Anal. Calcd for $C_8H_{10}BrNO_3$: C, 38.7; H, 4.1; N, 5.7. Found: C, 38.8; H, 4.2; N, 5.6.

7,7-Dibromo-8-oxo-1-azabicyclo[4.2.0]octane (29). A mixture of decomposition products (94 mg) collected by preparative GC of the esters **27** and **28** was chromatographed on kieselgel (11 g) with ether–petroleum ether (3:1 v/v), giving **29** (25 mg), intermediate fractions (16 mg) shown by GC to contain **22** to the extent of ~30%, then **22** (35 mg), identical with an authentic sample by ir, NMR comparison, and GC coinjection. **29** was recrystallized from hexane–$CHCl_3$: mp 73–74°; ir 1782 cm^{-1}; NMR (CCl_4) δ 1.2–2.3 (6 H, m), 2.82 (1 H, m), 3.5–4.0 (2 H, m); mass spectrum *m/e* (rel intensity) 285 (M^+, 1.7), 283 (M^+, 3.2), 291 (M^+, 1.7), 257 (<1), 255 (1), 253 (<1), 212 (46), 210 (80), 208 (50), 204, 202 (93), 176, 174 (86), 123 (82), 95 (27), 44 (100).

Anal. Calcd for $C_7H_9Br_2NO$: C, 29.7; H, 3.2; N, 4.9. Found: C, 30.0; H, 3.3; N, 4.9.

Registry No.—**3**, 4450-97-9; **4**, 42599-26-8; **5**, 42599-27-9; **7**, 54409-76-6; **11**, 759-65-9; **12**, 505-18-0; **13**, 42599-33-7; **14**, 35620-54-3; **15**, 54409-78-8; **16**, 54409-79-9; **17**, 42599-30-4; **19**, 54409-80-2; **20**, 54409-81-3; **21**, 42599-31-5; **22**, 53618-26-1; **23**, 40876-98-0; **24**, 54409-85-7; **25**, 54409-86-8; **26**, 54409-87-9; **27**, 42599-40-6; **28**, 42599-41-7; **29**, 42599-42-8; ethyl sodioethoxalylacetate, 54409-82-4; piperidine, 110-89-4; *N*-chlorosuccinimide, 128-09-6; ethyl 3-*tert*-butoxycarbonyl-2-oxopropionate, 54409-83-5.

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(22) X-Ray crystallographic and other stereochemical studies of **23**, **25**, and **26** will be presented in a subsequent paper.
(23) Solvent evaporations were carried out in vacuo using a Berkeley rotary evaporator. All melting points are uncorrected. Infrared (ir) spectra were measured in chloroform (unless otherwise indicated) on a Perkin-Elmer 137 or 337 spectrometer; ultraviolet (uv) spectra were measured using a Cary Model 14 spectrometer; and nuclear magnetic resonance (NMR) spectra were taken in $CDCl_3$ (unless otherwise indicated) on a Varian T-60 spectrometer and are reported as δ values relative to Me_4Si (δ 0). NMR line shape abbreviations include: dd, double doublet, br dd, broad double doublet. Mass spectra were obtained on a CEC 103 instrument. All reactions and continuous extractions were carried out in a nitrogen atmosphere. Chromatography was performed on Merck silica gel (70–230 mesh) or Camag kieselgel (>250 mesh) without binder as specified. Kieselgel chromatography was generally carried out in quartz columns using General Electric manganese-activated zinc silicate, Type T-1 (1%, w/w) as a short-wavelength uv indicator. Elemental analyses were performed by the Analytical Laboratory, Department of Chemistry, University of California, Berkeley.
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Fumaric Acid Formation in the Diels–Alder Reaction of 2-Methylfuran and Maleic Acid. A Reexamination[1]

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The exo-cis Diels–Alder adduct of 2-methylfuran and maleic acid in water slowly reverts to maleic acid, 2-methylfuran, endo-cis adduct, and fumaric acid. Fumaric acid formation in this system has previously been cited to support a nonconcerted [2 + 4] cycloaddition. Present kinetic measurements, however, show that fumaric acid is formed in a very minor side reaction. The sum of the rates of cycloaddition between maleic acid and 2-methylfuran and cycloreversion of exo-cis and endo-cis [2 + 4] adducts is at least 1000 times as fast as fumaric acid formation and suggests that the main reaction proceeds by a concerted path. Possible mechanisms of direct isomerization of the maleic acid in equilibrium with adduct have been tested. Other possible mechanisms leading to fumaric acid are discussed.

