anti-Tricyclo[3.1.0.0^{2,4}]hexanes. Synthesis and Reactions

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A facile synthesis of dimethyl *anti*-tricyclo[3.1.0.0^{2,4}]hexane-1,2-dicarboxylate (**4**) involving two intramolecular nucleophilic displacements is described. Thermolysis of **4** gives dimethyl cyclohexa-1,4-diene-1,2-dicarboxylate (**7**). Silver ion catalyzed reaction of 1,2-bis(acetoxymethyl)-*anti*-tricyclo[3.1.0.0^{2,4}]hexane (**8**) also results in ring opening, giving 1,2-bis(acetoxymethyl)cyclohexa-1,4-diene (**10**) and 2-acetoxymethyltoluene (**11**). Catalytic hydrogenation of **4** proceeds stereospecifically from an endo face, giving a product shown to be dimethyl bicyclo[3.1.0]hexane-1,*endo*-2-dicarboxylate (**17**). The addition of hydrogen bromide to **4** yields a pair of products shown to be the epimeric bicyclo[3.1.0]hexanes **20** and **21**, in accord with expectations for stereospecific attack of bromide ion on protonated **4**.

Although *anti*-tricyclo[3.1.0.0^{2,4}]hexane (**1**) and a few of its derivatives have been described, little chem-

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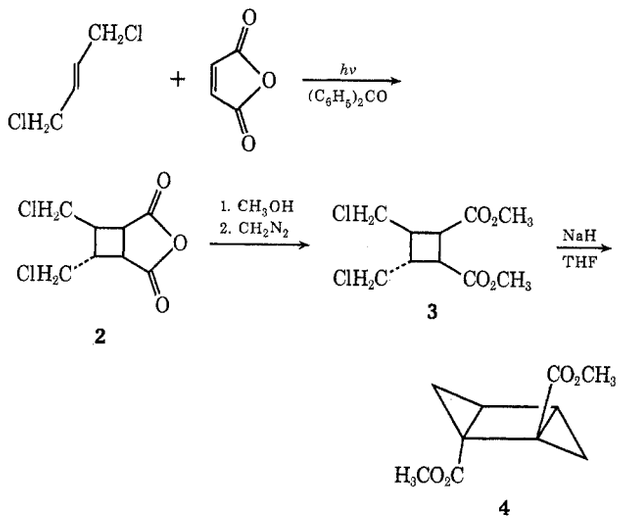
istry of this interesting strained ring system has been studied; only hydrogenation and thermolysis of the parent hydrocarbon[2] and thermolysis of various derivatives[3-5] have been reported. We would like to report a new, convenient synthesis of this ring system and to describe some of its thermal, catalytic, and ionic reactions.

Synthesis.—Previous syntheses of substituted *anti*-tricyclo[3.1.0.0^{2,4}]hexanes have relied on photochemical[4-7] or metal-catalyzed[3] dimerizations of cyclopropenes. The method which we have used provides much easier access to these compounds, as outlined in Scheme I. The benzophenone-sensitized photo-

SCHEME I



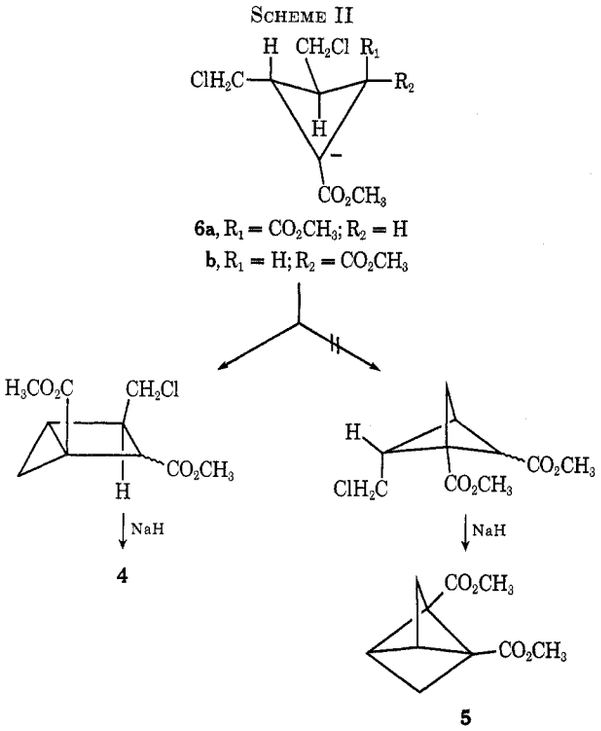
addition of maleic anhydride to *trans*-1,4-dichloro-2-butene afforded anhydride **2** in 76% yield (ν_{CO}^{KBr} 1865, 1800 cm^{-1}). The reaction of **2** first with methanol and then with diazomethane furnished the bis methyl ester **3** in 91% yield (ν_{CO}^{neat} 1740 cm^{-1}). The nmr spectrum of **3** confirmed the trans arrangement of the chloromethyl substituents. (Methoxyl resonances appeared at δ 3.65 and 3.70.) Refluxing a solution of **3** in tetrahydrofuran with an excess of sodium hydride produced dimethyl *anti*-tricyclo[3.1.0.0^{2,4}]hexane-1.2-dicarboxylate (**4**) in 59% yield.

