The Mechanism of Azo Ester Addition–Abstraction Reactions with Cyclic Dienes

BORIS FRANZUS

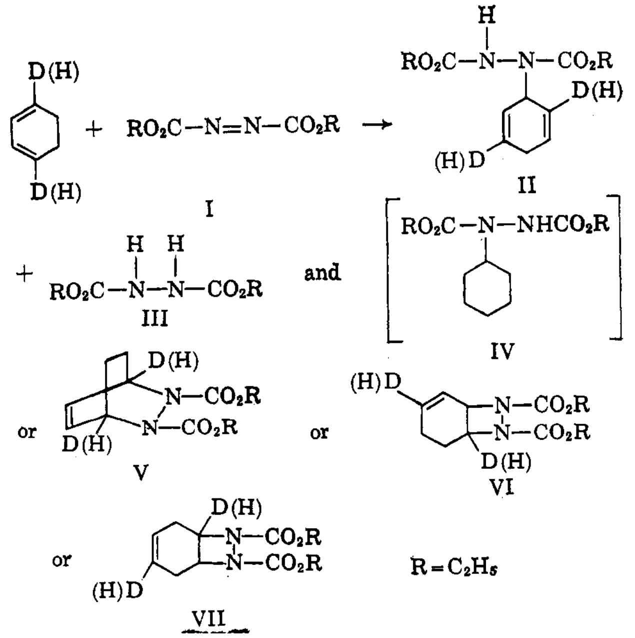
Central Basic Research Laboratory, Esso Research and Engineering Company, Linden, New Jersey

Received April 8, 1963

The structures of the Diels–Alder adduct and the addition–abstraction product from 1,4-dideuterio-1,3-cyclohexadiene and ethyl azodicarboxylate indicate that the formation of these compounds proceeds by entirely different paths. Lack of isomerization of both reactants and products and lack of deuterium exchange (in CH_3OD) for both reactants and products are consistent with a concerted cyclic process. These results are consistent with the energetics of the adduction reaction. Thus, the entropy of activation for the reaction of 1,3-cyclohexadiene and ethyl azodicarboxylate is −40.7 e.u., and it is −31.8 e.u. for ethyl azodicarboxylate and 1,4-cyclohexadiene. This high negative entropy of activation is consistent with a concerted process.

The reactions of ethyl azodicarboxylate with 1,3- and 1,4-cyclohexadienes[1a] and with sterically hindered conjugated dienes[1b] appear to proceed *via* an addition–abstraction mechanism. In order to verify the reaction path and to search more critically for the Diels–Alder adduct reported by both Cohen and Zand[2a] and Pirsch and Jorgl,[2b] an investigation on the mechanism of the reaction of ethyl azodicarboxylate with 1,3- and 1,4-cyclohexadienes was initiated.

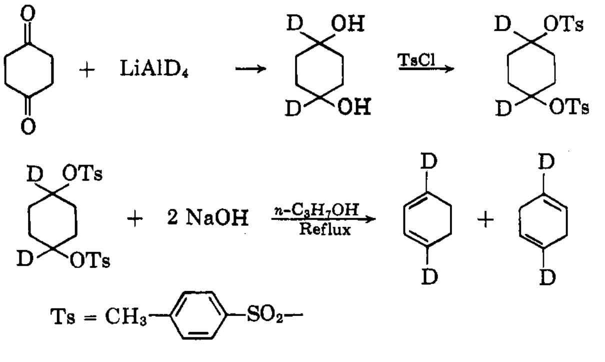
Vapor phase chromatographic analysis of the products from adduction of 1,3-cyclohexadiene with ethyl azodicarboxylate (I) indicated three compounds; the major product, the previously identified diethyl 2,5-cyclohexadien-1-yl-bicarbamate (II), has been further substantiated by Gillis and Beck.[1b] The formation of ethyl hydrazodicarboxylate (III) also had been substantiated by isolation of III from the reaction mixture.[1a] The third product, occurring only in 5 to 15% yields was tentatively identified as diethyl cyclohexylbicarbamate (IV) on the basis of similar v.p.c. retention times with an authentic sample.[1a] By column chromatography on an acid-washed alumina column, the third product has now been isolated and analyzed. The analysis does not agree with IV but is instead consistent with structures V, VI, or VII (without deuterium).



Since there was no N–H stretching at 3300 cm.$^{-1}$ in the infrared, and the n.m.r. indicated no hydrogen bound to nitrogen, this compound cannot be an addition–abstraction product. The relative hydrogen areas by n.m.r. are consistent with V, VI, or VII (nondeuterated). In Fig. 1a there can be seen six methyl hydrogens (triplet τ 8.7), two ring allyl hydrogens ($\tau \cong$ 8.1), four O–CH_2 hydrogens (τ 5.9), two hydrogens next to nitrogen (τ 5.2), and two vinyl hydrogens (τ 3.5).

The vinyl hydrogen triplet shown in Fig. 1a probably rules out VI as a possible structure but does not readily differentiate between compounds V and VII. The reaction of 1,4-dideuterio-1,3-cyclohexadiene with ethyl azodicarboxylate (I) could then have given rise to V, VI, or VII (with deuterium) along with ethyl hydrazodicarboxylate and a corresponding deuterated addition–abstraction product (II). The difference in the n.m.r. spectra of V *vs.* both VI and VII would be clearly demonstrated by a retention of vinyl hydrogen area and the complete disappearance of that peak due to the tertiary hydrogen next to the nitrogen. If, on the other hand, VI and VII were the product, both vinyl hydrogen and tertiary hydrogen would suffer a reduction in area to one-half of the original vinyl and tertiary hydrogen area. As is evident from Fig. 1b, the tertiary hydrogen next to nitrogen (τ 5.2) is no longer present, the vinyl hydrogen area is unchanged, and the vinyl triplet (τ 3.5) has collapsed to a singlet supporting only compound V, the Diels–Alder adduct. Thus the reaction of I and 1,3-cyclohexadiene does indeed give a 5–15% yield of Diels–Alder adduct (V), 5–15% of ethyl hydrazodicarboxylate (III), and about 80% of the addition–abstraction product (II).

The positional integrity of the deuterium in 1,4-dideuterio-1,3-cyclohexadiene was established in part by the synthesis of the diene and in part by the n.m.r. spectra of the resultant product.



---

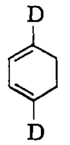
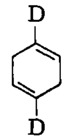
[1] (a) B. Franzus and J. H. Surridge, *J. Org. Chem.*, **27**, 1951 (1962); (b) B. T. Gillis and P. E. Beck, *ibid.*, **27**, 1947 (1962).

