THE REVERSE DIELS-ALDER OR RETRODIENE REACTION

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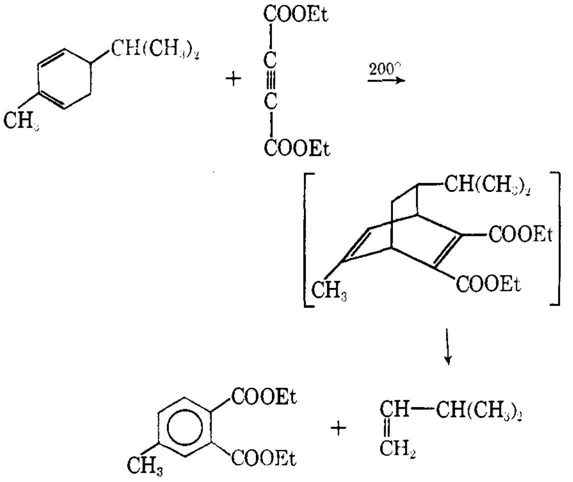
CONTENTS

I. SURVEY OF REACTIONS

The reverse Diels–Alder reaction, or as the German literature refers to it, the retrodiene decomposition, is almost as old as the Diels–Alder itself. In 1929 Diels and Alder[1] reported the preparation of the adduct of furan and maleic anhydride and found that it dissociated at its melting point of 125°. This was one of the earliest in a long series of papers which were to prove the versatility and generality of the reaction for which Diels and Alder were later to win the Nobel prize. The reaction is, however, older than this. In 1906 Albrecht[2] obtained two adducts containing 1 and 2 moles, respectively, of cyclopentadiene from the reaction of cyclopentadiene with benzoquinone. The fact that these adducts dissociate at their melting points was used by Staudinger as an argument for the assignment of a 1,2-addition structure to these compounds. The correct structure, that of 1,4 addition, was later proven by Diels and Alder.[3]

There have recently been a number of very extensive reviews of the Diels–Alder reaction, but the reverse Diels–Alder has not been previously reviewed except for small sections in reviews of the forward reaction.[4–6] Therefore, the present review will be confined almost exclusively to the reverse Diels–Alder reaction, insofar as this is possible. The first five sections are concerned with synthetic and analytic applications of the reverse Diels–Alder reactions. Sections VI and VII are concerned with the use of the reverse reaction in elucidation of the mechanism of the forward (and reverse) Diels–Alder reaction. Obviously it will be necessary in these sections to discuss some aspects of the forward reaction and touch upon some material reviewed earlier, but the emphasis is still on the reverse Diels–Alder. In section VIII it should be clear that the molecular orbital interpretations of Woodward and Hoffmann[7,8] have obviously much broader applicability than the reverse Diels–Alder reaction, but this does not lessen their usefulness as a basis for discussion and interpretation of the experimental material reviewed here.

In 1937 two papers by Alder and Rickert[9] summarized what was known at the time of the reverse Diels–Alder reaction. The most interesting example was the decomposition of adducts of cyclohexadienes with acetylenic dienophiles to give an olefin and an aromatic compound. Thus, α-phellandrene, when allowed to react with acetylenedicarboxylic ester for 2 hr at 200°, gives 4-methylphthalic acid and 3-methyl-1-



(1)

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(1) O. Diels and K. Alder, *Ber.*, **62**, 554 (1929).

(2) M. C. Kloetzel, *Org. Reactions*, 4, 6 (1948).

(3) O. Diels and K. Alder, *Ber.*, **62**, 2337 (1929).

(4) L. I. Onischenko, "Diene Synthesis," Israel Institute for Scientific Translations, Jerusalem, 1964.

(5) A. Wassermann, "Diels-Alder Reactions," Elsevier Publishing Co., New York, N. Y., 1965.

(6) J. Sauer, *Angew. Chem. Intern. Ed. Engl.*, **5**, 211 (1966); **6**, 16 (1967).

(7) R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **87**, 395, 2046, 2511, 4388, 4389 (1965).

(8) P. Millie, *Bull. Soc. Chim. France*, 4031 (1966).

(9) K. Alder and H. F. Rickert, *Ann.*, **524**, 180 (1936); *Ber.*, **70**, 1354 (1937).

butene (eq 1). Another illustration is that of 1,2-dihydrophthalic acid which, when treated in the same way with acetylenedicarboxylic ester, gives phthalic acid and maleic acid. This type of reaction constitutes a good diagnostic test for the cyclohexadiene structure in a compound, since only such structures are capable of manifesting this behavior. Thus, the adduct of cyclopentadiene and dimethyl acetylenedicarboxylate can be vacuum distilled at 134° (10 mm) but dissociates reversibly into its addends at higher temperatures. Decomposition of the acetylenedicarboxylic adducts of cycloheptadiene and furan has not been observed.

The ease of analysis of the aromatic products makes this reaction useful for stereochemical investigations of the Diels–Alder reaction. For instance, Wynn and Klein[10] studied the directive influence of substituents by noting the proportion of *ortho-* to *meta*-substituted benzoate obtained by reaction of ethyl 1,3-cyclohexadiene-1-carboxylate with monosubstituted acetylenes. The Diels–Alder additions were run at 320° in a sealed tube, and the intermediate bicyclic adduct was not isolable. No reaction occurred under milder conditions.

Maleic anhydride adducts dissociate much more readily than adducts of acetylenic dienophiles. Adducts of cyclic dienes are less stable than those of acyclic dienes, and adducts of cyclopentadiene decompose more readily than those of cyclohexadiene. Riemschneider and Becker[11] have determined the decomposition temperature of a number of maleic anhydride adducts by adding a mixture of adduct and *trans*-1,4-diphenylbutadiene to a heated flask containing glass beads. Diphenylbutadiene is a high-boiling, reactive diene which combines with the maleic anhydride from the dissociation of the adduct and therefore prevents recombination of the original addends. The diene thus set free then distils over. In all cases studied, the temperature required was above 250°. The adduct of 2,3-dimethylbutadiene decomposed at 290–310°, that of cyclohexadiene at 310–325°. The 5-norbornene-2,3-dicarboxylic anhydride was found[12] to exchange with 2,3-dimethylbutadiene and produce cyclopentadiene at 200°.