The structure of **4** was established on the basis of its spectral and chemical properties. Its mass spectrum showed a molecular ion at *m/e* 196 ($C_{10}H_{12}O_4$). The pmr spectrum showed no olefinic absorption; a single methoxyl absorption (6 H) appeared at δ 3.67; and three separated multiplets (2 H each) were found at δ 1.72, 1.95, and 2.20. While a detailed assignment of these absorptions was not attempted, they are clearly compatible with the structure proposed. The cmr spectrum of **4** (parts per million downfield from external TMS) showed, besides absorptions at 71.73 and 52.96 for the carbonyl and methyl carbons, three absorptions at 29.41, 31.09, and 32.66 assigned, respectively, to the quaternary, tertiary, and secondary carbon atoms on the basis of the ^{13}C–H coupling patterns. The fact that the bridgehead carbon atoms absorb at higher field than the bridge carbon atoms may be ascribed to these nuclei lying in the shielding region of the adjacent cyclopropane ring. The values obtained for the ^{13}C–H coupling constants ($J_{^{13}C-H}$ = 188 Hz, $J_{^{13}C-H_2}$ = 166 Hz) are in the range expected for a strained molecule of this type and are indicative of the high degree of *s* character associated with the bonds in this system.[8]

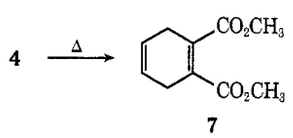
It is of interest that the dehydrohalogenation of **3** gives **4**, the result of two 1,3-intramolecular displacements, rather than **5**, the product which would have resulted from two 1,4 displacements. This preference may be rationalized on the basis of the relative activation energies expected for the initial displacements in carbanions **6a** and **6b**. These displacements can yield either a bicyclo[2.1.0]pentane, which should cyclize readily to **4**, or a bicyclo[1.1.1]pentane, which could cyclize to **5** (Scheme II). Insofar as the activation energies of these two displacements reflect the strain energies of the bicyclic products, we would expect to obtain the observed product **4**, since it has been calculated that bicyclo[1.1.1]pentane is more highly strained than bicyclo[2.1.0]pentane.[9]

(1) National Institutes of Health Postdoctoral Fellow, 1972.
(2) E. L. Allred and J. C. Hinshaw, *J. Amer. Chem. Soc.*, **90**, 6885 (1968).
(3) F. J. Weigert, R. L. Baird, and J. R. Shaply, *J. Amer. Chem. Soc.*, **92**, 6630 (1970).
(4) H. H. Stechl, *Chem. Ber.*, **97**, 2681 (1964).
(5) C. Deboer and R. Breslow, *Tetrahedron Lett.*, 1033 (1967).
(6) N. Obata and I. Moritani, *Bull. Chem. Soc. Jap.*, **39**, 2250 (1966).
(7) J. Trotter, C. S. Gibbons, N. Nakatsuka, and S. Masamune, *J. Amer. Chem. Soc.*, **89**, 2792 (1967).
(8) K. B. Wiberg, *Advan. Alicyclic Chem.*, **3**, 193 (1968).
(9) N. C. Baird, *Tetrahedron*, **26**, 2185 (1970).

SCHEME II

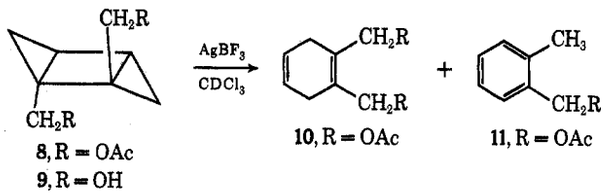


Thermolysis.—A sample of **4** maintained at 190° in an evacuated glass tube for 1.5 hr was quantitatively converted to dimethyl cyclohexa-1,4-diene-1,2-dicarboxylate (**7**), identified by comparison with an authentic



sample.[10] Although this isomerization is formally a $-[2_a + 2_a]$ cycloaddition, which, on the basis of orbital symmetry concepts, is not allowed,[11] whether this reaction is concerted or proceeds through a discrete diradical intermediate is, as yet, unanswered.[12]

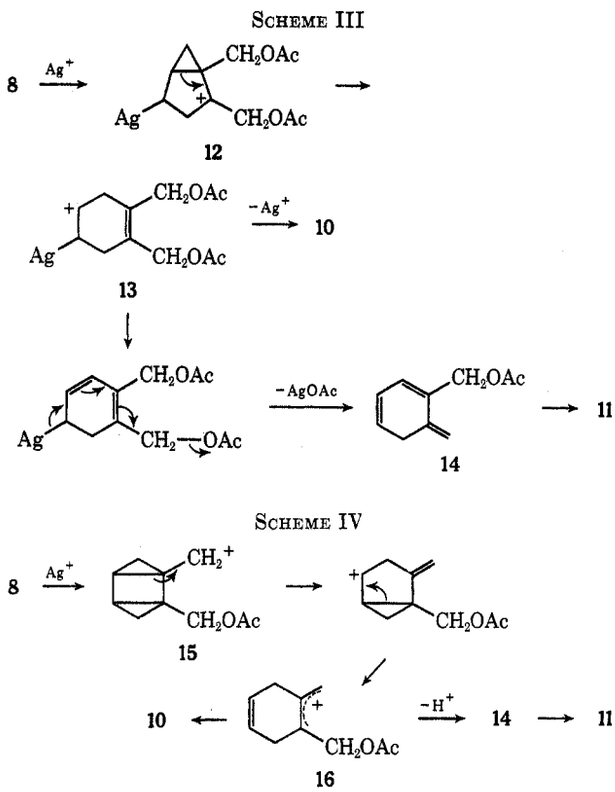
Silver-Catalyzed Rearrangement.—In view of the current interest shown in silver-catalyzed rearrangements of strained hydrocarbons,[13] we have examined the silver-catalyzed rearrangement of **4**. When a sample of **4** was refluxed in chloroform in the presence of silver fluoroborate, it was recovered unchanged. We noted that Eaton, *et al.*,[14] in their study of the silver-catalyzed rearrangement of the cubyl system, observed a rate-retarding effect by carbomethoxy groups. Consequently, we prepared the diacetate **8** (by reduction of **4** with lithium aluminum hydride to give diol **9**, followed by acetylation) with the expectation that the absence of the electron-withdrawing substituents would make reaction more likely. When a sample of **8** in chloroform-*d* containing a catalytic quantity of silver fluoroborate was heated to boiling for 1 min and allowed to stand at room temperature for 1 hr, the nmr spectrum of the resulting solution indicated a complete conversion of **8** to **10** (84%) and **11** (16%).[15]



The structure of **10** was proven by independent synthesis (see Experimental Section); the minor product (**11**) was identical with the compound obtained upon acetylation of 2-hydroxymethyltoluene.[16]

With the experimental data obtained thus far, either of two mechanisms for the formation of **10** and **11** appear plausible; these are shown in Schemes III and IV.