[2] (a) S. G. Cohen and R. Zand, *J. Am. Chem. Soc.*, **84**, 586 (1962); (b) L Pirsch and J. Jorgl, *Ber.*, **68**, 1324 (1935).

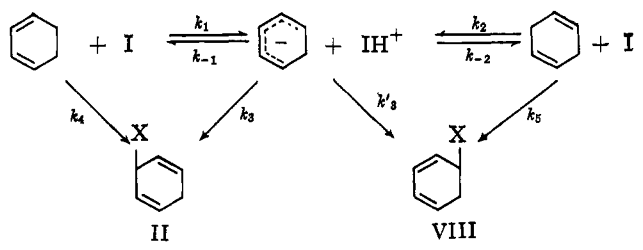
Reduction of 1,4-cyclohexanedione by lithium aluminum deuteride should involve no rearrangement[3] and the formation of the ditosylate involves no rearrangement.[4,5] Thus the only step of the synthesis which could conceivably give rise to deuterium scrambling is the elimination reaction since the dienes could isomerize in a basic media. If in a basic, protic media, proton abstraction occurs reversibly to form the carbanion of the cyclic diene, then not only would the 1,3- and 1,4-dienes interconvert but the resulting dienes would incur both deuterium scrambling and loss of deuterium to the protic solvent. However, the reaction of 1,4-cyclohexadiene and 1,3-cyclohexadiene with sodium hydroxide in 1-propanol gave no evidence of isomerization of the 1,4-diene to the 1,3-diene and vice versa. This means that the carbanion is not formed and the resultant 1,3- and 1,4-cyclohexadienes should be free of both deuterium scrambling and loss of deuterium. Final confirmation of structure resided in the analyses of the 1,4-dideuterio-1,3-cyclohexadiene and the 1,4-dideuterio-1,4-cyclohexadiene by n.m.r. as shown in Table I.

Table I

N.m.r. Hydrogen Areas for 1,4-Dideuterio-1,3- and -1,4-cyclohexadienes

		Calcd.	Found
	Allyl/vinyl	2.00/1	1.99/1
	% Allyl-H	66.7	66.7
	% Vinyl-H	33.3	33.3
	Allyl/vinyl	2.00/1	1.92/1
	% Allyl-H	66.7	65.7
	% Vinyl-H	33.3	34.3

For the addition–abstraction reaction, the extent of carbon–hydrogen cleavage by the azo-nitrogen can be measured by the amount of isomerization of the starting dienes and by the final mixture of products.



X = $C_2H_5O_2CNNHCO_2C_2H_5$ ϵ_{max} 3760 (λ_{max} 258 mμ)

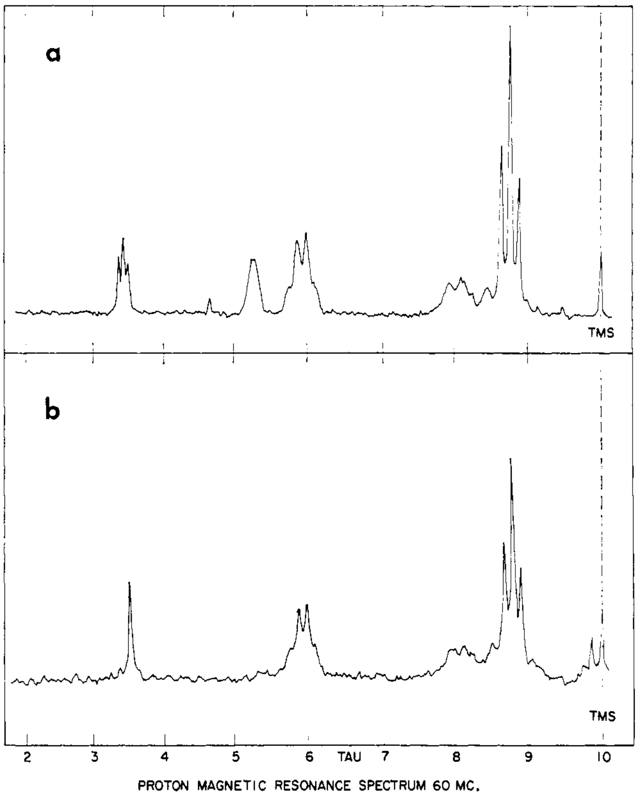


Fig. 1.—N.m.r. spectra of Diels–Alder adducts in CCl_4 at 25°: (a) Diels–Alder adduct from 1,3-cyclohexadiene and ethyl azodicarboxylate; (b) Diels–Alder adduct from 1,4-dideuterio-1,3-cyclohexadiene and ethyl azodicarboxylate.

If proton abstraction by the azo-nitrogen is complete and the reaction with diene is reversible (k_1, k_{-1}, k_2, k_{-2}, fast), then starting with either 1,3- or 1,4-cyclohexadiene one would anticipate an equilibrium mixture of the 1,2- and 1,4-dienes. This was not observed; the starting diene was not isomerized. However, one might anticipate that proton abstraction by the azo-nitrogen would be irreversible (also k_{-1} and k_{-2} are essentially zero), and this would be reflected by an equilibrium mixture of the final products (*via* k_3 and k'_3). This, too, was not observed. The 1,3-product VIII arising from 1,4-cyclohexadiene had a large molar extinction coefficient,[1a] and thus made traces of the 1,3-product easily detectable.

On the other hand, the 1,4-product II that arose from I and 1,3-cyclohexadiene was easily detectable by its n.m.r. spectrum shown in Fig. 2b. It will be noted that the hydrogens of the two ethyl groups of the azo ester are sufficiently different that a chemical shift is readily detectable by the two O–CH_2 quartets and the two CH_3 triplets. This n.m.r. spectrum is quite different from that of the 1,3-product VIII that arose from I and 1,4-cyclohexadiene (Fig. 2a). The latter n.m.r. spectrum (2a) only indicates one type of OCH_2 and CH_3. The observation that the 1,4-diene did not isomerize to the 1,3-diene and vice versa in the presence of I was further substantiated by the fact that *cis–trans* isomers also did not interconvert in their reactions with I.[6]

It became quite apparent that since both products and unchanged starting material did not undergo isomerization, complete removal of the proton by the azo-nitrogen did not occur. Furthermore, one can also rule out any solvated ion-pairs since there was no detectable deuterium in either unchanged starting diene or final product when I reacted with either 1,3- or 1,4-

---

[3] (a) L. W. Trevoy and W. G. Brown, *J. Am. Chem. Soc.*, **71**, 1675 (1949); (b) M. S. Newman and R. Gaertner, *ibid.*, **72**, 264 (1950).

