BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 43 3505—3510 (1970)

A Study on the Photochemistry of α,β-Unsaturated γ-Lactones. I. The Structures of the Photodimers of 4-Hydroxycrotonic Acid γ-Lactone[*1]

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(Received April 27, 1970)

The structures of the photodimers obtained from 4-hydroxycrotonic acid γ-lactone under several conditions were determined. The products of irradiations in the solution were a pair of *anti* dimers: one is a *head-to-head* cyclo-adduct, and the other a *head-to-tail* adduct. The corresponding product in the solid state, on the other hand, was a *head-to-head* cyclo-adduct in the *syn* form.

Irradiation of 2-cyclopentenone and 2-cyclohexenone has been well known to afford the photodimers only in the *anti* forms.[1] In the case of coumarine, however, a photodimer in the *syn* form was obtained provided that the reaction was carried out in polar solvents.[2] The stereo-specificities of these photo-dimerizations are very important both from theoretical and from practical points of view. In this connection, we studied the photochemical reactions of 4-hydroxycrotonic acid γ-lactone (I), the most simple α,β-unsaturated γ-lactone, in the liquid phase[*2] and also in the solid state. Three photodimers with a cyclobutane ring were obtained: two from the liquid phase and one from the solid state irradiations. The molecular structures of these photodimers were determined as described in the present paper.

Results and Discussion

Irradiation of I in polar solvents with a low-pressure mercury lamp yielded white, crystalline materials (yields calculated as the dimers, 20—30%). The solid material was later confirmed to consist of two components, Ia and Ib. At first, Ia was separated by recrystallizations. Several chemical treatments on the remaining fraction eventually yielded Ib″, which was identified with Ib as described in the experimental section. Irradiation of I in the solid state at low temperature (−78°C) with the same low-pressure mercury lamp yielded Ic (yield calculated as the dimer, 26%). The molecular weights, the results of elementary analyses, and the characteristic IR absorption bands indicate that Ia, Ib″(Ib), and Ic are isomeric dimers of I as shown in Table 1.

On the basis of the results of treating Ia, Ib″ and Ic with alkaline and then with acidic reagents, each of the above isomeric dimers is suggested to possess a lactone ring in the molecular structure. The NMR spectra also are in agreement with the proposed structure with a cyclobutane ring for each isomer as shown in Fig. 1. All of the conceivable structures of the dimers are listed in Fig. 2.

In order to distinguish the above stereo-isomers, the isolated products were oxidized at first. Ia was oxidized with potassium permanganate in acidic media, and then esterified with diazomethane. The product (overall yield, 54%) was identified with the authentic sample of 1,2,3,4-*cis*, *trans*, *cis*-tetramethoxycarbonyl cyclobutane (abbreviated to *cis*, *trans*, *cis*-TMCCB, hereafter), as prepared according to the method of Griffin *et al.*[3] by the NMR and IR spectra and the mixed melting-point measurements. *cis*, *trans*, *cis*-TMCCB was also obtained (yield, 69%) by the esterification of the oxidation products of Ib′, which was a dimer of 4-hydroxycrotonic acid obtained by the

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[*2] Photodimerization of the same compound was reported also by Odaira and his associates at the Discussion Meeting on the Photochemistry (Tokyo, November, 1967), where the present authors partially presented their results reported here.

1) P. J. Wagner and D. J. Bucheck, *J. Amer. Chem. Soc.*, **91**, 5090 (1969); J. L. Ruhlen and P. A. Leermakers, *ibid.*, **89**, 4944 (1967); *ibid.*, **88**, 5671 (1969); P. E. Eaton and W. S. Hurt, *ibid.*, **88**, 5038 (1966); P. E. Eaton, *ibid.*, **84**, 2344 (1962); *ibid.*, **84**, 2454 (1962); E. Y. Y. Lam, D. Valentine and G. S. Hammond, *ibid.*, **89**, 3482 (1967); D. Valentine, N. J. Turro, Jr., and G. S. Hammond, *ibid.*, **86**, 5202 (1964).

2) H. Morrison and R. Hoffmann, *Chem. Commun.*, **1968**, 1453; H. Morrison, H. Curtis and T. McDowell, *J. Amer. Chem. Soc.*, **88**, 5415 (1966); C. H. Kranch, S. Farid and G. O. Schenck, *Chem. Ber.*, **99**, 625 (1966).