SCHEME III



SCHEME IV

In Scheme III, silver ion adds across one of the strained σ bonds of **8** to produce the carbonium ion **12**, subsequent rearrangement of which (to **13**), followed by loss of silver ion, would give **10**. Loss of a proton from **13**, followed by loss of silver acetate as shown, would produce **14**. Tautomerization of **14** to give **11** would follow.

Scheme IV involves a silver ion assisted ionization of **8**[17] to give carbonium ion **15**, subsequent rearrangement of which would yield the allylic carbonium ion **16**. Recapture of acetate would yield **10**, while loss

(10) O. Diels and K. Alder, *Justus Liebigs Ann. Chem.*, **490**, 236 (1931).

(11) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N. Y., 1969, p 70.

(12) On the basis of a measurement of the activation energy for the thermal rearrangement of the parent hydrocarbon, it has recently been suggested that this reaction might be concerted: J. E. Baldwin and J. Ollerenshaw, *Tetrahedron Lett.*, 3757 (1972).

(13) For a leading reference, see R. J. Roth and T. J. Katz, *J. Amer. Chem. Soc.*, **94**, 4770 (1972).

(14) L. Cassar, P. E. Eaton, and J. Halpern, *J. Amer. Chem. Soc.*, **92**, 6366 (1970).

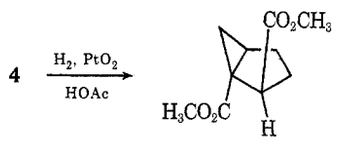
(15) That **11** is a primary product, and not simply the result of acetic acid elimination from **10**, was demonstrated by the observation that **10** was unchanged when subjected to the reaction conditions for a 24-hr period.

(16) G. H. Daub and R. N. Castle, *J. Org. Chem.*, **19**, 1571 (1954).

(17) Silver ion assisted ionization of some strained methyl ethers has recently been observed: L. A. Paquette and G. Zon, *J. Amer. Chem. Soc.*, **94**, 5096 (1972).

of a proton would give **14**. Tautomerization of **14** again completes the sequence.[18]

Hydrogenation.—Hydrogenation of the parent hydrocarbon **1** with platinum oxide in acetic acid at atmospheric pressure is reported[2] to yield cyclohexane and methylcyclopentane. In contrast to these results, hydrogenation of **4** under identical conditions proceeded with cleavage of a single bridging bond, giving dimethyl bicyclo[3.1.0]hexane-1,*endo*-2-dicarboxylate (**17**) stereospecifically within the limits of nmr detection.



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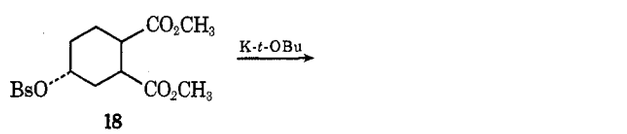
To assign the stereochemistry of **17**, we prepared brosylate **18** from the corresponding alcohol of known configuration,[19] with the expectation that a base-induced intramolecular displacement of the brosylate group would give dimethyl bicyclo[3.1.0]hexane-1,*exo*-2-dicarboxylate (**19**) as the major isomer, provided that conditions could be found which would minimize subsequent epimerization of **19**. This could be accomplished by the addition of potassium *tert*-butoxide to a solution of **18** in *tert*-butyl alcohol at room temperature, giving **19** and **17** in a 3:2 ratio.[20] That this ratio of products is not simply the equilibrium ratio was demonstrated by equilibration studies using sodium methoxide in methanol; an equilibrium mixture consisting of 78% **17** and 22% **19** was obtained. The above results indicate that the reaction of **18** with



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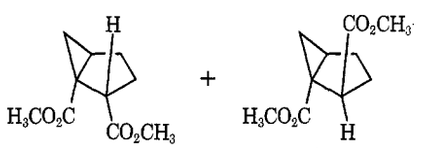
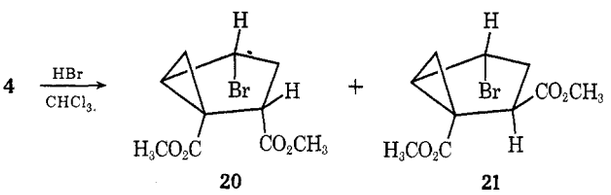


19 **17**

base gave **19** as the initial product. It follows that **19** has the exo configuration and that **17** is the corresponding endo epimer. These assignments were substantiated by the nmr spectra of **17** and **19**. While **17** showed a multiplet in the region of δ 3.33–3.60 for the proton α to the carboxylate group, **19** showed the corresponding absorption at 2.95–3.17. It is well established that, for 2-substituted bicyclo[3.1.0]hexanes, the proton α to the substituent absorbs at higher field when the substituent is exo, owing to the shielding properties of the cyclopropyl ring.[21]

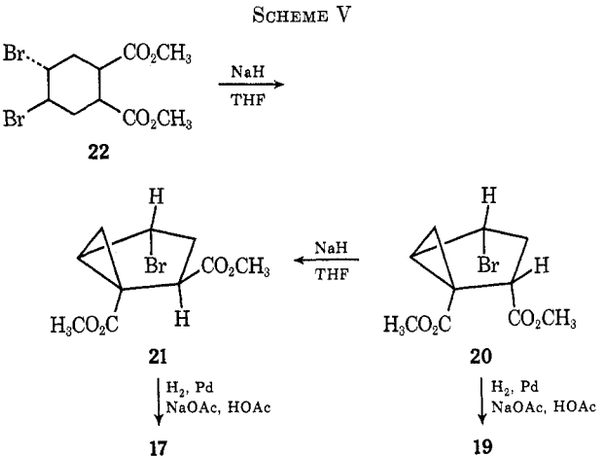
The most striking feature of the hydrogenation of **4** is its stereospecificity. This requires that the hydrogen must have added from the inside of one of the "flaps" of the *anti*-tricyclo[3.1.0.0^{2,4}]hexane skeleton. In this respect, the reaction bears a formal similarity to the cycloadditions described by Gassman,[22] in which bicyclo[2.1.0]pentane suffers attack from the concave face.

