A Short Synthesis of Dimethyl Tricyclo[3.3.0.0^{3,7}]octane-1,5-dicarboxylate and its 3,7-Dimethyl Derivative. A New Route to the Tricyclo[3.3.0.0^{3,7}]octane Skeleton

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Five-step syntheses of dimethyl tricyclo[3.3.0.0^{3,7}]octane-1,5-dicarboxylate (**13**) and its 3,7-dimethyl derivative **14** from the readily available *cis*-bicyclo[3.3.0]octane-3,7-diones **1** and **2**, respectively, are described. The key-step implies the iodine oxidation of the bis-enolate derived from the corresponding dimethyl *cis*-bicyclo-[3.3.0]octane-3,7-dicarboxylates **11** and **12**, thus being developed a new synthetic entry into the tricyclo[3.3.0.0^{3,7}]octane skeleton. Also, some attempts to synthesize diester **13** by using known methodology for the synthesis of compounds containing this tricyclic skeleton are described.

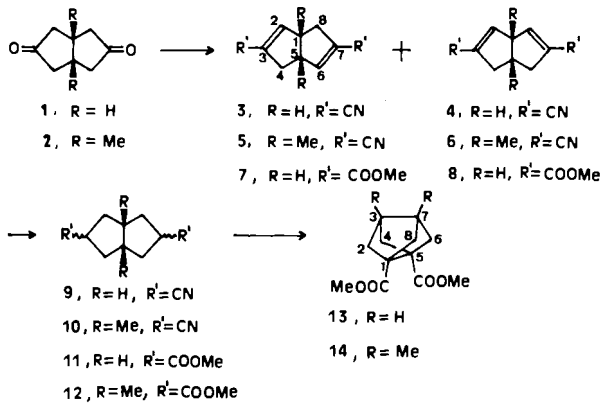
Eine kurze Synthese von Tricyclo[3.3.0.0^{3,7}]octan-1,5-dicarbonsäure-dimethylester und seines 3,7-Dimethylderivats. Ein neuer Weg zum Tricyclo[3.3.0.0^{3,7}]octan-Gerüst

Die 5-stufige Synthese von Tricyclo[3.3.0.0^{3,7}]octan-1,5-dicarbonsäure-dimethylester (**13**) und seines 3,7-Dimethylderivats **14** ausgehend von den leicht zugänglichen *cis*-Bicyclo[3.3.0]octan-3,7-dionen **1** bzw. **2** wird beschrieben. Schlüsselreaktion ist die Oxidation der Bis-enolate der *cis*-Bicyclo[3.3.0]octan-3,7-dicarbonsäure-dimethylester **11** und **12** mit Iod zum Tricyclo-[3.3.0.0^{3,7}]octan-Derivat **13** bzw. **14**. Zusätzlich wird die Synthese des Diesters **13** nach bekannten Methoden versucht.

Some time ago we published [1] several attempts to develop a new synthetic entry into the tricyclo[3.3.0.0^{3,7}]octane skeleton in order to synthesize dimethyl tricyclo-[3.3.0.0^{3,7}]octane-1,5-dicarboxylate (**13**) and reviewed the described routes to obtain compounds containing this strained carbocyclic skeleton. Since then no other new synthetic entry to this type of carbocyclic derivatives has been described [2]. We describe herein the synthesis of diester **13** and dimethyl 3,7-dimethyltricyclo[3.3.0.0^{3,7}]octane-1,5-dicarboxylate (**14**) in a straightforward manner from the readily available *cis*-bicyclo[3.3.0]octane-3,7-dione (**1**)[3] and *cis*-1,5-dimethylbicyclo[3.3.0]octane-3,7-dione (**2**)[3], respectively.

Reaction of diketone **1** with excess sodium cyanide in water gave a mixture of stereoisomeric bis-cyanohydrins that was dehydrated as such by reaction with phosphoryl chloride in boiling pyridine to give a mixture of *cis*-bicyclo-[3.3.0]octa-2,6-diene-3,7-dicarbonitrile (**3**) and -2,7-diene-3,7-dicarbonitrile (**4**) in 54% yield. This mixture, in which **3** was slightly predominant (GLC), was separated by semi-preparative HPLC. The 200-MHz ^{1}H NMR spectra of **3** and **4** could be fully assigned by double-resonance experiments (Table 1).

Scheme 1



Only four kinds of protons were observed for dinitrile **3** according to its C_2 symmetry. For dinitrile **4**, however, five kinds of protons were observed in accord to its C_s symmetry. Assignment of the *exo*-4(8)-H and *endo*-4(8)-H absorptions of **3** was made on the basis of their coupling constants and chemical shifts [4,5]. As expected from the Karplus equation, the coupling constant value 1-H,*exo*-8-H (6.6 Hz) is greater than that for 1-H,*endo*-8-H (2.2 Hz). The assignment of dinitrile **4** was carried out in a similar manner. The 50-MHz ^{13}C NMR spectra of dinitriles **3** and **4** (Table 2) were also in accord with their symmetry. The assignment was based mainly on the multiplicity and intensity of the absorptions. To assign the absorptions of C-1 and C-5 in **4**, the values predicted by using the data of Bremser et al.[6] were conclusive.

Hydrogenation of the mixture of dinitriles **3** and **4** was easily achieved. The product consisted essentially of one of the three possible stereoisomers, that was obtained in pure state by crystallization from ether. On the basis of its C_{2v} symmetry and the expected preferred hydrogenation of the carbon-carbon double bonds of **3** and **4** by their less hind-

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ered *exo* faces, it was considered to be *cis*-bicyclo-[3.3.0]octane-*endo*-3,*endo*-7-dicarbonitrile (*endo,endo*-**9**). A temptative assignment of the 200-MHz ^{1}H NMR spectrum of *endo,endo*-**9** and the assignment of its 50-MHz ^{13}C NMR spectrum, based on the same arguments used for dinitriles **3** and **4**, is shown in Tables 1 and 2.

Table 1. Proton NMR data (200 MHz) of some bicyclo-[3.3.0]octane derivatives ($CDCl_3$, 25°C). In symmetrical compounds, the chemical shift is given only for the lowest numbered proton among equivalent ones

		Compound						
		3	4	endo,endo-9	18	19	21	22
δ (ppm)	1-H	3.70	4.12	2.60				
	2-H	6.44	6.54		5.83	5.94	5.43	5.71
	exo-2-H			2.32				
	endo-2-H			1.81				
	3-H			2.80	5.83	5.80	5.81	5.71
	exo-4-H	2.92	3.01		2.7	2.75	2.48	2.40
	endo-4-H	2.55	2.48		3.1	3.22	3.18	3.09
	5-H		3.23					
J (Hz)	1-H,2-H	2.0	2.3					
	1-H,exo-2-H			6.9				
	1-H,endo-2-H			6.9				
	1-H,exo-4-H	4.4	2.3					
	1-H,endo-4-H	2.2	3.0					
	1-H,5-H		8.0					
	1-H,exo-8-H	6.6						
	1-H,endo-8-H	2.2						
	2-H,3-H					5.6	5.8	
	2-H,exo-4-H	2.2	2.3			2.2	1.4	
	2-H,endo-4-H	2.2	2.3			2.2	2.7	
	exo-2-H,endo-2-H			13.4				
	exo-2-H,exo-3-H			8.1				
	endo-2-H,exo-3-H			9.4				
	3-H,exo-4-H					2.2	2.7	
	3-H,endo-4-H					2.2	1.9	
	exo-4-H,endo-4-H	16.6	16.8		18.1	18.4	16.5	17.4
	exo-4-H,5-H		9.2					
	endo-4-H,5-H		4.0					