[4] H. Phillips, *J. Chem. Soc.*, **123**, 44 (1923).

[5] We are indebted to Prof. P. S. Skell for suggesting tosylate elimination as the best synthetic route to the dienes.

[6] Personal communication from Dr. W. A. Thaler of the Central Basic Research Laboratories, Esso Research and Engineering Co.

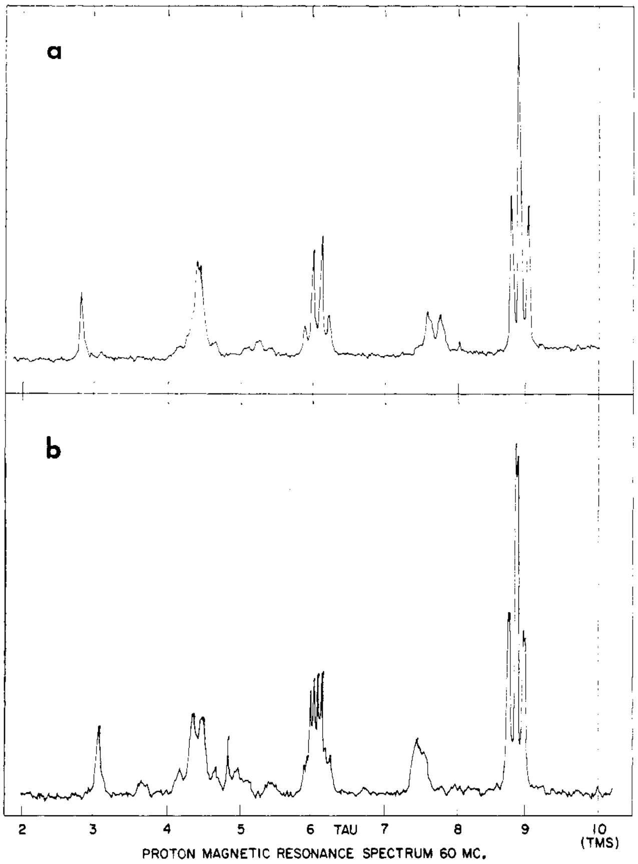


Fig. 2.—N.m.r. spectra of addition–abstraction products in CCl_4 at 25°: (a) compound VIII from 1,4-cyclohexadiene and ethyl azodicarboxylate; (b) compound II from 1,3-cyclohexadiene and ethyl azodicarboxylate [CH_3 (τ 8.8); ring alllyl hydrogens (τ 7.7 in a, τ 7.5 in b); OCH_2 (τ 6.1); vinyl hydrogens ($\tau \cong 4.4$); N-H ($\tau \cong$ 2.8–3.1 dependent on concentration)].

cyclohexadiene in the presence of methanol-D.[7] Because the N–H bond in products II and VIII exchanged H for D with the deuterated solvent very slowly, the fact that there was essentially no N–D in the final product further eliminates the possibility of a solvated ion-pair. One must conclude that under these reaction conditions, lack of deuterium exchange infers that reaction of 1,3-cyclohexadiene with I (k_4) and 1,4-cyclohexadiene with I (k_5) proceeds through either an intimate ion-pair, ion-dipole, or *via* a concerted process. Hydrogen–deuterium exchange has been observed in other systems using stronger base, higher temperatures, and benzylic-type compounds.[8] This exchange apparently does not apply to the azo ester–diene system.

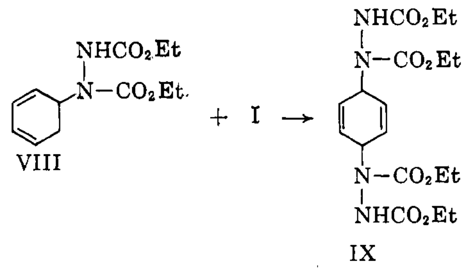
Kinetics of azo ester adduction with cyclic dienes should be second-order for a concerted process. As shown in Table II second-order kinetics is exactly what was observed. Kinetics were run both in cyclohexane and in ethanol with rate constants in ethanol being about twenty times greater than in cyclohexane. However, the data for the kinetics in ethanol are not reported here (except qualitatively) because competition between I and the diene, and I and ethanol[9] caused difficulty in obtaining reproducible results. The results of the kinetics were surprising since it was assumed, *a priori*, that the loss or gain of resonance energy by 1,3- or 1,4-cyclohexadiene to 1,4- and 1,3-diene products (II and VIII, respectively) would be a large driving force in the azo ester cyclic diene adduction. Thus it was assumed that 1,4-cyclohexadiene should react faster than 1,3-cyclohexadiene. It is quite evident from Table II that at 50° the 1,3-diene reacts some fifteen times faster than the 1,4-diene. In fact, reasonable kinetics for the 1,4-diene were obtainable only by using a high concentration of 1,4-diene since the 1,3-product VIII also reacted faster than 1,4-cyclohexadiene to form compound IX. The data in Table II were finally rationalized by the observation that the 1,3-diene is only 600 calories more stable than the 1,4-diene as determined by the thermodynamic equilibration of the 1,3- and 1,4-dienes in the presence of strong base.

TABLE II

SECOND-ORDER RATE CONSTANTS IN CYCLOHEXANE AS FUNCTION OF CONCENTRATION

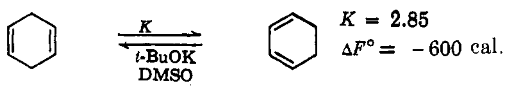
Cyclo-hexadiene	T, °C.	Diene	Azo ester	$10^5 k$ (l. mole^{-1} sec.$^{-1}$)
1,3	25	0.0615	0.0501	7.86
1,3	25	.0800	.0194	7.33
1,3	50	.1226	.0825	31.7
1,3	50	.2460	.0795	32.1
VIII	50	.166	.0974	6.99
1,4[a]	50	.1293	.1000	2.27
1,4	50	.2025	.0240	2.22
1,4	75	.0935	.0229	12.8
1,4	75	.1863	.0230	12.9

[a] Estimated from first 25% reaction, before reaction of VIII becomes dominant.



VIII

IX



The kinetic data in Table III embrace three reaction rate constants for 1,3-cyclohexadiene; the addition–abstraction reaction (k_{AA}), an oxidation–reduction reaction ($k_{ox\text{-}red}$) and a Diels–Alder adduction (k_{DA}). Similarly a k_{total} for 1,4-cyclohexadiene is comprised of an addition–abstraction reaction (k_{AA}) and an oxidation–reduction reaction ($k_{ox\text{-}red}$). (See p. 2957, col. 1).

