Syntheses of Tetracyclo[7.3.0.0^{3,7}.0^{4,10}]dodecane-2,8-dione ("[8]Diisotwistane-2,8-dione"[1]) and 8,9-Benzotricyclo[4.3.1.0^{3,7}]decane ("Benzoisotwistane")

Masao NAKAZAKI, Koichiro NAEMURA, and Hiroyuki YOSHIHARA

Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560

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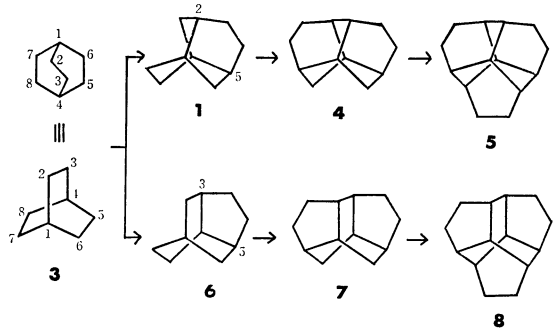
Tetracyclo[7.3.0.0^{3,7}.0^{4,10}]dodecane-2,8-dione ("[8]diisotwistane-2,8-dione") was synthesized from *trans-anti*-2,5-dioxo-7,8-diethoxycarbonylbicyclo[2.2.2]octane which was prepared by the Diels-Alder reaction of hydroquinone with diethyl fumarate. 8,9-Benzotricyclo[4.3.1.0^{3,7}]decane ("benzoisotwistane") was also synthesized from 2-oxo-5-*endo*-ethoxycarbonyl-7,8-benzotricyclo[2.2.2]octane which was obtained by the Diels-Alder reaction of β-naphthol with ethyl acrylate.

We have been interested in the preparation of "gyrochiral"[2] cage-shaped compounds such as twistane (D_2 point group) (**1**)[3] and twist-brendane (C_2 point group) (**2**)[4] as well as in the study of their chiroptical properties.

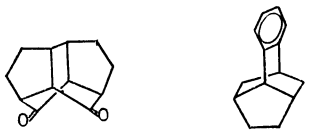
1 **2**

Although twistane (**1**) can be regarded as being constructed by the double 1–4 and 2–5 ethano-bridging over and below twist-cyclohexane (D_2 symmetry), one can also visualized it as being formed by the single diagonal ethano-bridging between 2 and 5 positions of bicyclo[2.2.2]octane (**3**). On continuance of this type of diagonal ethanol-bridging on twistane, there arise successively ditwistane (C_2 point group) (**4**)[5] and tritwistane (D_3 point group) (**5**). There remains another possible ethano-bridging, *i.e.* the collateral bridging between 3 and 5 positions this time, and this type of bridging on parent bicyclo[2.2.2]octane gives isotwistane (C_s point group) (**6**), "[8]diisotwistane"(C_2 point group) (**7**),[6] and the pentacyclic hydrocarbon (C_2 point group) (**8**)[8] successively.



3 **1** **4** **5** **6** **7** **8**

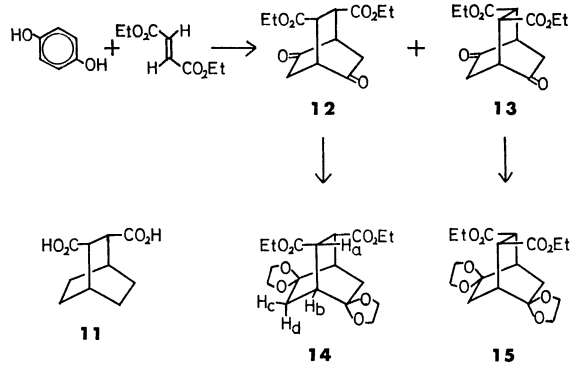
We have been making efforts to synthesize these "gyrochiral" tetra and pentacyclic compounds, and this paper reports the preparation of [8]diisotwistane-2,8-dione (**9**) as the first member of the tetracyclic compound with this unique structure. Although 8,9-benzotricyclo-[4.3.1.0^{3,7}]decane ("benzoisotwistane") (**10**) is achiral, since its preparation incidentlly follows an analogous scheme to the compound (**9**) in securing the starting material as well as in its final synthetic step, the synthesis of this compound will also be reported in the latter part of this paper.



9 **10**

[8]Diisotwistane-2,8-dione

Heating a mixture of hydroquinone and diethyl fumarate under a nitrogen atmosphere for 63 hr at 200—220 °C and chromatographic separation of the adduct gave two ketonic substances in a 3: 1 ratio; the major product melting at 88—89 °C and the minor product melting at 104.5—105.5 °C. The stereoisomeric nature of these compounds were demonstrated by their conversion to the same *trans*-2,3-dicarboxybicyclo[2.2.2]-octane (**11**) on Wolff-Kishner reduction. We resorted to the NMR spectra (Table 1) of their ketal derivatives (**14**) and (**15**) to securing the informations about their stereochemistry. A W-letter long-range coupling between proton H_a and proton H_d in ketalester (**14**) from the minor product which is clearly revealed on a spin decoupling experiment afforded the evidence to



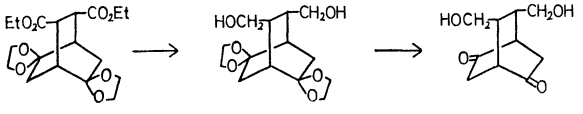
12 **13** **11** **14** **15**

Table 1. NMR spectra (in $CDCl_3$) of **14** and **15**

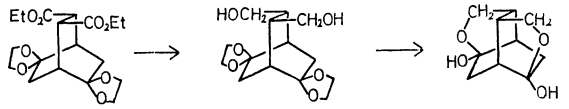
	14	**15**
Carboethoxy	δ 1.22 (t, 6H)	δ 1.21 (t, 6H)
	4.18 (q, 4H)	4.10 (q, 4H)
H_e	1.77 (q, 2H)	1.78 (q, 2H)
H_d	2.18 (q, 2H)	2.12 (q, 2H)
H_b	2.28 (m, 2H)	2.51 (m, 2H)
H_a	3.42 (d, 2H)	3.05 (d, 2H)
Ethylenedioxy	3.85—4.00 (m, 8H)	3.62—3.90 (m, 8H)

assign the *anti*-structure[9] (**12**) to the minor adduct whereas the *syn*-structure[9] (**13**) to the major adduct.