As might be expected, the liberated addends from adducts of maleic anhydride with cyclohexadienes can undergo an exchange reaction to give aromatic compounds. Thus Littmann[13] found that the maleic adduct of α-terpinene decomposes upon atmospheric pressure distillation using a free flame to give *p*-cymene and succinic anhydride. Strangely, however, the barium salt of this adduct does not show this disproportionation. Upon dry distillation it gives[14] α-terpinene and only 7% *p*-cymeme. A similar reaction occurs[15] when the adduct of anthracene and acetylenedicarboxylic acid is allowed to react with butadiene. The adduct of anthracene and acetylenedicarboxylic acid contains the maleic acid grouping and is thus a good dienophile. Upon attempted vacuum distillation of the adduct of this with butadiene, the products obtained are 3,6-dihydrophthalic anhydride and anthracene. However, if the temperature is raised slightly these products disproportionate to give phthalic anhydride and 9,10-dihydroanthracene.

Anthracene is not the only polycyclic aromatic compound which adds dienophiles. In general any aromatic compound for which complete Kekulé structures cannot be drawn for all the rings will add dienophiles.[16] Bachmann and Kloetzel[17] have treated maleic anhydride with a number of polycyclic aromatic compounds in boiling xylene. With a 1:1 mole ratio of diene to dienophile the reactions do not go to completion but instead reach an equilibrium. The following table, reproduced from Bachmann and Kloetzel, shows the per cent of adduct at equilibrium for a number of polycyclic aromatic compounds and demonstrates the existence of structural effects regulating the relative ease of the forward and reverse Diels–Alder reactions.

Diene	% adduct
Anthracene	99
9-Methylanthracene	99
9,10-Dimethylanthracene	98
9-Phenylanthracene	75
9,10-Diphenylanthracene	16

Synthetic applications of the retrodiene reaction are numerous. A great many of these involve use of the Diels–Alder reaction for much the same purpose as one introduces a protecting group during a synthesis. Probably the earliest example of this was the preparation of acetylenedicarbonyl chloride by Diels and Thiele.[18] When acetylenedicarboxylic acid is treated with PCl_5, the only product is chlorofumaroyl chloride. However, the adduct of anthracene and acetylenedicarboxylic acid will give a normal acid chloride upon treatment with PCl_5. If this is now treated with maleic anhydride at 190°, the products are acetylenedicarbonyl chloride and the anthracene–maleic anhydride adduct. Direct decomposition of the anthracene–$ClCOC{\equiv}CCOCl$ adduct requires such a high temperature that only oxidative degradation products, CO_2, CO, and phosgene, were obtained. In a similar spirit is the partial oxidation of cyclopolyenes to cyclo-

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[10] C. M. Wynn and P. S. Klein, *J. Org. Chem.*, **31**, 4251 (1966).

[11] R. Riemschneider and E. Becker, *Monatsh. Chem.*, **91**, 148 (1960).

[12] D. Craig, *J. Am. Chem. Soc.*, **73**, 4889 (1951).

[13] E. R. Littmann, *ibid.*, **57**, 586 (1935).

[14] E. Tischenko and A. I. Bogomolov, *Byull. Vsesoyuz Khim. Obshchestva im D. I. Mendeleeva*, **35** (1939); *Chem. Abstr.*, **34**, 4386 (1940).

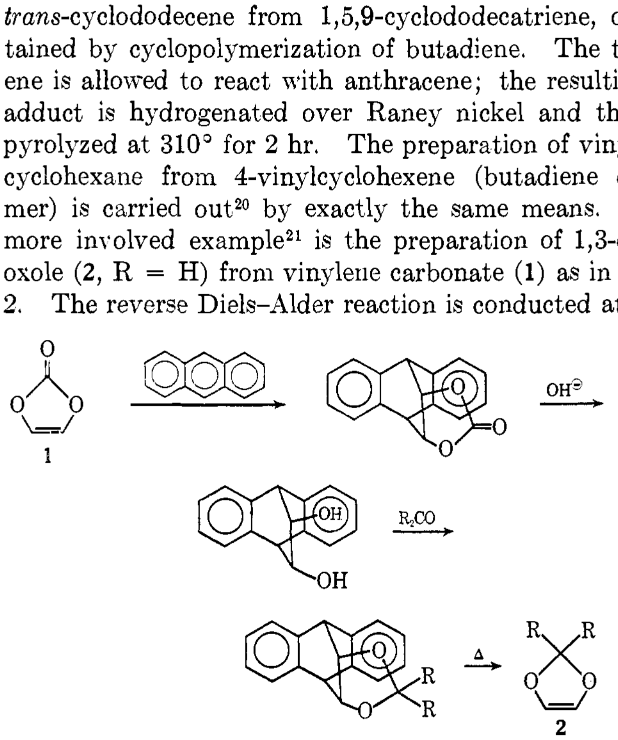
[15] O. Diels and W. Friedrichsen, *Ann.*, **513**, 145 (1934).

[16] J. A. Norton, *Chem. Rev.*, **31**, 319 (1942).

[17] W. E. Bachmann and M. C. Kloetzel, *J. Am. Chem. Soc.*, **60**, 481 (1938).

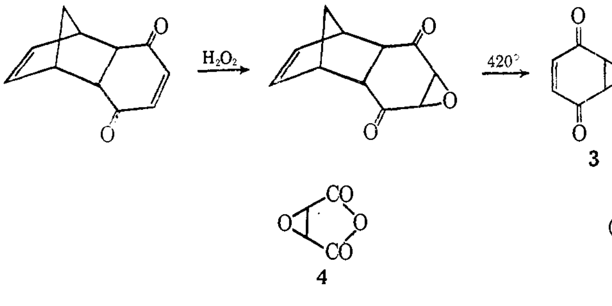
[18] O. Diels and W. E. Thiele, *Ber.*, **71**, 1173 (1938).

alkenes. Thus Waddan[19] claims an 80% yield of *trans*-cyclododecene from 1,5,9-cyclododecatriene, obtained by cyclopolymerization of butadiene. The triene is allowed to react with anthracene; the resulting adduct is hydrogenated over Raney nickel and then pyrolyzed at 310° for 2 hr. The preparation of vinylcyclohexane from 4-vinylcyclohexene (butadiene dimer) is carried out[20] by exactly the same means. A more involved example[21] is the preparation of 1,3-dioxole (**2**, R = H) from vinylene carbonate (**1**) as in eq 2. The reverse Diels–Alder reaction is conducted at a temperature such that the dioxole distils off while the anthracene remains behind. Consequently, the method is limited to fairly volatile dioxoles.



(2)

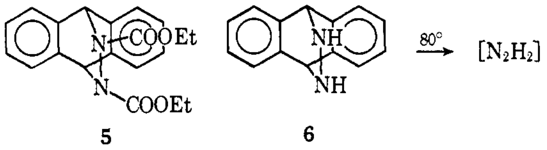
Anthracene is of course not the only diene which may be used in this sort of synthetic scheme. Alder[22] used cyclopentadiene in his preparation of benzoquinone epoxide (**3**) (see eq 3). Alkaline hydrogen peroxide is a mild reagent for epoxidation of α,β-unsaturated ketones including naphthoquinone, but with benzoquinone it gives only **4**. Using dimethylfulvene as the diene component of the adduct, the decomposition temperature may be lowered to 50°, but this diene fails to react with hindered benzoquinones such as 2,5-dimethylbenzoquinone.



