then separated, washed with water and 10% sodium bicarbonate (both precooled in ice-bath), dried over sodium sulfate and the solvent removed. The final traces of benzene were removed by azeotropic distillation with ethanol and the product crystallized directly from this latter solvent; yield 245 mg. (82%), m.p. 128–129°, $[\alpha]^{25}D$ +41.5°. The cholestanone has an infrared spectrum identical with authentic material and displayed no bands at the C–D stretching frequency. Deuterium analysis showed only the natural atom per cent. excess D.

Decomposition of Reduction Complex with D_2O.—The reduction was conducted as described above using 0.9 g. of cholestanone enol acetate and 4.2 mmoles of lithium aluminum hydride. After the solution had been stirred for one hour, 0.5 g. (25 mmoles) of D_2O (99.98%) was added and the solution allowed to stand under a nitrogen atmosphere for 10 hours. Additional anhydrous ether was added, the mixture stirred for another two hours and then centrifuged. The ether was decanted and the residue was leached twice with additional anhydrous ether. Evaporation of the filtered decantate yielded 685 mg. of solid which was dissolved in hexane and chromatographed on alumina which had been neutralized and activated.[13] After elution of the cholestanone (251 mg.), with 15% ether in hexane, a volume of this same solvent containing a few per cent. methanol was passed through the column to elute the sterols (412 mg.).[14] A second chromatograph on less active alumina[16] yielded 100 mg. of epicholestanol-2-d, m.p. 180–182°, and 286 mg. of cholestanol-2-d, m.p. 140–142°, recrystallized, m.p. 141.5–142.5°, $[\alpha]^{25}D$ +23°. Both of these steroids show the characteristic C–D stretching frequency. Deuterium analysis of the cholestanols showed 2.20 atom per cent. excess D (theory 2.08 atom per cent. excess D).

A portion of the cholestanol-2-d was oxidized to cholestanone-2-d in the same manner as described for the oxidation of cholestanol-3-d. The product, m.p. 129.5–130.0°, retained the C–D absorption band at 2060 cm.$^{-1}$ and deu-

terium analysis shows a 2.28 atom per cent. excess D. A sample of this ketone was dissolved in hexane and passed onto a column of basic alumina.[16] After a quantity of hexane saturated with water had been passed through the column, the cholestanone was eluted with 15% ether in hexane. This ketone, as directly eluted, had a m.p. 126–128° and no longer showed any absorption in the C–D stretching frequency region. Deuterium analysis showed only the natural atom per cent. excess D.

Reduction of Cholestenone Enol Acetate with Varying Amounts of Lithium Aluminum Hydride.—The experiments were performed at 25° in a manner described previously for an inverse reduction.[2] The only significant difference was that saturated sodium potassium tartrate solution was employed to decompose the reduction complex in place of dilute mineral acid. Considerable attention was given to the maintenance of anhydrous conditions, to the employment of scrupulously dried equipment and to the standardization of the hydride solutions used. The stock hydride solution was prepared, stored and standardized both by titration and hydrogen evolution before each run. All equipment was dried at 100° in a vacuum oven immediately prior to use and the cholestenone enol acetate dried at room temperature for 10 hours at 10^{-5} mm. All experiments were performed with 0.500 g. of ester in 10 ml. of anhydrous ether. The reaction products were separated by chromatography in the usual manner on alumina. The results are listed in Table I.

Attempted Reduction of Cholestenone Enolate Ion.—To 50 ml. of dry butyl ether there was added, in turn, 0.45 ml. (4.4 mmoles) of freshly distilled diethylamine, 3.3 mmoles of phenyllithium in 4.6 ml. ethereal solution and after three hours, 0.80 g. (2.1 mmoles) of cholestenone. The mixture was stirred for four hours at room temperature in a nitrogen atmosphere and was then heated on a steam-bath and approximately 10 ml. of solvent was removed under reduced pressure.

A solution of 5 mmoles of lithium aluminum hydride in 3.5 ml. of ethyl ether was added to the butyl ether solution and the mixture stirred overnight at room temperature. After decomposition of the reduction complex, the mixture was processed in the standard fashion. There was obtained, 248 mg. (34%) of cholestenone, m.p. 76–78°; 325 mg. (45%) of mixed Δ^4-cholesten-3-ols, m.p. 125–138°; 127 mg. (17%) of Δ^4-cholesten-3β-ol, m.p. 131–133°.

(13) C. W. Shoppee and G. H. R. Summers, *J. Chem. Soc.*, 687 (1950).

(14) The alumina employed for this chromatograph was sufficiently active to prevent ready elution of hydroxylated material by the ordinary solvents, ether and hexane. While the sterols were absorbed on this very active alumina, the solution containing methanol was passed through the column in order to "wash off" any deuterium from the oxygen of the alcohol. Elution in this manner did not give a satisfactory separation of the sterols so it was necessary to perform a second chromatograph on less active alumina in order to separate the epimers.

(15) Merck, Aluminum Oxide Reagent, suitable for chromatographic adsorption.