This assignment was further supported by their chemical behaviors as follows. Lithium aluminum hydride reduction converted these two ketals into two alcohols (**16**) and (**17**). Whereas treatment of *anti*-ketalalcohol (**16**) with 5% sulfuric acid led to the corresponding ketoalcohol (**18**), the same procedure led the *syn*-ketalalcohol (**17**) to the hemi-ketal (**19**) whose structure was confirmed by the IR spectrum.

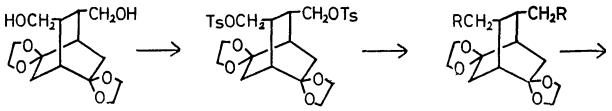


14 **16** **18**

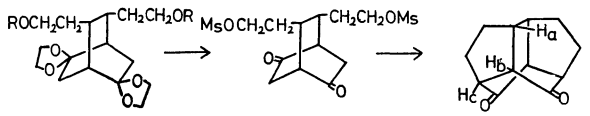


15 **17** **19**

Thus being convinced of the stereochemistry, we could carry on our syntheses. Tosylation of the *anti*-alcohol (**16**) provided the ketaltosylate (**20**) which was treated with sodium cyanide in DMF to give the *anti*-nitrile (**21**). Alkaline hydrolysis of the *anti*-nitrile (**21**) afforded the *anti*-carboxylic acid (**22**), which was reduced with lithium aluminum hydride to yield the *anti*-alcohol (**23**). After mesylation of the *anti*-alcohol (**23**), ketal functions were removed by treatment with 10% sulfuric acid. The resultant *anti*-ketomesylate (**25**) was treated with sodium hydride in DMF. Chromatography on silica gel followed by sublimation of the reaction product yielded a dione mp 88—89 °C, to which the structure (**26**) was assigned on the basis of the following spectral data. The NMR spectrum exhibited two multiplet signals centered at δ 2.53 due to protons H_b and at 2.83 due to protons H_c. The IR spectrum showed a carbonyl absorption at 1710 cm^{-1}. The UV spectrum showed absorption maxima at 258 (ε=40) and 289 (42) nm.

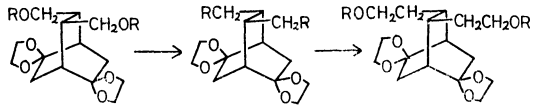


16 **20** **21** R=CN
22 R=CO_2H



23 R=H
24 R=Ms
25 **26**

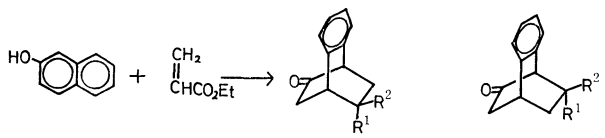
It seems in order here to divert attention from [8]diisotwistane series of compound to our sterile efforts to [8]ditwistane series of compound. The same procedure described for *anti*-form converted the *syn*-ketalalcohol (**17**) into *syn*-nitrile (**28**), *syn*-carboxylic acid (**29**), and *syn*-ketalalcohol (**30**) successively. On treatment with methanesulfonyl chloride and pyridine the *syn*-ketalalcohol (**30**) gave a corresponding ketal-mesylate (**31**) whose structure was confirmed on the basis of its NMR and IR spectra. But various fruitless attempts to remove the ketal functions at this stage forced us to abandon the hope to proceed further.



17 R=H
27 R=Ts
28 R=CN
29 R=CO_2H
30 R=H
31 R=Ms

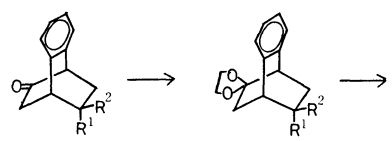
Benzoisotwistane

Diels-Alder reaction which was proved convenient to secure starting materials with functional groups suitable for the synthesis of the cage-shaped compound as described above, encouraged us to apply this reaction to β-naphthol and ethyl acrylate. Although formation of the four isomers (**32**)—(**35**) was theoretically expected, analysis of the adduct, bp 137—140 °C at 0.1 mmHg, by glc revealed a formation of only two components in a ratio of 2: 3. Reflection on steric and electric effects involved in the Diels-Alder reaction led to the conclusion that 2-oxo-5-ethoxycarbonyl-7,8-benzobicyclo[2.2.2]-octanes (**32**) and (**33**) should be formed preferentially over 2-oxo-6-ethoxycarbonyl-7,8-benzobicyclo[2.2.2]-octanes (**34**) and (**35**). Further structural information was accessible from the NMR spectrum which showed two three-protons triplets centered at 1.11 and 1.26 (relative ratio 4: 6 respectively). These signals were due to methyl protons of carboethoxy groups. The high field signal was assigned for *exo*-isomer (**33**)[10] and the low field one was due to *endo*-isomer (**32**).[10]

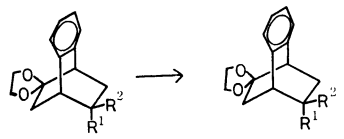


32 R^1=CO_2Et, R^2=H
33 R^1=H, R^2=CO_2Et
34 R^1=CO_2Et, R^2=H
35 R^1=H, R^2=CO_2Et

No attempt was made at this stage to separate these isomers because of difficulty encountered to accomplish the separation, and the product after ketalization with ethylene glycol was treated with lithium aluminum hydride to give a mixture of the ketalalcohols (**38**) and (**39**). Upon treatment with *p*-toluenesulfonyl chloride and pyridine the mixture of the ketalalcohols (**38**) and (**39**) was converted into the mixture of the tosylates (**40**) and (**41**). At this stage one isomer of the tosylates was separated as crystals and the other was liquid. The fact that this crystalline isomer was eventually led to benzoisotwistane implies the isomer has *endo*-structure (**40**) whereas the liquid one has *exo*-structure (**41**).