The retrodiene reaction,[2] exhibited by the exo-cis adduct (I) from maleic acid and 2-methylfuran, has been asserted to be a nonconcerted reaction.[3] Gagnaire et al.[3] reported that in aqueous solution adduct I undergoes cycloreversion to yield fumaric acid along with maleic acid and 2-methylfuran (eq 1). Fumaric acid, along with exo- and endo-cis adducts, were also reported to form if maleic acid and 2-methylfuran were mixed in aqueous solution. If, however, furan or 2,5-dimethylfuran was used instead of 2-methylfuran, no fumaric acid was observed to form from the maleic acid initially present under similar conditions. On this basis the authors concluded that reversion of I to its ad-

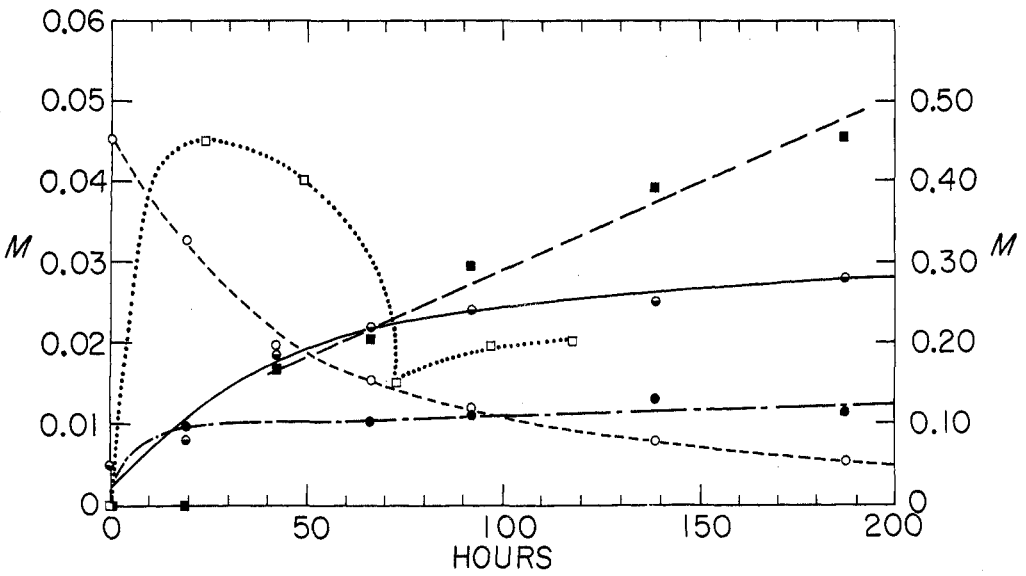
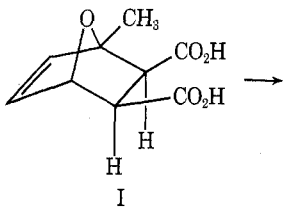


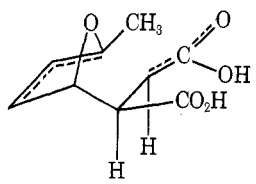
Figure 1. Concentration of products found in the aqueous layer as a function of time from decomposition of I in D_2O. Circles, use right ordinate; squares, use left ordinate. Reactants and product are designated as follows: I, open circles; maleic acid, half circles; endo-cis adduct, solid circles; 2-methylfuran, open squares; fumaric acid, solid squares. The aqueous solution becomes supersaturated in 2-methylfuran which, after a period of time, forms a second layer.



I

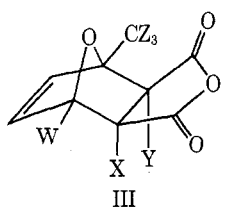
maleic acid + fumaric acid + 2-methylfuran (1)

dends involved rupture of the two bonds in separate steps. Cis–trans isomerization was presumed to occur in an intermediate such as II.



II

This conclusion, concerning the timing of bond rupture, appears to contradict that derived from earlier studies on adduct III; III is the anhydride of I. The results of extensive studies utilizing secondary deuterium isotope effects in III are in accord with a concerted and equal rupture of the



III

a, W = X = Y = Z = H
b, W = D; X = Y = Z = H
c, W = Z = H; X = Y = D
d, W = X = Y = H; Z = D
e/f, (W = X = Z = H; Y = D) / (W = Y = Z = H; X = D) (1 : 1)

two bonds during retrodiene reaction.[4] Since the mechanism for two such similar compounds undergoing reverse cycloaddition appears not to be the same, the usefulness of the methods used to investigate these reactions is weakened. Consequently we have repeated the experiments of Gagnaire et al. and examined them in greater detail.

In this report we show that fumaric acid is a very minor product and consequently the products of decomposition of I are consistent with a concerted two-bond rupture. Further experiments aimed toward the determination of the genesis of fumaric acid have been carried out and described below.