3) G. W. Griffin, A. F. Vellturo and K. Furukawa, *J. Amer. Chem. Soc.*, **83**, 2725 (1961).

TABLE 1. CHARACTERISTICS OF PHOTODIMERS

Isomer	Molecular* weight	Elementary analyses† C%	Elementary analyses† H%	Characteristic ν(C=O)	IR Bands ν(C-O-C)
Ia	168	56.93	4.77	1760	1168 cm^{-1}
Ib''(Ib)	168	57.20	4.86	1775	1160
Ic	168	57.11	5.02	1780	1174

* Obtained from *m/e* value for the parent peak of the mass spectra.

† Calculated values for $C_8H_8O_4$: C, 57.14; H, 4.80%.

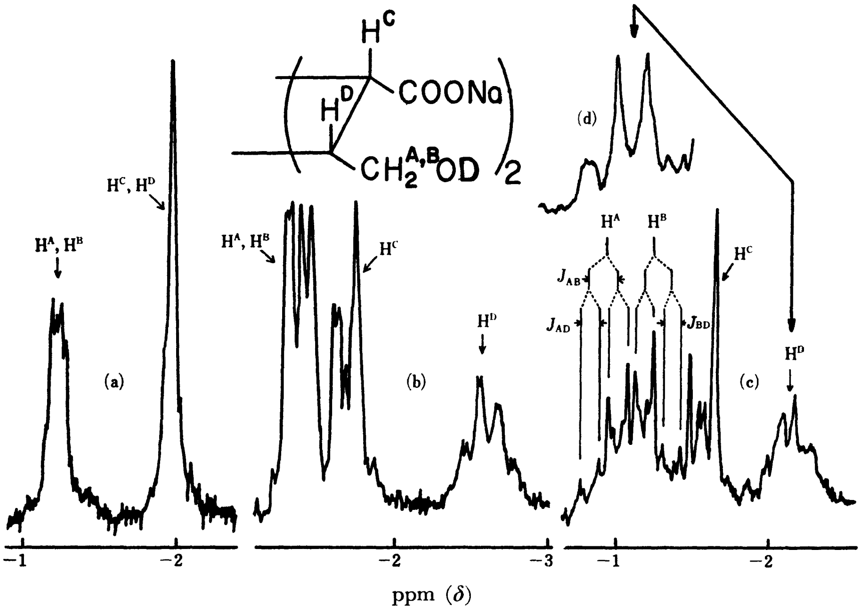

Fig. 1. NMR spectra of photodimers in 4 N NaOD/D_2O solution.
(a): Ia, (b): Ib'', (c): Ic ($\nu_{AB}=18, J_{AB}=11, J_{AD}=8$, and $J_{BD}=7$ Hz), and (d): the methylene proton signals of Ic when H^D protons were decoupled (difference frequency, +65 Hz). The chemical shifts were measured from the internal H_2O signal.

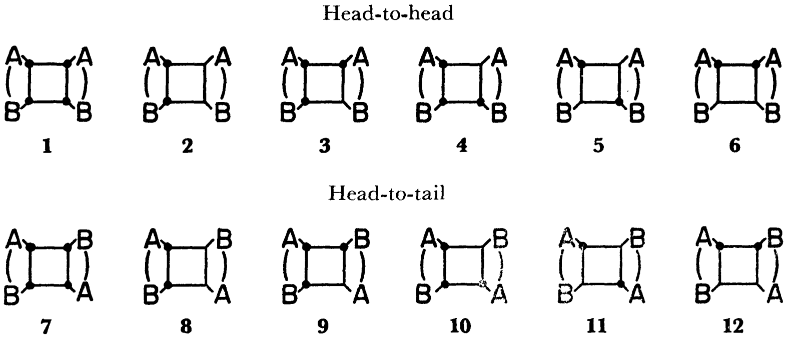

Fig. 2. Conceivable geometrical isomers of the photodimers.
The symbols A and B stand for C=O and CH_2O groups, respectively.

hydrolysis of Ib as described in the experimental section. As to TMCCB, it has been established that the most stable isomer is the one with the four methoxycarbonyl groups in all *trans* form.[3] Among the twelve isomers in Fig. 2, the isomers 5 and 11 are surely expected then to give *trans*, *trans*, *trans*-TMCCB. Four other isomers (**3**, **4**, **9** and **10**) will end up with either *cis*, *cis*, *trans*- or *trans*, *trans*, *trans*-TMCCB. Thus, the experimental results of oxidations are taken to indicate that neither Ia nor Ib could be one of the above six stereo-isomers (**3**, **4**, **5**, **9**, **10** and **11**). Since the yield of *cis, trans, cis*-TMCCB is fairly high, the isomers **1** and **7** should be also eliminated from the list of the possible isomers.

