 (6H, m), 7.73 (1H, dd, J=8, 2 Hz). Found: C, 81.43; H, 5.97%. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10%.

(+)-DMDC-1,6-dicarboxylic Acid [*(+)-(**27b**)*]. Mp 259—260 °C; $[\alpha]_D^{22}$ ±315.3°±5.7° (*c* 0.347, MeOH).

(+)-1,6-Diamino-DMDC [*(+)-(**29b**)*]. NaN_3 (1.11 g) was added in small portions to a solution of the (+)-dicarboxylic acid [(+)-(**27b**)] (612 mg) in concentrated H_2SO_4 (33 ml) at 40—45 °C over a period of 1 h with vigorous stirring. The mixture was then heated at 50 °C for 6 h, allowed to stand overnight, poured onto ice, made alkaline with 40% aqueous NaOH and extracted with benzene. The solution was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The crystalline residue was recrystallized from benzene and gave prisms (368 mg) (74.9%): mp 178—179 °C; $[\alpha]_D^{22}$ +736.1°±11.4° (*c* 0.357, MeOH); IR (Nujol) 3355 cm^{-1}; NMR ($CDCl_3$) δ 1.97 (1H, d, J=10 Hz), 2.41 (1H, dd, J=5, 10 Hz), 2.63 (1H, d, J=14 Hz), 3.12 (1H, dd, J=5, 14 Hz), 3.31 (1H, d, J=4 Hz), 3.51 (4H, s), 3.90 (1H, d, J=5 Hz), 6.2—7.4 (6H, m). Found: C, 81.29; H, 6.76; N, 11.78%. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85%.

(+)-4,9-Diamino-DMDC [*(+)-(**30b**)*]. The (+)-dicarboxylic acid [(+)-(**28b**)] (45 mg) was treated as above and gave prisms (21.5 mg): mp 224—225 °C; $[\alpha]_D^{23}$ +212.9°±4.1° (*c* 0.364, $CHCl_3$); IR (Nujol) 3465, 3375 cm^{-1}; NMR ($CDCl_3$-a drop of CD_3OD) δ 2.07 (1H, d, J=11 Hz), 2.42 (1H, dd, J=5, 11 Hz), 2.66 (1H, dd, J=5, 16 Hz), 3.15 (1H, dd, J=5, 16 Hz), 3.5 (1H, m), 3.81 (1H, d, J=5 Hz), 6.3—7.3 (6H, m). Found: C, 80.99; H, 6.66; N, 12.04%. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85%.

*1,5-bis(hydroxymethyl)-11-*endo*-hydroxy-DEA* (***15b***). A solution of the ester **9b** (99 mg) in dry tetrahydrofuran (3 ml) was added to a slurry of $LiAlH_4$ (0.1 g) in tetrahydrofuran (3 ml) with cooling in ice. The mixture was then heated under reflux for 2 h and treated as usual. The residue was chromatographed on thin silica gel plate [Merck, pre-coated plate; ethyl acetate] and recrystallized from chloroform, giving a powder (31.2 mg): mp 153—154 °C; IR ($CHCl_3$) 3607, 3484 cm^{-1} (1.495 M/l); NMR (CD_3OD) δ 1.33 (1H, ddd, J=3, 3, 13 Hz), 2.22 (1H, ddd, J=3, 9, 13 Hz), 4.13 (1H, m), 4.5—4.8 (m), 6.8—7.4 (6H, m). Found: C, 75.67; H, 5.41%. Calcd for $C_{18}H_{18}O_4$: C, 76.57; H, 6.43%.

(+)-4,9-Bis(hydroxymethyl)-DMDC [*(+)-(**34b**)*]. The (+)-diester (+)-**26b** (91 mg) was reduced as above. The product could not be crystallized and was converted into the bis(3,5-dinitrobenzoyl) ester according to the above procedure, giving crystals (109 mg): mp 176—178 °C; $[\alpha]_D^{22}$ +179.8°±2.5° (*c* 0.511, $CHCl_3$); IR (Nujol) 1720, 1550,

1288 cm^{-1}; NMR ($CDCl_3$) δ 2.20 (1H, d, J=11 Hz), 2.64 (1H, dd, J=5, 11 Hz), 2.86 (1H, d, J=16 Hz), 3.43 (1H, dd, J=5, 16 Hz), 3.78 (1H, m), 4.42 (1H, m), 5.55 (1H, s), 5.57 (1H, d, J=12 Hz), 5.82 (1H, d, J=12 Hz), 6.9—7.4 (6H, m), 9.1—9.3 (6H, m). Found: C, 58.63; H, 3.54; N, 8.18%. Calcd for $C_{32}H_{22}N_4O_{12}$: C, 58.72; H, 3.39; N, 8.56%.