(3)

The reverse Diels–Alder reaction is also the usual method for the preparation of maleimide.[23] Unlike succinimide, maleimide cannot be obtained simply by fusion of the corresponding ammonium salt. However, the maleic anhydride adducts of anthracene and cyclopolyenes will give imides by this method. When these imides are passed through a tube packed with chipped glass and heated to 200–500°, maleimide is obtained. Maleic anhydride can be used to trap the diene also liberated, but it is not necessary.[24] Prill also claims furan as a useful diene in this synthesis, but it has been mentioned that the instability of the furan–maleic anhydride adduct would not allow it to survive the ammonium salt fusion.[23,25] Furan adducts are further discussed in section VI.

The retrodiene reaction also serves for the generation of a number of unstable intermediates. Possibly the most important example of this is the procedure developed by Corey and Mock[26] for carrying out the diimide reduction in homogeneous medium. Reaction of ethyl azodicarboxylate with anthracene gives **5**, which is saponified with ethanolic sodium hydroxide at 25° under nitrogen. Upon standing 20 hr decarboxylation occurs to give **6**, the diimide precursor, which undergoes the retrodiene reaction at about 80°. The diimide reduction can subsequently be carried out simply by refluxing **6** and the compound to be reduced in the ethanol solution.



Another interesting intermediate[27] is ethenetetracarboxylic dianhydride, C_6O_6. Since maleic anhydride is a more active dienophile than maleonitrile, this oxide would be expected to be more active than tetracyanoethylene. Because of ring strain caused by the double bond, one would not expect this compound to be isolable, but it was generated in solution by making use of the fact that adducts of polycyclic aromatic compounds are in equilibrium in solution with a π complex of diene and dienophile. The diene chosen was 9,10-dimethoxyanthracene, the adduct of which with tetracyanoethylene is entirely decomposed in solution. Treatment of the adduct of this diene and ethenetetracarboxylic acid with acetyl chloride gave **7**, which precipitated out of ether or acetone solution. When dissolved in dioxane, **7** is in equilibrium with 20% C_6O_6, which is extremely reactive and may be trapped with almost any diene.

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[19] D. Y. Waddan, British Patent 1,015,875 (1966).

[20] H. Slaugh and E. F. Magoon, *J. Org. Chem.*, **27**, 1037 (1962).

[21] N. D. Field, *J. Am. Chem. Soc.*, **83**, 3504 (1961).

[22] K. Alder, F. H. Flock, and H. Beaumling, *Ber.*, **93**, 1896 (1960).

[23] E. J. Prill, U. S. Patent 2,524,136; *Chem. Abstr.*, **45**, 1162 (1951).

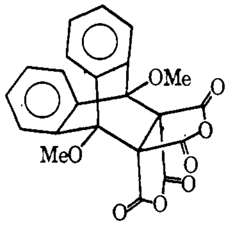
[24] P. O. Tawney, U. S. Patent 2,524,145; *Chem. Abstr.*, **45**, 1162 (1951).

[25] J. A. Berson and R. Swidler, *J. Am. Chem. Soc.*, **76**, 2835 (1954).

[26] E. J. Corey and W. L. Mock, *ibid.*, **84**, 685 (1962).

[27] J. Sauer, B. Schroder, and A. Mielert, *Ber.*, **100**, 315 (1967); J. Sauer, B. Schroder, and R. Wiemer, *ibid.*, **100**, 306 (1967).

Upon refluxing the dioxane solution of **7** for 90 hr, **8** is isolated. This compound is stable in solution. In spite of its instability in solution, **7** is extremely stable thermally, subliming unchanged at 400° and decomposing only above 500°.



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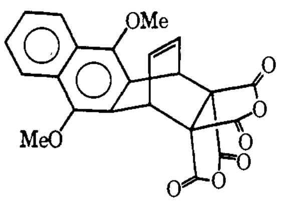

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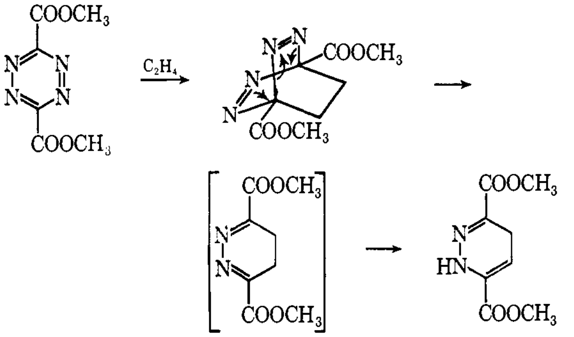
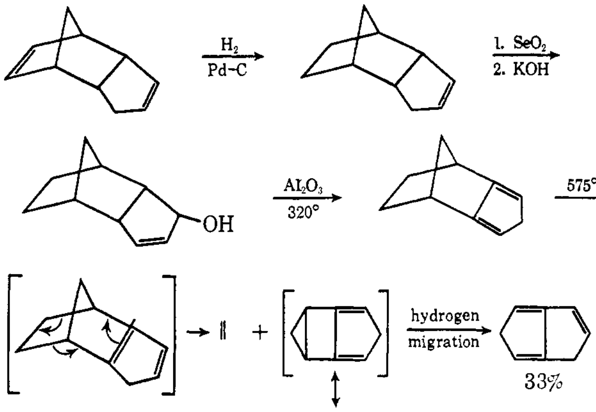
The above is part of Sauer's extensive investigations[27] into the electronic effects of substituents on diene and dienophile. Although extremely interesting, most of this work is not relevant to a study of the reverse Diels–Alder reaction. There is, however, one example which involves both the reverse Diels–Alder reaction and a forward Diels–Alder with inverse electronic effect, namely, the reaction of tetrazines with olefins to give dihydropyridazines,[28] as in eq 4. This has been suggested as a titrimetric reaction for olefins.[29] Tetrazines also react with acetylenes to give pyridazines, but, as expected of the inverse electronic effect, this reaction occurs less readily than the one with olefins.