At this point, one should notice that among the remaining four isomers (**2**, **6**, **8** and **12**), the isomer **2** alone does not have any symmetry element. In other words, one can expect that the isomer **2** exists as a racemate. This expectation was verified by resolving Ib′ into a pair of optically active isomers as described in the experimental section. The optical activities still remained even after the lactone ring was formed again (Fig. 3). Therefore, Ib (Ib″) is uniquely assigned to a racemate corresponding to the structure **2** in Fig. 2.

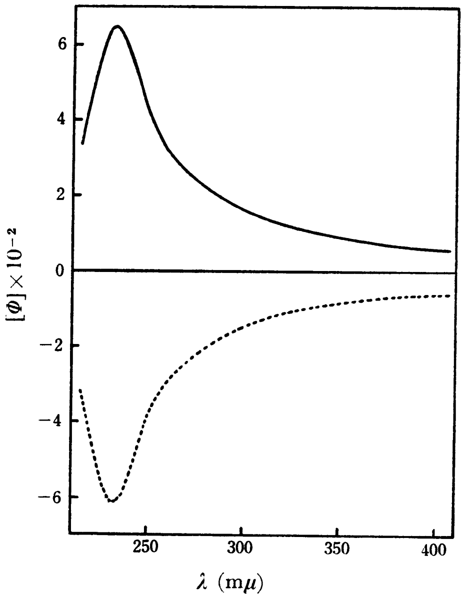

Fig. 3. ORD curves of Ib″(Ib) in acetonitrile at 24°C. The solid line represents (+)-enantiomer, and dotted line represents (−)-enantiomer.

For the rest, the isomers **6** and **12** are *trans* adducts, where the presence of extremely high steric strain is expected of the *trans*-fused lactone ring. Once such highly-strained lactone ring is opened, it will be quite difficult to be restored. Since **Ia** can be recovered from the alkaline solution, however, more easily than Ib, Ia can not be one of those *trans* adducts. Consequently, Ia may be assigned to the remaining *anti* dimer as represented by the structure **8** in Fig. 2.

On the other hand, Ic was converted into *cis, cis, cis*-TMCCB by the oxidation followed by the esterification (yield, 10%). From thermodynamicals points of view, *cis, cis, cis*-TMCCB is the most unstable among the stereo-isomers under discussion. Hence, Ic is suggested to be one of the two *syn* dimers (**1** and **7**) in Fig. 2, which will afford *cis, cis, cis*-TMCCB without any epimerization.

The structure of Ic may be further elucidated by the investigation of the NMR spectra. The methylene proton signals of Ic are much more complicated than those of Ia and Ib (Fig. 1). Then, the geminal protons of the methylene group in Ic are suspected to be in magnetically non-equivalent environments. In agreement with this suggestion, the methylene proton signals of Ic appear as a pattern close to AB type when H^A and H^B protons are decoupled from H^D (Fig. 1). The NMR parameters ($J_{AB}=11$ Hz. $\nu_{AB}=18$ Hz), thus obtained, are successfully applied to analyze the original signals of the methylene protons of Ic. In the case of the isomer **1** in Fig. 2, the geminal protons are certainly in magnetically non-equivalent environments. This is not true in the case of the isomer **7**, however, because there is a plane of symmetry which contains the carbon atom of the methylene group under consideration. Therefore, Ic is assigned to the isomer **1** in conclusion.