The ester was hydrolyzed with a 5% KOH solution in methanol by refluxing for 3 h giving an oily residue: $[\alpha]_D^{23}$ +407.5°±6.1° (c 0.402, MeOH); NMR ($CDCl_3$) δ 2.06 (1H, d, J=11 Hz), 2.48 (1H, dd, J=11Hz), 2.77 (1H, d, J=16 Hz), 3.28 (1H, dd, J=16, 5 Hz), 3.63 (1H, m), 4.34 (1H, d, J=5 Hz), 4.68 (2H, s), 4.80 (2H, s), 6.8—7.3 (6H, m). Found: C, 79.96; H, 6.79%. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49%.

*(+)-11-Hydroxy-DMDC-4,9-dicarboxylic Acid (**24b**).* A crude rearranged compound **18b** (4.1 g) was hydrolyzed with a solution of 5% KOH in methanol (60 ml) by heating under reflux for 3 h. The product could not be purified by recrystallization and was esterified with methanol in the presence of concentrated H_2SO_4 by heating under reflux for 16 h. The crude ester was chromatographed on a thick silica gel plate [Merck, pre-coated plate; benzene–ethyl acetate (5:2)]. The residue was crystallized from benzene–hexane giving a powder (1.0 g): mp 152—153 °C. Found: C, 71.32; H, 5.51%. Calcd for $C_{20}H_{18}O_5$: C, 70.99; H, 5.36%.

The ester was hydrolyzed as above. Mp 286 °C (dec); IR (Nujol) 1692 cm^{-1}; NMR (CD_3OD) δ 2.30 (2H, m), 4.32 (2H, broad s), 5.00 (1H, broad s), 6.9—7.9 (6H, m). Found: C, 70.22; H, 4.72%. Calcd for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55%.

*(+)-DMDC [(+)-(**35**)].* A mixture of the (+)-dicaboxylic acid [(+)-(**28b**)] (163 mg), copper chromite (220 mg) and quinoline, which was distilled over copper chromite, was heated under reflux for 1.5 h, poured into water and extracted with ether. The solution was washed with dilute HCl, aqueous $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was chromatographed on thin silica gel plate [Merck, pre-coated; hexane] and distilled at 140 °C (bath temperature) at 0.05 mmHg (1mmHg=133.322 Pa). $[\alpha]_D^{23}$ +206.5°±2.0° (c 0.3056, $CHCl_3$); IR (film) 750 cm^{-1}; NMR ($CDCl_3$) δ 2.08 (1H, d, J=11 Hz), 3.23 (1H, dd, J=15, 5 Hz), 3.46 (1H, m), 3.85 (1H, d, J=4 Hz), 7.8—7.4 (8H, m). Found: C, 92.92; H, 6.61%. Calcd for $C_{16}H_{14}$: C, 93.16; H, 6.84%.

*Ethyl 11-Hydroxy-DEA-11-acetate (**36**).* The procedure used was a modification of a reported method.[7] A solution of 11-oxo-DEA (10.3 g) and ethyl bromoacetate (10 ml) in dry tetrahydrofuran (70 ml) was added dropwise to a mixture of activated Zn powder (20 g) in tetrahydrofuran (80 ml) with vigorous stirring at refluxing temperature. The reaction was started by addition of a small piece of iodine. After completion of the addition, the mixture was heated for 1 h. Activated Zn powder (20 g) and a small piece of iodine was added together. The mixture was again heated for 30 min. A solution of ethyl bromoacetate (2 ml) in tetrahydrofuran (5 ml) and activated Zn powder (20 g) were added. Heating of the solution was continued for 1 h. Acetic acid (20 ml) was added with cooling in ice then water was added. The organic phase was separated and the aqueous phase was extracted with ether. The combined organic phases were washed with dilute NH_4OH and water, dried (Na_2SO_4) and concentrated *in vacuo*. The oily residue was crystallized from ether giving colorless crystals, 9.8 g (68.0%). All of the physicochemical properties were identical with those of the authentic samples.

*11-Hydroxy-DEA-11-acetic Acid (**37**).* A solution of the ester **36** (1.0 g) in 5% KOH solution of methanol (20 ml) was heated under reflux for 2 h then poured into ice-cold dilute HCl (1.8 ml of concentrated HCl in 80 ml of ice water). The mixture was extracted with ethyl acetate. The solution was washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. The crystalline residue, 0.877 g (96.4%), was washed with ether. Mp 211 °C.