Alkaline hydrolysis of the mixture of dinitriles **9** gave, after esterification with diazomethane, a liquid mixture of the three possible stereoisomers of dimethyl *cis*-bicyclo-[3.3.0]octane-3,7-dicarboxylate (**11**) in the approximate ratio *exo,exo*-**11**:*exo,endo*-**11**:*endo,endo*-**11** = 2:5:1 (^{13}C NMR) in 67% yield. Alternatively, hydrolysis of a mixture of dinitriles **3** and **4**, followed by acid-catalyzed esterification with methanol, gave in 44% yield, after chromatography and crystallization, a solid mixture of the corresponding diesters **7** and **8** in about the same ratio (approximately 1:1) as the starting mixture of dinitriles. Hydrogenation of this mixture gave a product consisting mainly of one of the C_{2v} stereoisomers of diester **11**, probably *endo,endo*-**11**, since hydrogenation of the carbon-carbon double bonds of diesters **7** and **8** must take place preferently from their *exo* faces. The comparison of the ^{13}C-NMR spectra of the mixture of diesters **11** and *endo,endo*-**11** let us differentiate the absorptions of all of the three stereoisomers and make the temptative assignment shown in Table 2. Also the ^{13}C-NMR spectrum of a mixture of diesters **7** and **8** in the approximate ratio 1:1 was temptatively assigned (Table 2) on the basis of the multiplicity and intensity of the absorptions and by comparison with the ^{13}C chemical shifts of dinitriles **3** and **4**.

Reaction of a mixture of diesters **11** with 2 equivalents of lithium diisopropylamide in anhydrous tetrahydrofuran, followed by reaction of the corresponding bis-enolate with one equivalent of iodine[7] gave dimethyl tricyclo-[3.3.0.0^{3,7}]octane-1,5-dicarboxylate (**13**) in 39% yield. A liquid product of approximately 95% purity (^{13}C NMR) was simply obtained by column chromatography or distillation in a rotary microdistillation apparatus. The analytical sample was obtained by HPLC of this 95% purity product, and it solidified on standing (m.p. 59–61°C). The spectroscopic data and elemental analysis of **13** were all concordant with

Table 2. Carbon-13 NMR data of some bicyclo[3.3.0]octane and tricyclo[3.3.0.0^{3,7}]octane derivatives[a]. In symmetrical compounds, the chemical shift is given only for the lowest numbered carbon atom among equivalent ones. Values underlined can be interchanged

Compound[b]	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	CH_3	OCH_3	CN	-COO-
3	48.5	149.9	113.4	38.4							115.7	
4	59.7	145.4	115.5	42.0	38.5						115.7	
7	48.5	146.0	134.0	36.0						51.5		165.5
8	59.2	141.3	136.3	39.8	38.9					51.5		165.5
endo,endo-9	43.4	37.5	30.0								121.8	
exo,exo-10	51.3	45.6	25.6						24.2		122.0	
endo,endo-11	44.2	36.65	47.8							51.6		175.5
endo,exo-11	42.4	37.9	42.2			36.5	45.5			51.6		175.5 and 176.1
exo,exo-11	44.0	37.6	42.15							51.6		176.1
endo,endo-12	51.0	45.3	42.1						24.6	51.6		176.1
endo,exo-12	50.4	45.8	40.0			44.8	41.4		24.1	51.6		176.0 and 176.2
exo,exo-12	52.8	42.7	41.9						21.9	51.6		176.8
13	57.3	50.2	37.2							51.7		173.6
14	58.0	56.2	47.7						16.0	51.6		173.4
18	69.7	128.6	133.2	41.9								173.9
19	79.2	127.9	132.6	44.6	59.8							171.5 and 175.9
21[c]	68.9	131.0	133.4	40.4						51.9		174.0
22[c]	76.5	130.4	131.1	44.9	61.8					51.9		173.5 and 175.3

[a] Except where otherwise stated, the spectra have been taken at 50 MHz in $CDCl_3$ solution at 25°C. — [b] The values of compounds **7**, **8**, *exo,exo*-**10**, **11**, and **12** have been determined from isomeric mixtures. — [c] This spectrum was taken at 20 MHz.

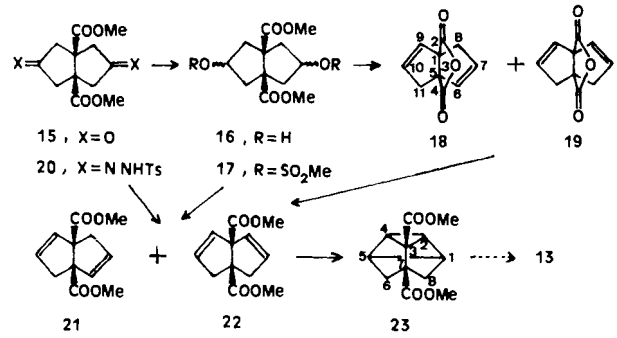
expectations, in particular the ^{13}C-NMR spectrum was in accord with its C_{2v} symmetry (Table 2).

In a similar manner, diketone **2** was converted into a solid mixture of dinitriles **5** and **6** in the approximate ratio 2.5:1 (^{13}C NMR) in 63% overall yield of crystallized product. Quast et al.[8] have described the conversion of **2** into a nearly 2:1 mixture of dinitriles **5** and **6** by reaction with trimethylsilyl cyanide followed by treatment of the stereoisomeric mixture of silylated bis-cyanohydrins with phosphoryl chloride in pyridine. An improved procedure based on the method of Quast hat been published recently[9]. This mixture of dinitriles **5** and **6** was hydrogenated in ethanol solution using 5% Pd on charcoal as catalyst. Hydrogenation took place slowly as compared with the mixture of dinitriles **3** and **4**, a fact that must be related to the presence of the methyl groups at the bridgehead positions. It is noteworthy that Hofmann et al.[9] have reported recently their failure to hydrogenate this mixture of dinitriles **5** and **6** that, however, they reduced in high yield with magnesium in methanol to a mixture of the three possible stereoisomers of *cis*-1,5-dimethylbicyclo[3.3.0]octane-3,7-dicarbonitrile (**10**) in the approximate ratio *endo,endo*-**10**:*endo,exo*-**10**:*exo,exo*-**10** = 5:9:6. According to their assignment of these stereoisomers, based on the chemical shift for the methyl protons, our mixture contained them in the approximate ratio *endo,endo*-**10**:*endo,exo*-**10**:*exo,exo*-**10** = 1:1:2, showing that hydrogenation takes place with slight preference from the *endo* faces of the carbon-carbon double bonds of **5** and **6** in marked contrast with the preferent *exo* hydrogenation of dinitriles **3** and **4**. Table 2 shows the assignment of the ^{13}C-NMR absorptions for the major stereoisomer, *exo,exo*-**10**. Alkaline hydrolysis of the mixture of dinitriles **10** followed by esterification with diazomethane gave a solid mixture of the three possible stereoisomers of dimethyl *cis*-1,5-dimethylbicyclo[3.3.0]octane-3,7-dicarboxylate (**12**) in 73% yield. The approximate ratio (^{1}H NMR) was found to be *endo,endo*-**12**:*endo,exo*-**12**:*exo,exo*-**12** = 2:4:1, showing that, at least, partial epimerization at C-3 and C-7 takes place during hydrolysis. Interestingly, the acidic hydrolysis occurs without epimerization[9]. Crystallization of this mixture from hexane gave a solid mixture of *endo,endo*-**12** and *endo,exo*-**12** in the approximate ratio 2:3. The comparison of the ^{13}C-NMR spectra of both mixtures led to the assignment of the carbon absorptions of all of the three stereoisomers of diester **12** (Table 2). The multiplicity and intensity of the absorptions, the different symmetry of *endo,exo*-**12** (C_s) vs *endo,endo*-**12** and *exo,exo*-**12** (C_{2v}), and the different proportion of stereoisomers greatly facilitated the assignment. As before, treatment of a mixture of diesters **12** with lithium diisopropylamide in anhydrous tetrahydrofuran followed by reaction of the corresponding bis-enolate with 1 equivalent of iodine gave, in 38% yield, dimethyl 3,7-dimethyltricyclo[3.3.0.0^{3,7}]octane-1,5-dicarboxylate (**14**). The spectroscopic data and elemental analysis were all concordant with expectations (^{13}C NMR in Table 2).