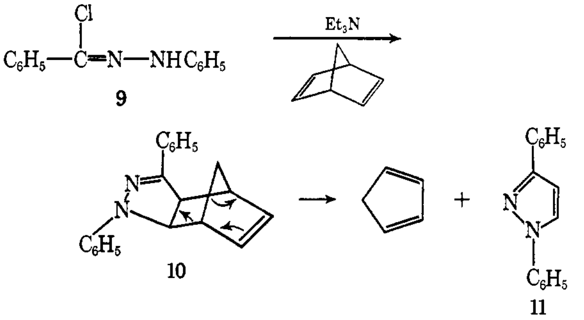
(4)

Some synthetic applications of the reverse Diels–Alder reaction clearly do not involve the forward reaction at any stage. One example is the preparation of dihydropentalene from dicyclopentadiene by the following series of reactions[30] in eq 5. This can be viewed[30a] as involving preliminary hydrogen migration followed by the reverse Diels–Alder. A similar isomerization appears to occur simultaneously with or just after the dehydration reactions forming isodicyclopentadiene, the structure of which has been proven.[30b] It should be recalled that cyclopentadiene is usually prepared[31] just before use by thermal decomposition of dicyclopentadiene. This procedure is illustrative of the very extensive synthetic utilization of the reverse Diels–Alder. It is applied whenever it is possible to preserve a reactive diene as a stable dimeric adduct, to be reversed at will by simple thermal means.



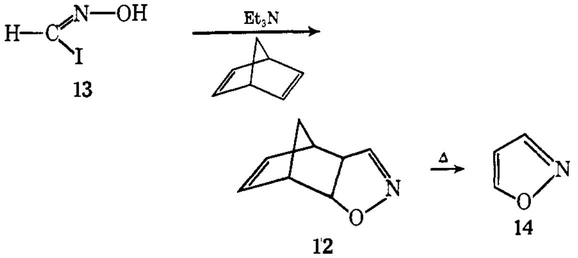
(5)

In a few cases the products of 1,3-dipolar addition undergo a retrodiene reaction. One example of this is **10**, the adduct of diphenyl nitrilimine (generated *in situ* from **9**) and norbornadiene. This decomposes at its melting point of 135° to give **11** in 98% yield along with 77% cyclopentadiene[32] (see eq 5a).



(5a)

Similarly **12**, the 1,3-dipolar adduct of norbornadiene and fulminic acid, generated *in situ* by dehydroiodination of **13**, undergoes the reverse Diels–Alder reaction at 140–160° to give cyclopentadiene and isoxazole (**14**), in 90% yield[33] (eq 5b).



(5b)

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(28) J. Sauer, A. Mielert, D. Lang, and D. Peter, *Ber.*, **98**, 1435 (1965).

(29) C. D. Nenitzescu, M. Avram, I. G. Dinulescu, and E. Marica, *ibid.*, **95**, 2248 (1962).

(30) (a) T. J. Katz, M. Rosenberger, and R. K. O'Hara, *J. Am. Chem. Soc.*, **86**, 249 (1964); K. Alder, F. H. Flock, and P. Janssen, *Ber.*, **89**, 2689 (1956).

(31) R. B. Moffett, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 238.

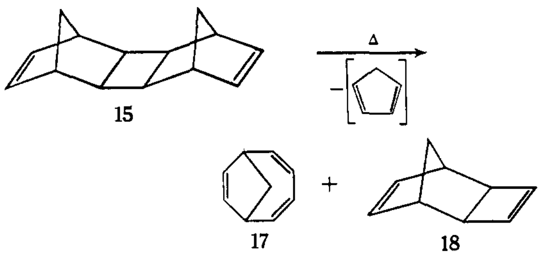
(32) R. Huisgen, M. Seidel, G. Wallbillich, and H. Knupfer, *Tetrahedron*, **17**, 3 (1962).

(33) R. Huisgen and M. Christl, *Angew. Chem. Intern. Ed. Engl.*, 5, 456 (1967).

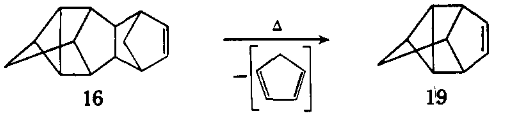
Norbornadiene serves as a starting material for the synthesis of a number of interesting fused ring hydrocarbons. Dimerization of norbornadiene by heat alone or by use of carbonyl or phosphite ester complexes of iron, cobalt, or nickel as catalysts leads to a mixture of **15** and **16**, with **15** predominating. There are many possible stereoisomers of these compounds, but only a few are actually obtained by the dimerization.[34] For example,[35] decomposition of **15** in a flow system at 400° with a residence time of 9.6 sec gives 44% of **17**, 10% of **18**, 29% of cyclopentadiene, and 17% of unreacted **15** (see eq 5c).

Similarly **16**, prepared in 65% yield by dimerization of norbornadiene on 5% Rh-C at 110° for 23 hr,[36] gives a 28% yield of **19** upon pyrolysis[37] at 550°.

The formation of **15** is a 2 + 2 cycloaddition, that is, the coming together of two olefinic double bonds, each with two π electrons, to form a cyclobutane ring. By obvious extension, the formation of **16** is a 2 + 2 + 2 cycloaddition, also known as a homo-Diels–Alder addition. Further discussion of this point will be found in sections VII and VIII. It should be noted, however, that **19** formed in eq 5d may arise directly by 2 + 2 + 2 cycloaddition of acetylene to norbornadiene using the catalyst system mentioned above.[34,36]



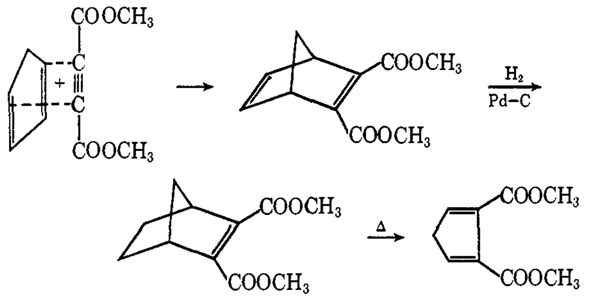
(5c)



(5d)

II. HYDROGENATED ADDUCTS OF ACETYLENEDICARBOXYLIC ACID

Adducts of acetylenedicarboxylic esters with dienes other than cyclohexadienes are very stable. When these adducts are hydrogenated under mild conditions, generally platinum or palladium catalyst at room temperature and 1–3 atm, 1 mole of hydrogen is absorbed. The double bond next to the carboxyl groups is not reduced except under forcing conditions. These dihydrogenated adducts are generally also quite stable. However, it can be seen from the structure of these adducts that they should be able to undergo a retrodiene reaction in the reverse direction from which the components added to give an olefin and a dicarboxylated diene (eq 6 and 7).