In short, the photodimerization of I in solution was found to afford a pair of *anti* dimers. One of them was a *head-to-tail* dimer (Ia), and the other was a *head-to-head* dimer (Ib). The scheme for the chemical separation and the structures of the dimers, thus determined, are summarized in Fig. 4. Because of the extremely low solubilities of the photodimers, the IR spectra could not be used in order to determine the isomer ratio. On the same reason, it could not be possible either to convert the dimers into more soluble derivatives suited to quantitative analysis. Then, the NMR spectra obtained in NaOD solutions were used to estimate the relative yield of the isomers. Even in this case, however, accurate data could not be obtained either because the signals of the two isomers overlapped each other. On the basis of the NMR spectra, anyhow, the relative yield of Ia was approximately the same as that of Ib, when the aqueous solution of I (0.2 M) was irradiated with a low-pressure mercury lamp. The relative yield of Ia with respect to Ib increased as the solvent was changed from water to acetonitrile and then to acetic acid.

The effect of internal irradiations with a high-pressure mercury lamp was also investigated. The same photodimers as above were obtained from the benzene or formic acid solutions of 4-hydroxycrotonic acid γ-lactone, provided that acetone was present in the solution. The relative yield of Ib with respect to Ia was higher in formic acid than that in benzene. Since the water jacket surrounding the lamp was made of pyrex glass, the most of the light should have been absorbed by acetone in these cases. In other words, the dimerization of I could be sensitized by acetone.

Although more quantitative data are required to clarify the mechanistic details of the present

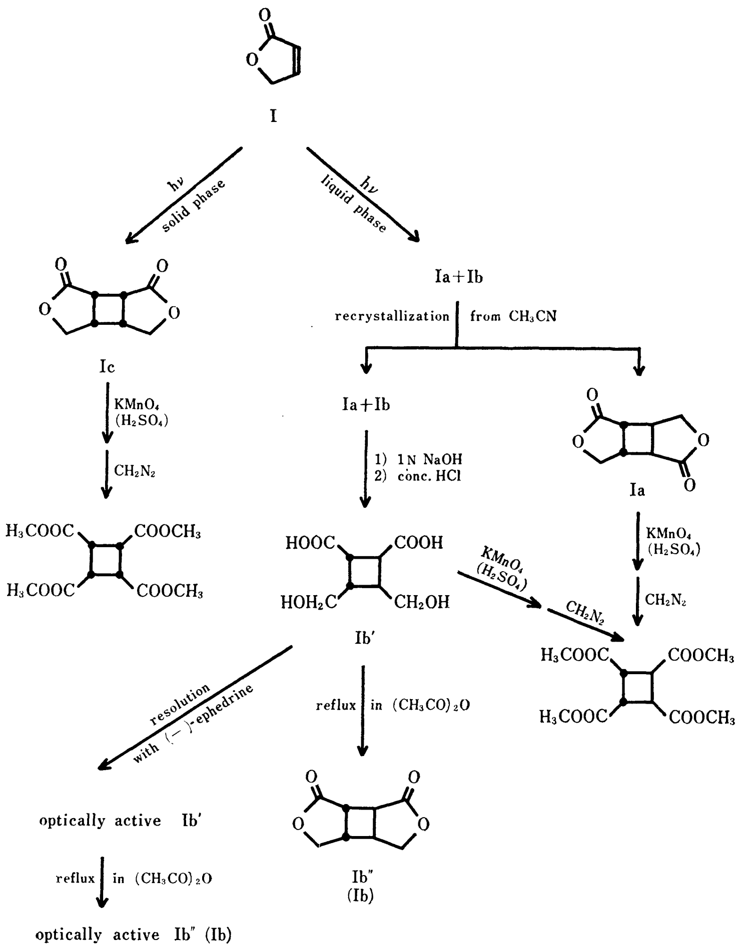

Fig. 4. The scheme for the chemical separation and the structure determination of the photodimers.

reaction, one may conclude now that at least a part of the reaction proceed *via* a triplet state. It is not clear, however, whether the photodimerization induced by the direct excitation of 4-hydroxycrotonic acid γ-lactone also proceeds *via* a triplet state or not. In any case, it should be noticed that the products of the present reactions are *anti* dimers just as in the cases of 2-cyclopentenone and 2-cyclohexenone. The solvent dependence of the isomer ratio is also interesting enough to be investigated. The investigation of this kind, however, should be waited until some reliable means for quantitative analysis are established in future.

Irradiation of I in the solid state with the low-pressure mercury lamp, on the other hand, yielded a *head-to-head*, *syn* dimer (Ic). The structure of the molecular crystal may be responsible for the unique mode of dimerization.