(16) Fisher, Alumina Adsorption. This alumina had previously been shown to have sufficient basic strength to cause the hydrolysis of cholesteryl acetate during normal chromatographic procedures.

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The Stereochemistry of the Furan–Maleic Acid Reaction[1]

BY JEROME A. BERSON AND RONALD SWIDLER

The reaction of furan with maleic acid in water is shown to be stereochemically heterogeneous. *endo*-Addition is kinetically favored but the *endo*-adduct gradually isomerizes to the more stable *exo*-adduct. A method is described for analysis of the diene reaction mixtures. The free energy change for isomerization of *endo* to *exo*-adduct is estimated to be not more than −1.2 kcal./mole. A discussion is given of the possible origins of energy differences in *endo*- and *exo*-isomers of 2,2,1-bicycloheptane derivatives.

The general occurrence of *endo*-stereospecificity in the products of diene additions investigated in a series of early studies was summarized in the well-known Alder rule.[2] Further investgations,[3–5] stimulated by the brief report[2] that the diene additions of fulvenes were stereochemically non-

(1) This work reported here will form a portion of the thesis to be submitted by Ronald Swidler in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) K. Adler and G. Stein, *Angew. Chem.*, **50**, 514 (1937).

(3) R. B. Woodward and H. Baer, THIS JOURNAL, **66**, 645 (1944).

(4) K. Alder, F. W. Chambers and W. Trimborn, *Ann.*, **566**, 27 (1950).

(5) K. Alder and R. Ruhmann, *ibid.*, **566**, 1 (1950).

homogeneous, brought to light the dependence of the steric outcome of these additions upon the reaction conditions, the *endo*-adduct being formed more rapidly but giving way at longer reaction times or higher temperatures to the thermodynamically-favored *exo*-isomer. The reaction of furan with maleimide[6] now seems to conform to this energetic scheme, and even in the difficultly mobile cyclopentadiene–maleic anhydride *endo–exo* adduct equilibrium,[7] the same kinetic order and relative

(6) H. Kwart and I. Burchuk, THIS JOURNAL, **74**, 3094 (1952).

(7) D. Craig, *ibid.*, **73**, 4889 (1951).

thermodynamic stabilities are maintained. However, the literature pertaining to the additions of furan to maleic acid and maleic anhydride affords no such detailed clarification of the factors controlling the stereochemistry of the product. The present communication reports results which place the furan–maleic acid addition in the customary energetic pattern.

Furan was observed to dissolve slowly when agitated for several days with an aqueous solution of maleic acid.[8] Although the expected adduct (I) was not isolated from the reaction mixture, bromination of the aqueous solution afforded a nearly quantitative yield ("crude") of the bromolactonic acid IIa. By contrast, the reaction of
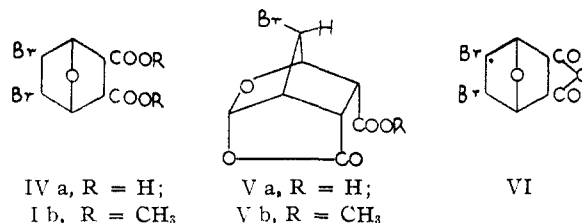
I   II a, R = H; II b, R = CH₃
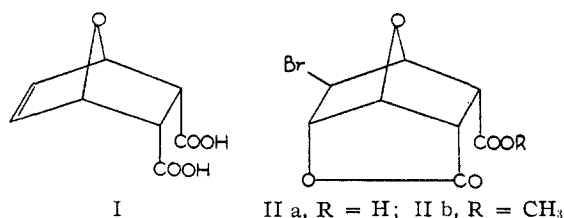
furan with maleic anhydride in ether[9] produced an excellent yield of an adduct which was subsequently shown[10] to be exo-cis-3,6-endoxo-Δ⁴-tetrahydrophthalic anhydride (III).[11] In an attempt to

III
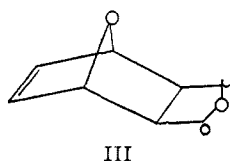
establish the origin of this unique stereochemical result, we have reinvestigated the furan–maleic acid addition. Contrary to the previous implication,[8] the reaction is not stereochemically homogeneous.

Analysis of the Reaction Mixtures.—The ease with which both the endo- and exo-adducts of furan and maleic acid dissociate[9,10] places severe limitations upon attempts to isolate the substances themselves. Accordingly, we have sought to isolate them as stable derivatives. Since saturation of the olefinic bond of the adducts renders them incapable of diene retrogression, our first analytical efforts involved attempts to fractionate the crude product resulting from direct bromination of the diene addition reaction mixture. The initial crystalline material which precipitated upon bromination consisted largely of crude endo-bromolactonic acid (IIa). The mother liquors deposited a mixture of IIa and an exo-dibromoacid (IVa) which was identical with the substance previously described by Woodward and Baer[10] in their elegant investigation of the bromination products of III. (The rearranged exo-bromolactonic acid (Va)[10]

(8) O. Diels and K. Alder, Ann., **490**, 243 (1931).