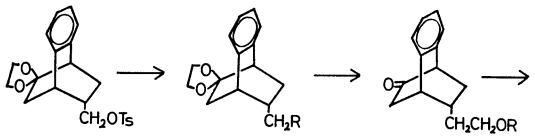


32 R^1=CO_2Et, R^2=H
33 R^1=H, R^2=CO_2Et
36 R^1=CO_2Et, R^2=H
37 R^1=H, R^2=CO_2Et

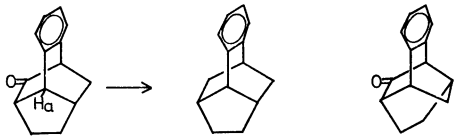


38 $R^1=CH_2OH$, $R^2=H$ **40** $R^1=CH_2OTs$, $R^2=H$
39 $R^1=H$, $R^2=CH_2OH$ **41** $R^1=H$, $R^2=CH_2OTs$

Upon treatment with sodium cyanide in DMF, the *endo*-tosylate (**40**) gave the *endo*-nitrile (**42**). Alkaline hydrolysis of the substance afforded the *endo*-carboxylic acid (**43**), which was reduced with lithium aluminum hydride to yield the *endo*-alcohol (**44**). After hydrolysis of the ketal function, the resultant ketoalcohol (**45**) was converted into the *endo*-ketomesylate (**46**), which was treated with sodium hydride in DMF. Sublimation of a solid product gave a tricyclic ketone mp 85—86 °C. We assigned benzoisotwistan-2-one (**47**) to the product on the basis of the NMR spectrum exhibiting double doublet signal centered at 3.38 for a proton H_a and this pattern ruled out twistane structure (**48**). The Wolff-Kishner reduction of the ketone (**47**) yielded benzoisotwistane (**10**) mp 56—57 °C.

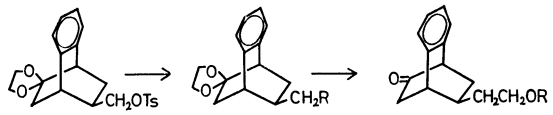


40 **42** R=CN **45** R=H
43 R=CO_2H **46** R=Ms
44 R=CH_2OH



47 **10** **48**

Turning to the oily *exo*-tosylate (**41**), the substance gave also a crystalline *exo*-nitrile (**49**), which was converted into the *exo*-carboxylic acid (**50**), ketalalcohol (**51**), ketoalcohol (**52**), and Ketomesylate (**53**) by the same procedure described for *endo*-isomer. The *exo*-mesylate (**53**) was treated with sodium hydride in DMF, but a cyclized product was not obtained.

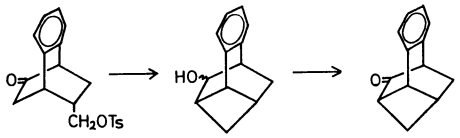


41 **49** R=CN **52** R=H
50 R=CO_2H **53** R=Ms
51 R=CH_2OH

Finally we made an effort to prepare the lower homolog of benzoisotwistane; 7,8-benzotricyclo[3.3.1.$0^{3,6}$]nonan-2-one (**56**). Upon treatment with acetone and *p*-toluenesulfonic acid, the *endo*-ketaltosylate (**40**) gave the *endo*-ketotosylate (**54**), which was heated with sodium hydride in DMF. Chromatographic separation of a product yielded a cyclized compound. It was not an expected ketone but an alcoholic compound. On oxidation with 8N Jones' reagent the substance gave a ketonic compound mp 90 °C, whose UV spectrum (Table 2) was very similar with that of benzoisotwistan-2-one (**47**). From the fact we assigned the structure (**56**) to the compound and its NMR and IR spectra were also consistent with the structure (**56**).

TABLE 2. UV SPECTRA (IN ISOOCTANE SOLUTION) OF **47** AND **56**

47		**56**	
nm	ε	nm	ε
259.5 (sh)	330	260 (sh)	320
265	409	265.5	368
271.5	361	272	327
291 (sh)	213	289 (sh)	268
299.5	261	296.5	309
309	254	305.5	297
319 (sh)	147	316 (sh)	177



54 **55** **56**

Experimental

All the melting points and the boiling points are not corrected. The IR spectra were measured with Hitachi EPI-S2 spectrophotometer. The NMR spectra were obtained on LNM-C-60HL and JNM-MH-100 spectrometer. The UV spectra were measured with Beckman DB spectrometer.

Diels-Alder Reaction of Hydroquinone with Diethyl Fumarate. A mixture of 160 g of hydroquinone and 320 g of diethyl fumarate was heated for 36 hr at 200—220 °C under a nitrogen atmosphere. After cooling, 105 g of hydroquinone was recovered by filtration and a liquid reaction mixture was distilled to recover 220 g of diethyl fumarate. A residue was chromatographed on neutral alumina (Woelm, activity III) and ealier fractions eluted with benzene gave an oily product, which was distilled to yield 14.6 g of **13**, bp 170—180 °C at 1.5 mmHg. This adduct was crystallized in a reciever, mp 88—89 °C. Followed fractions eluted with benzene gave a solid, which was recrystallized from benzene to yield 5.5 g of **12**, mp 104.5—105.5 °C.

13: IR (KBr): 1720 (s), 1260 (m), 1240 (m), 1190 (s), 1112 (m), and 1022 (m) cm^{-1}.

NMR ($CDCl_3$): δ 1.30 (t, 6H, J=7 Hz), 2.52—2.67 (m, 4H), 3.02—3.25 (m, 2H), 3.55 (s, 2H), and 4.20 (q, 4H, J=7 Hz).

Found: C, 59.15; H, 6.54%. Calcd for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43%.

12: IR (KBr): 1720 (s), 1253 (m), 1239 (m), 1190 (s), 1175 (m), and 1030 (m), cm^{-1}.

NMR ($CDCl_3$): δ 1.25 (t, 6H, J=7 Hz), 2.42—2.55 (m, 4H), 3.04—3.18 (m, 2H), 3.15 (s, 2H), and 4.18 (q, 4H, J=7 Hz).

Found: C, 59.48; H, 6.42%. Calcd for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43%.

trans-2,3-Dicarboxybicyclo[2.2.2]octane (11). *From* **12**: A mixture of 1.37 ml of 80% hydrazine hydrate, 1.34 g of potassium hydroxide, 14 ml of triethylene glycol and 1.33 g of **12** was heated for 3 hr at 130—140 °C and then water was removed from the reaction mixture. A residual solution was heated for further 6 hr at 200 °C and then diluted with water.