Experimental

Instrumental Analysis. The IR spectra were obtained with KBr disk on a JASCO Model DS-301 IR spectrophotometer. The NMR spectra were measured with a Varian Model A-60 analytical NMR spectrometer combined with a Varian Model V-5068A spin decoupler. The photodimers were dissolved in 4N deuterated alkali metal hydroxide solutions and the water signal was used as the internal standard. 1,2,3,4-Tetramethoxycarbonylcyclobutanes were measured as the deuteriochloroform solution with tetramethylsilane as the internal standard. The mass spectrum of Ia was recorded on a Hitachi Model RMU mass spectrometer, and the rest on a JEOL Model JMS-O1SG spectrometer. The optical rotatory dispersion curves were measured with a JASCO Model ORD/UV-5 optical rotatory dispersion recorder by the use of a 1 dm cell. The melting points were measured on a Yanagimoto micro melting-point measurement apparatus and are uncorrected.

Preparation of 4-Hydroxycrotonic Acid γ-Lactone (I). The preparation of I was carried out, according to the method of a literature,[4] through hydrolysis of glycerol-α-cyanohydrin and purification with

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[4] J. W. E. Glattfeld, G. Leavell G. E. Spieth and D. Hutton, *ibid.*, **53**, 3164 (1931).

aqueous silver nitrate solution, followed by distillation under reduced pressure (bp 90.0°C/13 mmHg). The distillate showed a single peak on inspection by the gas chromatography (25% Silicon DC200 on Shimalite, 2.25 m × 3 mm). The NMR spectra were also in good agreement with that reported by Freeman.[5] UV absorptions: ε, 8.0×10^3 (at 206 mμ, the absorption maximum), 1.6×10^1 (at 254 mμ) in water; ε, 3.4×10^3 (at 216 mμ), 2.5×10^1 (at 254 mμ) in *n*-hexane.

Irradiation of the Solution with a Low-Pressure Mercury Lamp. In the experiments with various solvent such as acetic acid, acetonitrile, and water, the solution (0.2—0.6 M) was internally irradiated with a 30 W low-pressure mercury lamp (Riko-Sha UVL 303 Q) equipped with a quartz jacket. The reactions were carried out at temperatures between 20 and 30°C in nitrogen atmosphere. White crystals had separated out of the solution during the irradiation which continued for the period of 20—30 hr.

Irradiation of the Solution with a High-Pressure Mercury Lamp. Either benzene solution (0.6 M) or formic acid solution (0.4 M) of I was internally irradiated with a high-pressure mercury lamp (Riko-Sha UVL-700P) equipped with a pyrex water-jacket for the period between 40 and 50 hours at 20°C. Acetone was added as the sensitizer: 0.7 M for the benzene solution and 0.1 M for the formic acid solution, respectively.

Irradiation of I in the Solid State. The reaction vessel containing neat liquid of I was held so that one side could be dipped into a dry ice-methanol mixture. The vessel was rotated slowly. After a short period of time, the wall was coated with a thin film of I. Then the vessel was held in the dry ice-methanol mixture, and was internally irradiated with the above-mentioned low-pressure mercury lamp under nitrogen flow.

Isolation of the Isomers. After the irradiation of the solution, the solvent and the raw material were removed by distillation under reduced pressure to leave white crystalline materials. Recrystallization of the crystalline materials from acetonitrile afforded pure samples of Ia (mp 292—293°C). The filtrate was dissolved into 1 N sodium hydroxide solution, and the pH of the solution was adjusted with concentrated hydrochloric acid to a value between 2 and 4. At this point, Ib′ separated out as white crystals. The presence of both hydroxyl and carbonyl groups was indicated by the IR spectra (KBr disk, 3360 (broad); 3260; 3100—2400 (broad); 1722 and 1700 cm^{-1}). Since the same treatments on Ia could only reproduce Ia, the origin of Ib′ must be a compound Ib but not Ia. Ib′ was quantitatively converted into a lactone Ib″ (mp 280—281°C, as recrystallized from acetonitrile) by refluxing the acetic anhydride solution for 3 hr. Ib′ was also converted into Ib″ during the measurement of the melting point. On the basis of the above behaviors, Ib′ was suggested to be a dimer of 4-hydroxycrotonic acid obtained by the hydrolysis of Ib. In agreement with this suggestion, the mass spectra of Ib′ showed a peak (m/e=168) which corresponded to a fragmention formed on the release of two water molecules from the molecular ion. Furthermore, Ib′ was resolved into a pair of optically active isomers as described later. The results of elementary analyses of the isomers were also in good agreement with the values calculated from the dimer of 4-hydroxycrotonic acid.