In the reaction of 1,3-cyclohexadiene with ethyl azodicarboxylate, the variation in product distribution as a function of temperature was determined by v.p.c. Since the differences in product distribution were of the same order of magnitude as the errors in the analytical

---

(7) Methanol-D was chosen because of its high dielectric constant ($D \cong 31$); however, in the presence of methanol the amount of oxidation–reduction increases at the expense of the addition–abstraction product. This was not true of solvents such as ethanol ($D = 24$), and dimethyl sulfoxide ($D = 46.7$) where the ratio of all three products remained essentially unchanged from those results obtained either in the absence of solvent or in cyclohexane as solvent.

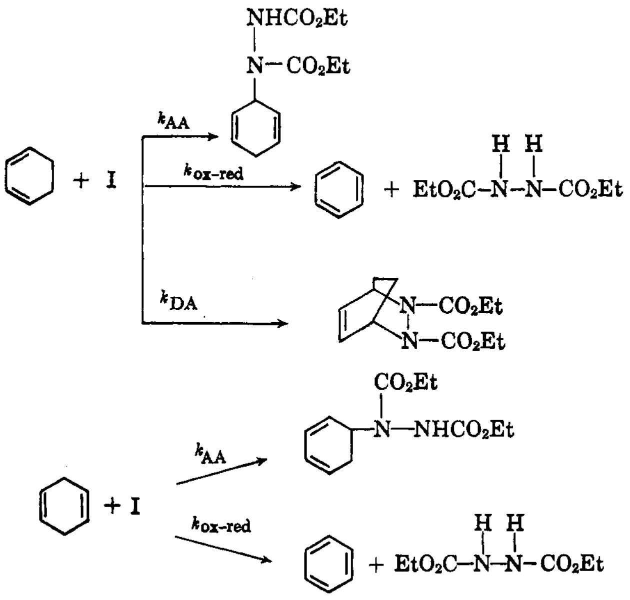
(8) D. J. Cram, C. C. Kingsbury, B. Rickborn, *J. Am. Chem. Soc.*, **81**, 5835 (1959).

(9) O. Diels and C. Wulff, *Ann.*, **437**, 309 (1924).

TABLE III
PARTIAL AND RELATIVE RATES FOR 1,3- AND 1,4-CYCLOHEXADIENE AT 50°

Diene	10^5k_{total}, l. mole^{-1} sec.$^{-1}$	$k_{1,3(total)}$/ $k_{1,4(total)}$	10^5k_{AA}, l. mole^{-1} sec.$^{-1}$	k_{AA}(1,3)/ k_{AA}(1,4)
1,3-	31.9		24.0	
		14.5		18.5
1,4-	2.2		1.3	

Diene	$k_{ox\text{-}red}$ l. mole^{-1} sec.$^{-1}$	$k_{ox\text{-}red}$(1,3)/ $k_{ox\text{-}red}$(1,4)	10^5k_{DA}, l. mole^{-1} sec.$^{-1}$
1,3-	3.5		4.4
		3.9	
1,4-	0.9		



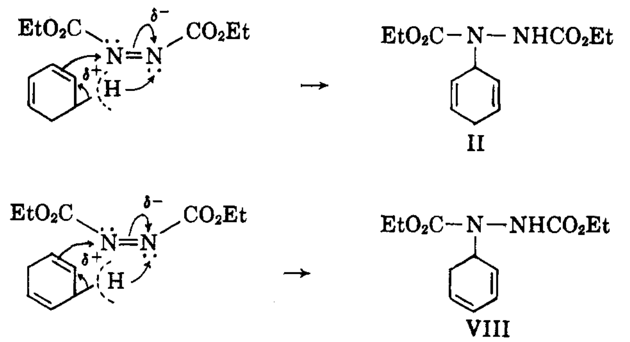
technique (±1%) an average product distribution was used for computation of k_{AA}, k_{DA} and $k_{ox\text{-}red}$. This same product distribution held (essentially unchanged) down to −25° both without solvent[1a] and in ethanol from room temperature to 62°. The addition–abstraction product from 1,4-cyclohexadiene forms a 1,3-product VIII with a reasonably large molar extinction coefficient so analyses of products were feasible even though the variation of product distribution as a function of temperature was small. These results are shown in Tables III and IV.

TABLE IV
ENTHALPY AND ENTROPY OF ACTIVATION FOR VARIOUS REACTION PATHS

Diene	ΔH^* (total), kcal.	ΔS^* (total), e.u.	ΔH^* (A A), kcal.	ΔS^* (A A), e.u.
1,3-	10.9	−40.7	10.9	−41.0
1,4-	15.6	−31.8	14.4	−36.4

Diene	ΔH^* (ox-red), kcal.	ΔS^* (ox-red), e.u.	ΔH^* (D A), kcal.	ΔS^* (D A), e.u.
1,3-	10.9	−45.0	10.9	−44.5
1,4-	16.0	−32.3		

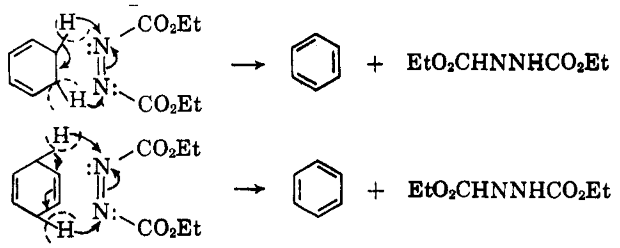
A favorable mechanism for the addition–abstraction reaction is *via* a concerted process with a partial charge development.[1a,b]



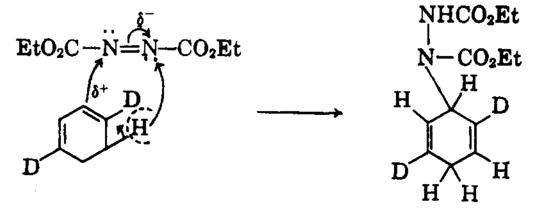
II

VIII

A similar mechanism also could be written for the oxidation–reduction reaction.

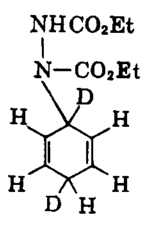


Consistent with these results is the rate enhancement in ethanol (over cyclohexane), the lack of hydrogen–deuterium exchange in reactants and products (when run in CH$_3$OD) and lack of isomerization of both starting dienes and final products. In addition, the observance of a kinetic isotope effect in the reaction of I with 1,4-dideuterio-1,4-dihydronaphthalene[10] also is consistent with a cyclic concerted mechanism. The high negative entropy of activation also fits the cyclic concerted mechanism just as it fits a Diels–Alder adduction. However, the addition–abstraction mechanism should not have the same transition state or go *via* the same intermediate as the Diels–Alder adduct. By a concerted cyclic mechanism, the product obtained by the reaction of ethyl azodicarboxylate with 1,4-dideuterio-1,3-cyclohexadiene (X), should have two vinyl hydrogens, two allyl hydrogens, and a tertiary hydrogen (next to nitrogen).