(9) O. Diels and K. Alder, Ber., **62**, 557 (1929).

(10) R. B. Woodward and H. Baer, THIS JOURNAL, **70**, 1161 (1948).

(11) The difference in the stereochemical courses of these two additions has been attributed to a solvent dependence.[6,12]

(12) R. C. Elderfield and T. N. Dodd, Jr., in "Heterocyclic Compounds," edited by R. C. Elderfield, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 139.

IV a, R = H;   V a, R = H;   VI
I b, R = CH₃   V b, R = CH₃

was not isolated in this procedure.) Separation of IIa and IVa was facilitated by the discovery that the sodium salt of IVa is virtually insoluble in water. The exo-stereochemistry of IVa was confirmed by its independent synthesis from III. Bromination of III in methylene chloride produced the dibromo anhydride VI, hydrolysis of which afforded IVa. VI was regenerated from IVa by treatment with acetic anhydride or by pyrolysis.

Although the stereochemical heterogeneity of the diene addition was thus unequivocally established, this fractionation procedure was found inconvenient for the determination of the relative proportions of the isomers, since purification of the first crop of crude IIa was achieved only with severe losses of material.

A successful fractionation was finally based upon the observation that addition of slightly less than one equivalent of sodium bicarbonate to the reaction mixture before bromination caused the preferential precipitation of a considerable proportion of the exo-adduct (VII) as well as unreacted maleic acid in the form of a mixture (A) of sodium salts. Hydrogenation of the aqueous mother

VII   VIIIa   VIIIb
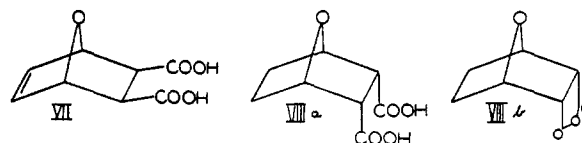
liquors (B) from the salt precipitation afforded the saturated endo-adduct (VIIIa), identified as the corresponding anhydride (VIIIb) in small yield. Hydrogenation of (A) yielded succinic acid but no saturated exo-adduct could be isolated.

However, bromination of (A) produced virtually pure exo-bromolactonic acid (Va). It is of interest that, in contrast to the procedure (vide supra) employing direct bromination of the reaction mixture, bromination of the sodium salts (A) produced little or no dibromoacid (IVa).[13] Bromination of the mother liquors (B) produced mainly IIa admixed with small quantities of Va. Purification of IIa was accomplished by fractionation from 90% methanol. The course of purification was readily followed, since the presence of even a small quantity of Va in solid samples of IIa is sufficient to cause darkening upon fusion. Accordingly, fractionation was continued until the material melted to a colorless liquid. An additional quantity of endo-derived material was obtained by esterifying the combined tail fractions and fractionating the mixed methyl esters (IIb and Vb).

(13) In most of the runs, IVa could not be isolated (via its sodium salt). Only in runs in which the exo-adduct concentration was high did IVa appear at all, and then only in quantities never exceeding 0.005 mole per mole of Va.

Although IIb was obtained in pure form, a small tail fraction (C) consisting of an inseparable mixture of esters always remained. This mixture remained almost constant in weight and melting point throughout several runs regardless of the relative amounts of *exo-* and *endo*-derived material obtained in the first part of the separation scheme.[14]

Results and Discussion.—The gravimetric values for product composition as a function of time are given in Table I and the results are shown graphically in Fig. 1. The somewhat greater scattering of the points in the initial portion of the curve (up to 72 hours) is presumably attributable to the less efficient thermostating used during the period when the reaction mixture is heterogeneous (see the second paragraph of the Experimental section). The total yields of isolated products as a function of time are plotted in Fig. 2. Although some irreversible destruction of furan (by hydrolysis in the acidic medium and self-condensation of the hydrolysis products) undoubtedly occurs as evidenced by the darkening of the reaction mixtures and by the observed presence of carbonyl bodies, this process must be slow compared to diene additions and retrogressions of the adducts, since Fig. 2 shows no downward drift in total yield over a period greater than one-third of the total reaction time examined.

TABLE I[a]

PRODUCT COMPOSITION IN THE FURAN–MALEIC ACID REACTION

Time, hours	exo,[b] mole Va	endo,[c] mole IIa and IIb	Total yield,[d] %
23	...	0.061	30
32	...	.066	32
48	0.018	.068	42
55	. .021	.075	47
72	.025	.080	51
91	.038	.079	57
105	.051	.078	63
118	.061	.072	65
165	.076	.067	70
213	.092	.054	71
285	.101	.045	70

[a] All runs were at $27.5 \pm 0.7°$ to 72 hours, at $27.5 \pm 0.1°$ afterwards. Values are for single determinations. From preliminary duplicate runs, the reproducibility of a given value in moles was estimated at ± 0.001 mole; reagents: furan, 0.205 mole; maleic acid, 0.306 mole. [b] The weight of IVa was neglected. [c] The weight of IIa was corrected for hydrate water. [d] Pure products only. The methyl ester tail fraction (C) was neglected.