The method used to synthesize diesters **13** and **14** represents a new and rapid synthetic entry into the strained tricyclo[3.3.0.0^{3,7}]octane skeleton, that does not require separation of stereoisomers at any moment in the sequence and might be applied to other substrates easily obtainable from the readily available *cis*-bicyclo[3.3.0]octane-3,7-diones.

We also attempted to obtain diester **13** by using known methodology for the synthesis of tricyclo[3.3.0.0^{3,7}]octane derivatives, as shown in Scheme 2. Dimethyl *cis*-3,7-dioxobicyclo[3.3.0]octane-1,5-dicarboxylate (**15**) was transformed into a mixture of dimethyl *cis*-bicyclo[3.3.0]octa-2,6-diene-1,5-dicarboxylate (**21**) and -2,7-diene-1,5-dicarboxylate (**22**) by several procedures, only one of them being satisfactory.

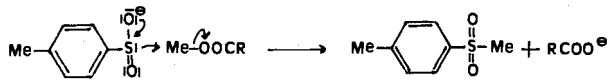
Scheme 2



First, diketo diester **15** was reduced with $NaBH_4$ in methanolic solution to give in high yield a mixture of the three possible stereoisomers of dimethyl *cis*-3,7-dihydroxybicyclo[3.3.0]octane-1,5-dicarboxylate (**16**), in which one of them, possesing C_{2v} symmetry, was predominant. Several attempts to selectively crystallize it were fruitless. Reduction of **15** with lithium tri-*tert*-butoxyaluminum hydride in anhydrous tetrahydrofuran gave a mixture of stereoisomers of **16** in about the same ratio as that obtained with $NaBH_4$. Reaction of the mixture of dihydroxy diesters **16** with 2 equivalents of methanesulfonyl chloride in pyridine gave in high yield a mixture of stereoisomers of dimesylate **17**. Crystallization of this mixture from methylene chloride gave in 21% yield the major stereoisomer. The ^{1}H-NMR spectrum of this compound clearly showed its C_{2v} symmetry, being difficult to differentiate among the two possible stereoisomers *endo,endo*-**17** and *exo,exo*-**17**. Many attempts to carry out the bis-dehydromesylation of the stereoisomeric mixture **17** with aluminum oxide in methylene chloride, sodium methoxide in methanol, or dimethyl sulfoxide, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in dimethyl sulfoxide or toluene, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene showed the different reactivity of the three stereoisomers of **17**. Together with the desired diene diesters **21** and **22**, products of partial dehydromesylation were generally obtained. The best results gave DBU as the base in toluene under reflux leading to a mixture of **21** and **22** (ratio $\approx$2:1) in 56% yield. By repeated chromatography and crystallization pure solid samples of both diesters were obtained. The spectral data and elemental analyses were all in accord with expectations, in particular the ^{1}H- and ^{13}C-NMR spectra clearly showed the C_2 symmetry of **21** and the C_s symmetry of **22**.

Alternatively, diketo diester **15** was transformed into the corresponding bis-tosylhydrazone **20**, which was treated with sodium methoxide in anhydrous methanol. The corresponding disodium salt was pyrolyzed at 135°C/0.5 Torr to give a mixture of diesters **21** and **22** (approximately 46% yield, working on a 2-g scale; 26% **21** and 20% **22**) plus another product that was characterized as methyl *p*-tolyl sulfone[10] (**24**). Starting from 20 g of bis-tosylhyrazone **20**, the yield of diesters was only 33%, while the amount of sulfone **24** greatly increased. The formation of this by-product can be easily explained by nucleophilic attack of the *p*-toluene-sulfinate anion, formed during the pyrolysis, to a methyl of an ester group, either of the starting compound or of any of the intermediate or final product with simultaneous formation of the carboxylic acid sodium salt (Scheme 3), thus decreasing the yield of diesters **21** and **22**. Separation of these diesters from sulfone **24** could not be easily carried out by distillation or column chromatography. Consequently, this method of obtaining diesters **21** and **22** did not offer any advantage over the bis-dehydromesylation of the bis-mesylate **17**.

Scheme 3



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A better preparation of these diesters was carried out by heating a mixture of dihydroxy diesters **16** with a mixture of phosphorus pentoxide and 85% phosphoric acid. The product consisted of a mixture of the anhydrides **18** and **19** in the approximate ratio 7:3. This mixture was hydrolyzed and esterified with diazomethane to give the corresponding mixture of diesters **21** and **22** in 78% overall yield from **16**. Pure samples of anhydrides **18** and **19** were obtained by saponification of the corresponding diesters followed by reaction with acetic anhydride and sublimation.

Table 1 shows a temptative assignment of the ^{1}H-NMR spectra of diesters **21**, **22** and anhydrides **18**, **19**, based on double resonance experiments. It is noteworthy that the 200-MHz ^{1}H-NMR spectra of diester **22** and anhydride **18**, for which the ethylenic protons have about the same chemical shifts, showed virtual coupling between these and the methylene protons. Irradiation of the ethylenic protons left the methylene absorption as two doublets. The 200-MHz ^{1}H-NMR spectrum of anhydride **18** was simulated perfectly by using the LAOCOON 3 program and the following parameters: δ ethylenic protons (A and B): 1165 and 1167 Hz; δ allylic protons (C and D): 620 and 543 Hz; $J_{AB} = 5.5$, $J_{AC} = -2.1$, $J_{AD} = -2.2$, $J_{BC} = 2.2$, $J_{BD} = 2.2$, and $J_{CD} = -18.1$ Hz. These values are in close proximity to those obtained experimentally for anhydride **19**.

We next attempted to convert diester **22** into diester **13**. We irradiated a mixture of **21** and **22** in the approximate ratio 18:82 in anhydrous ether with a 400-W mercury lamp. After 130 h diester **22** had been consumed, most of diester **21** remained unchanged, and two new compounds of the same molecular mass of **22** (GLC/MS) had been formed. Then, we irradiated pure samples of **21** and **22** and established that the new products had been formed from diester **22**. From the crude of irradiation of a 3:1 mixture of **21** and **22** (1.5 g) we could isolate, after many column chromatographies and distillation, a fraction of about 1 mg consisting mainly of one of the new products formed on irradiation of **22**. Its ^{1}H NMR and mass spectra (chemical ionization and electron impact) were compatible for dimethyl tetracyclo-[3.3.0.0^{2,4}.0^{3,7}]octane-3,7-dicarboxylate (**23**). The mass spectrum using chemical ionization (isobutane) showed two peaks at *m/z* 223 ($M + H^+$) and 191 ($M - MeOH + H^+$). The mass spectrum (electron impact) showed peaks whose *m/z* values and intensities were very close to those observed for diester **22**, a fact that can be explained by assuming that the excited diester **23**, by breaking of the cyclobutane ring, gives an excited diester **22**. The 80-MHz ^{1}H-NMR spectrum of this product in hexadeuteriobenzene is compatible with structure **23**. The small amount of product available did not let us obtain the ^{13}C-NMR spectrum and try its conversion into diester **13** by catalytic hydrogenation.

Also, we irradiated a mixture of anhydrides **18** and **19** under similar conditions to those used with diesters **21** and **22** but, after 80 h irradiation, no evidence of the formation of cyclized products could be obtained.