Results and Discussion

The NMR spectrum of a relatively concentrated aqueous solution of I initially exhibits resonances attributed to the protons of I but shortly after mixing there appear peaks that can be assigned to maleic acid, 2-methylfuran, and the corresponding endo-cis adduct formed from the diene and dieneophile generated from decomposition of I. After standing at ambient temperature for 100 hr, however, a new vinyl singlet, due to fumaric acid, begins to appear. At further extended reaction times fumaric acid precipitates from solution. A typical plot of the percent composition of the aqueous phase vs. time is shown in Figure 1. With an initial exo-adduct concentration (~0.5 *M*) suitable for NMR measurements, a pseudo-steady state is reached after about 150 hr. At this concentration the bulk of the 2-methylfuran formed is immiscible with water and forms a second phase. The amount of diene in the aqueous phase reaches a plateau of 0.02 *M* after about 70 hr. It is readily apparent that maleic acid appears long before and in greater quantity than fumaric acid. The question arises: Does fumaric acid form solely from free maleic acid or is it generated as a direct consequence of the formation and decomposition of cycloadducts?

Since a pseudo-steady state is reached at about the time that fumaric acid is first detected, it was of interest to determine the rate constant for decomposition of the exo-cis adduct in aqueous solution. 2-Methylfuran and maleic acid both absorb strongly at 215 nm while the adduct absorbs only weakly. The kinetics of formation of addends were thus followed. The results of such a run are shown in Figure 2. The average rate constant for decomposition at 22° is 4.84×10^{-5} sec^{-1} ($t_{1/2}$ = 3.9 hr). The apparent slow rate of exo-adduct disappearance shown in Figure 1 is thus due to the reversibility of the reaction, which becomes important at the high concentrations used by Gagnaire and Payo-Subiza to observe continuous wave NMR spectra. Under these conditions a true equilibrium between exo adduct, maleic acid, and 2-methylfuran is never reached because fumaric acid is continually being formed at the expense of maleic acid but this latter reaction is slow enough that an

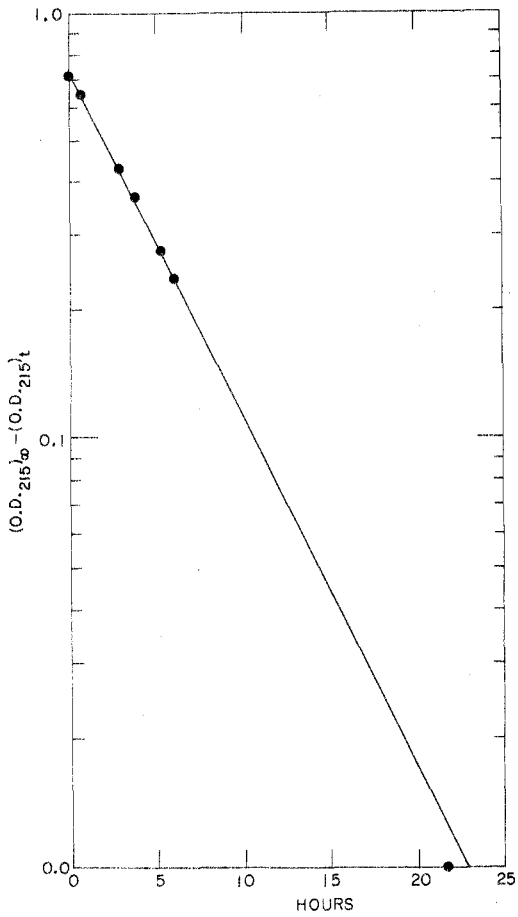


Figure 2. Kinetics of decomposition of I in ethanol–water (5:95) followed at 215 nm. $[I]_0 = 5 \times 10^{-5}$ *M*.

approximate dissociation equilibrium constant (K'_{eq}) can be calculated at t = 250 hr: K'_{eq} (aqueous phase) = [maleic acid][2-methylfuran]/[exo adduct] = 0.028 *M*. From the approximate equilibrium constant, the relatively constant concentration of diene in the aqueous phase, and the rate constant for exo-adduct decomposition, a pseudo-first-order rate constant for exo-adduct *formation* in the aqueous phase can be determined. This turns out to be 3.7×10^{-5} sec^{-1}.

Each time the adduct decomposes to addends or the addends combine to yield adduct, an intermediate and/or transition state is formed. It is interesting to compare the number of passes which yield maleic to the number which yield fumaric acid. Using the rate constants obtained above for the forward and backward reaction it can be calculated that only 2.8 per 1000 yield fumaric acid. This is a maximum value, since the number of passes over the energy surface leading to the formation and decomposition of the endo adduct has not also been included. Similar kinetic studies on decomposition of the endo adduct are precluded because of its greater instability with respect to I. NMR experiments at ambient temperature, however, show that starting with maleic acid and 2-methylfuran, endo adduct forms about twice as fast as the exo adduct. Moreover, if I is allowed to decompose in aqueous medium the endo to exo concentration ratio steadily climbs, reaching the value of about 2 after about 150 hr. Consequently, the rate of endo decomposition is about the same but formation is about twice as fast as the exo adduct. Thus a fumaric acid molecule is really formed about once per 1000 passes through the transition states leading to either formation or decomposition of Diels–Alder adducts.