The variation of product composition with time (Fig. 1) unambiguously establishes the furan–maleic acid reaction in the typical kinetic-energetic pattern. *endo*-Addition is the rate-favored process but the *endo*-adduct is thermodynamically unstable with respect to the *exo*-adduct which gradually accumulates at its expense.

Two kinetically discrete sets of processes have been proposed to account for the isomerization of

(14) This may be due, at least in part, to the apparent ability of IIb and Vb to form a crystal compound. A melting point vs. composition diagram of synthetic mixtures of IIb and Vb showed a maximum in the region of ca. 40% of Vb. However, since Vb decomposes upon fusion, the observed melting points are somewhat dependent upon the rate of heating and the curve has not been reproduced here.
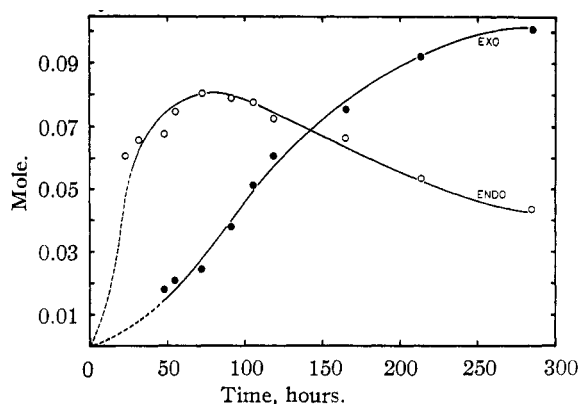

Fig. 1.—Variation of product composition with time in the furan–maleic acid reaction.
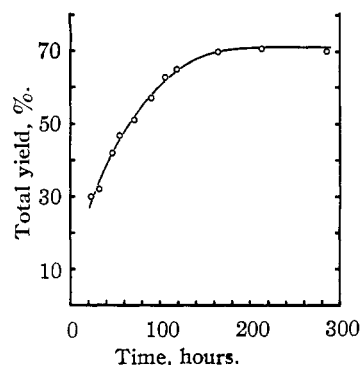

Fig. 2.—Variation of total yield with time.

endo-diene adducts to *exo*-isomers. The first of these, proposed[3,15] for the interconversion of the stereoisomeric adducts in the fulvene series, considers that the isomerization occurs by dissociation of the *endo*-adduct to the addends which then recombine at a slower rate to give the relatively stable *exo*-adduct. The process is summarized in equation (1). Craig[16] has proposed an alternate mechanism to account for certain phenomena in the

$$exo\text{-adduct} \rightleftharpoons \text{addends} \rightleftharpoons endo\text{-adduct} \quad (1)$$
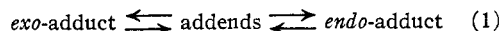
interconversion of the cyclopentadiene–maleic anhydride adducts (IXa and b). This author suggests that the *endo*-adduct (IXa) is isomerized to

the *exo*-adduct (IXb) directly through some non-isolable intermediate without prior dissociation to the addends. While certain details of the intimate mechanism of this process suggested by Craig appear implausible to us on energetic grounds, the general nature of the scheme, summarized in equation (2) is not refuted by any data now available in the literature. If both *endo-* and *exo-*

$$\text{addends} \rightleftharpoons endo\text{-adduct} \rightleftharpoons exo\text{-adduct} \quad (2)$$
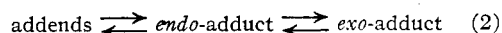
adducts are formed directly from addends in simultaneous, competing reactions (equation 1), the

(15) K. Alder and W. Trimborn, Ann., **566**, 58 (1950).

(16) D. Craig, THIS JOURNAL, **73**, 4889 (1951).

slopes (dc_{endo}/dt and dc_{exo}/dt) of the adduct formed vs. time plots for the two isomers should have maximum values when the addend concentration is highest, i.e., at the beginning of the reaction. This follows from the rate expression (assuming second-order kinetics), $dc/dt = k[\text{furan}][\text{maleic acid}]$. If the situation is represented by equation (2), however, dc_{endo}/dt will have a maximum value at the onset of reaction, but dc_{exo}/dt will gradually increase and will reach its maximum value at a time corresponding to or following the time at which the concentration of endo-adduct is at a maximum. Inspection of Fig. 1 reveals that dc_{exo}/dt gradually increases with time and that an inflection occurs in the general neighborhood of the maximum endo-adduct concentration. While this result seems to provide support for a set of processes governed by equation (2), it must be emphasized that the non-availability of the endo-adduct per se[10] has prevented a test of our analytical scheme upon synthetic mixtures of known composition. Therefore, the possibility exists that serious preferential manipulative losses of exo-material at low exo-adduct concentrations are to blame for the apparent shape of the curve. A decision between the mechanisms represented by equations (1) and (2) cannot, therefore, be made on the basis of the present data.