After washing with ether, a water layer was acidified with hydrochloric acid and extracted with ether. The extract was washed with water and dried over magnesium sulfate. Removal of the solvent gave a solid which was recrystallized from ethanol to yield 692 mg of **11**, mp 232 °C (lit,[11] mp 234 °C).

Found: C, 60.74; H, 7.19%. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12%.

From ***13***: *trans*-2,3-Dicarboxybicyclo[2.2.2]octane (550 mg) was obtained from 1.25 g of **13** by the same method described above.

trans-anti-*2,5-Bisethylenedioxy-7,8-diethoxycarbonylbicyclo[2.2.2]octane (**14**).* A solution of 3.34 g of **12**, 24 mg of *p*-toluenesulfonic acid, and 40 ml of ethylene glycol in 176 ml of benzene was boiled for 25 hr during which time water generated was removed from the reaction mixture as the azeotrope with benzene. After cooling to room temperature, benzene layer was separated and washed with satd. aqueous sodium bicarbonate and water. Removal of the solvent gave a solid which was recrystallized from hexane to yield 4.22 g of **14**, mp 80—81 °C.

IR (KBr): 1728 (s), 1288 (m), 1220 (m), 1185 (s), 1110 (s), 1032 (s), and 1025 (s) cm^{-1}.

Found: C, 58.20; H, 7.27%. Calcd for $C_{18}H_{26}O_8$: C, 58.37; H, 7.08%.

trans-syn-*2,5-Bisethylenedioxy-7,8-diethoxycarbonylbicyclo[2.2.2]octane (**15**).* *syn*-Ketoester (**13**) (8.54 g) was converted into **15** (7.34 g), mp 98—98.5 °C, by the same method described above.

IR (KBr): 1740 (s), 1730 (s), 1312 (m), 1235 (m), 1185 (s), 1150 (m), 1105 (s), and 1020 (s) cm^{-1}.

Found: C, 58.38; H, 7.17%. Calcd for $C_{18}H_{26}O_8$: C, 58.37; H, 7.08%.

trans-anti-*2,5-Bisethylenedioxy-7,8-bis(hydroxymethyl)bicyclo[2.2.2]octane (**16**).* To a suspension of 1.15 g of lithium aluminum hydride in 50 ml of dry ether was added a solution of 6.30 g of **14** in 150 ml of dry ether at room temperature and then the mixture was refluxed for 2 hr. After cooling with ice, to the chilled reaction mixture was carefully added satd. aqueous ammonium chloride solution and then a solid was filtered off. A filtrate was washed with water and dried over magnesium sulfate. Removal of the solvent gave a solid which was recrystallized from acetone to yield 5.27 g of **16** mp 163—165 °C.

IR (KBr): 3350 (s), 1130 (m), 1098 (m), 1062 (s), 1038 (m), and 990 (m) cm^{-1}.

Found: C, 58.70; H, 7.80%. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.75%.

trans-syn-*2,5-Bisethylenedioxy-7,8-bis(hydroxymethyl)bicyclo[2.2.2]octane (**17**).* Reduction of 14.0 g of **15** with 3.4 g of lithium aluminum hydride in dry ether afforded 9.65 g of **17**, mp 132 °C, by the same procedure described above.

IR (KBr): 3300 (s), 1155 (m), 1090 (s), 1045 (s), and 995 (s) cm^{-1}.

Found: C, 58.55; H, 7.81%. Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.75%.

trans-anti-*2,5-Dioxo-7,8-bis(hydroxymethyl)bicyclo[2.2.2]octane (**18**).* A solution of 500 mg of **16** in 10 ml of 5% sulfuric acid was kept for 3 days at room temperature. The reaction mixture was neutralized with solid sodium bicarbonate and concentrated under reduced pressure. Acetone was added to a residue and an insoluble solid was filtered off. A filtrate was concentrated to give a solid which was recrystallized from acetone to yield 210 mg of **18**, mp 126—127 °C.

IR (KBr): 3400 (s), 1725 (s), 1705 (s), 1080 (m), 1070 (m), and 1020 (s) cm^{-1}.

Found: C, 60.36; H, 7.17%. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12%.

Hydrolysis of trans-syn-*2,5-Bisethylenedioxy-7,8-bis(hydroxymethyl)bicyclo[2.2.2]octane (**17**).* A mixture of 10.3 g of **17** and 5% sulfuric acid was kept for 3 days at room temperature. After working up as the same manner described above, a solid product was recrystallized from acetone to give 3.83 g of **19**, mp 125 °C.

IR (KBr): 3300 (s), 1160 (m), 1090 (m), 1070 (m), and 980 (s) cm^{-1}.

Found: C, 60.46; H, 7.27%. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12%.

trans-anti-*2,5-Bisethylenedioxy-7,8-bis(cyanomethyl)bicyclo[2.2.2]octane (**21**).* To a solution of 5.05 g of **16** in 25 ml of dry pyridine was added 15.0 g of *p*-toluenesulfonyl chloride with ice cooling and then the mixture was stirred for 2 hr at this temperature. After standing overnight at room temperature, the mixture was poured onto ice water and acidified with hydrochloric acid. A solid was collected and washed with dilute hydrochloric acid, satd. aqueous sodium bicarbonate, and water. After drying over calcium chloride, 9.05 g of tosylate (**20**) was obtained, mp 156—157 °C. A mixture of 9.00 g of **20**, 4.7 g of sodium cyanide and 45 ml of *N,N*-dimethylformamide (DMF) was heated for 4 hr at 120—130 °C and then for further 8 hr at 140—150 °C. After cooling to room temperature, a solid was filtered off and a filtrate was concentrated under reduced pressure. A residue was poured into water and a solid was collected, which was washed with water. Recrystallization from benzene gave 4.10 g of **21**, mp 162—164 °C.

IR (KBr): 2260 (w), 1135 (s), 1110 (m), 1053 (s), 1025 (s), 983 (s), and 950 (m) cm^{-1}.