Further proof that fumaric acid is only a minor product

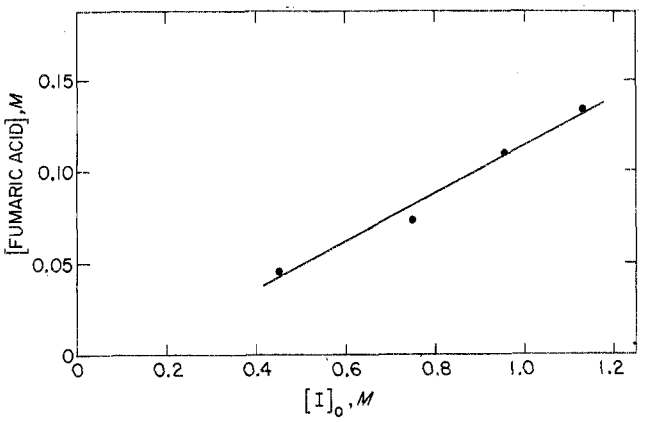


Figure 3. Fumaric acid formed from different initial concentrations of I in D_2O after 187 hr.

during apparent exo-adduct decomposition comes from direct examination of the product under conditions where the reaction is not reversible. Decomposition of I in aqueous solution at high dilution (4×10^{-5} *M*) followed by freeze drying yields maleic acid as product with no detectable fumaric acid as determined by averaging 200 NMR scans. In a control experiment, 2 l. of an aqueous solution, containing maleic and fumaric acids in a ratio of about 10:1 and a total concentration of 2.5×10^{-3} *M*, was subjected to the same isolation procedure. Fumaric acid was easily visible in an NMR spectrum of the residue in D_2O. Thus if fumaric acid were formed in the high-dilution experiment it would have been detected.

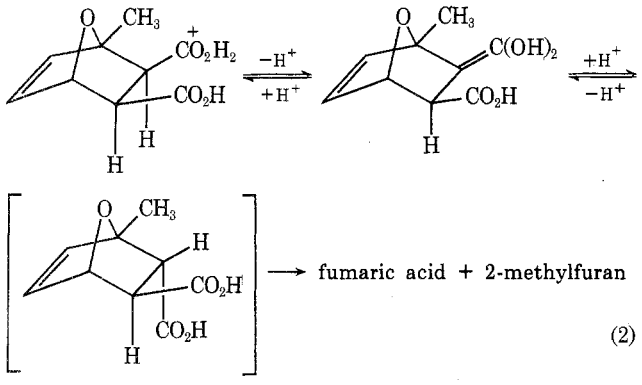
When decomposition of I is carried out in acetone-d_6 or dimethyl sulfoxide-d_6 at NMR concentrations, no fumaric acid is observed. In these solvents the equilibrium between adduct and addends lies completely to the side of addends. The first-order rate constant for disappearance of adduct in acetone-d_6 was found by NMR to be 4.8×10^{-5} sec^{-1} (22°), essentially the same as in dilute aqueous solutions. Thus the decomposition rate is about the same but the cycloaddition rate is substantially reduced in these solvents as compared to water.

The rate of appearance of fumaric acid was also examined as a function of initial exo-diacid concentration. In several parallel runs where the initial adduct concentration varied between 0.45 and 1.3 *M*, the concentrations of fumaric acid generated at various reaction times were measured by NMR. Data obtained well after the system reached pseudoequilibrium (t = 187 hr) are shown in Figure 3 and demonstrate that the rate of formation of fumaric acid is first order in exo-diacid concentration.

These results suggest two broad ways in which fumaric acid can be generated. (1) At NMR concentrations and for the period of observation (i.e., t > 100 hr) the ongoing reversible [2 + 4] cycloaddition reactions provide numerous passes through an intermediate and/or transition state. If [2 + 4] cycloaddition can be accomplished by either of two paths, one requiring a higher energy than the other, then the very large number of traverses across the lower energy path will be accompanied by a few across the higher energy path. The higher energy path could be identified with a two-step cycloaddition reaction (to be discussed below). The lower energy path is the concerted cycloaddition mechanism. (2) Alternatively, the rate of fumaric acid formation could be dependent on the product of the concentrations of free 2-methylfuran and maleic acid or in some other way on the concentration of a species, other than cycloadduct, derived from reaction of these addends. The concentration of 2-methylfuran in either phase is relatively

constant and the kinetic pattern exhibited by reactions in categories 1 and 2 would be similar, and therefore other criteria must be used to establish the genesis of fumaric acid. In the latter category reasonable mechanisms can be suggested to account for the generation of fumaric acid. These have been tested and are discussed below.