In order to make an approximate evaluation of the equilibrium constant for the reaction endo ⇌ exo in the present case, we have allowed the pure exo-adduct (VII) to stand in solution at room temperature for varying lengths of time. An appropriate quantity of excess maleic acid was added to the reaction mixtures so that the analytical conditions would simulate those existing in the diene addition runs, and the reaction mixtures were analyzed by the scheme described above. The gravimetric values are indicated in Table II and plotted in Fig. 3. The recovery of only 88% of exo-material even when no endo-product could be isolated probably represents the limit of accuracy of the method at high exo-adduct concentrations, although a part of the unrecovered 12% of material may be in the form of addends generated by retrogression. The small decrease in total recovery from 261 to 1304 hours probably is attributable to some irreversible destruction of furan. (The reaction mixture becomes quite dark after prolonged standing.) While the final figures of Table

II (1304 hour run) probably do not represent the true equilibrium ratio, it is clear that the experimental equilibrium value lies somewhere between these figures and those of the 285 hour run of Table I. That the concentration changes after 1304 hours of equilibration are very slow is indicated by the shallow slope of the curves of Fig. 3. The failure to achieve quantitative material balance in the equilibration runs prevents, of course, the accurate estimation of the equilibrium constant for the isomerization, $K_i = [exo]/[endo]$. However, a maximum value of K_i is obtainable by assuming the unrecovered material at 1304 hours to be of exo-origin. This gives a value for K_i of $0.181/0.024 = 7.55$, a figure which can only be diminished by a closer approach to equilibrium than was achieved after 1304 hours. From the relationship $\Delta F_i = -RT \ln K_i$, the free energy change for the interconversion in water at 28° cannot be larger than ca. -1.2 kcal./mole.

TABLE II[a]

EQUILIBRATION OF exo-cis-3,6-ENDOXO-Δ^4-TETRAHYDRO-PHTHALIC ACID (VII) IN AQUEOUS MALEIC ACID AT 28°

Time, hours	exo, mole Va	endo, mole IIa and IIb	Total yield, %
20	0.180	...	88
261	.135	0.013	72
1304	.114	.024	67

[a] Reagents: exo-adduct (VII), 0.205 mole (prepared from 0.205 mole of III); maleic acid, 0.100 mole (prepared from 0.100 mole of maleic anhydride); water 75 cc.

On the basis of available information[3-7,17] it seems likely that the energy differences in previously observed pairs of endo-exo isomers are not very much greater than the maximum value of 1.2 kcal./mole observed in the present case. It is striking that, despite the small differences in energy, the thermodynamic stability order (exo > endo) persists in all the cases studied so far. The reasons for this are not immediately apparent. A qualitative estimate of the stability relationship in the case of the completely saturated pair of isomers derived from dicyclopentadiene (Xa and Xb) may be made on the basis of the non-bonded interaction effects believed[18-21] to operate in alicyclic and paraffinic hydrocarbon derivatives. The "boat" form of cyclohexane (XI) may be considered as the simple prototype of Xa and Xb. In XI, by the conformational criteria developed[18] for the cases of methylcyclohexane and the dimethylcyclohexanes, the energy of interaction of an equatorial (e) methyl group at C_2 or C_3 with a polar (p) methyl group at C_1 or C_4, respectively, will be equivalent to that of a p-methyl group at C_2 or C_3 with a p-hydrogen at C_6 or C_5, respectively. It seems reasonable to suppose that the same relationship would hold for the methylene–methylene interaction as compared to methylene–hydrogen with the exception that the actual values of the energy for each such interaction will be slightly smaller than
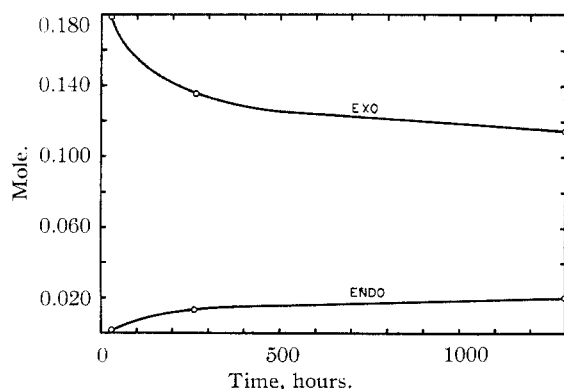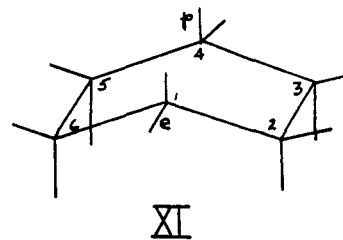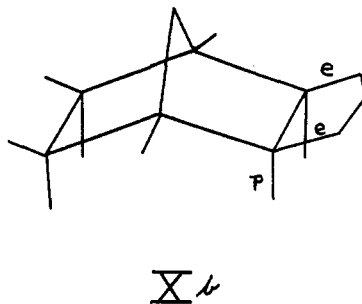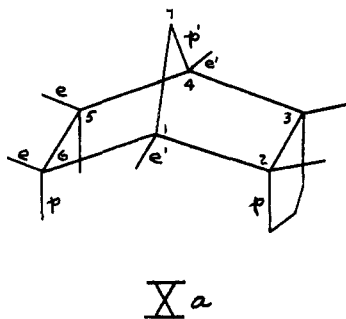
(17) K. Alder and G. Stein, Ber., 67, 613 (1934).