X

On the other hand, if one works out details, the addition–abstraction product one would obtain from a transition state (or intermediate) arising from a Diels–Alder adduct (after the appropriate hydrogen migra-



XI

---

(10) R. Huisgen and H. Pohl, *Ber.*, **93**, 527 (1960).

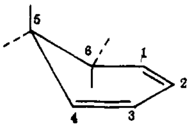
TABLE V

N.M.R. HYDROGEN AREAS OF X AND XI FROM 1,4-DIDEUTERIO-1,3-CYCLOHEXADIENE AND I

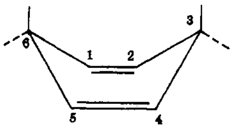
N.m.r. % area of hydrogens	% calcd. for X	% calcd. for XI	Found
CH_3	37.5	37.5	40.7
OCH_2	25.0	25.0	24.6
Ring CH_2	12.5	6.25	12.1
Vinyl	12.5	25.0	12.2
t-H (next to N)	6.25	0	5.2
N-H	6.25	6.25	5.2

tion) would have a structure corresponding to XI with four vinyl hydrogens and one allyl hydrogen. It is apparent from Table V that X is the observed product substantiating the concerted cyclic mechanism.

If one builds molecular models of the azo ester–cyclic diene system, one can rationalize the observed enthalpies and entropies of activation from the steric effects manifested by interactions of various atoms in the molecular models. Both Dreiding and Stuart–Briegleb models show that the two axial hydrogens (5 and 6 in 1,3-cyclohexadiene) extend in opposite directions perpendicular to the plane of the 1,3-cyclohexadiene ring (XII); axial hydrogens 3 and 6 in 1,4-cyclohexadiene extend in the same direction perpendicular to the plane of the 1,4-cyclohexadiene ring (XIII).[11]



XII



XIII

If one assumes that I approaches perpendicular to the cyclohexadiene rings to abstract an axial hydrogen, a steric effect from the other axial hydrogen is noted in the case of the 1,4-diene but not with the 1,3-diene. This effect could then show up in part in the ΔH^* term.[12] This could explain the greater reactivity of the 1,3-diene over the 1,4-diene since the entropy of activation for both the 1,3- and 1,4-dienes are very nearly the same The oxidation–reduction rate constants for the 1,3- and 1,4-dienes are very nearly the same. Again the 1,3-diene has a lower ΔH^* than the 1,4-diene probably due in part to a hindering effect of the other axial hydrogen. The more favorable entropy for the 1,4-diene over the 1,3-diene could be rationalized by simultaneous abstraction of axial hydrogens 3 and 6 by I; this favorable conformation cannot be realized by the 1,3-diene.

Experimental

All melting points were corrected and were taken on a Fisher-Johns melting point apparatus. Infrared spectra were determined using a Beckman IR-5 spectrophotometer. Ultraviolet and visible spectra for the kinetic experiments were obtained using an Optika CF-4 double-beam recording spectrophotometer. N.m.r. spectra were determined with a Varian Associates A-60 spectrometer. Vapor phase chromatographic analyses were carried out on a Perkin-Elmer Model 154-D vapor fractometer. Elemental analyses were performed by both the Analytical Research Division of Esso Research and Engineering Company and by Galbraith Laboratories, Inc., Knoxville, Tenn. Molecular weight analyses were done by Galbraith Laboratories, Inc.

N,N-Dicarboxyethyl-1,4-*endo*-hydrazocyclohexene (V).—The reaction of I with 1,3-cyclohexadiene has been described elsewhere.[1a,b] Compound V, the Diels–Alder adduct, was separated from II the addition–abstraction product and ethyl hydrazodicarboxylate by chromatography on an acid-washed alumina column using methylene chloride as eluent. The Diels–Alder adduct (V) was the first compound to be eluted, followed by a mixture of II and ethyl hydrazodicarboxylate. The last compound to be eluted was ethyl hydrazodicarboxylate. Compound V is a viscous liquid whose infrared spectra differs mainly from compound II by the absence of the N–H stretching at 3300 cm.$^{-1}$.[13] The liquid chromatography samples were analyzed by v.p.c.[14] The Diels–Alder adduct (V) had a perfect analysis for a one-to-one adduct.

Anal. Calcd. for $C_{12}H_{18}N_2O_4$: C, 56.88; H, 7.13; N, 11.02. Found: C, 56.85; H, 6.93; N, 10.93.

1,4-Dideuterio-1,4-cyclohexanediol.—Into a dry 2-l. resin flask containing 5.0 g. (0.119 mole) of lithium aluminum deuteride, equipped with a vibromix stirrer, thermometer, and dropping funnel was distilled (from lithium aluminum hydride) 100 ml. of tetrahydrofuran. To this deuteride solution was slowly added 22.4 g. (0.2 mole) of 1,4-cyclohexanedione (Aldrich Chemical Co., Milwaukee, Wis.) in 300 ml. of dry tetrahydrofuran. Addition of the dione (which took 35 min.) was accompanied by slight heat evolution. Agitation was continued for 3 hr. after addition and the reaction mixture allowed to stand overnight. After decomposition of excess lithium aluminum deuteride with 200 ml. of methanol, all the solvent was removed (under aspirator vacuum) using a rotary evaporator. Extraction of the 1,4-diol was accomplished by dissolving the 1,4-diol from the combination of salts with tetrahydrofuran (150 ml.). This gave 6.0 g. of diol (after evaporation of the tetrahydrofuran). The solid was then further extracted with boiling tetrahydrofuran in a Soxhlet extractor to yield more 1,4-diol (6.4 g.). Finally the remaining solid was dissolved in dilute sulfuric acid, neutralized with sodium hydroxide, concentrated to dryness under vacuum on a rotary evaporator, and extracted with acetone to yield 1.9 g. of 1,4-diol. The yield of 1,4-dideuterio-1,4-cyclohexanediol (14.3 g., 0.133 mole) was 66.5%. The infrared and n m.r. spectra of the 1,4-diol were consistent with deuteriums in the 1,4-position.