Possible Reversible Enolization. If a 0.5 *M* solution of I and its reaction products were sufficiently acidic to protonate a substantial fraction of carbonyl oxygens a reversible enolization of the adduct with concomitant isomerization could take place (eq 2).[5] Fumaric acid, obtained from



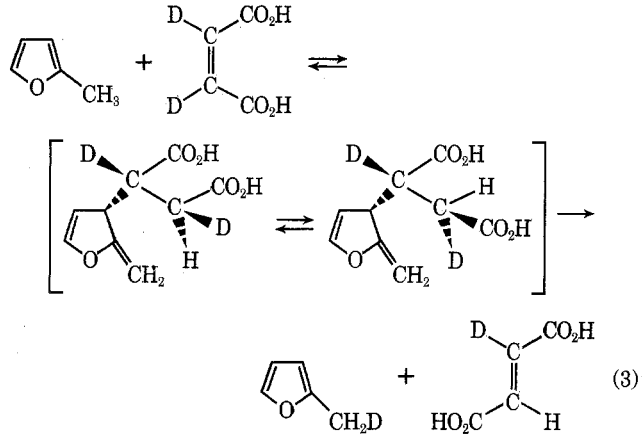
(2)

decomposition of the adduct in D_2O and then recrystallized from water, contained no excess deuterium as indicated by NMR and mass spectrometry. Thus isomerization by eq 2 is ruled out.

Catalyzed Isomerization of Maleic Acid by Reversible Radical Addition Has Been Known for Some Time.[6] This is an important path to consider, since Schenck[7] had reported previously that 2-methylfuran forms a peroxide in the presence of oxygen. Indeed, freshly distilled 2-methylfuran exposed to air quickly develops a yellow color which fails to form in the absence of oxygen. The peroxide decomposes rapidly at 70–80° and could possibly supply oxy radicals which might be effective in catalyzing cis–trans isomerization. Several experiments carried out to see if oxy radical formation is important on the time scale of fumaric acid appearance indicate that it is not. Neither the presence of *N,N,N′,N′*-tetramethylphenylenediamine in the aqueous phase nor 2,4,6-tri-*tert*-butylphenol in the 2-methylfuran phase had any effect on the ability of the reaction mixture to generate fumaric acid. Moreover, bubbling oxygen into a dimethyl sulfoxide-d_6 solution of I, allowing cycloreversion of the aqueous solution to take place in the dark, or degassing an aqueous solution of adduct prior to decomposition neither increased nor retarded the rate of fumaric acid formation. These results suggest that radicals are not responsible for the isomerization. Neither does the isomerization appear to take place in the 2-methylfuran phase.

Possible Reversible Ene Reaction. The reversible ene reaction[8] was investigated as a possible path for formation of fumaric acid. Maleic acid-*2,3*-d_2 was mixed with an excess of 2-methylfuran in D_2O. As shown for an exo arrangement of ene and eneophile in eq 3, vinyl-proton exchange would be expected for such a pathway. The fumaric acid collected after an extended reaction time was crystallized from a 250-fold excess of water. The dried fumaric acid, examined by NMR, showed no evidence of vinyl-protium incorporation.

Possible Nucleophilic Catalysis. Cis–trans isomerization of carbonyl-conjugated olefins by nucleophiles is well known.[9] To see whether the small quantity of carboxylate anion in equilibrium with I might possibly be catalyzing cis–trans isomerization of maleic acid,[5] 5,6-dihydro-I was prepared and added to an aqueous solution of maleic acid.



(3)

Use of 5,6-dihydro-I instead of I allows inspection of this type of pathway without the possibility of isomerization via reverse cycloaddition taking place. No fumaric acid could be detected by NMR, however, after a D_2O solution of maleic acid (0.38 *M*) and 5,6-dihydro-I was kept at ambient temperature for 7 days.

Conclusions

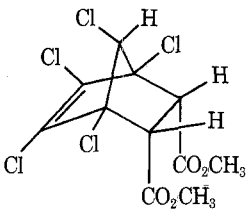
Fumaric acid formation is a minor side reaction during reversible cycloaddition of 2-methylfuran and maleic acid. For every 1000 journeys along the normal path leading to formation or decomposition of adduct, about one molecule of fumaric acid is formed. Several possible mechanisms for its formation have been tested. The results suggest that it is unlikely that carboxylate anions present, nor oxy radicals that may be formed from the expected presence of 2-methylfuran peroxide, cause maleic acid to isomerize. Neither a reversible ene reaction (eq 3) nor a reversible enolization (eq 2) appear to be responsible for the isomerization.