Found: C, 63.31; H, 6.69; N, 9.20%. Calcd for $C_{16}H_{20}O_4N_2$: C, 63.14; H, 6.62; N, 9.21%.

trans-syn-*2,5-Bisethylenedioxy-7,8-bis(cyanomethyl)bicyclo[2.2.2]octane (**28**).* Tosylation of 7.90 g of **17** with 15.7 g of *p*-toluenesulfonyl chloride and 42 ml of pyridine was carried out by the same procedure described above and 11.3 g of **27** was obtained. A mixture of 11.0 g of **27**, 5.8 g of sodium cyanide, and 55 ml of DMF was heated for 4 hr at 120—130 °C and then for further 10 hr at 140—150 °C. After working up as described above, a solid was collected and recrystallized from benzene to yield 2.09 g of **28**, mp 217—219 °C.

IR (KBr): 2260 (w), 1140 (s), 1100 (s), 1075 (s), 980 (m), and 960 (m) cm^{-1}.

Found: C, 63.25; H, 6.69; N, 9.06%. Calcd for $C_{16}H_{20}O_4N_2$: C, 63.14; H, 6.62; N, 9.21%.

trans-anti-*2,5-Bisethylenedioxy-7,8-bis(carboxymethyl)bicyclo[2.2.2]octane (**22**).* A mixture of 3.82 g of **21**, 4.23 g of potassium hydroxide and 35 ml of ethylene glycol was heated for 6 hr at 150—160 °C. After cooling to room temperature, the reaction mixture was diluted with water and acidified with hydrochloric acid. A solid was collected, washed with water, and dried over calcium chloride to yield 1.92 g of **22**, mp 208 °C dec.

IR (KBr): 2900 (broad), 1705 (s), 1295 (m), 1140 (m), 1120 (m), 1020 (m), and 998 (m) cm^{-1}.

Found: C, 55.65; H, 6.51%. Calcd for $C_{16}H_{22}O_8$: C, 56.13; H, 6.48%.

trans-syn-*2,5-Bisethylenedioxy-7,8-bis(carboxymethyl)bicyclo[2.2.2]octane (**29**).* Hydrolysis of 9.22 g of **28** with potassium hydroxide in ethylene glycol gave 3.95 g of **29**, mp 238 °C dec., by the same procedure described above.

IR (KBr): 2900 (broad), 1720 (s), 1205 (m), 1130 (m), 1090 (s), and 960 (m) cm^{-1}.

Found: C, 55.97; H, 6.44%. Calcd for $C_{16}H_{22}O_8$: C, 56.13; H, 6.48%.

trans-anti-*2,5-Bisethylenedioxy-7,8-bis(2-hydroxyethyl)bicyclo-*

[2.2.2]octane (23). To a suspension of 0.48 g of lithium aluminum hydride in 20 ml of dry tetrahydrofuran (THF) was added a solution of 1.82 g of **22** in 20 ml of dry THF at room temperature and then a mixture was heated under reflux for 2 hr. After cooling with ice, satd. aqueous ammonium chloride solution was carefully added to the chilled reaction mixture and a solid was filtered off. A filtrate was dried over magnesium sulfate and removal of the solvent gave a solid which was recrystallized from acetone to yield 1.39 g of **23**, mp 138—139 °C.

IR (KBr): 3300 (s), 1140 (m), 1118 (s), 1060 (m), 1012 (s), 995 (m), and 948 (m) cm^{-1}.

Found: C, 61.09; H, 8.52%. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34%.

trans-syn-*2,5-Bisethylenedioxy-7,8-bis(2-hydroxyethyl) bicyclo-[2.2.2]octane (30).* Reduction of **29** (3.95 g) with lithium aluminum hydride was carried out by the same procedure described above and recrystallization of a product gave 2.10 g of **30**, mp 183 °C.

IR (KBr): 3450 (m), 1110 (s), 1060 (m), 1045 (m), and 970 (m) cm^{-1}.

Found: C, 61.26; H, 8.28%. Calcd for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34%.

[8]Diisotwistane-2,8-dione (26). To a solution of 1.6 g of **23** in 20 ml of dry pyridine was added 2.28 g of methanesulfonyl chloride at 0—5 °C and then a reaction mixture was stirred for 2 hr at this temperature. After standing for further 20 hr at room temperature, it was poured onto ice and extracted with ether. The extract was washed with dilute hydrochloric acid, satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. Removal of the solvent gave 1.11 g of **24**, to which was added 30 ml of 10% sulfuric acid. After standing for 3 days at room temperature, it was extracted with ether. The extract was washed with satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. Removal of the solvent afforded 0.78 g of **25** as an oily product.

IR (neat film): 1725 (s), 1350 (m), 1175 (m), and 945 (m) cm^{-1}.

The mesylate (**25**), without purification, was dissolved in 25 ml of dry DMF and a solution was added to a suspension of 1.0 g of sodium hydride in 10 ml of dry DMF. A reaction mixture was heated for 48 hr at 60—70 °C under a nitrogen atmosphere. After cooling to room temperature, a few drops of methanol was added to the mixture and then it was diluted with water and extracted with ether. The extract was washed with dilute hydrochloric acid, satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. After evaporation of the solvent, a residue was chromatographed on neutral alumina (Woelm, activity III) and fractions eluted with ether–pentane (1:1 volume) gave a wax. The wax was sublimed to yield 85 mg of [8]diisotwistane-2,8-dione (**26**), mp 88—89 °C (in a sealed tube). A sample for elemental analysis was further purified by tlc (Kieselgel 60 PF_{254}, Merck) and sublimation.

IR (KBr): 1710 (s), 1222 (m), 1160 (m), and 1030 (m) cm^{-1}.

NMR ($CDCl_3$): δ 1.6—2.2 (m, 10H), 2.45—2.60 (m, 2H), and 2.68—2.88 (m, 2H).

UV: $\lambda_{max}^{ethanol}$ 258 nm (ε=40), 289 nm (42).

Found: C, 75.68; H, 7.49%. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42%.

Mesylation of 30. To a solution of 1.90 g of **30** in 20 ml of dry pyridine was added 2.70 g of methanesulfonyl chloride with ice cooling. After stirring for 5 hr at 0—5 °C, a mixture was stand overnight at room temperature and then poured onto ice. A solid was collected and washed with water to give 2.08 g of **31**, mp 169 °C dec.