Hydrobromination.—When **4** is allowed to stand in a chloroform solution of hydrogen bromide for 30 min, it is completely converted to a mixture of dimethyl *exo*-4-bromobicyclo[3.1.0]hexane-1,*exo*-2-dicarboxylate (**20**, 44%) and dimethyl *exo*-4-bromobicyclo-[3.1.0]-hexane-1,*endo*-2-dicarboxylate (**21**, 56%). The stereochemistry of **20** and **21** was determined as follows. The reaction of the dibromo diester **22**[23] with sodium hydride in tetrahydrofuran gave a 65% yield of a product identical with the major product obtained in the reaction of **4** with hydrogen bromide. Since the bromine atoms of **22** are trans to each other, the bromine substituent in **21**, obtained by this intramolecular nucleophilic displacement, must then be exo to the three-membered ring. The endo configuration of the ester group in **21** was demonstrated by hydrogenolysis of **21** to give **17**. When a sample of **20** was allowed to react with sodium hydride in tetrahydrofuran, it was epimerized to **21**, along with small amounts of dimethyl phthalate and an unidentified product. It therefore can be concluded that the bromine atom of **20** is also exo. The exo configuration of the ester group of **20** was confirmed by hydrogenolysis to give **19** (Scheme V).



20 **21**

SCHEME V



(18) An attempt has been made to distinguish between the mechanisms presented in Schemes III and IV by conducting the reaction in acetic acid-*d*$_4$. However, under these conditions the reaction proceeded much more slowly, and **10** and **11** were no longer the major products, but were accompanied by at least four additional components. Since it is likely that a different mechanism is operating in acetic acid, any attempt to extrapolate the information obtained under these conditions to the reaction conducted in chloroform would be unreliable.

(19) J. Klein, E. Dunkelblum, and D. Avrahami, *J. Org. Chem.*, **32**, 935 (1967).

(20) This reaction is a direct extension of the bicyclo[3.1.0]hexane synthesis developed by N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957).

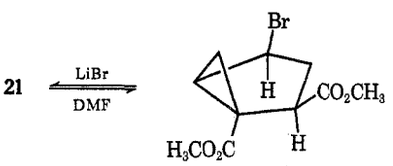
(21) C. D. Poulter, R. S. Borkess, J. I. Brauman, and S. Winstein, *J. Amer. Chem. Soc.*, **94**, 2291 (1972).

(22) P. G. Gassman, K. T. Mansfield, and T. J. Murphy, *J. Amer. Chem. Soc.*, **91**, 1684 (1969).

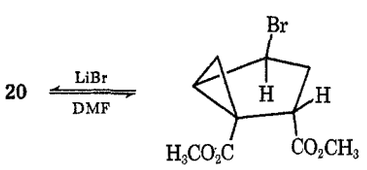
(23) U. F. Kucherov, A. L. Shabanov, and A. S. Onishchenko, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 884 (1963).

To gain further insight into the hydrobromination of **4**, we performed several other experiments. It was found that, when both **20** and **21** were resubmitted to the reaction conditions, they were recovered unchanged. When a sample of **4** was allowed to react with deuterium bromide in chloroform, the nmr spectra of the isolated products showed that the absorptions at δ 3.20 and 3.83, assigned to the protons α to the carboxylate group in **20** and **21**, were absent; no other deuterium incorporation in either isomer was apparent.

To determine whether the reaction of **4** with hydrogen bromide is thermodynamically or kinetically controlled, equilibration studies were conducted with **20** and **21**. A sample of **21** treated with lithium bromide in dimethylformamide gave an equilibrium mixture consisting of **21** (56%) and the new epimer **23**



23



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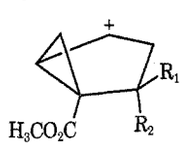
(44%), as determined from the nmr spectrum of the mixture. Similarly, treatment of **20** with lithium bromide in dimethylformamide gave an equilibrium mixture consisting of **20** (20%) and **24** (80%). These results clearly indicate that the reaction of **4** with hydrogen bromide is kinetically controlled, since epimers **23** and **24** are not observed.

An important feature of the hydrobromination of **4** is the stereochemistry of the resulting bicyclo[3.1.0]-hexanes, **20** and **21**. While there is essentially no stereochemical preference shown for the carboxylate group in the products, the reaction is stereospecific with respect to the bromine substituents. One of the first mechanisms which we considered involves addition of a proton to a strained bridgehead bond, giving the bicyclo[3.1.0]hexyl cations **25** and **26**. Stereo-



25, $R_1 = CO_2CH_3$; $R_2 = H$
26, $R_1 = H$; $R_2 = CO_2CH_3$

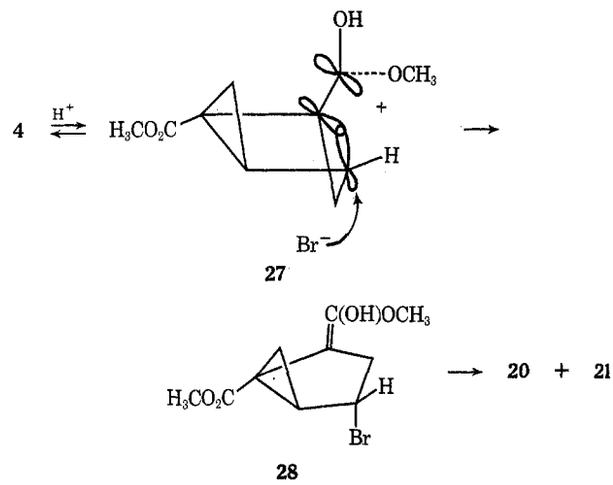
specific (exo) addition of bromide ion would give the observed products. However, it appears that, when the 2-bicyclo[3.1.0]hexyl cation has been generated under a variety of conditions, addition of a nucleophile to the cation is generally not stereospecific.[24]

(24) (a) K. B. Wiberg, R. A. Fenoglio, U. Z. Williams, and R. W. Obersax, *J. Amer. Chem. Soc.*, **92**, 568 (1970); (b) E. C. Friedrich and M. A. Saleh, *Tetrahedron Lett.*, 1373 (1971); (c) P. R. Brook, R. M. Ellam, and A. S. Bloss, *Chem. Commun.*, 425 (1968); (d) G. H. Schmid and A. Brown, *Tetrahedron Lett.*, 4695 (1968); (e) R. N. McDonald and G. E. Davis, *J. Amer. Chem. Soc.*, **94**, 5078 (1972).