*Optical Resolution of the Carboxylic Acid **37**.* A solution of the acid **37** (0.877 g) in methanol (5 ml) was added to a solution of cinchonidine (0.925 g) in methanol (10 ml). The solvent was changed to ethyl acetate. The crystals were collected by filtration and recrystallized from methanol four times to give a pure diastereomer (0.34 g): $[\alpha]_D^{25}$ −89.5°±1.7° (c 0.784, MeOH).

The salt was shaken with ethyl acetate and dilute HCl. The organic phase was separated and the aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was crystallized from methanol–water giving crystals (0.15 g): mp 139—140 °C, 158—159 °C (dimorphism), $[\alpha]_D^{27}$ −21.6°±0.6° (c 1.060, MeOH); IR (Nujol) 3330, 1708 cm^{-1}. Found: C, 75.83; H, 6.04%. Calcd for $C_{18}H_{16}O_3 \cdot 1/2H_2O$: C, 74.72; H, 5.92%.

*(−)-Methyl 11-Hydroxy-DEA-11-acetate [(−)-(**38**)].* A solution of the (−)-carboxylic acid (−)-**37** (0.685 g) in ether (10 ml) was added to a solution of excess diazomethane in ether. The solution was allowed to stand at 5 °C for 30 min and concentrated *in vacuo*. The crystalline residue was recrystallized from ether–hexane giving crystals (0.707 g): mp 117—118 °C; IR (Nujol) 3520, 3490, 1726, 1715 cm^{-1}; $[\alpha]_D^{24}$ +15.2°±0.5° (c 1.246, $CHCl_3$), CD $\Delta\varepsilon$ −0.175 (272.5 nm), +0.04 (270), −0.10 (267), +0.09 (262), +5.33 (232) (94.4% optical purity). Found: C, 77.82; H, 6.42%. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16%.

*(−)-11-Hydroxy-11-(2-hydroxymethyl)-DEA [(−)-(**39**)].* The (−)-ester (−)-**38** was reduced with $LiAlH_4$ by the same method reported for the reduction of the racemic ethyl ester **36**.[7] Mp 131—132 °C; $[\alpha]_D^{24}$ −21.4°±0.6° (c 1.027, MeOH), CD $\Delta\varepsilon$ −0.118 (273 nm), +0.023 (270), +0.052 (266), +6.33 (231), −7.78 (213) (94.4% optical purity).

*(−)-Monomesylate [(−)-(**40**)] of (−)-11-Hydroxy-11-(2-hydroxyethyl)-DEA.* The optically active compound (0.427 g, 95.3%) was synthesized from (−)-**39** (0.347 g) by the same procedure cited for the racemic compound.[7] The oily residue was used for the next preparation without further purification.

*(−)-Spiro[9,10-dihydro-9,10-ethanoanthracene-11,2′-oxetane] [(−)-(**41**)].* The optically active compound was also prepared by the same method cited for the racemic one. Mp 136—138 °C, $[\alpha]_D^{24}$ −67.0°±1.0° (c 1.119, $CHCl_3$), CD $\Delta\varepsilon$ +0.03 (276.5 nm), −0.16 (273), +0.087 (269.5), −0.12 (266), +0.056 (263), +2.20 (228) (94.4% optical purity).

*2,3,3a,12b-Tetrahydro-3a,8-methano-8H-dibenzo[3,4:6,7]cyclohepta[b]furan [(+)-(**42**)].* 1) The (−)-oxetane (−)-**41** (9.51 mg) was dissolved in chloroform (1 ml) containing *p*-toluenesulfonic acid (10 mg). After 3 min, $[\alpha]_D^{24}$ +145.8°±2.0°. The value did not change after 6 h.

2) The (−)-oxetane (−)-**41** (0.15 g) was dissolved in a solution of *p*-toluenesulfonic acid (0.1 g) in chloroform (10 ml). The solution was shaken for 10 min, washed with aqueous $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated *in vacuo*. The oily residue (0.137 g) was distilled at 180 °C (bath temp) at 0.4 mmHg through a short path distillation apparatus. $[\alpha]_D^{24}$ +132.2°±3.6° (c 0.481, $CHCl_3$).

*(+)-10-(2-Hydroxyethyl)-DMDC [(+)-(**43**)].* A

mixture of the rearranged material (+)-**42** (63 mg, 94.4% e.e.), 30% palladium charcoal (0.4 g), a drop of 70% perchloric acid, and ethanol (4 ml) was stirred in a hydrogen atmosphere for 5 d. The catalyst was removed by filtration. The filtrate was concentrated *in vacuo*. The residue was chromatographed on florisil (5 g) in dichloromethane and crystallized from ether. Mp 131—134 °C; $[\alpha]_D^{25}$ +180.0° ±2.6° (*c* 0.845, MeOH).