(18) C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, 69, 2488 (1947).

(19) C. W. Beckett, N. K. Freeman and K. S. Pitzer, ibid., 70, 4227 (1948).

(20) O. Hassel and B. Ottar, Acta Chem. Scand., 1, 929 (1947).

(21) D. H. R. Barton, Experientia, 6, 316 (1950).

Fig. 3.—Equilibration of VII.

Xa   Xb   XI

the value of 0.9 kcal. suggested[18] for the methyl–methyl and methyl–hydrogen cases. However, in Xa and Xb the substituents at C_1 and C_4 no longer have the true polar conformation but are displaced to a distorted conformation which we have designated p'. A group in the p'-conformation (C_7) is further away from an e-substituent at C_2 or C_3 than is the case with a group in the p-conformation and therefore the non-bonded interaction will be less.[22] On the other hand, interaction effects between p-substituents at C_2 or C_3 with p-hydrogens at C_6 or C_5, respectively, would be expected to retain their normal values. Assuming (i) that the distortion introduced by the endomethylene bridge has the maximum conceivable effect and completely eliminates two sources of non-bonded interaction between exo-C_2 and C_3 substituents and the bridge methylene group, (ii) that each interaction contributes a maximum of 0.9 kcal. of "Pitzer-strain," and (iii) that the only source of difference in heat content between Xa and Xb is "Pitzer-strain," then we may estimate the maximum difference in heat content for this pair of endo–exo isomers to be not greater than 1.8 kcal./mole.[23]

While similar conformational considerations apply to diene adducts themselves, the argument requires modification with respect to several new factors which are not yet capable of easy evaluation. Thus, in a diene adduct such as IXa, the π-orbitals of the olefinic bond and of the carbonyl groups are directed toward each other. Whether this will result in a mutual net attraction (through dispersion forces, for example) or repulsion of the groups seems difficult to assess. Further, the occurrence of strong dipole effects arising from the presence of polar substituents, solvation effects and intramolecular hydrogen-bonding (particularly in a case such as the furan–maleic acid adducts) may take energetic contributions of far greater magnitude than the non-bonded interactions. It seems entirely conceivable that, under the proper circumstances, these and other effects may supplement or oppose each other so that the energy differences between endo- and exo-isomers will be greater than have previously been observed or, conversely, so that there may be a reversal of the stability order.

(22) The e'-hydrogens are correspondingly closer to e-substituents at C_2 or C_3. This interaction is neglected.

(23) The argument applies strictly only to heat content. The comparable rigidity and symmetry of a pair of endo–exo-isomers, however, justifies the omission of entropy considerations (cf. ref. 3) and we therefore have assumed in the sequel that *free energy* values (derivable from equilibrium data) will be affected to a similar extent.

Experimental[24]

Reaction of Furan with Maleic Acid.—The reaction vessels were stout 150-cc. ground-glass stoppered bottles of uniform dimensions. Maleic acid was prepared by dissolving the necessary quantity (30.0 g., 0.306 mole) of freshly recrystallized maleic anhydride in 75 cc. of water in each reaction vessel. The contents were chilled to −5° and to each bottle was added 15.0 cc. (0.205 mole) of redistilled furan (du Pont). The bottles were sealed by heavily tapping the stoppers and dipping the heads of the vessels into molten paraffin.

The bottles were shaken in a constant temperature room at 27.5 ± 0.7° on a mechanical shaker. The furan slowly dissolved and apparent homogeneity was achieved after about 72 hours, whereupon the bottles were transferred to a thermostat at 27.5 ± 0.1°.

exo-Bromolactonic Acid (Va).—Each reaction mixture was worked up as follows: The bottle was chilled to 0°, opened and the contents diluted to 125 cc. with water. The solution was treated at 0° with 22.6 g. of solid sodium bicarbonate (added in portions during 10 minutes). The colorless precipitate (A) was collected at the pump and washed with two 25-cc. portions of ice-water. The filtrate (B) was preserved for the subsequent isolation of IIa. The salt (A) was suspended in 125 cc. of water, the mixture chilled to 5°, and bromine was added until a faint yellow color persisted. The reaction mixture was made strongly acidic with concentrated hydrochloric acid and treated with solid sodium bisulfite to decompose the excess bromine. The product was collected at the pump, redissolved in 10% potassium carbonate, reprecipitated with concentrated hydrochloric acid, collected and dried *in vacuo* to constant weight over calcium chloride. This material melted sharply at 158° with violent decomposition when it was slowly heated (0.5° per minute) after insertion into a bath at 140°, [reported[10] m.p. 153° (dec.)]. Its infrared spectrum was identical with that of an authentic specimen prepared by the method of Woodward and Baer.[10] There was no change in melting point or infrared spectrum upon recrystallization from water. In the runs at longer reaction times, trace amounts of the dibromoacid (IVa) were isolated from the mother liquors by the sodium salt precipitation technique (*vide infra*). For example, in a run in which 28.5 g. of Va was obtained, 0.25 g. of IVa was isolated.