Consequently, it is unlikely that **25** and **26** are intermediates in the hydrobromination of **4**.

The mechanism shown in Scheme VI appears to offer the best explanation of the experimental results.

SCHEME VI



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In this scheme, protonation of **4** occurs at an ester carbonyl oxygen, giving cation **27**. Attack of bromide ion at the back lobe of the appropriate σ orbital would yield enolized ester **28**, tautomerization of which to the observed products would follow. The specificity of attack by bromide ion and the formation of both epimers at the ester site are thereby simply accommodated.

Experimental Section

***trans*-1,2-Bis(chloromethyl)cyclobutane-*cis*-3,4-dicarboxylic Acid Anhydride (2).**—A solution of 30.0 g (0.306 mol) of maleic anhydride and 14.0 g (0.077 mol) of benzophenone in 370 ml of *trans*-1,4-dichloro-2-butene was placed in a photochemical apparatus equipped with a 450-W Hanovia lamp, Pyrex filter, and a water-cooled quartz immersion well. The reaction mixture was flushed with nitrogen for 8 min. The mixture was irradiated with stirring for 48 hr, at which time a white solid began to separate. The unreacted *trans*-1,4-dichloro-2-butene was removed by distillation [35° (4 mm); this material can be used in further runs without additional purification]. The residue was refluxed with 300 ml of hexane for ~15 min. The hot hexane solution was decanted and discarded. The mixture was then stirred at reflux in 250 ml of ether. The mixture was allowed to cool to room temperature. An off-white solid (51.6 g, 76%) was collected by filtration. An analytical sample was prepared by dissolving the anhydride in hot chloroform and adding ether until the solution became cloudy. Cooling to room temperature gave colorless crystals of the anhydride **2**: mp 121–123.5°; ν_{max}^{KBr} 3020, 2960, 1865, 1800 cm^{-1}; nmr $\delta_{TMS}^{acetone\text{-}d_6}$ 2.90–4.05 (series of multiplets).

Anal. Calcd for $C_8H_8O_3Cl_2$: C, 43.07; H, 3.62; Cl, 31.79. Found: C, 42.98; H, 3.44; Cl, 31.61.

Dimethyl *trans*-1,2-Bis(chloromethyl)cyclobutane-*cis*-3,4-dicarboxylate (3).—To 90 ml of methanol was added 5.5 g (0.0246 mol) of **2**. The mixture was heated on a steam bath until it became homogeneous (~15 min). The solution was cooled to 0° and an ethereal solution of diazomethane was slowly added until a permanent yellow color remained. Excess diazomethane was destroyed by the addition of a few drops of acetic acid. The solvent was removed by rotary evaporation. The residue was distilled [156.5–157.5° (4 mm)] to give 5.98 g (91%) of **3**. After standing several weeks in the freezer, this material crystallized: mp 37–39°; ν_{max}^{neat} 2985, 2950, 1740 cm^{-1}; *m/e* 237 (M − OCH_3), 209 (M − $COOCH_3$); nmr $\delta_{TMS}^{acetone\text{-}d_6}$ 3.77–3.93 (m, 4 H), 2.65–3.55 (m, 4 H), 3.65 (s, 3 H, CH_3), 3.70 (s, 3 H, CH_3).

Anal. Calcd for $C_{10}H_{14}O_4Cl_2$: C, 44.63; H, 5.24; Cl, 26.35. Found: C, 44.47; H, 5.24; Cl, 26.16.

Dimethyl *anti*-Tricyclo[3.1.0.0^{2,4}]hexane-1,2-dicarboxylate (4).—A mixture of 8.0 g (0.0297 mol) of **3**, 1.65 g (0.0687 mol) of sodium hydride, and 1 drop of methanol was stirred at reflux in 170 ml of tetrahydrofuran (THF) for 48 hr. The mixture was filtered from the precipitated salts and the THF removed by rotary evaporation. The mixture was mixed with a saturated solution of ammonium chloride. The aqueous mixture was extracted with ether. The ether solution was dried over magnesium sulfate and treated with Norit. The ether was removed at reduced pressure. The residue was distilled. The fraction boiling at 77–79° (0.02 mm) was collected, and 3.45 g (59%) of **4** was obtained as a liquid which, on standing several hours, crystallized: mp 44–46°; ν_{max}^{neat} 3014, 3000, 1740, 1335, 1260, 1205, 1165, 1097, 770, 735, 717 cm^{-1}; cmr (neat, parts per million downfield from external TMS) 29.41 ($CCOOCH_3$), 31.09 (CH, $J_{^{13}C-H}$ = 188 Hz), 32.66 (CH_2, $J_{^{13}C-H}$ = 166 Hz), 52.96 (CH_3), 71.73 (CO); pmr $\delta_{TMS}^{CDCl_3}$ 1.72 (m, 2 H), 1.95 (m, 2 H), 2.20 (m, 2 H), 3.67 (s, 6 H, CH_3); uv $\lambda_{max}^{n\text{-heptane}}$ 227 mμ (ϵ 82.2); mass spectrum *m/e*, 196.

Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 60.96; H, 6.23.