IR (KBr): 1335 (s), 1170 (s), 985 (m), and 840 (m), cm^{-1}.

NMR ($CDCl_3$): δ 1.6—2.1 (m, 6H), 2.4—2.5 (m, 2H). 3.09 (s, 6H), 3.60—3.70 (m, 12H), and 4.22—4.31 (m, 4H),

Found: C, 45.78; H, 6.44; S, 13.56%. Calcd for $C_{18}H_{30}O_{12}S_2$: C, 45.95; H, 6.43; S, 13.60%.

Attempts to Hydrolyze Ethylenedioxy Group of 31. Mesylate (**31**) was quantitatively recovered unchanged from 10% sulfuric acid (for 2 days at room temperature), *p*-toluenesulfonic acid in acetone (for 4 days at room temperature), 1 N hydrochloric acid in THF (for 5 hr at room temperature), and 50% aqueous acetic acid (for 1 hr at 70 °C).

Diels-Alder Reaction of β-Naphthol with Ethyl Acrylate. A mixture of 90 g of β-naphthol and 120 g of ethyl acrylate was heated for 70 hr at 170—180 °C under a nitrogen atmosphere. From the reaction mixture, 75 g of ethyl acrylate was recovered by distillation. A residue was chromatographed on alumina (Sumitomo). Fractions eluted with benzene were distilled to give 22.1 g of a mixture of adducts, bp 137—140 °C at 0.1 mmHg. Analysis by glc on a 10% SE-30 column at 190 °C revealed the presence of two components having relative retention times 1.00: 1.24 (relative yield 39: 61 respectively). The structure (**33**) was assigned to a minor adduct and **32** to a major adduct.

IR (neat film): 1720 (s), 1625 (w), 1600 (w), 1170 (m), and 755 (m) cm^{-1}.

NMR ($CDCl_3$): δ 1.11 (t, J=7 Hz, 1.0*), 1.26 (t, J=7 Hz, 1.5), 1.8—3.0 (m, 4.5), 3.4—4.3 (m, 3.5), 7.13 (s, 1.5), and 7.16 (s, 2.0).

Found: C, 73.49; H, 6.63%. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60%.

*Ketalization of a mixture of 2-Oxo-5-*endo*-ethoxycarbonyl-7,8-benzobicyclo[2.2.2]octane (32) and 2-Oxo-5-*exo*-ethoxycarbonyl-7,8-benzobicyclo[2.2.2]octane (33).* A solution of 22.0 g of a mixture of **32** and **33**, 300 ml of ethylene glycol, 1.40 g of *p*-toluenesulfonic acid in 1400 ml of benzene was boiled for 30 hr. During this period, the water generated was separated as benzene azeotrope from the reaction mixture. After cooling to room temperature, a benzene layer was separated and washed with satd. aqueous sodium bicarbonate, water and dried over magnesium sulfate. After evaporation of the solvent, a residue was distilled to give 23.8 g of a mixture of **36** and **37**, bp 153—155 °C at 0.1 mmHg.

IR (neat film): 1725 (s), 1625 (w), 1600 (w), 1185 (m), 1120 (m), 1095 (m), 1030 (m), 1010 (m), and 755 (m) cm^{-1}.

Found: C, 69.51; H, 8.33%. Calcd for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27%.

*A Mixture of 2-Ethylenedioxy-5-*endo*-hydroxymethyl-7,8-benzobicyclo[2.2.2]octane (38) and 2-Ethylenedioxy-5-*exo*-hydroxymethyl-7,8-bicyclo[2.2.2]octane (39).* A solution of 23.7 g of a mixture of **36** and **37** in 200 ml of dry ether was added to a suspension of 5.00 g of lithium aluminum hydride in 150 ml of dry ether at room temperature. It was refluxed for 2 hr and then cooled with ice. A chilled reaction mixture was added with satd. aqueous ammonium chloride solution and a solid was filtered off. A filtrate was washed with water and dried over magnesium sulfate. After evaporation of the solvent, a residue was distilled to yield 16.6 g of a mixture of **38** and **39**, bp 172—173 °C at 0.1 mmHg.

IR (neat film): 3400 (s), 1625 (w), 1600 (w), 1120 (m), 1080 (m), 1030 (m), and 750 (s) cm^{-1}.

Found: C, 72.98; H, 7.38%. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37%.

Tosylation of a Mixture of 38 and 39. To a solution of 16.5 g of a mixture of **38** and **39** in 40 ml of dry pyridine was

* Relative ratio of peak areas.

added 16.0 g of *p*-toluenesulfonyl chloride at 0—5 °C. The mixture was agitated at this temperature for 2 hr and then kept for further 24 hr at room temperature. After pouring onto ice, it was acidified with hydrochloric acid and extracted with benzene. The extract was washed with satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. After evaporation of the solvent, a residue was added with ether and a solid precipitated was collected. The solid was recrystallized from benzene to yield 9.10 g of **40**, mp 139—140 °C.

IR (KBr): 1360 (s), 1175 (s), and 750 (m) cm^{-1}.

Found: C, 66.09; H, 6.11; S, 7.69%. Calcd for $C_{22}H_{24}O_5S$: C, 65.99; H, 6.04; S, 7.99%.

The solvent was removed from a filtrate to give 15.4 g of an oily substance (**41**), which was, without further purification, used for a subsequent reaction.

IR (neat film): 1360 (s), 1175 (s), and 755 (m) cm^{-1}.

*2-Ethylenedioxy-5-*endo*-cyanomethyl-7,8-benzobicyclo[2.2.2]octane (42).* A mixture of 11.5 g of **40**, 6.30 g of sodium cyanide, and 75 ml of DMF was heated for 1 hr at 120 °C and then for further 8 hr at 150—160 °C. After cooling to room temperature, a solid was filtered off and a filtrate was concentrated under reduced pressure. A residue was diluted with water and extracted with ether. The extract was washed with dilute hydrochloric acid, satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. Removal of the solvent gave a solid, which was recrystallized from benzene–hexane to yield 6.10 g of **42**, mp 120—120.5 °C.

IR (KBr): 2250 (w), 1125 (m), 1090 (m), 1035 (m), 1010 (m), and 750 (m) cm^{-1}.