endo-Bromolactonic Acid (IIa).—The filtrate (B) from the bicarbonate precipitation was treated with 10 g. of solid sodium bicarbonate, chilled to 5°, swirled and treated with bromine until the color of excess bromine persisted. The clear solution was slowly acidified with concentrated hydrochloric acid, the excess bromine decomposed with solid sodium bisulfite, and the mixture cooled to 0°. The precipitate of crude *endo*-bromolactonic acid (IIa) was collected at the pump and dried *in vacuo* over calcium chloride for 48 hours. This material melted at 200–204° with pre-darkening and extensive decomposition. Recrystallization from 90% methanol, and then from water, gave glittering, bold staves, melting at 207–209° to a colorless liquid, reported[8] m.p. 205°. The melting point was unchanged by further recrystallization. This material was dried to constant weight over calcium chloride *in vacuo*.

(24) Melting points are corrected. The infrared spectra were determined in Nujol mulls with a Baird Associates Recording spectrometer. We are grateful to Dr. H. L. Holmes and his associates of Riker Laboratories, Inc., for the measurement of the spectra. The microanalyses were performed by Mr. Joseph Pirie.

endo-**Bromolactonic Ester (IIb).**—The methanol mother liquor from the purification of IIa was evaporated in a current of dry air and the solid residue dried *in vacuo* over calcium chloride and potassium hydroxide. The dried product was taken up in 100 cc. of absolute methanol, decolorized with charcoal, filtered, treated with 2 cc. of 30% fuming sulfuric acid and heated at reflux for two to three hours. The mixture was cooled to 0°, the solid ester collected at the pump and recrystallized from absolute methanol to constant melting point. The pure ester was obtained as glistening, micaceous platelets, m.p. 176–177°, reported[8] m.p. 175°.

Evaporation of the methanolic mother liquors left a small residue melting at 150–155°. Attempts to obtain pure material by fractional crystallization from a variety of solvents were generally unsuccessful.

Direct Bromination Procedure.—If the diene addition reaction mixture was brominated directly, without prior addition of sodium bicarbonate, crude IIa separated from solution as a white precipitate, melting over a range from *ca.* 180–200°. Recrystallization from water produced pure material but was attended by severe losses. Thus, in a typical run, from 32 g. of crude precipitate was obtained 9.5 g. of pure IIa.

The bromination mother liquors were cooled to 0° for 24 hours and the second crop of crystals collected. These usually melted at 141–148° with decomposition. The solid was triturated with 10% sodium bicarbonate and filtered. Acidification of the basic mother liquor produced a small additional quantity of IIa. The bicarbonate-insoluble filter cake was warmed with concentrated hydrochloric acid and the resultant solution, upon being cooled, deposited shining, transparent laths of the dibromoacid (IVa) **hydrate**, m.p. 163–164°. (The m.p. seems to depend on the rate of heating; occasionally a m.p. of 159–160° was observed; reported[10] m.p. 155°.) A mixed m.p. with material prepared by the method of Woodward and Baer[10] was not depressed. No Va was isolated. Recrystallization of IVa from a minimum quantity of water failed to change the melting point. The analytical sample was dried at room temperature for eight hours at 3 mm. over phosphorus pentoxide.

Anal. Calcd. for $C_8H_8O_5Br_2 \cdot H_2O$: C, 26.54; H, 2.98; Br, 44.15. Found: C, 26.92; H, 2.96; Br, 43.89.

After drying for four hours at 100° and 3 mm. over P_2O_5, the crystals became opaque, m.p. 163–164°.

Anal. Calcd. for $C_8H_8O_5Br_2$: C, 27.93; H, 2.34. Found: C, 27.79; H, 2.46.

The acid (IVa) dissolved readily in concentrated aqueous ammonia. When this solution was treated with saturated sodium chloride solution, the sodium salt of IVa precipitated immediately. Treatment of the solid salt with hydrochloric acid regenerated IVa.

The dimethyl ester (IVb) melted at 114.5–115.5°, reported[10] m.p. 115.9–116.3°.

Dibromoanhydride (VI). A.—To a solution of 16.8 g. of the furan–maleic anhydride adduct (III)[9] in 400 cc. of dry, freshly distilled methylene chloride was added 5.2 cc. of bromine in one portion. The reaction mixture was kept at room temperature for four hours, after which time the color of the bromine had disappeared. The crystalline precipitate (10.0 g.), m.p. 331°,[25] was filtered off and the mother liquor evaporated to dryness. The residue weighed 22.1 g. and melted at 157–160°. Recrystallization from chloroform–acetone afforded 18.6 g. of silky, clustered blades, m.p. 159–160°. The analytical sample, m.p. 162–163°, was recrystallized from carbon tetrachloride–acetone.