At this stage it is clear that a possible synthesis of diester **13** from diketo diester **15** by photocycloaddition of diester **22**, followed by catalytic hydrogenation[11], would have serious drawbacks as compared with the method described above.

Work is in progress to transform diesters **13** and **14** into more complex polycyclic compounds.

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Experimental

Infrared spectra: Perkin-Elmer Infracord 720, 577, 781, or 843 spectrometers. – 80-MHz ^{1}H and 20-MHz ^{13}C NMR spectra: Bruker model WP 80 SY spectrometer; 200-MHz ^{1}H and 50-MHz ^{13}C NMR spectra: Varian XL 200 spectrometer, internal TMS (δ scale). – Mass spectra: Hewlett-Packard spectrometers 5930 A 5985 B, electron impact and chemical ionization techniques, always at 70 eV. – Microanalyses: Microanalysis Service of the Centro de Investigación y Desarrollo, C. S. I. C. of Barcelona (Spain). – GLC analyses: Hewlett-Packard model 5830 A or Perkin-Elmer model Sigma-1 chromatographs. – HPLC separations: Waters HPLC chromatograph, model 6000 A, 30-cm μ-porasil semipreparative column. – Photochemical reactions: Medium pressure 125- and 400-W mercury lamps. – Hydrogenations: 300-ml Parr pressure

reactor, model 4561. – Melting points: Kofler hot-stage, uncorrected.

cis-Bicyclo[3.3.0]octa-2,6-diene-3,7-dicarbonitrile (**3**) *and cis-Bicyclo[3.3.0]octa-2,7-diene-3,7-dicarbonitrile* (**4**): A well-stirred mixture of sodium cyanide (10 g, 194 mmol), water (30 ml), and diketone **1** (5.0 g, 36.2 mmol) was cooled in an ice bath, and 40% aqueous H_2SO_4 (52 ml) was added dropwise over 3 h, keeping the temperature between 10 and 15°C. Ethyl ether (50 ml) was added, the organic phase was separated and the aqueous phase extracted with ether (3 × 250 ml). The combined organic phases were washed with water and dried with Na_2SO_4. Evaporation of the solvent gave the crude mixture of stereoisomeric bis-cyanohydrins. A solution of this crude product in pyridine (100 ml) was heated at 140°C and treated dropwise with $POCl_3$ (20 ml) and then heated under reflux for 4 h. The cold mixture was poured onto a mixture of conc. HCl (66 ml) and crushed ice (100 g) and extracted continuously with hexane for 48 h. The dried extract (Na_2SO_4) was concentrated at reduced pressure to give a solid mixture of dinitriles **3** and **4** (3.07 g, 54%), in which **3** slightly predominated (GLC). This mixture was separated by semipreparative HPLC using ethyl acetate/hexane (1:4) as eluent (flow 1.7 ml/min) with a pressure of 2000 psi in the column. The mixture of **3** and **4** (300 mg) was dissolved in CH_2Cl_2 (5 ml) and chromatographed in portions of 0.3 ml. Dinitrile **4** showed t_r 19 min and **3** 23 min.

3: M.p. 169–171°C (hexane). – IR (KBr): ν = 3060 cm^{-1} (m), 2930 (m), 2860 (m), 2210 (s), 1610 (s), 1445 (s), 1330 (m), 1310 (m), 1270 (m), 1260 (m), 1170 (m), 1160 (m), 1030 (s), 890 (s), 865 (s), 850 (s).

$C_{10}H_8N_2$ (156.2)	Calcd.	C 76.90	H 5.16 N 17.94
	Found	C 76.92	H 5.28 N 17.77

4: M.p. 128–130°C (hexane). – IR (KBr): ν = 3060 cm^{-1} (m), 2960 (m), 2920 (m), 2850 (m), 2210 (s), 1600 (s), 1440 (s), 1320 (m), 1110 (m), 1012 (m), 1000 (s), 900 (s), 870 (m), 860 (m).

$C_{10}H_8N_2$ (156.2)	Calcd.	C 76.90	H 5.16 N 17.94
	Found	C 76.67	H 5.10 N 17.81

cis-Bicyclo[3.3.0]octane-endo-3,endo-7-dicarbonitrile (*endo,endo*-**9**): A mixture of dinitriles **3** and **4** (11.31 g, 72.5 mmol), 5% Pd on charcoal (1.13 g), and methanol (100 ml) was hydrogenated in a Parr pressure reactor at 4 atm and room temperature in approximately 3 h. The reaction was followed through the disappearance of the ethylenic hydrogens (^{1}H NMR). The mixture was filtered and the filtrate concentrated at reduced pressure to give, in nearly quantitative yield, a product consisting mainly of *endo,endo*-**9**, m.p. 59–61°C (ether). – IR (KBr): ν = 2240 cm^{-1}.

$C_{10}H_{12}N_2$ (160.2)	Calcd.	C 74.97	H 7.55 N 17.48
	Found	C 75.20	H 7.44 N 17.07

Dimethyl cis-Bicyclo[3.3.0]octane-3,7-dicarboxylate (**11**): A mixture of dinitriles **9** (6.84 g, 42.7 mmol) and a 40% solution of KOH in methanol (50 ml) was heated under reflux for 3 h. Water (150 ml) was added, and the mixture was heated for 3 h more under reflux. The cold mixture was acidified with conc. HCl and evaporated to dryness at reduced pressure. The solid residue was extracted with hot ether (5 × 100 ml), and the combined extracts were dried with Na_2SO_4. Evaporation of the solvent gave a crude diacid (6.22 g) that was esterified as such with excess ethereal solution of diazomethane. Glacial acetic acid was added to destroy the excess of diazomethane. The volatile materials were eliminated at reduced pressure, and the residue was distilled in a rotary microdistillation apparatus to give **11** (6.5 g, 28.8 mmol, 67% from **9**) as a liquid mixture of the three possible stereoisomers, b.p. 140°C (oven)/0.5 Torr. – IR ($CHCl_3$): ν = 1725 cm^{-1}. – 200-MHz ^{1}H NMR ($CDCl_3$): δ = 1.2–2.3 (complex absorption, 8H), 2.4–3.0 (complex absorption, 4H), 3.66 (s), 3.67 (s), 3.68 (s) (total 6H).

$C_{12}H_{18}O_4$ (226.2)	Calcd.	C 63.70	H 8.02
	Found	C 63.45	H 8.34

Dimethyl cis-Bicyclo[3.3.0]octa-2,6-diene-3,7-dicarboxylate (**7**) *and Dimethyl cis-Bicyclo[3.3.0]octa-2,7-diene-3,7-dicarboxylate* (**8**): A mixture of dinitriles **3** and **4** (1.96 g, 12.6 mmol) and 96% H_2SO_4 (4 ml) was stirred for 2 days at room temperature. Water (100 ml) was added and then solid NaOH (6.31 g) until the solution became basic. The mixture was heated under reflux for 6 h and then filtered to eliminate a pinky precipitate (340 mg). The filtrate was evaporated to dryness, 96% H_2SO_4 (5 ml) and distilled methanol (80 ml) were added and the mixture heated under reflux for 6 h. The solution was concentrated at reduced pressure, diluted with water, and extracted thouroughly with CH_2Cl_2. The combined organic extracts were dried with Na_2SO_4, and the solvent eliminated at reduced pressure to give a crude mixture that contained partially esterified products (^{1}H NMR). This mixture was treated with distilled methanol (80 ml) and 96% H_2SO_4 (5 ml) as described before giving rise to 1.82 g of a mixture of diesters **7** and **8** that was purified by chromatography (silica gel/$CHCl_3$) and crystallization from hexane, obtaining a solid mixture, m.p. 75–86°C, of both diesters in the approximate ratio 1:1 (^{13}C NMR) (1.24 g, 5.6 mmol, 44%). – IR (KBr): ν = 1710 cm^{-1} (s), 1635 (m). – 200-MHz ^{1}H NMR ($CDCl_3$): δ = 2.34–2.60 (m), 2.75–3.04 (m), 3.04–3.30 (m), 3.726 (s), 3.732 (s), 3.96–4.10 (m), 6.57 (m), 6.67 (m).