Thermolysis of 4.—In a thick-walled glass tube was placed 0.075 g (0.446 mmol) of **4**. The tube was evacuated (0.05 mm) and sealed. The tube was heated to 190° for 1.5 hr. The contents of the tube were subjected to molecular distillation [bath temperature 70° (0.05 mm)] to give dimethyl cyclohexa-1,4-diene-1,2-dicarboxylate (**7**). This material was identified by comparing its nmr and ir spectra with those of an authentic sample.[10]

1,2-Bis(hydroxymethyl)-*anti*-tricyclo[3.1.0.0^{2,4}]hexane (9).—To a stirred slurry of 0.425 g (11.2 mmol) of lithium aluminum hydride in 10 ml of ether was added dropwise a solution of 1.0 g (5.1 mmol) of **4** in 10 ml of ether at such a rate as to maintain reflux. The mixture was stirred at room temperature for an additional 1 hr and 45 min. Excess reducing agent was destroyed by the dropwise addition of a saturated sodium sulfate solution. The mixture was filtered, and the salts were washed with additional ether. The combined ether solutions were dried ($MgSO_4$). The ether was removed at reduced pressure, leaving 0.68 g (95%) of **9**. An analytical sample was obtained *via* molecular distillation [bath temperature 80° (0.3 mm)]: ν_{max}^{neat} 3305, 3015, 2995, 2949, 2889, 2835, 1005 cm^{-1}; nmr $\delta_{TMS}^{CDCl_3}$ 3.59 [AB, 4 H, CH_2OH, $\Delta\nu_{AB}$ = 33.7 Hz, J_{AB} = −11.4 Hz (the low field portion of the AB pattern is further coupled, J = 1.0 Hz)], 4.16 (b s, 2 H, OH), 1.55 (m, 2 H), 1.33 (m, 2 H), 0.93 (m, 2 H).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 67.26; H, 8.70.

1,2-Bis(acetoxymethyl)-*anti*-tricyclo[3.1.0.0^{2,4}]hexane (8).—A solution of 0.30 g (2.14 mmol) of **9** and 0.075 g of sodium acetate in 2 ml of acetic anhydride was refluxed for 2 hr. The acetic anhydride was removed by distillation. The residue was mixed with water. Solid sodium bicarbonate was added until gas evolution ceased. The mixture was extracted with ether, and the ether solution was dried. The ether was removed by rotary evaporation. The residue was subjected to molecular distillation, giving 0.374 g (91%) of **8**. An analytical sample was isolated *via* preparative vpc (6 ft × 0.25 in. glass column, 5% Carbowax 20M on 60–80 mesh Chromosorb Q, 145°): ν_{max}^{neat} 3090, 2970, 2930, 2859, 1740 cm^{-1}; nmr $\delta_{TMS}^{CDCl_3}$ 2.16 (s, 6 H, CH_3), 4.33 (s, 4 H, CH_2OAc), 0.80–1.15 (m, 2 H), 1.32–1.76 (m, 4 H).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.32; H, 7.40.

Reaction of 8 with Silver Fluoroborate.—A solution of 0.240 g (1.25 mmol) of **8** in 1 ml of $CDCl_3$ was placed in an nmr tube. Several crystals of silver fluoroborate were added. The solution was heated to boiling on a steam bath for 1 min and allowed to stand at room temperature in the dark for 1 hr. At this time, the nmr spectrum of the dark brown solution showed the presence of **1,2-bis(acetoxymethyl)cyclohexa-1,4-diene (10**, 84%) and **2-acetoxymethyltoluene (11**, 16%). The products were identified by comparison of their nmr spectra in the mixture and vpc retention times (5% Carbowax 20M on 60–80 mesh Chromosorb W, 150°) with independently prepared samples.

When a sample of **10** was subjected to the above reaction conditions for 24 hr, it was observed to be unchanged.

1,2-Bis(acetoxymethyl)cyclohexa-1,4-diene (10).—To a slurry of 0.68 g (17.9 mmol) of lithium aluminum hydride in 15 ml of ether was added with stirring 1.6 g (8.16 mmol) of dimethyl cyclohexa-1,4-diene-1,2-dicarboxylate (**7**)[10] in ether at such a rate as to maintain reflux. The mixture was stirred an additional 1 hr 45 min at room temperature. Excess reducing agent was destroyed by the dropwise addition of a saturated sodium sulfate solution. The mixture was filtered, and the ether was removed at reduced pressure. The residue was dissolved in 6 ml of acetic anhydride. To this solution was added 0.30 g of sodium acetate. The mixture was refluxed for 1 hr and 15 min. The excess acetic anhydride was removed by distillation, and the residue was mixed with water. Solid sodium bicarbonate was added until gas evolution ceased. The mixture was extracted with ether, and the ether solution was dried ($MgSO_4$) and treated with Norit. The ether was removed at reduced pressure, giving 1.16 g (74%) of a liquid which was distilled [98–100° (0.1 mm)]. Analysis by nmr of the distillate indicated that this material was **10** contaminated with 9% 1,2-bis(acetoxymethyl)benzene. An analytical sample of the diene was isolated *via* vpc (6 × 0.25 in. glass column, 5% Carbowax 20M on 60–80 mesh Chromosorb Q, 175°): mp 34–35°; ν_{max}^{neat} 3005, 2850, 2790, 1739, 1655, 1225 cm^{-1}; nmr $\delta_{TMS}^{CDCl_3}$ 2.14 (s, 6 H, CH_3), 2.87 (b s, 4 H, CH_2, $W_{1/2}$ = 3.0 Hz), 4.83 (s, 4, CH_2OAc), 5.90 (b s, 2 H, vinyl, $W_{1/2}$ = 2.7 Hz).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 63.91; H, 7.20.

Hydrogenation of 4.—A solution of 0.20 g (1.02 mmol) of **4** in 2 ml of acetic acid containing 0.06 g of platinum dioxide was hydrogenated at atmospheric pressure. Hydrogen uptake ceased after 1 hr. The mixture was filtered, poured into water, and extracted with ether. The ether solution was washed with a saturated solution of sodium bicarbonate and dried ($MgSO_4$). The ether was removed by rotary evaporation. The residue was subjected to molecular distillation [bath temperature 70° (0.05 mm)]; 0.180 g (92%) of dimethyl bicyclo[3.1.0]hexane-1,*endo*-2-dicarboxylate (**17**) was obtained. An analytical sample was isolated by preparative vpc (UCON nonpolar on 60–80 mesh Chromosorb W, 190°): ν_{max}^{neat} 2960, 2870, 1730 cm^{-1}; nmr $\delta_{TMS}^{CDCl_3}$ 1.14–2.12 (m, 7 H), 3.33–3.60 (m, 1 H, $CHCOOCH_3$), 3.67 (s, 3 H, CH_3), 3.70 (s, 3 H, CH_3); mass spectrum *m/e* 198.