Anal. Calcd. for $C_8H_6O_4Br_2$: C, 29.48; H, 1.86. Found: C, 29.56; H, 1.96.

Hydrolysis of the anhydride in boiling water produced the dibromoacid (IVa), m.p. 163–164° alone or mixed with a sample prepared as above or by the method of Woodward and Baer.[10]

B.—A mixture of 3.5 g. of IVa in 15 cc. of acetic anhydride was heated at reflux for one hour. The reaction mixture was diluted with 20 cc. of chloroform, evaporated to 15 cc. volume, treated with an additional 20 cc. of chloroform, filtered hot and allowed to cool. The product (0.9 g.) had m.p. 161.5–162.5° alone or mixed with a sample of VI prepared by method A.

C.—Two grams of IVa was heated above its melting point for ten minutes. The pyrolysis residue was sublimed at a

pressure of 1 mm. and a bath temperature of 165° to yield 1.7 g. of VI, m.p. and mixed m.p. 159–161°.

Hydrogenation of Diene Addition Reaction Mixtures.—The reaction mixture was subjected to preliminary fractionation with sodium bicarbonate (*vide supra*). The mother liquor (B) was hydrogenated over 0.5 g. of palladized barium sulfate (10%) at an initial pressure of 35 lb./sq. in. After about 0.03 mole of gas had been consumed, 0.1 g. of platinum oxide was added and hydrogenation was continued until the total consumption of gas amounted to 0.144 mole whereupon the reaction ceased spontaneously. The solution was filtered, acidified with concentrated hydrochloric acid and cooled. The precipitated solid was heated above its melting point for ten minutes and recrystallized from acetic anhydride–Skellysolve B to yield 2.5 g.of the *endo-cis*-anhydride (VIIIb), m.p. 158–160°, reported[26,27] m.p. 158–159°.

Hydrogenation of the sodium salt precipitate (A) from the bicarbonate fractionation in aqueous suspension over platinum oxide yielded succinic acid as the only isolable product.

Epimerization of the *endo*-Bromolactonic Acid (IIa).—The procedure of Diels and Alder[8] for epimerizing IIa was found to be inconvenient. We have prepared the epimeric acid (XII) by a new method. A mixture of 10 g. of IIa
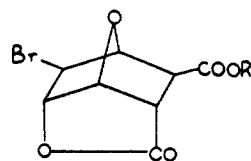

XII a; R = H; XII b; R = CH₃

and 50 cc. of acetic anhydride was heated at reflux for 15 minutes. The clear solution was then concentrated by distillation until the vapor temperature reached 136°. Acetic anhydride was added to restore the volume to 50 cc. The solution was then heated at reflux an additional 30 minutes, and the concentration and dilution procedure repeated. After an additional four-hour period of boiling, the solution was concentrated to half its volume, treated with 75 cc. of water to decompose the acetic anhydride and allowed to cool. The epimerized acid (XIIa) separated as 7.2 g. of white needles, m.p. 236–238°, reported[8] m.p. 231–232°.

The methyl ester (XIIb) had m.p. 170–171°, reported[8] m.p. 167–168°.

Application of this epimerization procedure to the methyl ester of the *endo*-bromolactonic acid (IIb) resulted in recovery of 88% of unchanged starting material.

endo-**Dilactone (XIII).**—The procedure used for preparation of this substance was based upon the one used by Alder and Stein[28] for the preparation of the analogous dilactone (XIV) from the *endo*-adduct of cyclopentadiene with maleic anhydride. To a solution of 3.9 g. of potassium hydroxide
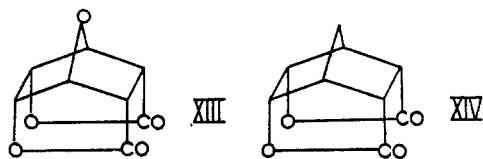
in 50 cc. of methanol was added 5.2 g. of IIa. The mixture was heated to reflux and a colorless precipitate appeared. After two hours, water was added to dissolve the precipitated salt, and the solution was neutralized to congo red with concentrated hydrochloric acid. The solution was evaporated to dryness and the residue heated on the steam-bath with 50 cc. of acetic anhydride. The reaction mixture was filtered from the insoluble inorganic residue and allowed to cool. The dilactone (XIII) crystallized as 0.75 g. of stout, sharply defined rhombohedra, m.p. 261.5–265.5°. Recrystallization from acetone–methanol raised the m.p. to 269.5°. The substance is insoluble in cold 10% potassium carbonate.

Anal. Calcd. for $C_8H_6O_5$: C, 52.75; H, 3.32. Found: C, 52.49; H, 3.28.

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(25) This substance is isomeric with VI. Its nature is now being investigated.

(26) K. Alder and K. H. Backendorf, *Ann.*, **535**, 113 (1938).

(27) *Cf.* reference 10 for the correct configurational assignment.

(28) K. Alder and G. Stein, *Ann.*, **514**, 1 (1934).