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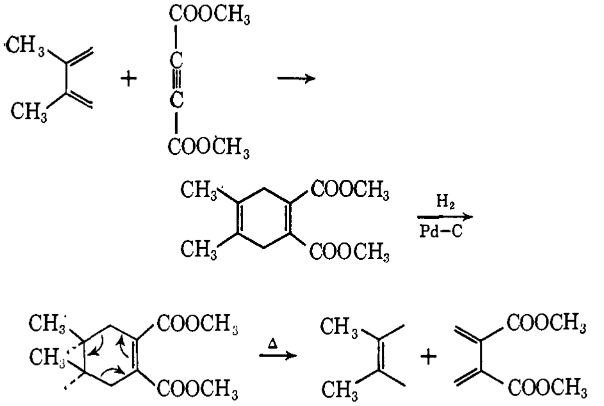

(7)

The first example of this type of reaction was observed by Alder and Rickert[9] in 1937. These workers found that when the dihydrogenated adduct of furan and dimethylacetylenedicarboxylate was vacuum distilled, two fractions were obtained. The larger, and higher boiling, of the two fractions boiled at 140–165° (11 mm) and was identified as 3,4-dicarbomethoxyfuran. A similar reaction was obtained with sylvan (2-methylfuran). In both cases the lower boiling fraction was found to be undecomposed adduct. Hoffmann and coworkers[38] have used this reaction for the synthesis of oxybiotin. The dihydrogenated adduct of 2-furanpentanol and diethyl acetylenedicarboxylate was found to evolve ethylene at about 190°.

Furan is known to have about 18 kcal/mole of resonance stabilization, and the presence of a carboxyl group increases the stability of the ring toward acidic reagents.[39] Thus, furan can be considered "semiaromatic" and its carboxyl derivatives even more aromatic. Consequently, if aromaticity has anything to do with the tendency for this reaction to occur, pyrrole and its derivatives should react very nicely. Unfortunately pyrrole is so aromatic that it tends to react with dienophiles by substitution at the 2 and 5 positions rather than by 1,4 addition. However, certain N-sub-

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[34] L. G. Cannell, *Tetrahedron Letters*, 5967 (1966).

[35] L. G. Cannell, French Patent 1,435,268; *Chem. Abstr.*, **66**, 10659v (1967).

[36] T. J. Katz and J. J. Mrowca, *J. Am. Chem. Soc.*, **88**, 4012 (1966).

[37] T. J. Katz, J. C. Carnahan, and R. Boecke, *J. Org. Chem.*, **32**, 1301 (1967).

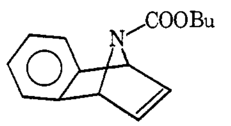
[38] K. Hoffmann, A. Bridgewater, and A. E. Axelrod, *J. Am. Chem. Soc.*, **71**, 1254 (1949); K. Hoffmann, *ibid.*, **67**, 421, 1495 (1945).

[39] A. P. Dunlop and F. N. Peters, "The Furans," Reinhold Publishing Corp., New York, N. Y., 1953, pp 6, 489.

stituted pyrroles will undergo Diels–Alder addition. For instance, Gabel[40] found that 1-carbethoxy-2,5-dimethylpyrrole reacted with acetylenedicarboxylic ester at 160° to produce 1,3,4-tricarbethoxy-2,5-dimethylpyrrole and acetylene. The acetylene was identified by leading it into ammoniacal cuprous chloride and noting the precipitate of cupric acetylide. The acetylene evolution begins at 140°, but using a reaction temperature below this leads only to starting materials; the adduct itself was never isolated. N-Carbethoxypyrrole undergoes the same reaction, but 1-carbethoxy-2,5-diphenylpyrrole is inert to dienophiles. Gabel[40] explains that the electron-withdrawing carbethoxy group on the nitrogen decreases the aromatic character of the pyrrole ring sufficiently for it to react as a diene.

Mandell and Blanchard[41] refluxed N-benzylpyrrole and acetylenedicarboxylic acid in ether for 24 hr. They obtained 9% of addition product and 45% of substitution products. The adduct was stable to hot water but decomposed to the addends upon treatment with hot 10% aqueous $NaHCO_3$. The dihydrogenated adduct, upon refluxing 24 hr in 10% aqueous $NaHCO_3$, gave an N-benzylpyrroledicarboxylic acid, which lost 2 moles of CO_2 upon treatment with 10% aqueous HCl. The carboxyl groups were assigned the 3 and 4 positions on the basis of analogy to the furan case. This analogy is rendered somewhat doubtful by the fact that the reaction occurred only in base, which is not a normal requirement for a retrodiene reaction. The authors ascribe the ability of this pyrrole to undergo the normal diene addition to steric inhibition of resonance by the benzyl group.

N-Carbalkoxypyrroles also add benzyne. Addition[42] of N-carbo-*t*-butoxypyrrole to benzyne generated from *o*-fluorobromobenzene gave a 40% yield of **20**. Decarboxylation of **20** by passing dry HCl through a solution of the compound in nitrobenzene gave the parent **21** as its hydrochloride. This could not be prepared[43] by direct reaction of benzyne with pyrrole.



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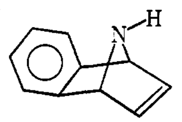

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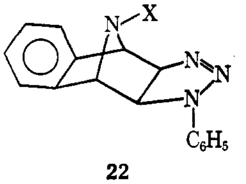

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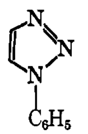

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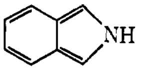

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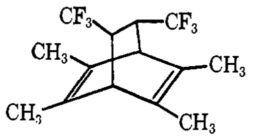
Both **20** and **21** reacted with phenyl azide to give **22**, which underwent a retrodiene reaction at 70° (X = H) or 120° (X = COOBu) to give **23**. The other expected product, isoindole (**24**), is known to be extremely unstable, although Kreher and Seubert[44] have succeeded in trapping it with maleic anhydride.