$C_{12}H_{14}O_4$ (222.2)	Calcd.	C 64.85	H 6.35
	Found	C 64.81	H 6.44

11 *by Hydrogenation of a Mixture of Diesters* **7** *and* **8**: A mixture of **7** and **8** (0.50 g, 2.26 mmol), methanol (30 ml), and 5% Pd on charcoal (0.1 g) was smoothly hydrogenated in a Parr pressure reactor at 5 atm and room temperature in approximately 3 h. The mixture was filtered and the solvent eliminated from the filtrate at reduced pressure to give nearly quantitatively a mixture of diesters **11**, in which *endo,endo*-**11** was the major component.

Dimethyl Tricyclo[3.3.0.0^{3,7}]octane-1,5-dicarboxylate (**13**): Lithium diisopropylamide was prepared by treating a solution of diisopropylamine (4.38 ml, 31.3 mmol) in anhydrous tetrahydrofuran (30 ml) with an ethereal solution of methyllithium (30 ml, 1.042 N, 31.3 mmol) at –60°C under argon. A solution of the stereoisomeric mixture of diesters **11** (3.0 g, 13.04 mmol) in anhydrous tetrahydrofuran (12 ml) was added dropwise with magnetic stirring keeping the temperature at –78°C. Stirring was continued for 10 min at this temperature after completion of the addition and then a solution of iodine (3.31 g, 13.0 mmol) in anhydrous tetrahydrofuran (90 ml) was added dropwise. The stirred mixture was maintained 30 min at –78°C and then allowed to come to room temperature. The mixture was neutralized with a saturated aqueous solution of ammonium chloride and extracted with ether (3 × 250 ml). The combined organic extracts were washed with brine (20 ml) and dried with Na_2SO_4. Evaporation of the volatile materials at reduced pressure gave a crude product (4.18 g) that was chromatographed through silica gel. On elution with hexane/ethyl acetate (98:2) **13** of approximately 95% purity (^{13}C NMR) (1.22 g, 39% yield) was obtained. The analytical sample was prepared by semipreparative HPLC (hexane/ethyl acetate 7:1, 1.2 ml/min, t_r 24.6 min). An unidentified impurity showed t_r 22.2 min. The purified product solidified on standing, m.p. 59–61°C. – IR (KBr): ν = 3000 cm^{-1} (m), 2980 (m), 2950 (m), 2900 (m), 2830 (w), 1720 (s), 1685 (w), 1480 (m), 1440 (m), 1430 (m), 1320 (s), 1290 (m), 1270 (m), 1260 (m), 1200 (m), 1190 (m), 1180 (m), 1090 (s), 1060 (m), 990 (m), 950 (m), 850 (m), 810

(m), 755 (m). – 200-MHz ^{1}H NMR ($CDCl_3$): δ = 1.84 (broad s, 8H), 2.47 (broad s, 2H), 3.69 (s, 6H).

$C_{12}H_{16}O_4$ (224.2) Calcd. C 64.27 H 7.19
Found C 64.00 H 7.16

cis-1,5-Dimethylbicyclo[3.3.0]octa-2,6-diene-3,7-dicarbonitrile (**5**) *and cis-1,5-Dimethylbicyclo[3.3.0]octa-2,7-diene-3,7-dicarbonitrile* (**6**): A well-stirred mixture of potassium cyanide (39.0 g, 0.60 mmol), diketone **2** (14.0 g, 84 mmol), and water (63 ml) was cooled in an ice bath and 40% aqueous H_2SO_4 (118 ml) was added dropwise over a period of 4 h, keeping the temperature between 10 and 15°C. Water (100 ml) was added, and the mixture was extracted with ethyl acetate (6 × 75 ml). The combined extracts were washed with water, dried with Na_2SO_4, and the solvent was removed at reduced pressure to give a crude mixture of stereoisomeric bis-cyanohydrins (17.82 g) that was used without further purification in the next step. A magnetically stirred mixture of the above crude product and pyridine (275 ml) was heated at 140°C, $POCl_3$ (50 ml, 0.54 mol) added dropwise, and then heated under reflux for 8 h. The cold mixture was poured onto a mixture of conc. HCl (154 ml) and crushed ice (200 g). The precipitate was separated by filtration and washed with diluted HCl and water. This solid was dissolved in methylene chloride (250 ml), and the solution was washed with water and dried with Na_2SO_4. Evaporation of the solvent gave a crude product (11.51 g) that was crystallized from diethyl ether to give a mixture of dinitriles **5** and **6** in the approximate ratio 2.5:1 (^{13}C NMR), m.p. 111–121°C (9.76 g, 63% overall yield).

cis-1,5-Dimethylbicyclo[3.3.0]octane-3,7-dicarbonitrile (**10**): A mixture of dinitriles **5** and **6** (7.1 g, 38.6 mmol), 5% Pd on charcoal (0.71 g), and 96% ethanol (100 ml) was hydrogenated in a Parr pressure reactor at 4 atm and room temperature. The course of the reaction was followed through the disappearance of the ethylenic protons (^{1}H NMR). More catalyst (approximately 2 × 200 mg) was added to complete hydrogenation, that required 48 h. The mixture was filtered and the solvent removed from the filtrate at reduced pressure to give nearly quantitatively a mixture of the three possible stereoisomers of **10** in the approximate ratio *endo,endo*-**10**:*endo,exo*-**10**:*exo,exo*-**10** = 1:1:2, m.p. 67–79°C (ether/hexane). – IR (KBr): ν = 2210 cm^{-1}. – 200-MHz ^{1}H NMR ($CDCl_3$): δ = 0.95 (s, CH_3), 1.04 (s, CH_3), 1.18 (s, CH_3), 1.18–2.10 (m, CH_2), 2.6–3.0 (m, CH). For the major stereoisomer, *exo,exo*-**10**: 1.18 (s, CH_3), 1.88 (dd, J = 13.7, J' = 9.3 Hz), and 2.04 (dd, J = 13.7, J' = 7.6 Hz, CH_2), 2.72 (tt, J = 7.6, J' = 9.3 Hz, CH). – 50-MHz ^{13}C NMR ($CDCl_3$): δ = 22.2 (q), 23.5 (q), 24.2 (q), 24.4 (d), 25.2 (d), 25.3 (d), 25.6 (d), 44.3 (t), 45.2 (t), 45.6 (t), 45.8 (t), 50.9 (s), 51.3 (s), 52.5 (s), 122.0 (s).

$C_{12}H_{16}N_2$ (188.3) Calcd. C 76.56 H 8.57 N 14.88
Found C 76.80 H 8.84 N 14.88

Dimethyl cis-1,5-Dimethylbicyclo[3.3.0]octane-3,7-dicarboxylate (**12**): A mixture of stereoisomeric dinitriles **10** (3.19 g, 19.45 mmol) and a 40% solution of KOH in methanol (23 ml) was heated under reflux for 3 h. Water (30 ml) was added and the mixture heated for 3 h more under reflux. The cold mixture was acidified with conc. HCl and evaporated to dryness at reduced pressure. The solid residue was extracted with hot ether (5 × 50 ml), and the combined extracts were dried with Na_2SO_4. Evaporation of the solvent gave a crude diacid (3.50 g) that was esterified as such with excess ethereal solution of diazomethane. The volatile materials were eliminated at reduced pressure, and the residue was distilled in a rotary microdistillation apparatus to give diester **12** as a solid mixture of the three possible stereoisomers, b.p. 150°C (oven)/0.5 Torr, m.p. 58–74°C (3.22 g, 14.2 mmol, 73% yield of distilled product from dinitriles **10**). – IR ($CHCl_3$): ν = 1720 cm^{-1}. – 200-MHz ^{1}H NMR ($CDCl_3$): δ = 0.94 (s), 1.00 (s), 1.04 (s) (total 6H), 1.6–2.2 (m, 8H), 2.7–3.1 (m, 2H), 3.664 (s), 3.671 (s) (total 6H). – On crystallization from hexane, a mixture of *endo,endo*-**12** and *endo,exo*-**12** in the approximate ratio 2:3 was obtained, m.p. 72–83°C.