*DMDC-10-Acetic Acid (**44**).* A Jones' reagent was added to a solution of the alcohol **39** (3.3 g) in acetone (50 ml) with cooling in ice until the characteristic brown color persisted. After 10 min, the mixture was diluted with water and extracted with ether. The solution was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The oily residue was crystallized from benzene–hexane giving a powder, 2.5 g (71.7%): mp 155—156 °C; IR (Nujol) 1700 cm^{-1}. Found: C, 82.70; H, 6.21%. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10%.

*Optical Resolution of **44**.* Cinchonidine (2.60 g) was added to a solution of the carboxylic acid **44** (2.33 g) in methanol (40 ml). The mixture was warmed to a clean solution then allowed to stand at room temperature overnight. The crystals were collected by filtration and recrystallized from methanol three times to give the pure diastereomer (1.25 g): $[\alpha]_D^{24}$ −163.8°±5.6° (*c* 0.469, MeOH).

The salt was shaken with dilute HCl and ether. The organic phase was separated and the aqueous phase was extracted with ether. The combined organic phases were washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The oily residue, 0.578 g, could not be crystallized. $[\alpha]_D^{24}$ −170.0°±1.6° (*c* 1.329, MeOH).

*(−)-Methyl DMDC-10-Acetate [(−)-(**45**)].* A solution of the (−)-carboxylic acid (−)-**44** (0.157 g) in ether (3 ml) was added dropwise to a solution of excess diazomethane in ether with ice cooling. The mixture was stirred for 30 min and concentrated *in vacuo*. The residue was distilled at 200 °C (bath temperature) at 0.4 mmHg giving a viscous oil, 0.162 g (98.0%): $[\alpha]_D^{23}$ −158.4°±2.4° (*c* 0.826, $CHCl_3$); IR (film) 1738 cm^{-1}. Found: C, 81.82; H, 6.48%. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52%.

*(−)-1-(2-Hydroxyethyl)-DMDC [(−)-(**43**)].* The ester (−)-**45** (0.148 g) was reduced with $LiAlH_4$ as for (−)-**38**. The residue was distilled at 180 °C at 0.4 mmHg. The distillate (0.113 g) crystallized quickly and then was recrystallized from ether giving a powder (0.088 g): mp 133—134 °C; $[\alpha]_D^{23}$ −190.6°±3.1° (*c* 0.745, MeOH). Found: C, 86.51; H, 7.25%. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25%.

*Mesylate (−)-**46** of (−)-1-(β-Hydroxyethyl)-DMDC.* (−)-**43** (0.341 g) was mesylated as usual. The residue crystallized on standing and was used for the next preparation.

*(−)-10-Ethyl-DMDC [(−)-(**47**)].* A solution of the (−)-mesylate (−)-**46** (0.40 g) in dry tetrahydrofuran (5 ml) was added to a slurry of $LiAlH_4$ (0.3 g) in tetrahydrofuran (10 ml) with ice cooling. The mixture was then heated under reflux for 6 h. Excess $LiAlH_4$ was decomposed with a solution of methanol in ether then dilute HCl with ice cooling. The mixture was extracted with ether. The solution was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was chromatographed on alumina (Merck grade 2, 7 g) in hexane. The elute was recrystallized from hexane: mp 81—82 °C, $[\alpha]_D^{25}$ −187.1°±2.0° (*c* 1.150, $CHCl_3$) (0.175 g); IR (Nujol) 755 cm^{-1}; NMR ($CDCl_3$) δ 1.00 (3H, t, J=7.0 Hz), 1.7—2.1 (2H, m), 2.34 (1H, ddd, J=1, 5, 10 Hz), 2.50 (1H, dd, J=1, 16 Hz), 3.10 (1H, d, J=16 Hz), 3.92 (1H, d, J=5 Hz), 6.8—7.3 (8H, m). Found: C, 92.47; H, 7.70%. Calcd for $C_{18}H_{18}$: C, 92.26; H, 7.74%.