1,4-Dideuterio-1,4-cyclohexanediol-di-*p*-toluenesulfonate.—To 165 ml. (2.31 moles) of freshly distilled dry pyridine was dissolved 14.3 g. (0.133 mole) of 1,4-dideuterio-1,4-cyclohexanediol. To this solution was added (with stirring) 50.6 g. (0.266 mole) of *p*-toluenesulfonyl chloride. Exothermicity was apparent after 10 min., and a white crystalline precipitate appeared after 20 min. The mixture was allowed to stand at room temperature for 2 days after which the reaction mixture was poured into 1500 ml. of cold 2.0 *M* hydrochloric acid. The solid that precipitated was vacuum dried (35° at 1.0 mm.) for 20 hr. The weight of 1,4-dideuterio-1,4-cyclohexanediol-di-*p*-toluenesulfonate was 47.8 g. (0.1125 mole) representing an 84.5% yield.

1,4-Dideuterio-1,3- and -1,4-cyclohexadiene.—To a 500-ml. distillation flask containing 270 ml. of redistilled propanol and 9.9 g. (0.247 mole) of sodium hydroxide was added 47.8 g. (0.112 mole) of 1,4-dideuterio-1,4-cyclohexanediol-di-*p*-toluenesulfonate. The 500-ml. flask was the distillation pot of a Todd distillation assembly so that as the contents of the flask were heated to reflux, the condensate with boiling point less than 97° was collected. Four fractions of condensate were collected totaling 70 ml. To the condensate was added 50 ml. of water; this mixture extracted with *n*-pentane. The pentane layer was washed once with water and the combined water layers extracted with *n*-pentane. The combined pentane layers were washed twice with water. A total of 55 ml. of *n*-pentane was used for extraction; the final volume was 59 ml. Most of the pentane (after drying) was carefully distilled until 10 ml. of hydrocarbon (dienes and pentane) remained. The 1,4-dideuterio-1,3-cyclohexadiene was separated from the 1,4-dideuterio-1,4-cyclohexadiene by preparative gas chromatography. A 10 ft. × 0.5 in. column packed with 160 g. of a substrate consisting of Ucon nonpolar on acid-washed Chromosorb P was used at 65° in conjunction with a Perkin-Elmer Model 154-D vapor fractometer. Samples of 0.70 ml. were in-

---

(11) F. H. Herbstein, *J. Chem. Soc.*, 2292 (1959).

(12) H. C. Brown and G. K. Barbaras, *J. Am. Chem. Soc.*, **75**, 6 (1953).

(13) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1957, p. 207.

(14) Obtained with a 1 m. × 0.25 in. column packed with 20% diethylene glycol succinate on acid-washed Chromosorb W at 170° and 210 cc./min. helium as carrier gas. The column packing was purchased from Wilkens Instrument and Research, Inc., Walnut Creek, Calif.

jected and the 1,3-diene (13.8 min. retention time from air) was collected first and the 1,4-diene (retention time 21.8 min. from air) was the second compound to be collected. The 2.3 g. (0.028 mole) of 1,4-dideuterio-1,3-cyclohexadiene represents a 25% yield.

Reaction of 1,4-Cyclohexadiene with Sodium Hydroxide in 1-Propanol.—To a distillation flask containing 125 ml. of 1-propanol, 4.6 g. (0.115 mole) of sodium hydroxide, and 19 g. (0.1 mole) of sodium *p*-toluenesulfonate was added 5.0 ml. (0.05 mole) of 1,4-cyclohexadiene. This mixture was refluxed for 2 hr. (on a Todd distillation assembly) after which condensate was collected and worked up as in the preparation of the deuterated dienes. The v.p.c. analysis[15] of the starting diene was 98.3% 1,4-cyclohexadiene, 1.6% benzene, and 0.1% cyclohexane. The v.p.c. analysis of the cyclohexadiene after refluxing with sodium hydroxide in propanol was 98.3% 1,4-cyclohexadiene, 1.6% benzene, and 0.1% cyclohexane. *No* 1,3-cyclohexadiene was formed.

Thermodynamic Equilibration of 1,3- and 1,4-Cyclohexadiene.—Using dimethyl sulfoxide as the solvent and potassium *t*-butoxide as the base, a solution 0.0402 *M* in base and 0.428 *M* in 1,4-cyclohexadiene (99.4% pure) was equilibrated at 35°. The system was in equilibrium in less than 5 min. since at 5, 15, 30, 60, 120, and 1180 min. the ratio of 1,3- to 1,4-cyclohexadiene was essentially unchanged. The analysis of the diene mixture by v.p.c.[15] gave a ratio of 1,3/1,4-cyclohexadiene of 1.86 ± 0.02. In an identical manner, 0.403 *M* 1,3-cyclohexadiene (analyzed[15] 96.0% 1,3-cyclohexadiene, 3.4% cyclohexene, 0.5% benzene, 0.1% 1,4-cyclohexadiene) and 0.033 *M* potassium *t*-butoxide in dimethyl sulfoxide was equilibrated at 35°. Again analyses[15] showed equilibration complete in less than 5 min. and the ratio of 1,3/1,4-cyclohexadiene was 1.84 ± 0.01.

Reaction of I and 1,3-Cyclohexadiene in Methanol-D.—Methanol-D was synthesized by cautiously adding 27 g. (0.5 mole) of sodium methylate to 33.5 ml. (1.175 moles) of 99.5% deuterium oxide. The whole operation was carried out in a dry-box in a 100 ml. flask with stirring. The methanol-D was distilled from the excess deuterium oxide under "anhydrous" conditions. The yield of CH_3OD was 17.5 ml. (0.42 mole) which represented an 84% yield. The isotopic purity of the methanol-D was 99.5% as determined by comparing the area of the hydrogen on the OH to the hydrogen area due to the splitting resulting from the natural abundance of C^{13}. Thus the $-C^{13}H_3-$ (1.1% abundance) area was compared to the OH area to determine isotopic purity.