$C_{14}H_{22}O_4$ (254.3) Calcd. C 66.12 H 8.72
Found C 66.03 H 8.98

Dimethyl 3,7-Dimethyltricyclo[3.3.0.0^{3,7}]octane-1,5-dicarboxylate (**14**): Lithium diisopropylamide was prepared by treating a solution of anhydrous diisopropylamine (0.84 ml, 60 mmol) in 5 ml of anhydrous tetrahydrofuran with an ethereal solution of methyllithium (8.8 ml, 0.683 N, 6.0 mmol) at –60°C under argon. A solution of the mixture of diesters **12** (635 mg, 2.5 mmol) in anhydrous tetrahydrofuran (2 ml) was added dropwise with magnetic stirring keeping the temperature at –78°C. Stirring was continued for 10 min at this temperature after completion of the addition, and then a solution of iodine (0.635 g, 2.5 mmol) in anhydrous tetrahydrofuran (15 ml) was added dropwise. The stirred mixture was maintained 30 min at –78°C and then allowed to come to room temperature. The mixture was neutralized with a saturated aqueous solution of ammonium chloride and extracted with ether (3 × 50 ml). The combined organic extracts were washed with brine (10 ml) and dried with Na_2SO_4. Evaporation of the volatile materials at reduced pressure gave 781 mg of a crude product that was distilled in a rotary microdistillation apparatus to give diester **14** (240 mg, 0.95 mmol, 38% yield), b.p. 150°C (oven)/0.5 Torr, m.p. 95–97°C (hexane). – IR ($CHCl_3$): ν = 1730 cm^{-1}. – 200-MHz ^{1}H NMR ($CDCl_3$): δ = 1.18 (s, 6H), 1.70 (d, J = 7.2 Hz, 4H), 1.92 (d, J = 7.2 Hz, 4H), 3.67 (s, 6H).

$C_{14}H_{20}O_4$ (252.3) Calcd. C 66.65 H 7.99
Found C 66.80 H 8.38

Dimethyl cis-3,7-Dihydroxybicyclo[3.3.0]octane-1,5-dicarboxylate (**16**): To a magnetically stirred solution of diketo diester **15** (1.0 g, 3.97 mmol) in anhydrous methanol (15 ml) $NaBH_4$ (1.5 g, 39.4 mmol) was added in small portions and the mixture stirred at room temperature for 16 h. Aqueous acetic acid (25 ml, 50%) was added, and stirring was continued for 24 h more. The mixture was extracted with CH_2Cl_2 (20 × 10 ml), and the combined extracts were dried with Na_2SO_4. Evaporation of the solvent at reduced pressure gave dihydroxy diester **16** (950 mg, 93% yield) as a solid mixture of the three possible stereoisomers in which one of them predominated (GLC), b.p. 165–180°C (oven)/0.3 Torr. – IR (KBr): ν = 3700–3100 cm^{-1} (m), 1730 (s). – 80-MHz ^{1}H NMR ($CDCl_3$): δ = 1.40–2.95 (complex absorption, 10H), 3.62 (s), 3.66 (s), and 3.70 (s) (total 6H), 4.07–4.71 (complex absorption, 2H). For the major stereoisomer the absorptions at δ 1.63, 1.69, 1.80, 1.87, 2.52, 2.60, 2.69, and 2.77 constitute the AB part of an ABX system with J_{AB} = 13.9, J_{AX} = 5.1, and J_{BX} = 6.2 Hz. – MS (Chemical ionization/isobutane): m/z = 259 ($M + H^+$), 227 (M – $MeOH + H^+$). – MS (electron impact): m/z (%) = 240 (12), 227 (17), 226 (58), 208 (100), 179 (53), 149 (41), 97 (70), 93 (63), 91 (79), 79 (36), 77 (38), 59 (56).

$C_{12}H_{18}O_6$ (258.3) Calcd. C 55.81 H 7.02
Found C 55.94 H 7.08

Dimethyl cis-3,7-Bis(methylsulfonyloxy)bicyclo[3.3.0]octane-1,5-dicarboxylate (**17**): Methanesulfonyl chloride (0.75 ml, 9.6 mmol) was added through a syringe to a cold (–78°C) solution of dihydroxy diester **16** (1.032 g, 4.0 mmol) in CH_2Cl_2 (20 ml) and pyridine (4 ml). After standing at room temperature for 72 h, the mixture was poured onto cold aqueous 2 N HCl (40 ml). The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (6 × 15 ml + 4 × 10 ml). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ and water and dried with Na_2SO_4. Evaporation of the solvent gave the bis-mesylate **17** as a

mixture of stereoisomers (1.616 g, 97% yield). Crystallization of this crude mixture from CH_2Cl_2 yielded the major stereoisomer (343 mg) of m.p. 148–151°C. – IR ($CHCl_3$): ν = 1745 cm^{-1} (s), 1370 (s), 1350 (s), 1215 (s), 1180 (s), 970 (s). – 80-MHz ^1H NMR ($CDCl_3$): δ = 2.14, 2.24, 2.31, and 2.41 (dd, J = 13.8, J' = 7.6 Hz, 4H), 2.52, 2.63, 2.69, and 2.80 (dd, J = 13.8, J' = 8.4 Hz, 4H), 3.03 (s, 6H), 3.70 (s, 6H), 5.04 (m, 2H). – MS (chemical ionization/isobutane): m/z = 415 ($M + H^+$), 319 ($M - MsOH + H^+$). – MS (electron impact): m/z (%) = 383 (25), 286 (11), 275 (15), 190 (16), 163 (59), 162 (85), 105 (64), 91 (37), 79 (100), 59 (28).

$C_{14}H_{22}O_{10}S_2$ (414.5) Calcd. C 40.57 H 5.35 S 15.47
Found C 40.53 H 5.49 S

Dimethyl cis-Bicyclo[3.3.0]octa-2,6-diene-1,5-dicarboxylate (**21**) *and Dimethyl cis-Bicyclo[3.3.0]octa-2,7-diene-1,5-dicarboxylate* (**22**): A mixture of stereoisomeric bis-mesylates **17** (0.828 g, 2.0 mmol), anhydrous toluene (30 ml), and 1,8-diazabicyclo[5.4.0]-undec-7-ene (1.52 g, 10 mmol) was heated at 160°C for 17 h in a glass pressure reactor. The cold mixture was acidified with aqueous 1 N HCl, the organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (3 × 15 ml). The combined organic phases were washed with water and dried with Na_2SO_4. Evaporation of the solvent gave a crude product (518 mg) that was chromatographed through silica gel (25 g, 230–400 mesh) with mixtures of hexane/CH_2Cl_2 as eluent. The different fractions were analyzed by GLC and combined into three groups: a) 117 mg of **21** + **22** (95:5 relative area by GLC), b) 84 mg of **21** + **22** (80:20 relative area by GLC), and c) 50 mg of **21** + **22** (9:91 relative area by GLC). Total yield 56% (41% of diester **21** and 15% of diester **22**, assuming the chromatographic areas to be proportional to the molar concentration). Crystallization of the fraction a) from methanol gave a pure sample of **21**, m.p. 88–91°C. After a new chromatography and crystallizing from methanol, **22** could be obtained in pure form, b.p. 92°C (oven)/1 Torr, m.p. 34–37°C.