On the treatment with alkaline and then with acid solutions, Ib″ afforded Ib′. Hence Ib″ was identified with Ib, the counterpart of Ia in the original mixture. This suggestion was verified by comparing the IR, far IR, and NMR spectra of the concerning materials.

Ic was easily separated from I, after the irradiation, by the same procedure as described in the cases of the irradiation of the solution. The obtained solid material was purified by recrystallization from acetone (mp 235—236°C). Ic was recovered again when the sample was dissolved into sodium hydroxide solution, and then acidified with hydrochloric acid.

Oxidation and Esterification of Ia. Ia (168 mg) was suspended in 15 m*l* of 0.7 N sulfuric acid, and aqueous solution (20 m*l*) of potassium permanganate (520 mg) was added dropwise into it under vigorous stirring. The reaction temperature was kept to 60°C by the use of a water bath. After 2 hr, sodium hydrogensulfite was added to the solution, and then 2 N sodium hydroxide solution was added until the solution became basic to litmus. The solution was acidified with concentrated hydrochloric acid. The acidic solution was evaporated to dryness and the residue was extracted with 100 m*l* of dry acetone by the use of a Soxlet extractor. Diazomethane in ether was added to the extracts dissolved in methanol at 0°C. The solution was evaporated to dryness. The residue was purified by the column chromatography on a silica gel column with benzene-ethyl acetate (20 : 1) as the eluting solvent, and then recrystallized from benzene. Yield, 154 mg (54%); mp 149.0—150.5°C; Found: C, 50.08; H, 5.64%. Calcd for $C_{12}H_{16}O_8$: C, 50.00; H, 5.60%. The product was identified with *cis, trans, cis*-TMCCB by means of the mixed melting point measurements and comparison of the NMR and IR spectra with those of the authentic sample, prepared by the method of Griffin *et al.*[3]

Oxidation and Essterification of Ib′. Ib′ (77 mg) was oxidized at 70°C by the similar procedure applied to Ia (1.6 N sulfuric acid, 240 mg $KMnO_4$/5 m*l* H_2O). After the reaction was completed, methanol was added to the solution, which was succeedingly made basic to litmus with 2 N sodium hydroxide solution. Manganese dioxide was filtered off and the filtrate was acidified with concentrated hydrochloric acid, and thne evaporated to dryness. The residue was extracted, treated with diazomethane as described in the case of Ia. The product was also purified as above, and was identified with *cis, trans, cis*-TMCCB. Yield, 77 mg (69%); mp 148—150°C; Found: C, 50.07; H, 5.66%. Calcd for $C_{12}H_{16}O_8$: C, 50.00; H, 5.60%.

Oxidation and Esterification of Ic. Ic (163 mg) was oxidized and esterified by the same procedure as applied to Ia. The product was purified by the column chromatography on a silica gel column with ethyl acetate as the eluting solvent and then recrystallized from methanol. Yield, 29 mg (10%); mp 222—223°C; Found: C, 49.97; H, 5.57%. Calcd for $C_{12}H_{16}O_8$: C, 50.00; H, 5.60%. The IR spectra (KBr) presented the same characteristic absorption bands as those of *cis, cis, cis*-TMCCB[6] at 2990 (m), 2940 (m), 2845 (w),

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[5] R. Freeman *Mol. Phys.*, **5**, 499 (1962).

[6] M. Avram, I. G. Dinulescu, E. Marica, G. Mateescu, E. Slaim and C. D. Nenitzescu, *Chem. Ber.*, **97**, 382 (1964); G. W. Griffin and D. Veber, *J. Amer. Chem. Soc.*, **82**, 6417 (1960).