In a typical experiment 4.3 g. (0.0246 mole) of ethyl azodicarboxylate (I), 5.0 ml. (0.050 mole) of 1,3-cyclohexadiene, and 5.0 ml. (0.122 mole) of methanol-D were added to a graduate which was then stoppered, and placed in a 62° bath until the yellow color of the azo ester had faded. The unchanged 1,3-cyclohexadiene, methanol-D, methanol, and benzene[1a] was stripped from the reaction mixture, analyzed by v.p.c.[15] and then analyzed by n.m.r. The allyl and vinyl hydrogens (n.m.r.) of the 1,3-cyclohexadiene are shifted widely from the OCH_3, OH, and benzene hydrogens. The areas of the allyl and vinyl hydrogens were equal indicating the lack of deuterium exchange. The products from the reaction were mixed with methylene chloride and filtered giving 2.2 g. of ethyl hydrazodicarboxylate and 1.7 g. of a viscous oil (after stripping the methylene chloride). V.p.c. analysis[14] indicated (by area per cent) 14% ethyl hydrazodicarboxylate, 53% of the Diels–Alder adduct (V), and 33% of the addition-abstraction product (II). Column chromatography as described in the isolation of the Diels–Alder adduct (V) was used to isolate the addition–abstraction product (II). The n.m.r. of compound II showed no deuterium incorporation; its n.m.r. spectra and infrared spectra were identical to authentic samples previously prepared.[1a]

In an identical experiment, 1,4-cyclohexadiene reacted with ethyl azodicarboxylate in the presence of methanol-D at 62°. Similarly the unchanged1,4-cyclohexadiene had equal allyl and vinyl areas in the n.m.r. indicating no deuterium exchange. The product VIII was isolated in a manner similar to the isolation of II and in a manner previously described.[1a] This product had an n.m.r. and infrared spectrum identical to the product derived in the absence of any deuterium[1a] indicating no deuterium incorporation.

Preparation of Va and X from Reaction of 1,4-Dideuterio-1,3-cyclohexadiene with Ethyl Azodicarboxylate (I).—To 2.3 g. (0.028 mole) of 1,4-dideuterio-1,3-cyclohexadiene was added 4.5 g. (0.026 mole) of ethyl azodicarboxylate. The reaction mixture was kept at room temperature with stirring for 64 hr. after which time the reaction mixture had become colorless. As in the isolation of V, acid-washed alumina was the column packing and dichloromethane was the eluent. The first product off the column was V (analyses of fractions were done by v.p.c.).[14] This was then followed by compound X. Each of these compounds were then analyzed by n.m.r. and the results shown in Fig. 1b (for V) and Table V (for X).

Preparation of 1,4-Bis(1′,2′-dicarbethoxyhydrazyl)-2,5-cyclohexadiene (IX).—Compound VIII, diethyl 2,4-cyclohexadien-1-yl-bicarbamate (1.39 g. 0.0055 mole), was diluted with benzene so that the volume of solution was 3 ml. To this solution was added 0.95 g. (0.0055 mole) of ethyl azodicarboxylate. The solution was heated for 1 hr. on a steam bath, allowed to stand overnight, and once again heated on a steam bath for 45 min. Overnight a white solid had precipitated which did not redissolve on heating; this solid, after drying weighed 1.18 g. (0.00276 moles, 50% yield) had m.p. 155.5–157° and an n.m.r. consistent with IX.

Anal. Calcd. for $C_{18}H_{28}N_4O_8$: C, 50.45; H, 6.59; N, 13.08, mol. wt., 428. Found: C, 50.46, 50.32; H, 6.61, 6.52; N; 13.19; mol. wt., 395 (osmometer).

Determination of Rate Constants.—Purity of the cyclohexadienes was determined by v.p.c.[15] 1,3-Cyclohexadiene (purchased from Farchan Research Lab., Wickliffe, Ohio) was 99.1% pure; the other impurities were benzene and cyclohexane which did not react with ethyl azodicarboxylate. Similarly, analysis of 1,4-cyclohexadiene (purchased from Columbia Organic Chemical Co., Columbia, S. C.) indicated a purity of 99.5%; the impurity in the 1,4-diene was benzene. Both the dienes and the ethyl azodicarboxylate (purchased from Aldrich Chemical Co., Milwaukee, Wis.) were distilled prior to kinetic runs. Spectro Grade cyclohexane (as the solvent) carefully was redistilled from anhydrous calcium sulfate and analyzed at least 99.9% pure.[15] For the determination of rate constants for 1,3-cyclohexadiene, samples of 1,3-diene in about 80 ml. of cyclohexane (in a 100-ml. volumetric flask) were placed for 30 min. in a thermostated bath; a weighed amount of ethyl azodicarboxylate was added to the 100-ml. volumetric flask and the volume adjusted to 100.0 ml. at the desired temperature with thermostatted solvent (cyclohexane). Samples of the solution were removed from time to time, quickly brought to room temperature, and a known volume diluted (with cyclohexane) for measurement of optical density. Usually dilution was 1 to 5; however, it would vary with the concentration of azo ester. The concentration of azo ester was determined from the optical density at 403 mμ. The initial concentration of azo ester was determined both by optical density of a sample taken immediately after adding the azo ester to the diene, and by calculation from the weight of the added azo ester. Since Beer's law held at all concentrations from 0.025 *M* down, the reactions were followed to 50–80% completion. Plots of the rate data, using a standard equation for the second-order rate law[16] gave good straight lines. The determination of rate constant for compound VIII going to IX by reaction with I was done in the same way as the reaction of 1,3-cyclohexadiene with I except that optical density was measured at 258 mμ. The determination of rate constants for reaction of 1,4-cyclohexadiene with ethyl azodicarboxylate was done by making (at room temperature) a solution (100.0 ml.) 0.02 to 0.1 *M* in azo ester I and 0.1 to 0.2 *M* in 1,4-cyclohexadiene. Approximately 7 ml. of the solution was pipeted into each of nine tubes which were sealed and placed in a thermostated bath. Initial concentration of azo ester was determined both by the weight of the azo ester and by optical density at 403 mμ of an initial sample appropriately diluted. From time to time samples were removed from the bath, cooled to room temperature, opened and a known volume of solution diluted (usually about 1 to 5) for measurement of optical density. Usually after 20% reaction the amount of ethyl hydrazodicarboxylate formed was sufficient to cause cloudiness of the solution at room temperature; these solutions were filtered through sintered glass with a slight nitrogen pressure above the liquid. The concentration of reactants was corrected for the expansion of solvent[17] and the rate data plotted to good straight lines using the standard equation for a

---

(15) Analysis for 1,3- and 1,4-cyclohexadiene was done with a Perkin-Elmer 2-m. R column, at 55° on a Model 154-D Perkin-Elmer vapor fractometer.

(16) S. J. Cristol, *J. Am. Chem. Soc.*, **67**, 1494 (1945).

(17) G. Egloff, "Physical Constants of Hydrocarbons," Vol. II, Reinhold Publishing Corp., New York, N. Y., 1940, pp. 78–80.