Fumaric acid appears to be generated in aqueous solution only when there is a substantial steady-state concentration of exo and/or endo adduct present at ambient temperature over periods of days. Adduct decomposition, of course, is a first-order reaction while cycloaddition is second order. When the initial exo-adduct concentration is low enough the cycloaddition rate is substantially reduced without affecting the cycloreversion rate; fumaric acid cannot be detected under these conditions although the reaction is carried out in water. Fumaric acid does not form in either acetone or dimethyl sulfoxide solution even when the initial concentration of exo adduct in these solvents would have been sufficient to generate fumaric acid in aqueous medium. In acetone or dimethyl sulfoxide, the adduct at these concentrations reverts completely to maleic acid and 2-methylfuran in a clean first-order reaction; the cycloaddition rate here is much reduced. Conditions which allow continuous forward and backward reactions provide an amplification of an irreversible side reaction. Several possible mechanisms have been tested and discarded. Reasonable mechanisms which remain to be considered are reversible nonconcerted [2 + 2] and [2 + 4] cycloaddition.

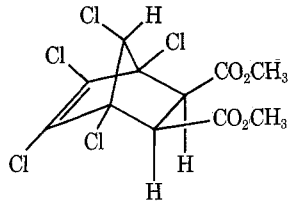
One striking observation is that fumaric acid only appears to be generated in those systems capable of supporting a substantial steady-state concentration of endo and exo [2 + 4] cycloadducts. It seems reasonable, therefore, to attribute the fumaric acid to an uncommon stepwise [$_\pi 2_s$ + $_\pi 4_s$] cycloaddition reaction. The stepwise path would be expected to require a higher activation energy than the symmetry-allowed concerted reaction. The intermediate would have a strong driving force for internal rotation provided by the steric crowding resulting from the proximity of the two carboxyls. An indication of the magnitude of this driving force is provided by the relative stabilities of cis and

trans pairs. In aqueous solution, maleic is 5 kcal/mol less stable than fumaric acid.[10]

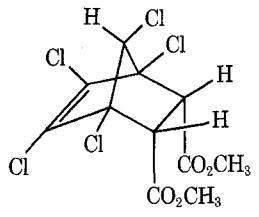
The conclusions derived from the studies of Williamson et al.[11] also suggest that *cis*-5,6-dicarboxyl groups in a bicyclo[2.2.1]-2-heptene skeleton suffer from steric crowding. Williamson and coworkers treated 1,2,3,4,5-pentachlorocyclopentadiene with dimethyl maleate and observed the formation of approximately equal quantities of IV, V, and VI,



IV

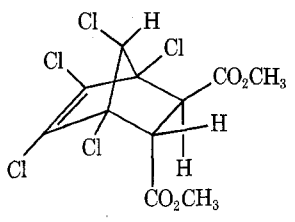


V



VI

the relative amounts presumably determined by kinetic control. The reaction of the same diene with dimethyl fumarate, however, gives a single adduct, VII. No adduct having both chlorine in the 7-anti position and an exo carbomethoxy group was detected. It is most noteworthy that when each of the four adducts was treated with sodium methoxide in methanol, VI and VII were unchanged but both IV and V yielded a product containing only VII and devoid of adduct reactant. These studies clearly demonstrate the strong driving force for the relief of steric crowding experienced by the endo-cis (IV) and exo-cis (V) 5,6-dicarbomethoxy groups.



VII

NMR spectra taken of an aqueous solution of I at successive reaction times indicates the appearance of one and only one additional adduct. The new adduct has been assigned the endo-cis configuration.[3] The spectrum which it exhibits is in agreement with coupling constants measured in similar bicyclo[2.2.1]-2-heptene systems.[12] The assignment also agrees with the ability of this compound to yield maleic acid. Therefore, for this stepwise path to be important, predominant reversion of the intermediate to fumaric acid and diene must result in spite of the expectation that formation of the second bond would result in a trans [2 + 4] adduct of greater stability than that of the cis-exo or cis-endo compound.[11] If it is assumed that the fate of every intermediate formed from stepwise addition results in internal rotation and reversion, then $\Delta\Delta G^{\ddagger}$ between concerted and stepwise [2 + 4] reaction is about 4 kcal/mol.[13]

Bartlett and coworkers[14] have shown that in the cycloaddition reactions of 1,1-dichloro-2,2-difluoroethylene to either 2,4-hexadienes or 1,4-dichloro-1,3-butadiene, recovered diene is isomerized to the extent of 3–7%. The concerted [$_{\pi}2_s + {}_{\pi}2_s$] reaction is symmetry forbidden and thus the diradical intermediate which is initially formed in the stepwise reaction can undergo internal rotation. Internal rotation competes with formation of the second bond as shown by substantial amounts of isomerized adduct along with nonisomerized product. However, another reaction competes with formation of the second bond and that is the rupture of the first bond to give recovered diene of retained and isomerized structures. In these systems formation of the second bond is three to four times faster than cleavage of the first.