Work in this laboratory[45] was undertaken in the attempt to demonstrate this reaction with adducts of hydrocarbon dienes. The results only show that it does not occur readily. However, the reaction can be made to occur. Barney and Stevenson[46] obtained 2,3-dicarbomethoxybutadiene by pyrolysis of 1,2-dicarbomethoxy-1-cyclohexene at 700–800°. The preferred method is to pass the compound through a heated tube at a pressure of less than 50 mm. The reaction does not occur below 500°; above 1000° "deep-seated decomposition" tends to occur.[46] The product obtained is purified by distillation at 40° (0.1 mm) and by freezing, the melting point being 16–18°. The dicarbomethoxybutadiene polymerizes readily to give a polymer with molecular weight 5000 or more; an inhibitor must be added to prevent polymerization during distillation. Analogously, pyrolysis of 1-carbomethoxycyclohexene at 750–850° gives the dimer of 2-carbomethoxybutadiene.[47] Even though the pyrolyzate was collected in a Dry Ice cooled receiver, monomeric 2-carbomethoxybutadiene could not be isolated. On the other hand, 2-norbornene-2,3-dicarboxylic anhydride and the corresponding dimethyl ester gave only tar upon attempted retrodiene decomposition at 350–400°. No cyclopentadiene-3,4-dicarboxylate could be found.[45]

By exactly similar means, 2,3-di(trifluoromethyl)-butadiene has been prepared from hexafluoro-2-butyne and butadiene. In this case, the cyclohexene ring was cleaved at a temperature of 800° and a pressure of 5 mm.[48] Hexafluoro-2-butyne is a very interesting dienophile in other respects too, for it reacts with durene at 200° in an autoclave to give **25**, thus providing one of the few examples[49] of a Diels–Alder reaction of a monocyclic aromatic compound. At 250° **25** undergoes a reverse Diels–Alder reaction to give **26**. Even benzene itself reacts with hexafluoro-2-butyne at 250°,



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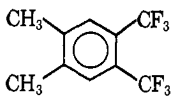

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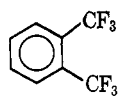

27

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(40) N. W. Gabel, *J. Org. Chem.*, **27**, 301 (1962).

(41) L. Mandell and W. A. Blanchard, *J. Am. Chem. Soc.*, **79**, 6198 (1957).

(42) L. A. Carpino and D. E. Barr, *J. Org. Chem.*, **31**, 764 (1966).

(43) G. Wittig and B. Reichel, *Ber.*, **91**, 2358 (1963).

(44) R. Kreher and J. Seubert, *Z. Naturforsch.*, **20B**, 75 (1965).

(45) H. Kwart and K. King, unpublished results.

(46) A. L. Barney and H. B. Stevenson, U. S. Patent 2,870,196; *Chem. Abstr.*, **53**, 11237 (1959).

(47) J. C. Westfahl, U. S. Patent 2,480,892; *Chem. Abstr.*, **44**, 4024 (1950).

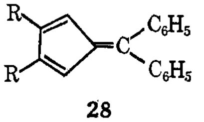
(48) R. E. Putnam, R. J. Harder, and J. E. Castle, *J. Am. Chem. Soc.*, **83**, 391 (1961).

(49) T. L. Cairns, C. G. Krespan, and B. C. McKusick, *ibid.*, **83**, 3428 (1961).

but the only isolable product is **27**, resulting from retrodiene decomposition.

The preparation of 2,3-dicarbomethoxybutadiene by other means has also been reported, but there is no record of the corresponding anhydride.[50] A cyclopentadiene-3,4-dicarboxylic ester has never been reported in any form. Clearly, this compound, if it can be prepared at all, cannot be rescued from the circumstances of pyrolysis of a 2-norbornene-2,3-dicarboxylic ester. In addition, the compound reported by Baeyer[51] as a 1,3-cyclohexadiene-2,3-dicarboxylic ester, prepared by reduction of phthalic acid, and long accepted as such, has now been shown[52,53] to be a 1,4-cyclohexadiene-2,3-dicarboxylic ester.

Further discussion of the retrodiene reaction of hydrogenated adducts of acetylenedicarboxylic acid derivatives is remanded to section VI in connection with *endo–exo* isomerism. In passing, it must be emphasized, however, that the stability of the retrodiene products at the temperatures which induce measurable amounts of reaction often may be the sole factor determining whether the true products can be identified. Thus, while **28** can be readily obtained at temperatures as low as 195° from **29**, the analogous dimethylfulvene-derived substrate, **30**, affords only tarry products on attempted retrodiene decomposition.



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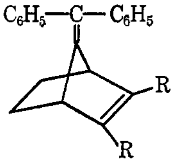

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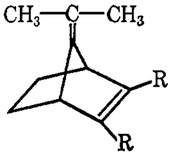


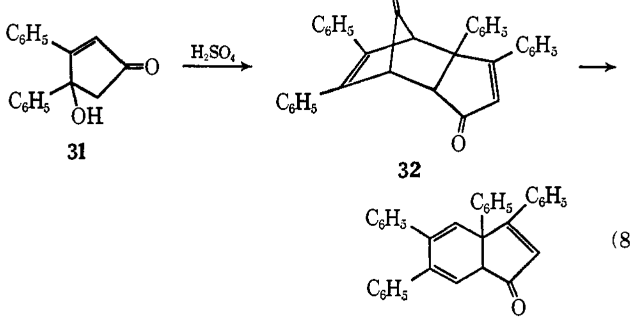
R = —$COOCH_3$

30

III. CYCLOPENTADIENONES

Cyclopentadienone and most of its derivatives have never been isolated because of their tendency to undergo Diels–Alder dimerization. This dimerization is irreversible because the dimers, which are highly strained 7-ketonorbornene derivatives, lose carbon monoxide by a reverse Diels–Alder mechanism on mild heating. The cause of this dimerization has been studied by Garbisch and Sprecher.[54] These workers prepared 2-*t*-butylcyclopentadienone and 2,4-di-*t*-butylcyclopentadienone. Steric hindrance prevents the facile dimerization of these compounds, so their spectra could be obtained. The results show an unusually small energy difference between the highest occupied and lowest unoccupied molecular orbitals. Since the Diels–Alder transition state involves an interaction[55] of the highest occupied orbital of one addend with the lowest unoccupied orbital of the other, the facile dimerization becomes obvious.

The 3,4-diphenylcyclopentadienone system is a typical example.[56] The starting material, anhydracetonebenzil (**31**), can easily be dehydrated to form **32**. Upon being heated to 210°, **32** loses CO to form **33** (eq 8). The latter is very difficult to isolate because, on further heating at the same temperature, it rearranges to **34**; however, it can be trapped with maleic anhydride to give **35**. If **31** is heated with maleic anhydride to 200°, dehydration and loss of carbon monoxide occur with production of **36**. Similarly,[16] attempts to produce tetrachlorocyclopentadienone result in **37**.



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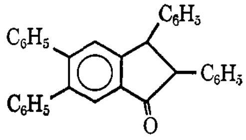

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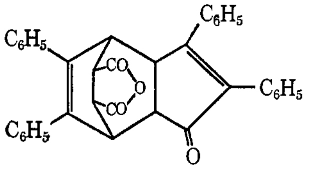

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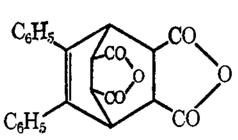

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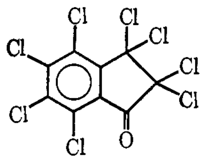

37

As might be expected, adducts of cyclopentadienones with acetylenic dienophiles cannot be isolated, since loss of carbon monoxide from these gives an aromatic system. Thus[16] dehydration of triphenylcyclopentenolone in the presence of phenylacetylene gives tetraphenylbenzene. The same product can be obtained using styrene as dienophile, since the cyclohexadiene produced is very easily dehydrogenated.