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.82; H, 7.32.

Preparation of the Brosylate of Dimethyl *trans*-4-Hydroxycyclohexane-*cis*-1,2-dicarboxylate.—To a solution of 1.80 g (9.0 mmol) of dimethyl *trans*-4-hydroxycyclohexane-*cis*-1,2-dicarboxylate[19] in 10 ml of dry pyridine was added 3.0 g (11.7 mmol) of brosyl chloride. The mixture was allowed to stand overnight in the refrigerator. The solution was filtered from the pyridine hydrochloride and poured into water. The aqueous mixture was extracted with ether. The ether solution was washed with dilute hydrochloric acid, followed by a saturated solution of sodium bicarbonate. The ether solution was dried (K_2CO_3, Na_2SO_4) and the ether removed by rotary evaporation. The residue (1.85 g) was dissolved in an ether–pentane mixture. The solution was cooled; the brosylate, which first oiled out, crystallized on standing several days in the freezer. The crystalline cake was crushed under pentane. The solid was washed with more pentane and dried at reduced pressure. The resulting brosylate showed mp 58–64°; nmr $\delta_{TMS}^{CDCl_3}$ 1.50–2.23 (m, 6 H, methylenes), 2.76–3.11 (m, 2 H, $CHCOOCH_3$), 3.73 (s, 6 H, CH_3), 4.63–4.98 (m, 1 H, CHOBs), 7.71 (s, 4 H, aromatic).

Anal. Calcd for $C_{16}H_{19}BrO_7S$: C, 45.83; H, 4.57. Found: C, 45.54; H, 4.32.

The Reaction of the Brosylate of Dimethyl *trans*-4-Hydroxycyclohexane-*cis*-1,2-dicarboxylate with Potassium *tert*-Butoxide.—A solution of potassium *tert*-butoxide in 20 ml of *tert*-butyl alcohol was prepared by refluxing 0.251 g (6.425 mmol) of potassium in the alcohol. This solution was added dropwise with stirring to a solution of 2.8 g (6.425 mmol) of **18** in 10 ml of *tert*-butyl alcohol over a 20-min period. The mixture was stirred for an additional 15 min. Solid ammonium chloride (1.0 g) was added. The *tert*-butyl alcohol was removed by rotary evaporation. The residue was diluted with water and extracted with ether. The ether solution was dried ($MgSO_4$) and the ether was removed by rotary evaporation. The residue (1.10 g) was distilled [bath temperature 110° (0.1 mm)] to give a 3:2 mixture (0.88 g, 67%) of **dimethyl bicyclo[3.1.0]hexane-1,*exo*-2-dicarboxylate (19)** and **17** as determined by nmr analysis.

Equilibration of 17 and 19.—A solution of 0.150 g (0.757 mmol) of **17** in 2 ml of methanol containing a small amount of sodium methoxide was refluxed for 24 hr. The mixture was

diluted with ether, treated with Norit, and filtered. The ether was removed by rotary evaporation. Nmr analysis of the residue showed the presence of the endo and exo isomers in a 78:22 ratio.

When an isomer mixture containing 60% exo isomer and 40% endo isomer was subject to the above reaction conditions, the endo–exo ratio was found to be 76:24.

Hydrobromination of 4.—Hydrogen bromide was bubbled into a solution of 0.50 g (2.55 mmol) of **4** in 8 ml of chloroform for 45 sec. The mixture was allowed to stand at room temperature for 30 min. The solvent was removed at reduced pressure, leaving 0.69 g (100%) of a mixture of **20** and **21**. The mixture was taken up in boiling hexane. The solution was allowed to stand for several hours at room temperature. Filtration gave 0.250 g of pure dimethyl *exo*-4-**bromobicyclo[3.1.0]hexane-1,*exo*-2-dicarboxylate** (**20**): mp 103–105°; ν_{max}^{KBr} 2985, 2935, 2912, 2810, 1741, 1720 cm^{-1}; nmr $\delta_{TMS}^{CDCl_3}$ 0.70–1.35 (AB of an ABX, 2 H, cyclopropyl methylene, $J_{AB} = -5.7$ Hz), 2.23–2.47 (m, 2 H, cyclopentyl methylene), 2.52–2.77 (X of an ABX, 1 H, cyclopropyl methine, $J_{AX} + J_{BX} = 13.5$ Hz), 3.20 (t, 1 H, CHCOOCH$_3$), 4.32 (t, 1 H, CHBr), 3.68 (s, 3 H, CH$_3$), 3.72 (s, 3 H, CH$_3$).

Anal. Calcd for $C_{10}H_{13}O_4Br$: C, 43.34; H, 4.73; Br, 28.84. Found: C, 43.53; H, 4.75; Br, 28.72.

The hexane was removed from the filtrate by rotary evaporation, leaving 0.403 g of a liquid which was subjected to molecular distillation, giving **dimethyl *exo*-4-bromobicyclo[3.1.0]hexane-1,*endo*-2-dicarboxylate** (**21**) contaminated with only a trace of **20**: ν_{max}^{neat} 2970, 2930, 2830, 1735 cm^{-1}; nmr $\delta_{TMS}^{CDCl_3}$ 1.13–1.68 (AB of an ABX, 2 H, cyclopropyl methylene, $J_{AB} = -5.9$ Hz), 1.95–2.63 (m, 3 H, cyclopropyl methine, cyclopentyl methylene), 3.83 (m, 1 H, CHCOOCH$_3$), 3.67 (s, 6 H, CH$_3$), 4.49 (d, 1 H, CHBr, $J = 4.8$ Hz).

Anal. Calcd for $C_{10}H_{13}O_4Br$: C, 43.34; H, 4.73, Br, 28.84. Found: C, 43.60; H, 4.85; Br, 28.53.

The ratio of **20** to **21** was found to be 44:56 by integration of the methyl resonances in the nmr spectrum of the mixture; the methyl resonances were resolved by the addition of Eu(fod)$_3$-d_{30}. Samples of both isomers, when subjected to the reaction conditions, were recovered unchanged.