If 2-methylfuran and maleic acid were able to enter into the path of [2 + 2] cycloaddition, internal rotation would be expected to compete strongly with any subsequent reaction. No [2 + 2] adduct is observed to form, however, in any of the solvents used in this study. Consequently the diradical would have to undergo bond rupture many times faster than second bond formation in order to satisfy the present observations.

Several examples of parallel [2 + 2] and [2 + 4] cycloaddition reactions progressing under one set of conditions are known.[15] In two of the systems amenable to stereochemical analysis, the results suggest that the [2 + 4] cycloadducts are formed by a concerted mechanism while the parallel [2 + 2] addition is a stepwise reaction[15c,f] and a common intermediate is ruled out.[16]

In the absence of cycloaddition products having a trans diacid structure, it is at present impossible to choose between a reversible [2 + 2] and a reversible stepwise [2 + 4] cycloaddition as the reaction responsible for generating fumaric acid.

Experimental Section

Preparation of 4-Methyl-7-oxabicyclo[2.2.1]-2-heptene-*exo-cis*-5,6-dicarboxylic Acid (I). The anhydride of the title compound was prepared as described previously.[4] Finely divided anhydride (10 g) was stirred in 50 ml of water for 2.5 hr at ambient temperature. Water was removed from the solution on a rotary evaporator at ambient temperature and the wet diacid was dried in vacuo: yield 10 g; mp 136–138° dec; NMR (D_2O, external TMS) δ 1.65 (s, 3 H), 3.06 (s, 2 H), 5.34 (d, J = 1.5 Hz, 1 H), 6.34, 6.60 (split AB quartet, J = 1.5, 5.6 Hz, 2 H).

Preparation of 4-Methyl-7-oxabicyclo[2.2.1]heptane-*exo-cis*-2,3-dicarboxylic Acid (5,6-Dihydro-I). 4-Methyl-7-oxabicyclo[2.2.1]-2-heptene-*exo-cis*-5,6-dicarboxylic acid anhydride[4] (1.74 g) in 30 ml of ethyl acetate was hydrogenated at atmospheric pressure and ambient temperature using 490 mg of 5% palladium on charcoal catalyst. Reduction was complete in about 20 min, thereby avoiding extensive reversion. The catalyst was removed by filtration whereupon the product began to precipitate out. The solution was cooled and the product was removed by filtration: NMR ($CDCl_3$) δ 1.67, 1.77 (s, m, respectively, 7 H), 3.07, 3.30 (AB quartet, J = 7.5 Hz, 2 H), 4.92 (d, J = 4.5 Hz, 1 H). The anhydride (1.1 g) was stirred with 15 ml of water at 35–50° for 1.5 hr, whereupon all the solid dissolved. The solution was concentrated in vacuo and dried in a vacuum desiccator: mp 153.6–155°; NMR (D_2O) δ 1.72 (s, 3 H), 1.97 (m, 4 H), 3.47 (s, 2 H), 5.17 (m, 1 H), 4.93 (internal HDO).

Kinetics of Decomposition of I and Formation of Fumaric Acid. Most of the kinetic studies were followed by proton NMR with a Varian A-60 instrument. Generally 1 ml of solution ranging in concentration from about 0.4 to 1.5 M in I were prepared and stored in NMR tubes. Studies were carried out in room light and in darkness, at ambient and elevated temperatures. Spectra and integrated peak areas were obtained at various times. The identifications of products (2-methylfuran, maleic and fumaric acids) peaks were made by adding authentic samples to parallel runs. Endo-cis adduct (4-methyl-7-oxabicyclo[2.2.1]-2-heptene-*endo-cis*-5,6-dicarboxylic acid) was identified by the similarity of its NMR spectrum to that of I: NMR (D_2O) δ 1.71 (s, CH_3), 3.50, 3.74 (AB quartet, H-5 and H-6, J = 10 Hz, lower half split into doublet of doublets, J = 4.6 and ~2 Hz), 5.21 (dd, J = 1.5, 4.5 Hz, H-1), ~6.35 and 6.60 (AB quartet, J = 5.5 Hz, H-2 and H-3, further splitting was obscured because of the presence of maleic acid).

Kinetics of decomposition of I were measured in a Beckman DU spectrophotometer. Solutions of I in 5% alcohol–water, ranging in concentration between 4.4×10^{-5} and 2.2×10^{-4} *M*, were prepared and the reaction was followed by measuring the optical density at 215 nm due to the appearance of maleic acid and 2-methylfuran at various times until no further increase was observed. The cell compartment was at ambient temperature (22°).