Tetracyclone (tetraphenylcyclopentadienone) is a common starting material for preparation of many interesting aromatic systems. The usefulness of this reagent is enhanced by the fact that it does not dimerize

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(50) W. J. Bailey, R. L. Hudson, and E. T. Yates, *J. Org. Chem.*, **28**, 828 (1963).

(51) A. Baeyer, *Ann.*, **258**, 145 (1890); **269**, 145 (1892).

(52) V. F. Kucherov and N. Ya. Grigoreva, *Izv. Akad Nauk SSSR*, 2196 (1962); English transl., p 2100.

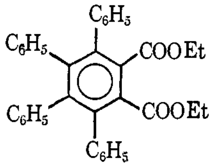
(53) M. J. Goldstein and G. L. Thayer, *J. Am. Chem. Soc.*, **87**, 1933 (1965).

(54) E. W. Garbisch and R. F. Sprecher, *ibid.*, **88**, 3433 (1966).

(55) K. Fukui, "Molecular Orbitals in Chemistry, Physics, and Biology," P. O. Lowdin and B. Pullman, Ed., Academic Press Inc., New York, N. Y., 1964, p 513.

(56) C. F. H. Allen and E. W. Spanagel, *J. Am. Chem. Soc.*, **55**, 3773 (1933).

and thus need not be generated *in situ*. Thus, reaction of tetracyclone with diethyl acetylenedicarboxylate in a sealed tube at 300° for 2 hr gives diethyl tetraphenylphthalate (**38**), which is so hindered that it cannot be saponified, even by molten NaOH.[57] Similarly **39** is prepared[58] in 59% yield by reaction of tetracyclone with 2-butyne-1,4-diol in refluxing *p*-cymene. In all these cases loss of carbon monoxide from the adduct is extremely rapid. In fact, Becker and Dudkowski[59] have used the CO evolution to follow the kinetics of addition of tetracyclone to a number of phenylacetylenes of the type $PhC\equiv CY$ in order to study the electronic effects of the substituent Y.



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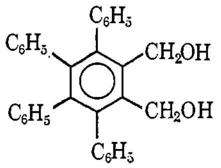

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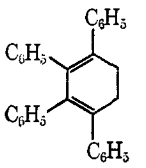

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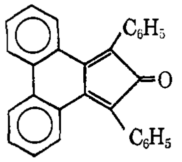
Even with ethylenic dienophiles, tetracyclone adducts are rarely isolable. For example, tetracyclone reacts with ethylene at 105° and a pressure of 100 psi to give[60] a mixture of tetraphenylbenzene and tetraphenylcyclohexadiene (**40**). However, use of an aluminum chloride catalyst permits isolation of the adduct, which melts with loss of CO at 90–95°. Only with maleic anhydride is the adduct easily isolable;[57] it forms at 155°, melts at 220°, and loses carbon monoxide at 235°.

Even highly hindered aromatic systems are accessible *via* cyclopentadienones. For example, 2,3,5-tri-*t*-butylcyclopentadienone reacts with *t*-butylacetylene at 250° to give 1,2,4,5-tetra-*t*-butylbenzene in 70% yield.[61] Infrared and ultraviolet spectra indicate that steric strain due to the *o*-*t*-butyl groups forces the benzene ring into a boat form. Tri-*t*-butylcyclopentadienone results in 12% yield from the reaction of *t*-butylacetylene, di-*t*-butylacetylene, and cobalt octacarbonyl. It also reacts with dimethyl acetylenedicarboxylate at 200° to give 70% of the corresponding dimethyl tri-*t*-butylphthalate.

MacKenzie[62] treated tetracyclone with norbornadiene to give tetraphenylbenzene and cyclopentadiene. By carrying out the reaction in boiling xylene swept with nitrogen, and leading the effluent nitrogen into an ethereal solution of maleic anhydride, the adduct of cyclopentadiene and maleic anhydride could be isolated from the ether. Phencyclone (**41**) underwent the same reaction. However, in this case the adduct **42** was itself isolable. Compound **42** lost CO and cyclopentadiene at 200° to give **43**, but, while decomposition of the adduct of phencyclone with 2,3-dicarbomethoxy-2,5-norbornadiene (**44**) also gave **43**, no evidence for 3,4-dicarbomethoxycyclopentadiene (**45**) was found, even when the adduct **44** was decomposed in boiling nitrobenzene containing maleic anhydride.



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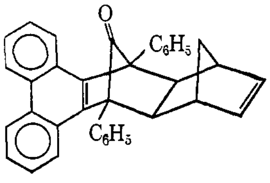

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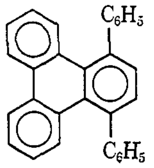

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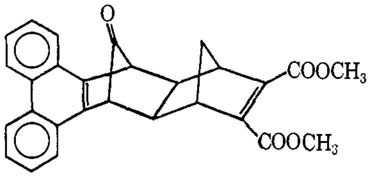

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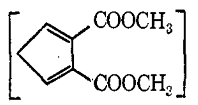

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2,5-Dimethyl-3,4-diphenylcyclopentadienone is the only cyclopentadienone shown to form a dimer reversibly.[63] When the precursor reagent dimethylanhydracetonebenzil is dehydrated, a colorless solid dimer is obtained. Solutions of this dimer, however, rapidly became colored, indicating the presence of monomer. All phenylcyclopentadienones are colored. When the dimer is treated with 2,4-dinitrophenylhydrazine, a monomeric dinitrophenylhydrazone is obtained.

The retrodiene decomposition of cyclopentadienone adducts involves breaking two bonds from the same carbon atom, thus producing a carbene. Carbon monoxide is a stable carbene and forms readily. We must then expect adducts of cyclopentadienol derivatives to decompose similarly to give aldehydes. Allen and VanAllan[64] added phenylmagnesium bromide and benzylmagnesium bromide to tetracyclone and treated the carbinols obtained with styrene and with acetylenedicarboxylic ester. At 290–300° (15 mm), the adduct of pentaphenylcyclopentadienol with styrene gave 35% styrene and 24% benzaldehyde. The moiety remaining after loss of benzaldehyde was isolated as pentaphenylbenzene. The adduct of pentaphenylcyclopentadienol and acetylenedicarboxylic ester gave benzaldehyde and tetraphenylphthalic ester cleanly at this temperature.