Found: C, 75.58; H, 6.78; N, 5.58%. Calcd for $C_{16}H_{17}O_2N$: C, 75.27; H, 6.71; N, 5.49%.

*2-Ethylenedioxy-5-*exo*-cyanomethyl-7,8-benzobicyclo[2.2.2]octane (49)* Treatment of 15.3 g of **41** with 8.20 g of sodium cyanide by the same manner described above yielded a solid which was recrystallized from benzene–hexane to give 5.20 g of **49**, mp 116.5—118 °C.

IR (KBr): 2250 (w), 1095 (s), 1075 (s), 1030 (m), 1015 (m), and 755 (m), cm^{-1}.

Found: C, 75.51; H, 6.78; N, 5.55%. Calcd for $C_{16}H_{17}O_2N$: C, 75.27; H, 6.71; N, 5.49%.

*2-Oxo-5-*endo*-(2-hydroxyethyl)-7,8-benzobicyclo[2.2.2]octane (45).* A mixture of 5.80 g of **42**, 10.0 g of potassium hydroxide, and 85 ml of ethylene glycol was heated for 2 hr at 120 °C and then for further 8 hr at 150—160 °C. After cooling to room temperature, a reaction mixture was diluted with water and acidified with hydrochloric acid. It was extracted with ether. The extract was washed with water and dried over magnesium sulfate. Removal of the solvent gave 6.53 g of an oily product (**43**), which was dissolved in 200 ml of dry ether. A solution was slowly added to a suspension of 2.00 g of lithium aluminum hydride in 50 ml of dry ether and a mixture was refluxed for 3 hr. After cooling with ice, to the chilled mixture was carefully added satd. aqueous ammonium chloride solution. A solid was filtered off and a filtrate was concentrated to give 5.92 g of a viscous oily product (**44**).

IR (neat film): 3450 (s), 1050 (m), 1110 (m), 1080 (m), 1030 (m), 1010 (m), and 755 (m) cm^{-1}.

To a solution of this substance in 400 ml of acetone was added 1.00 g of *p*-toluenesulfonic acid and the mixture was allowed to stand overnight at room temperature. After removal of acetone under reduced pressure, a residue was diluted with water and extracted with ether. The extract was washed with satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. After evaporation of the solvent, a residue was distilled to yield 3.64 g of **45**, bp 180 °C at 0.5 mmHg.

IR (neat film): 3450 (s), 1725 (s), 1625 (w), 1600 (w), 1050 (m), and 755 (m) cm^{-1}.

Found: C, 76.99; H, 7.33%. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46%.

The substance was very hygroscopic.

*2-Ethylenedioxy-5-*exo*-carboxymethyl-7,8-benzobicyclo[2.2.2]octane (50).* Hydrolysis of 4.17 g of **49** with 8.00 g of potassium hydroxide in 70 ml of ethylene glycol was carried out by the same manner described above. A solid was obtained and recrystallized from benzene–hexane to yield 4.06 g of **50**, mp 119.5—120 °C.

IR (KBr): 3000 (broad), 1710 (s), and 755 (m) cm^{-1}.

Found: C, 70.27; H, 6.65%. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61%.

*2-Oxo-5-*exo*-(2-hydroxyethyl)-7,8-benzobicyclo[2.2.2]octane (52).* Reduction of 4.20 g of **50** with 2.10 g of lithium aluminum hydride in dry ether gave 3.66 g of an oily product (**51**).

IR (neat film): 3450 (s), 1050 (m), 1110 (m), 1080 (m), 1030 (m), 1010 (m), and 755 (m) cm^{-1}.

The substance was dissolved in 280 ml of acetone and to the solution was added 0.72 g of *p*-toluenesulfonic acid. The solution was stirred for 8 hr at room temperature and then worked up as described above to yield 2.30 g of **52**, bp 167—168 °C at 0.2 mmHg.

IR (neat film): 3450 (s), 1720 (s), 1050 (m), and 755 (m) cm^{-1}.

Found: C, 77.66; H, 7.50%. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46%.

8,9-Benzotricyclo[4.3.1.0^{3,7}]decan-2-one (47). To a solution of 3.32 g of **45** in 10 ml of dry pyridine was added 3.42 g of methanesulfonyl chloride with ice cooling and then a mixture was kept for 20 hr at room temperature. It was poured onto ice and acidified with hydrochloric acid. It was extracted with ether. The extract was washed with satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. Removal of the solvent gave 4.40 g of **46**.

IR (neat film): 1720 (s), 1350 (s), 1170 (s), and 755 (m) cm^{-1}.

The methanesulfonate (**46**) was, without purification, dissolved in 45 ml of dry DMF and the solution was added to a suspension of 8.00 g of sodium hydride in 100 ml of dry DMF. It was stirred for 22 hr at 60 °C under a nitrogen atmosphere. After cooling with ice, to a chilled reaction mixture was added 3 ml of methanol and then poured onto ice. It was extracted with ether. The extract was washed with dilute hydrochloric acid, satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. After evaporation of the solvent, to a residue was added pentane to give a solid which was collected and sublimed to yield 2.62 g of **47**, mp 85—86 °C (in a sealed tube).

IR (KBr): 1725 (s), 1630 (w), 1475 (m), 1455 (m), and 755 (s) cm^{-1}.

NMR (CCl_4): δ 1.4—1.6 (m, 2H), 1.6—2.3 (m, 4H), 3.17 (t, 2H), 3.38 (d,d, J=3.3 Hz, J=1.4 Hz, 2H), and 7.12 (s, 4H).

Mass spectrum: *m/e* 198 (parent peak).

Found: C, 84.60; H, 7.15%. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12%.

Tosylhydrazone; mp 182 °C dec.

Found: C, 69.11; H, 6.38; N, 7.32; S, 8.56%. Calcd for $C_{21}H_{22}O_2N_2S$: C, 68.83; H, 6.05; N, 7.65; S, 8.74%.