The effect of *N,N,N',N'*-tetramethyl-*p*-phenylenediamine on the rate of appearance of fumaric acid from I was measured. A solution of I (1.0 *M*) in D_2O was prepared and the kinetics of fumaric acid formation at ambient temperature were followed by NMR and compared to the observed rate when the solution also contained *N,N,N',N'*-tetramethyl-*p*-phenylenediamine dihydrochloride.

In another run 1.0 ml of a 1.0 *M* solution of I in D_2O was placed in an NMR tube together with a 1.0 *M* solution of 2,4,6-tri-*tert*-butylphenol (recrystallized twice from ethanol) in 1.0 ml of $CDCl_3$. A control contained 1.0 ml of $CDCl_3$ and 1.0 ml of a 1.0 *M* solution of I. After 6 days the layers were separated and the quantity of fumaric acid was measured in each D_2O phase.

The relative rates of endo- and exo-adduct formation from 2-methylfuran and maleic acid were measured by NMR. To 1 ml of a 1.5 *M* solution of maleic acid in D_2O, 0.5 ml of 2-methylfuran was added. NMR spectra were recorded periodically. The relative quantities of endo and exo adducts were measured by comparison of their methyl peak heights at δ 1.71 and 1.65.

Effect of 5,6-Dihydro-I on Maleic Acid. Maleic acid (30.8 mg) and 49.8 mg of 5,6-dihydro-I were mixed and dissolved in 0.7 ml of D_2O. The solution was added to an NMR tube and the tube was sealed. Spectra were recorded periodically for 7 days from the time of mixing and stored at room temperature during that time.

Product Studies with Deuterated Reactions. Maleic acid-*2,3-d*$_2$ was prepared as previously described.[18] Maleic acid-*2,3-d*$_2$ (1.0354 g, 96.4% vinyl deuteration by NMR) was dissolved in 3.0 ml of D_2O in an ampoule. To this was added 1.50 ml of freshly distilled 2-methylfuran. The ampoule was cooled, flushed with nitrogen, and sealed at atmospheric pressure. The ampoule was maintained at 56° for 16 hr. Fumaric acid crystallized upon cooling. It was dried in vacuo at 100°, yield 0.264 g (~25% conversion). The fumaric acid was recrystallized from 10 ml of boiling water and dried in vacuo at 100°. A solution of known concentration of the product fumaric acid in DMSO-d_6 was prepared and its NMR spectrum compared to that for a solution of natural fumaric acid of the same concentration. The integrals for the vinyl and carboxyl protons were compared internally and between the two solutions.

In another study 2.93 g of I was dissolved in 10 ml of D_2O in an ampoule. The system was flushed with nitrogen and sealed at atmospheric pressure. The contents were heated at 56° for 5.5 hr. Upon cooling, fumaric acid precipitated and was collected. It was recrystallized and dried as described above. The recovered fumaric acid (50.81 mg) was mixed with 43.04 mg of maleic anhydride and dissolved in 0.4 ml of DMSO-d_6. The ratio of vinyl proton peak intensities (maleic anhydride/fumaric acid) for the two compounds was found to be 1.02 as compared to 1.003 for 0% exchange.

The fumaric acid product was examined by mass spectroscopy.

Registry No.—I, 54384-22-4; 5,6-dihydro-I, 54384-23-5; 4-methyl-7-oxabicyclo[2.2.1]-2-heptene-*exo-cis*-5,6-dicarboxylic acid anhydride, 54422-97-8; 2-methylfuran, 534-22-5; maleic acid, 110-16-7; fumaric acid, 110-17-8; 4-methyl-7-oxabicyclo[2.2.1]-2-heptene-*endo-cis*-5,6-dicarboxylic acid, 54384-24-6.

References and Notes

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(13) Alternatively, a referee has suggested, [2 + 4] cycloadditions in the present system proceeds in stepwise fashion and $\Delta G^{\ddagger}$ for internal rotation in the intermediate is 4 kcal/mol larger than that for cleavage or formation of the second bond. While this scheme can also account for the kinetics, the stereochemistry of the products is more consistent with the proposition that the major reaction (99.9%) proceeds by a concerted mechanism.
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(16) (a) Concertedness is inferred from the stereochemistry of the product and is based on the assumption that internal rotation of a biradical intermediate in a stepwise [2 + 4] cycloaddition would compete effectively with formation of the second bond as it does in the [2 + 2] cycloaddition. (b) Recently Mark[17] in a communication reported that the reaction of hexachlorocyclopentadiene and several trans-disubstituted olefins led to considerable 1,2,3,4,7,7-endo-cis 5,6-disubstituted bicyclo[2.2.1]-2-heptenes. This would suggest that these [2 + 4] cycloadditions are stepwise and internal rotation occurs in the intermediate. Before this conclusion is firmly accepted, however, appropriate control experiments must be carried out to show that chlorine atoms, capable of isomerizing the dieneophile prior to cycloaddition, are absent from the system during reaction.
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