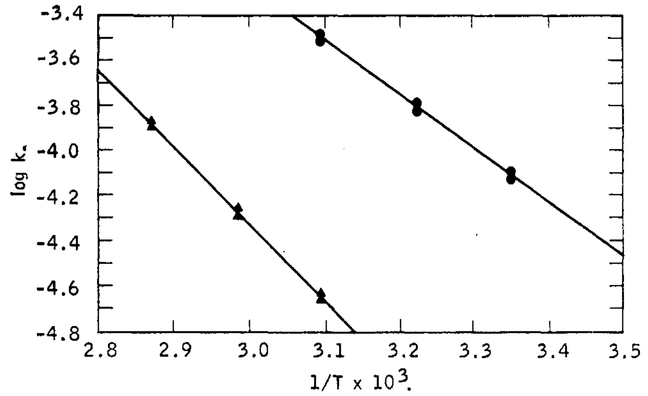


Fig. 3.—Enthalpy of activation from log *k vs.* 1/*T*: ▲, 1,3-cyclohexadiene; ●, 1,4-cyclohexadiene.

second-order reaction.[16] Quantitative analysis for amount of compound VIII (from 1,4-cyclohexadiene and I) at different temperatures was based on the ultraviolet absorption of VIII at 258 mμ (ϵ_{max} 3760). After all solvent and unchanged diene were removed from the reaction mixture the product was diluted with ethanol and the concentration of VIII determined from the ultraviolet absorption. Reproducibility of results by this method was ±0.3%. Qualitative verification for the validity of this method was based on the analysis of benzene (and therefore ethyl hydrazodicarboxylate) by v.p.c.[15] Quantitative analysis for II, V, and ethyl hydrazodicarboxylate from the reaction of 1,3-cyclohexadiene and I was done by v.p.c.[14] Molar response data[18] from known mixtures of ethyl hydrazodicarboxylate and II and ethyl hydrazodicarboxylate and V were sufficient for the quantitative analysis of all three components. Reproducibility was good to ±1%. Reaction temperatures for 1,3-cyclohexadiene and I were 25.05 ± 0.05°, 37.07 ± 0.05°, and 49.96 ± 0.05°; for 1,4-cyclohexadiene and I reaction temperatures were 49.96 ± 0.05°, 61.86 ± 0.05° and 75.22 ± 0.05°. The plot of log *k vs.* 1/*T* is shown in Fig. 3 for the reaction of ethyl azodicarboxylate and both 1,3- and 1,4-cyclohexadiene. As can be seen from Fig. 3 the plots are quite good so that over-all enthalpies of activation are good to at least ±0.5 kcal.

Acknowledgment.—The author is greatly indebted to Mr. John H. Surridge for his invaluable assistance in the experimental work. Credit is given to my colleagues, Drs. W. A. Thaler, W. C. Baird, E. I. Snyder, and J. L. Kurz, along with Professors W. E. von Doering H. C. Brown, S. J. Cristol, and P. S. Skell for their helpful discussions and suggestions. The determination of the n.m.r. spectra is credited to Dr. Boyd E. Hudson, Jr.

---

[18] A. E. Messner, D. M. Rosie, and P. A. Argabright, *Anal. Chem.*, **31**, 230 (1959).

Synthesis of Bicyclic Nitriles and Related Compounds. II[1,2]

PETER SCHEINER,[3,4] KLAUS K. SCHMIEGEL,[5] GEORGE SMITH, AND WYMAN R. VAUGHAN

Department of Chemistry of the University of Michigan, Ann Arbor, Michigan

Received January 10, 1963

A number of polynitriles and related compounds derived from bicyclic systems have been prepared *via* the Diels–Alder reaction. Of particular interest is the reaction of chloromaleic anhydride with 1-carbomethoxycyclohexa-1,3-diene, which affords but one of the two structurally possible isomers; chlorine appears in the 2-position of the adduct. The preparation of 2,3-diacetoxycyclohexa-1,3-diene is described, but the compound failed to react satisfactorily in the Diels–Alder synthesis.

A previous publication[1] in this series described the synthesis of a number of bicyclic nitriles and related compounds whose synthesis was stimulated by the unexpected antileukemia activity of the Diels–Alder adduct of fumaronitrile and cyclohexa-1,3-diene. The present paper is, in part, an extension of this exploratory synthesis and, in part, related to the broader problem of the scope and limitations of the Diels–Alder reaction with functionally substituted cyclic dienes and the steric course of this reaction.

Following up the reaction of fumaronitrile with cyclopentadiene[6] and cyclohexa-1,3-diene, it has been found that it is in general a practicable dieneophile, good yields of adducts being obtained with furan and cyclohepta-1,3-diene.[7]

A potential intermediate[8] in the preparation of fumaronitrile, α-chloroacrylonitrile, also proved to be a practicable dieneophile, with cyclopentadiene and cyclohexa-1,3-diene. The two purified adducts, which probably are the less soluble members of two epimeric pairs, surprisingly showed complete inertness to refluxing with silver nitrate solution. Thus, one may tentatively assign an *endo* configuration to the chlorine, for in the *exo* configuration one might reasonably expect comparatively labile chlorine.

An examination of the α-chloroacrylonitrile adducts by n.m.r. affords additional support for the *endo*-chlorine configuration: the vinyl protons in *exo*- and *endo*-bicyclo[2.2.1]hept-5-ene-2-carbonitrile appear as multiplets, respectively, at 3.83 and 3.72 τ (deuteriochloroform, internal tetramethylsilane reference, 60 Mc.), whereas in the 2-chlorobicyclo[2.2.1]hept-5-ene-2-carbonitrile, the vinyl protons appear as two multiplets at 3.79 and 3.52 τ suggesting that one of them (on C-6) is in approximately the same environment as in the unchlorinated compound while the other is less shielded due to the *endo*-chlorine. In 2-chlorobicyclo[2.2.2]oct-5-ene-2-carbonitrile a multiplet for two protons falls at 3.64 τ, which suggests about the same environment as for the [2.2.1] analog.

Further evidence for the *endo*-chlorine configuration appears in the reduction of 2-chlorobicyclo[2.2.1]heptane-2-carbonitrile by lithium aluminum hydride. The product, isolated as the hydrochloride, consists of

---

[1] Previous paper in this series: P. Scheiner and W. R. Vaughan, *J. Org. Chem.*, **26**, 1923 (1961).

[2] Work supported in part by a research grant (CY 5406) from the National Cancer Institute to The University of Michigan.

[3] National Institutes of Health Predoctoral Fellow, 1960–1961.

[4] Abstracted in part from a portion of the Ph.D. dissertation of P. Scheiner, The University of Michigan, 1961.

[5] American Cancer Society Institutional Research Grant Fellow, Summer, 1961.

[6] A. T. Blomquist and E. C. Winslow, *J. Org. Chem.*, **10**, 149 (1945).

[7] Hi-Laboratory, Whitmore Lake, Mich.

[8] D. T. Mowry and W. H. Yanko, to Monsanto Chemical Co., U. S. Patent 2,471,767 (1949).