*Oxidation of (−)-10-Ethyl-DMDC [(−)-(**47**)].* A mixture of the (−)-hydrocarbon (−)-**47** (0.325 g), *N*-bromosuccinimide (0.3 g), *m*-chloroperbenzoic acid (10 mg), and dry carbon tetrachloride (10 ml) was heated under reflux for 8 h. After cooling, the mixture was filtered and the solid was washed with carbon tetrachloride. The filtrate was concentrated *in vacuo*. The residue was chromatographed on thin silica gel plate [Merck, pre-coated plate; benzene]. The fraction of the larger R_f value was recrystallized from ether giving colorless crystals (62.5 mg): $[\alpha]_D^{25}$ 0°, $[\alpha]_{365}^{25}$ 0° (*c* 0.727, $CHCl_3$): mp 173—175 °C; IR (Nujol) 810, 770, 753 cm^{-1}; NMR ($CDCl_3$) δ 1.41 (3H, d, t, J=7, 1 Hz), 2.31 (2H, m), 4.40 (1H, t, J=3 Hz), 4.63 (1H, s), 5.56 (1H, m), 6.9—7.4 (8H, m). Found: C, 92.45; H, 6.82%. Calcd for $C_{18}H_{16}$: C, 93.05; H, 6.94%. The fraction with the smaller R_f value was recrystallized from hexane and gave (−)-**48** (46.4 mg): mp 130—134 °C; $[\alpha]_D^{23}$ −111.0° ±1.7° (*c* 0.928, $CHCl_3$); IR 1687, 763 cm^{-1}; δ ($CDCl_3$) 0.95 (3H, t, J=7 Hz), 1.87 (1H, q, J=7 Hz), 2.45 (1H, q, J=7 Hz), 2.72 (2H, d, J=3 Hz), 4.17 (1H, t, J=3 Hz), 6.9—7.4 (7H, m), 7.8—8.0 (1H, m). Found: C, 86.87; H, 6.49%. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49%.

We thank Dr. Kazuo Tori for the NMR measurement, Mr. Mamoru Takasuka for the IR measurements, and Mr. Tatsuo Iwata for assistance in performing the variable-temperature CD measurement.

References

1) S. Hagishita and K. Kuriyama, *Tetrahedron*, **28**, 1435 (1972).
2) J. A. Schellman, *Acc. Chem. Res.*, **1**, 1448 (1968); R. Grinter and S. F. Mason, *Trans. Faraday Soc.*, **60**, 274 (1964); S. F. Mason and G. W. Vane, *J. Chem. Soc., B*, **1966**, 370.
3) S. Hagishita and K. Kuriyama, *Bull. Chem. Soc. Jpn.*, **44**, 617 (1971).
4) S. Hagishita and K. Kuriyama, *J. Chem. Soc., Perkin Trans. 2*, **1978**, 59.
5) S. J. Cristol, J. R. Mohrig, and D. E. Plorde, *J. Org. Chem.*, **30**, 1956 (1965).
6) S. J. Cristol, F. P. Parungo, and D. E. Plorde, *J. Am. Chem. Soc.*, **87**, 2870 (1965); S. J. Cristol and M. C. Kochansky, *J. Org. Chem.*, **40**, 2171 (1975) and references cited therein.
7) P. F. Hudrlik, A. M. Hudrlik, and C.-N. Wan, *J. Org. Chem.*, **40**, 1116 (1975).
8) H. Tatemitsu, F. Ogura, Y. Nakagawa, K. Naemura, and M. Nakazaki, *Bull. Chem. Soc. Jpn.*, **48**, 2473 (1975).
9) J. A. Schellman, *J. Chem. Phys.*, **44**, 55 (1966); G. Snatzke and P. C. Ho, *Tetrahedron*, **27**, 3645 (1971); K. Kuriyama, T. Iwata, M. Moriyama, K. Kotera, Y. Hamada, R. Mitsui, and K. Takeda, *J. Chem. Soc., B*, **1967**, 46.
10) A. Moscowitz, K. Wellman, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 3515 (1963).
11) K. Kotera, Y. Hamada, and R. Nakane, *Tetrahedron*, **24**, 759 (1968), we thank Dr. Hamada for giving us the samples.
12) H. Arakawa, *Bull. Chem. Soc. Jpn.*, **41**, 2541 (1968).
13) T. R. Govindachari, S. J. Patankar, and N. Viswanathan, *Phytochemistry*, **10**, 1603 (1971).
14) B. Bosnich, *Acc. Chem. Res.*, **2**, 266 (1969).
15) S. F. Mason, *J. Chem. Soc., Chem. Commun.*, **1973**, 239.
16) D. J. Caldwell and H. Eyring, *Ann. Rev. Chem.*, **15**, 281 (1964); A. Moscowitz, A. Rosenberg, and A .E. Hansen, *J. Am. Chem. Soc.*, **87**, 1813 (1965).