1743 (vs), 1452 (m), 1437 (m), 1350 (s), 1220 (s), 1195 (vs), 1175 (vs), 1115 (m), 1072 (m), 955 (m), 830 (m), 770 (m) cm^{-1} (w: weak, m: medium, s: strong, vs: very strong). The NMR spectrum ($CDCl_3$ solution) consisted of two singlet peaks at 3.64 and 3.73 ppm (the ratio of the area under the peak, 1 : 3). The mass spectrum gave the base peak at *m/e* 257, which corresponds to the loss of a methoxyl group from the molecular ion. On the basis of these data, the product is identfied with *cis*, *cis*, *cis*-TMCCB.

Resolution of Ib′. Ib′ (342 mg) was dissolved into 30 m*l* of methanol containing 508 mg of (−)-ephedrine. The solution was concentrated to 2 m*l* and then 15 m*l* of acetonitrile was added to it. After the solution was allowed to stand overnight, the salt crystallized out (334 mg, mp 130—136°C). Recrystallization was repeated twice by the similar procedure (yield, 193 mg; mp 134.5—135.5°C). The purified salt was decomposed with dilute hydrochloric acid. The separated white needles were filtered off and washed with water and methanol. Yield, 68 mg; Found: C, 46.40; H, 6.14%. Calcd for $C_8H_{12}O_6$: C, 47.06; H, 5.92%. The characteristic IR absorption bands (KBr disk) were found at 3400 (broad), 3320, 3100—2400 (broad), 1715 and 1693 cm^{-1}. This compound, (+)-Ib′, exhibited a positive Cotton effect curve in 0.2 N sodium hydroxide solution (C, 0.600) at 24°C: $[\Phi]_{690}$ $+20^\circ$, $[\Phi]_{589}$ $+28^\circ$, $[\Phi]_{235}$ $+311^\circ$ (infl.), $[\Phi]_{218}$ $+492^\circ$. The filtrate, which contained the fraction of more soluble ephedrine salt of Ib′, was treated with dilute hydrochloric acid as above. The isolated acid was purified by the treatment with aqueous sodium hydroxide solution and then with concentrated hydrochloric acid. Yield, 59 mg. Found: C, 46.62; H, 6.13%. Calcd for $C_8H_{12}O_6$: C, 47.06; H, 5.92%. The IR spectrum was similar to that of (+)-Ib′. This compound, (−)-Ib′, exhibited a negative Cotton effect curve in 0.2 N sodium hydroxide (C, 0.695) at 24°C: $[\Phi]_{690}$ -23°, $[\Phi]_{589}$ -32°, $[\Phi]_{235}$ -327° (infl.), $[\Phi]_{218}$ -522°.

Preparation of Optically Active Ib. Dehydration of (+)-Ib′ with acetic anhydride gave optically active Ib which exhibited a negative Cotton effect curve in acetonitrile. Repeated recrystallization from acetonitrile afforded a pure sample (mp 288—289°C). In the same way, (−)-Ib′ was dehydrated to give the other enantiomer which exhibited a positive Cotton effect curve in acetonitrile (mp 290.0—290.5°C). These enantiomers showed characteristic IR absorption bands at 1778, 1755, 1179 and 1160 cm^{-1}. The ORD curves of the same compounds (Fig. 3) in acetonitrile at 24°C are as the following: (a) the (+)-enantiomer (C, 0.250): $[\Phi]_{690}$ $+20^\circ$, $[\Phi]_{589}$ $+23^\circ$, $[\Phi]_{232}$ $+646^\circ$ (peak), $[\Phi]_{214}$ $+332^\circ$, and (b) the (−)-enantiomer (C, 0.642): $[\Phi]_{690}$ -19°, $[\Phi]_{589}$ -22°, $[\Phi]_{232}$ -614° (trough), $[\Phi]_{214}$ -317°.

The authors are grateful to Dr. H. Kobayashi and Mr. H. Saito at the Department of Organic Synthesis of Kyushu University, for their helpful suggestions in the resolution of the optical isomers. Thanks are also due to Dr. I. Aiga and T. Matsui, at the Biotron Institute of the same university, and Miss. Y. Inatsu at the Faculty of Medicine, for their helps in the measurements of ORD and mass spectra, respectively. The authors are also indebted to Hitachi Manufacturing Co., Ltd., and Japan Electron Optics Laboratory Co., Ltd. for the measurements of mass spectra.