The above reaction was repeated, using deuterium bromide. Nmr analysis of the separated isomers indicated that in each case only the hydrogen α to the carbomethoxy group was replaced by deuterium.

The Reaction of Dimethyl *trans*-4,5-Dibromocyclohexane-*cis*-1,2-dicarboxylate (22) with Sodium Hydride.—A solution of 12.0 g (0.0355 mol) of **dimethyl *trans*-4,5-dibromocyclohexane-*cis*-1,2-dicarboxylate** (**22**) in 400 ml of dry THF containing 1.85 g (0.077 mol) of sodium hydride was refluxed with stirring for 48 hr. The mixture was filtered and the THF removed by rotary evaporation. The residue was mixed with an aqueous solution of ammonium chloride and extracted with ether. The ether solution was dried (MgSO$_4$) and the solvent was removed by rotary evaporation. The residue was distilled [95–100° (0.05 mm)], giving 6.0 g (65%) of **21**. This material is identical with the major isomer isolated from the hydrobromination of **4** as determined by nmr and ir spectra, as well as vpc retention times.

Hydrogenolysis of 21.—A solution of 0.25 g (0.91 mmol) of **21**, 0.5 g of sodium acetate, and 0.10 g of Pd/C (5%) in 3 ml of acetic acid was hydrogenated at atmospheric pressure for 23 hr. The mixture was filtered and poured into water. The aqueous mixture was extracted with ether. The ether solution was washed with a saturated solution of sodium bicarbonate and dried (MgSO$_4$). The ether was removed by rotary evaporation, leaving 0.180 g (100%) of **17**, determined from its nmr spectrum and vpc retention time.

Hydrogenolysis of 20.—A 0.080-g (0.289 mmol) sample of **20** was hydrogenated for a total of 48 hr using the above procedure, giving 0.053 g (93%) of **19**. An analytical sample was isolated *via* preparative vpc (6 ft × 0.25 in. glass column, Carbowax 20M on 60–80 mesh Chromosorb Q, 160°): $\nu_{max}^{CCl_4}$ 2915, 2845, 2813, 1731 cm^{-1}; nmr $\delta_{TMS}^{CDCl_3}$ 3.60 (s, 3 H, CH$_3$), 3.66 (s, 3 H, CH$_3$), 2.95–3.17 (m, 1 H, CHCOOCH$_3$), 0.75–2.30 (m, 7 H, saturated).

Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.72; H, 7.17.

The Interconversion of 20 and 21.—A solution of 0.100 g (0.37 mmol) of **20** and 0.014 g of sodium hydride in 2 ml of THF was stirred at reflux for 2 hr and at room temperature for 16 hr. A few drops of acetic acid were added, and the mixture was poured into a saturated solution of ammonium chloride. The mixture was extracted with ether. The ether solution was washed with a saturated solution of sodium bicarbonate and dried (MgSO$_4$). The ether was removed at reduced pressure, giving 0.065 g of a liquid. Nmr and vpc analysis (Carbowax 20M on 60–80 mesh Chromosorb W, 165°) of the liquid indicated it was composed of **21**, dimethyl phthalate, and an unidentified component; the ratio of the respective areas of the vpc trace was 69:13:18.

Equilibration of Dimethyl *exo*- and *endo*-4-Bromobicyclo[3.1.0]hexane-1,*endo*-2-dicarboxylates (21 and 23).—To a solution of 0.150 g (0.54 mmol) of **21** in 1 ml of DMF was added 0.30 g (3.5 mmol) of lithium bromide. The solution was stirred at room temperature for 30 min, poured into water, and extracted with ether. The ether solution was washed with water and dried (MgSO$_4$). The ether was removed at reduced pressure, giving 0.110 g (73%) of a mixture of 21 and **23**; the ratio of the two isomers was found to be 56:44 by integration of the methyl resonances in the nmr spectrum of the crude reaction mixture; the methyl resonances were resolved by the addition of Eu(fod)$_3$-d_{30}.

These isomers were shown to differ only in the configuration at the carbon atom bearing the bromine by hydrogenolysis of the mixture (5% Pd/C, NaOAc, HOAc, 48 hr) to give **17**.

A similar mixture of isomers was obtained by passing **21** through a column packed with UCON nonpolar on 60–80 mesh Chromosorb W at 190°.

Equilibration of Dimethyl *exo*-and *endo*-4-Bromobicyclo[3.1.0]hexane-1,*exo*-2-dicarboxylates (20 and 24).—To a solution of 0.080 g (0.289 mmol) of **20** in 0.75 ml of DMF was added 0.20 g (2.3 mmol) of lithium bromide. The mixture was maintained at 100° for 1 hr and then poured into water. The aqueous mixture was extracted with ether. The ether solution was washed with water and dried (MgSO$_4$). The ether was removed at reduced pressure, giving 0.074 g (92%) of a mixture of **20** and **24** in a ratio of 20:80, respectively; the ratio was determined from integration of the methyl resonances in the nmr spectrum of the crude reaction mixture; these resonances were resolved by the addition of Eu(fod)$_3$-d_{30}.

These isomers were shown to differ only in the configuration at the carbon atom bearing the bromine by hydrogenolysis of the mixture (5% Pd/C, NaOAc, HOAc, 72 hr) to give **19** as the major product.

Registry No.—**2**, 38665-90-6; **3**, 38665-91-7; **4**, 38665-92-8; **7**, 14309-54-7; **8**, 38665-94-0; **9**, 38665-95-1; **10**, 38665-96-2; **17**, 38665-97-3; **19**, 38665-98-4; **20**, 38665-99-5; **21**, 38666-00-1; maleic anhydride, 108-31-6; *trans*-1,4-dichloro-2-butene, 110-57-6; dimethyl *trans*-4-hydroxycyclohexane-*cis*-1,2-dicarboxylate, 7731-16-0; dimethyl *trans*-4-hydroxycyclohexane-*cis*-1,2-dicarboxylate brosylate, 38666-01-2.

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