21: GLC (column: DEGS/2 m; oven temperature 180°C; flow 20 ml N_2/min), t_r 5.2 min. – IR ($CHCl_3$): ν = 3050 cm^{-1} (m), 1735 (s), 1255 (s). – MS (chemical ionization/isobutane): m/z = 223 ($M + H^+$), 191 ($M - MeOH + H^+$). – MS (electron impact): m/z (%) = 222 (0.5), 191 (10), 190 (25), 163 (28), 162 (100), 131 (10), 103 (70), 91 (10), 77 (19), 59 (12).

$C_{12}H_{14}O_4$ (222.2) Calcd. C 64.85 H 6.35
Found C 64.96 H 6.35

22: GLC (column DEGS/2 m; oven temperature 180°C; flow 20 ml N_2/min), t_r 6.1 min. – IR ($CHCl_3$): ν = 3040 cm^{-1} (w), 1735 (s), 1255 (m), 1200 (m). – MS (chemical ionization/isobutane): m/z = 223 ($M + H^+$), 191 ($M - MeOH + H^+$). – MS (electron impact): m/z (%) = 222 (M^+, 0.9), 191 (5), 190 (27), 163 (37), 162 (95), 131 (9), 103 (100), 102 (28), 91 (12), 77 (16), 59 (14).

$C_{12}H_{14}O_4$ (222.2) Calcd. C 64.85 H 6.35
Found C 64.96 H 6.29

Dimethyl cis-3,7-Bis(p-tolylsulfonylhydrazono)bicyclo-[3.3.0]octane-1,5-dicarboxylate (**20**): A mixture of diketo diester **15** (15.0 g, 59.1 mmol) in glacial acetic acid (100 ml) and tosylhydrazine (45.0 g, 241.9 mmol) in glacial acetic acid (360 ml) was stirred at room temperature for 16 h. The white precipitate was filtered, washed with acetic acid, and dried in vacuo over KOH pellets. Yield of **20** 33.7 g (97%), m.p. 218–219°C. – IR (KBr): ν = 3240 cm^{-1} (m), 1735 (s), 1410 (m), 1340 (m), 1165 (s), 1095 (m), 1025 (m). – 80-MHz ^1H NMR ($CDCl_3$): δ = 2.23 and 2.46 (dm, J = 18.4 Hz, 2H), 2.43 (s, 6H), 2.38 and 2.61 (dm, J = 18.4 Hz, 2H), 2.90 and 3.13 (dm, J = 18.4 Hz, 2H), 3.01 and 3.24 (dm, J = 18.4 Hz, 2H), 3.62 (s, 6H), 7.06 (s, 2H), 7.25 and 7.35 (d, J = 7.6 Hz, 4H), 7.75 and 7.84 (d, J = 7.6 Hz, 4H). – MS (chemical ionization/isobutane): m/z = 407 ($M - TsNHN + H^+$), 157 ($TsH + H^+$). – MS (electron impact): m/z (%) = 347 (3), 251 (10), 219 (8), 191 (27), 163 (41), 139 (30), 131 (19), 103 (43), 91 (100), 65 (84), 59 (60).

$C_{26}H_{30}N_4O_8S_2$ (590.7) Calcd. C 52.87 H 5.12 N 9.48
Found C 52.51 H 5.05 N 9.61

Pyrolysis of the Sodium Salt of Bis-Tosylhydrazone **20** *with Formation of Diesters* **21** *and* **22** *and Methyl p-Tolyl Sulfone* (**24**): A mixture of **20** (2.0 g, 3.4 mmol), anhydrous sodium methoxide (550 mg, 10.2 mmol), and anhydrous methanol (70 ml) was heated under reflux for 2 h. The solvent was removed under reduced pressure and the residue dried in vacuo at room temperature for 19 h. The flask containing the sodium salt of **20** was connected to a rotary microdistillation apparatus and heated at 135°C/0.5 Torr. A product (468 mg) consisting mainly of a mixture of diesters **21** and **22** distilled in a few minutes. Column chromatography through silica gel (30 g, 230–400 mesh) with mixtures of hexane/CH_2Cl_2 as eluent gave different fractions that were combined according to their composition (GLC) into three groups: a) 117 mg of a mixture of **21** and **22** (84:16 relative area by GLC), b) 144 mg of a mixture of **21** and **22** (55:45 relative area by GLC), c) 197 mg of a mixture of **21** and **22** and sulfone **24** (19:64:17 relative area by GLC). Approximate yield of **21** and **22** 46% (26% **21** and 20% **22**, assuming the chromatographic areas to be proportional to the molar concentration). Repeated chromatography and crystallization gave pure samples of all of the three compounds.

24[10]: GLC (column: DEGS/2 m; oven temperature 180°C; flow 20 ml N_2/min), t_r 30.0 min. – IR ($CHCl_3$): ν = 3040 cm^{-1} (m), 1315 (s), 1300 (s), 1290 (m), 1200 (m), 1150 (s), 1090 (m), 955 (m). – 80-MHz ^1H NMR ($CDCl_3$): δ = 2.45 (s, 3H), 3.03 (s, 3H), 7.36 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H). – 20-MHz ^{13}C NMR ($CDCl_3$): δ = 21.4, 44.4, 127.2, 129.8, 137.9, 144.5 – MS (electron impact): m/z (%) = 170 (M^+, 95), 155 (76), 139 (5), 107 (61), 91 (100), 77 (20), 65 (40), 39 (15).

3-Oxa[3.3.3]propella-6,9-diene-2,4-dione (**18**) *and 3-Oxa-[3.3.3]propella-6,10-diene-2,4-dione* (**19**): A mixture of stereoisomeric dihydroxy diesters **16** (100 mg, 0.39 mmol), 85% phosphoric acid (0.5 ml), and P_2O_5 (0.5 g) was placed in a 10-ml flask that was connected to a rotary microdistillation apparatus and heated at 140°C/15 Torr to give a product that was sublimed at 90°C/0.7 Torr giving rise to a mixture of anhydrides **18** and **19** in the ratio 70:30 (relative areas by GLC) (0.55 g, 82% total yield).

$C_{10}H_8O_3$ (176.2) Calcd. C 68.18 H 4.58
Found C 67.88 H 4.68

Conversion of the Mixture of Anhydrides **18** *and* **19** *into the Mixture of Diesters* **21** *and* **22**: A mixture of **18** and **19** (200 mg, 1.13 mmol), NaOH (136 mg, 3.39 mmol), and water (2 ml) was heated under reflux for 4 h. The cold solution was acidified with aqueous 6 N HCl and extracted with ether (20 × 10 ml). The organic extracts were dried with Na_2SO_4, and the solvent was removed under reduced pressure to give a crude mixture of the corresponding diacids (215 mg) that was treated with excess of an ethereal solution of diazomethane. The solution was dried with Na_2SO_4 and the solvent removed under reduced pressure giving rise to a mixture of diesters **21** and **22** (240 mg, 96% yield).