8,9-Benzotricyclo[4.3.1.0^{3,7}]decane (10). A mixture of 300 mg of **47**, 0.13 g of potassium hydroxide, 0.22 ml of 80% hydrazine hydrate, and 2 ml of triethylene glycol was heated for 90 min at 160 °C and then water was removed from the

reaction mixture. A residual solution was heated for further 3 hr at 200 °C and then diluted with water. It was extracted with pentane. The extract was washed with water and dried over magnesium sulfate. Removal of the solvent gave a solid which was sublimed to yield 131 mg of **10**, mp 56—57 °C (in a sealed tube).

IR (KBr): 2920 (m), 2870 (m), 1480 (m), 1450 (m), and 755 (s) cm^{-1}.

NMR (CCl_4): δ 1.3—2.1 (m, 10H), 2.81 (m, 2H), and 7.03 (s, 4H).

Mass spectrum: *m/e* 184 (parent peak).

Found: C, 90.98; H, 8.85%. Calcd for $C_{14}H_{16}$: C, 91.25; H, 8.75%.

Attempt to Cyclize exo-*Methanesulfonate (53).* Treatment of 2.30 g of **52** with 2.50 g of methanesulfonyl chloride and 7 ml of dry pyridine by the same manner described for *endo*-isomer gave 2.28 g of **53**, which was dissolved in 30 ml of dry DMF. This solution was added to a suspension of 4.80 g of sodium hydride in 60 ml of dry DMF. The mixture was agitated for 25 hr at 60 °C under a nitrogen atmosphere and 2 ml of methanol was added to the reaction mixture with ice cooling. It was then poured onto ice and extracted with ether. The extract was washed with dilute hydrochloric acid, satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. Removal of the solvent gave an oily product which was chromatographed on neutral alumina (Woelm, activity III). But 8,9-benzotricyclo[4.3.1.$0^{3,7}$]-decan-2-one (**47**) was not obtained.

Hydrolysis of Ethylenedioxy Group of 40. A mixture of 8.21 g of **40**, 1.50 g of *p*-toluenesulfonic acid and 600 ml of acetone was stirred for 2 days at room temperature. The mixture was concentrated under reduced pressure and a residue was diluted with water. It was extracted with ether. The extract was washed with satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. After evaporation of the solvent, a residue was added with benzene–hexane to yield 6.31 g of **54**, mp 121.5—123 °C.

IR (KBr): 1730 (s), 1595 (m), 1355 (s), 1175 (s), 970 (s), 845 (s), and 755 (m) cm^{-1}.

Found: C, 68.04; H, 6.01; S, 8.78%. Calcd for $C_{20}H_{20}O_4S$: C, 67.40; H, 5.66: S, 8.98%.

7,8-Benzotricyclo[3.3.1.$0^{3,6}$*]nonan-2-ol (55).* A solution of 4.50 g of **54** in 50 ml of dry DMF was added to a suspension of 8.00 g of sodium hydride in 100 ml of dry DMF and a mixture was agitated for 72 hr at 70 °C. After cooling to room temperature, the reaction mixture was diluted with water and extracted with ether. The extract was washed with dilute hydrochloric acid, satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. After evaporation of the solvent, a residue was chromatographed on silica gel (Mallinckrodt) and fractions eluted with ether–pentane (1: 1 volume) gave 0.23 g of **55**, mp 95—98 °C.

IR (KBr): 3250 (s), 1030 (s), and 745 (s) cm^{-1}.

Mass spectrum: *m/e* 186 (parent peak).

Found: C, 83.78; H, 7.68%. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58%.

7,8-Benzotricyclo[3.3.1.$0^{3,6}$*]nonan-2-one (56).* To a solution of 150 mg of **55** was added 0.5 ml of 8N-Jones' reagent at 0—5 °C and a mixture was stirred for 30 min at the same temperature. After dilution with ether, it was washed with satd. aqueous sodium bicarbonate, water, and dried over magnesium sulfate. Removal of the solvent gave a solid which was sublimed to yield 61 mg of **56**, mp 90 °C (in a sealed tube).

IR (KBr): 1720 (s) and 750 (s) cm^{-1}.

NMR ($CDCl_3$): δ 1.4—1.7 (m, 2H), 2.30 (m, 1H), 2.70 (m, 3H), 3.82 (m, 2H), and 7.12 (s, 4H).

Mass spectrum: *m/e* 184 (parent peak).

Found: C, 84.80; H, 6.54%. Calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57%.

References

1) Presented at the 30th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1974, preprint Vol. III p. 1798.

2) This name has been given to describe symmetry of a shape which is chiral but not asymmetric. Collectively we call a shape "gyrochiral" when it belongs to anyone of C_n ($n \neq 1$), D_n, T, O, and I point groups.

3) H. W. Whitlock, Jr., *J. Amer. Chem. Soc.*, **84**, 3412 (1962). J. Gauthier and P. Deslongchamps, *Can. J. Chem.*, **45**, 297 (1967). K. Adachi, K. Naemura, and M. Nakazaki, *Tetrahedron Lett.*, **1968**, 5467. M. Tichy and J. Sicher, *Collect. Czech. Chem. Commun*, **37**, 3106 (1972).

4) B. R. Vogt, *Tetrahedron Lett.*, **1968**, 1579. R. R. Sauers and J. A. Whittle, *J. Org. Chem.*, **34**, 3579 (1969). K. Naemura and M. Nakazaki, This Bulletin, **46**, 888 (1973).

5) K. Hirao, T. Iwakura, M. Taniguchi, E. Abe, O. Yonemitsu, T. Date, and K. Kotera, *Chem. Commun.*, **1974**, 691.

6) According to the proposed nomenclature[5,7], we name tetracyclo[7.3.$0^{3,7}$.$0^{4,10}$]dodecane (**7**) [8]diisotwistane.

7) W. D. Graham, P. v. R. Schleyer, E. W. Hagaman, and E. Wenkert, *J. Amer. Chem. Soc.*, **95**, 5785 (1973).

8) The symmetry of the parent compound (**3**) forces the last ethano-bridging to become diagonal.

9) As a matter of convenience, an isomer with 7 and 8-carboxyl groups near to 2 and 5-keto groups respectively is termed *syn*-form and the other is named *anti*-form.

10) We call an isomer with 5-carboxy group near to benzene ring *exo*-form and the other isomer *endo*-form.

11) O. Diels and K. Alder, *Ann.*, **478**, 152 (1930).