18: A mixture of diester **21** (98% pure by GLC, 400 mg, 1.80 mmol) and aqueous 2 N KOH (8 ml) was heated under reflux for 18 h. The cold solution was acidified with aqueous 6 N HCl and extracted with ether (3 × 40 ml). The combined organic extracts were dried with Na_2SO_4, and the solvent was removed under reduced pressure to give the crude diacid (350 mg). This product was

heated under reflux for 1 h with acetic anhydride (4 ml). The volatile materials were removed at 3 Torr, and the residue was dried at room temperature/3 Torr for 2 h over P_2O_5. The crude product was sublimed at 130°C/0.5–1 Torr to give anhydride **18** (229 mg, 72% yield), m.p. 122–123°C (hexane). GLC (column: DEGS/2 m; oven temperature 180°C; flow 20 ml N_2/min) t_r 6.7 min. – IR (KBr): ν = 3060 cm^{-1} (w), 1820 (m), 1775 (s). – MS (chemical ionization/isobutane): *m/z* = 177 ($M + H^+$). – MS (electron impact): *m/z* (%) = 104 (85), 78 (39), 63 (54), 51 (42), 50 (48), 39 (100).

$C_{10}H_8O_3$ (176.2) Calcd. C 68.18 H 4.58
Found C 67.86 H 4.65

19: A mixture of diester **22** (99% pure by GLC, 100 mg, 0.45 mmol) and aqueous 2 N KOH (2 ml) was heated under reflux for 18 h. The cold solution was acidified with aqueous 6 N HCl and extracted with ether (3 × 20 ml). The combined organic extracts were dried with Na_2SO_4, and the solvent was removed under reduced pressure. The crude material was heated under reflux for 1 h with acetic anhydride (1 ml). The volatile materials were removed at 1 Torr, and the residue was dried at 50°C/1 Torr for 2 h over P_2O_5. The crude product was sublimed at 110°C/1 Torr giving rise to anhydride **19** (35.5 mg, 45% yield), m.p. 139–141°C (hexane). GLC (column: DEGS/2 m; oven temperature 180°C; flow 20 ml N_2/min): t_r 7.8 min. – IR (KBr): ν = 3040 cm^{-1} (w), 1820 (m), 1780 (s). – MS (chemical ionization/isobutane): *m/z* = 177 ($M + H^+$). – MS (electron impact): *m/z* (%) = 104 (90), 89 (11), 78 (23), 63 (38), 51 (42), 50 (57), 39 (100).

$C_{10}H_8O_3$ (176.2) Calcd. C 68.18 H 4.58
Found C 68.58 H 4.59

Dimethyl Tetracyclo[3.3.0.0^{2,4}.0^{3,7}]octane-3,7-dicarboxylate (**23**)

a) *Irradiation of a Mixture of Diesters* **21** *and* **22**: A solution of a mixture of **21** and **22** (18:82 relative area by GLC, 25 mg) in anhydrous ether (5 ml) was placed in a quartz tube, deoxygenated by bubbling argon, and the tube was stoppered with a septum. The solution was irradiated with a 400-W mercury lamp using a quartz refrigeration jacket, and the course of the reaction was followed by GLC and GLC/MS. After 130 h irradiation, **22** had been consumed, most of **21** remained unchanged, and two new products of the same molecular mass as **21** and **22** had been formed. GLC (column: DEGS/2 m; oven temperature 180°C; flow 20 ml N_2/min): t_r 8.3 and 9.6 min.

b) *Irradiation of Diester* **21**: The same procedure described before was followed, starting from **21** (7 mg) in anhydrous ether (3 ml). After 70 h irradiation only the starting compound was observed by GLC.

c) *Irradiation of Diester* **22**: The same procedure described before was followed, starting from **22** (25 mg) in anhydrous ether (5 ml). After 120 h irradiation, the formation of the new compounds of t_r 8.3 and 9.6 min (by GLC) was observed, although the major component was the starting compound.

Isolation of Diester **23**: A solution of a mixture of **21** and **22** (75:25 relative area by GLC, 1.5 g) in anhydrous ether (650 ml) was deoxygenated by bubbling argon for 1 h and irradiated with a 400-W mercury lamp provided with a quartz refrigeration jacket. When the relative area of **22** remained unchanged (288 h), the irradiation was stopped. Evaporation of the solvent gave a crude product containing polymeric material (3.29 g). After several column chromatographies through silica gel with mixtures of hexane/CH_2Cl_2 as eluent a fraction (less than 1 mg, distilled at 50–70°C (oven)/15 Torr) was isolated whose GLC analysis showed it to be mainly (90% relative area by GLC) the product of t_r 9.6 min. – 80-MHz ^{1}H NMR (C_6D_6): δ = 1.06 (dm, *J* = 10 Hz, 2H), 1.90–2.10 (complex absorption), 1.96 (d, *J* = 10 Hz, total 4H), 2.57 (t, *J* = 2 Hz, 2H), 3.18 (s, 3H), 3.57 (s, 3H). – 80-MHz ^{1}H NMR ($CDCl_3$): δ = 1.39 (dm, *J* = 10 Hz, 2H), 2.08 (dm, *J* = 10 Hz, 2H), 2.68 (m, 2H), 2.82 (t, *J* = 2 Hz, 2H), 3.57 (s, 3H), 3.80 (s, 3H). – MS (chemical ionization/isobutane): *m/z* = 223 ($M + H^+$), 191 ($M - MeOH + H^+$). – MS (electron impact): *m/z* (%) = 191 (14), 163 (29), 162 (83), 131 (23), 103 (100), 91 (17), 77 (33), 59 (16).

Attempt to Photocyclize Anhydride **19**: A solution of a mixture of **18** and **19** (70:30 relative area by GLC, 27 mg) in anhydrous ether (10 ml) was irradiated as described before. After 80 h irradiation most of the starting compounds remained unchanged, and no other products of the same molecular mass as the starting compounds were detected by GLC/MS analysis.

CAS Registry Numbers

1: 51716-63-3 / **1** (bis-cyanohydrin): 111717-99-8 / **2**: 21170-10-5 / **2** (bis-cyanohydrin): 111718-07-1 / **3**: 111718-00-4 / **4**: 111718-01-5 / **5**: 85433-62-1 / **6**: 85433-63-2 / **7**: 111718-04-8 / **7** (free diacid): 111718-25-3 / **8**: 111718-05-9 / **8** (free diacid): 111718-26-4 / **9** (*endo,endo* isomer): 111742-46-2 / **10** (*endo,endo* isomer): 103260-00-0 / **10** (*endo,exo* isomer): 103260-01-1 / **10** (*exo,exo* isomer): 103260-02-2 / **11** (*endo,endo* isomer): 111742-29-1 / **11** (*endo,endo* isomer-free diacid): 111718-30-0 / **11** (*exo,exo* isomer): 111718-02-6 / **11** (*exo,exo* isomer-free diacid): 111718-28-6 / **11** (*endo,exo* isomer): 111718-03-7 / **11** (*endo,exo* isomer-free diacid): 111718-29-7 / **12** (*endo,endo* isomer): 111718-08-2 / **12** (*endo,endo* isomer-free diacid): 103260-03-3 / **12** (*endo,exo* isomer): 111718-09-3 / **12** (*endo,exo* isomer-free diacid): 103260-04-4 / **12** (*exo,exo* isomer-free diacid): 103260-05-5 / **13**: 111718-06-0 / **14**: 111718-10-6 / **15**: 91758-62-2 / **16** (*endo,endo* isomer): 111718-11-7 / **16** (*exo,exo* isomer): 111718-12-8 / **16** (*endo,exo* isomer): 111718-13-9 / **17** (*endo,endo* isomer): 111718-14-0 / **17** (*exo,exo* isomer): 111718-15-1 / **17** (*endo,exo* isomer): 111718-16-2 / **18**: 111718-20-8 / **18** (free diacid): 111718-22-0 / **19**: 111718-21-9 / **19** (free diacid): 111718-23-1 / **20**: 111718-27-5 / **20** (sodium salt): 111718-19-5 / **21**: 111718-17-3 / **22**: 111718-18-4 / **23**: 111718-24-2 / **24**: 3185-99-7

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