These are not the only examples of this sort of reaction. The adduct of dimethyl acetylenedicarboxylate and 1,1-difluoro-2,3,4,5-tetrachlorocyclopentadiene decomposes at 480° to give[65] dimethyl tetrachloro-

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[57] C. F. H. Allen and L. J. Sheps, *Can. J. Res.*, **11**, 171 (1936).

[58] E. I. Becker, E. F. Bonner, and A. G. Finkensieper, *J. Org. Chem.*, **18**, 426 (1953).

[59] E. I. Becker and J. J. Dudkowski, *ibid.*, **17**, 201 (1952).

[60] C. F. H. Allen, J. A. VanAllan, and R. W. Ryan, *ibid.*, **27**, 778 (1962).

[61] G. Hoogzand and W. Hubel, *Tetrahedron Letters*, 637 (1961).

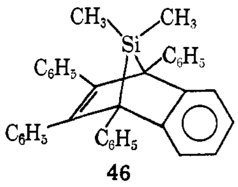
[62] K. MacKenzie, *J. Chem. Soc.*, 473 (1960).

[63] C. F. H. Allen and J. A. VanAllan, *J. Am. Chem. Soc.*, **64**, 1260 (1942).

[64] C. F. H. Allen and J. A. VanAllan, *ibid.*, **65**, 1384 (1943).

[65] E. T. McBee, D. K. Smith, and H. E. Ungnade, *ibid.*, **77**, 387 (1955)

phthalate in 83% yield. The fate of the CF_2 group was not reported. Furthermore, **46**, prepared from **47** and benzyne, decomposes at 300° to give 72% of 1,2,3,4-tetraphenylnaphthalene and a dimethylpolysilane, $(Me_2Si)_x$.[66] When the decomposition is conducted in the presence of diphenylacetylene, **48** is obtained in 50% yield. This compound is also obtained from decomposition of the adduct of **47** and diphenylacetylene. However, **48** cannot be obtained from the adduct of **47** and dimethyl acetylenedicarboxylate, although dimethyl tetraphenylphthalate is produced.



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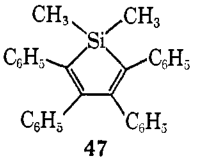

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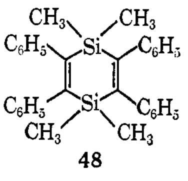

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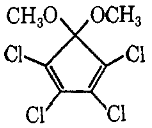
Cyclopentadienone ketals have recently been very thoroughly investigated.[67,68] Reaction of **49** with dimethyl acetylenedicarboxylate at 145° does not give the expected adduct, but instead gives **50** in 59% yield, along with methyl chloride. Similarly **51**, allowed to react with dimethyl acetylenedicarboxylate at room temperature, gives an 88% yield of **52**. However, when **49** is allowed to stand with phenylacetylene at 70° for several days, the expected adduct, **53**, is obtained in about 50% yield. This adduct decomposes above 120° to a mixture of **54** and **55**, the relative yields of each depending on solvent. Nonpolar solvents favor **54**, whereas polar solvents favor **55**; the yield of **54** is 63% in CCl_4 but only 28% in pyridine.[63,67] Decomposition of solid **53** at 130° (4 mm) gives 55% of **54** and 40% of **55**.



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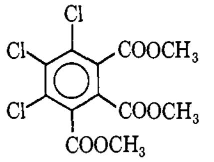

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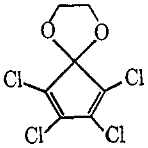

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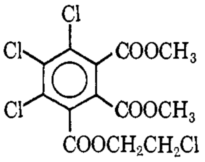

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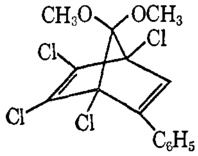

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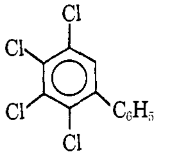

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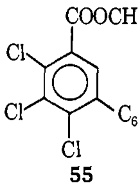

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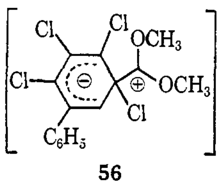

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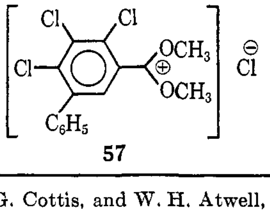

57

Of greatest interest is the fate of the bridge ketal group. In the absence of air and water, the only product traceable to the bridge is tetramethoxyethylene. In the presence of oxygen a complex mixture including methyl formate, acetate, oxalate, and carbonate is obtained. When **53** is dropped into hot decalin, trimethyl orthoformate is obtained in about 50% yield.[68] On the other hand, the adduct of **51** and phenylacetylene decomposes cleanly to ethylene, CO_2, and **54**. Correspondingly, vapor-phase decomposition of 7,7-dimethoxynorbornadiene, prepared from trimethyl orthoformate and quadricyclanone, at a pressure less than 20 mm gives 25% each of ethane, CO_2, and methyl acetate.[69] When **53** is decomposed in a mass spectrometer, no peak corresponding to dimethoxycarbene is observed; the peak at m/e 74 was shown to result from methyl acetate.[70]

As might be expected, the kinetics of this reaction also show[68] a great dependence on solvent. The kinetic parameters for the decomposition of **53** are

	$\Delta H^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, eu
In cyclohexane	34.2	+8.7
In acetonitrile	24.7	−8.8

All this suggests a zwitterionic intermediate such as **56**, which could either lose dimethoxycarbene or rearrange to the ion pair **57**. The presence of polar groups such as carbomethoxy would naturally favor the ion pair; this explains the results with dimethyl acetylenedicarboxylate. The decomposition of the adduct of **51** and phenylacetylene could be formulated either as involving a zwitterion similar to **56** or as a concerted reaction; the fact that in cyclohexane at 115° this reaction occurs eight times more slowly than the corresponding decomposition of **53** renders the concerted mechanism perhaps less likely.[68] It is clear that the decomposition of norbornadiene ketals is not a reverse Diels–Alder reaction. The same conclusion probably does not apply to the loss of CO from ketonorbornadienes since these reactions are extremely rapid and show little in the way of solvent effects. Such a difference in mechanism is not surprising when one considers the tremendous difference in stability between carbon monoxide and dimethoxycarbene.

The first approach to cyclopentadienone itself was that of Alder and Flock[71] who obtained 1-ketodicyclopentadiene by oxidation of dicyclopentadiene. When this ketone was passed through a tube filled with as-

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(66) H. Gilman, G. Cottis, and W. H. Atwell, *J. Am. Chem. Soc.*, **86**, 1596 (1964).

(67) R. W. Hoffmann and H. Hauser, *Tetrahedron*, **21**, 891 (1965).

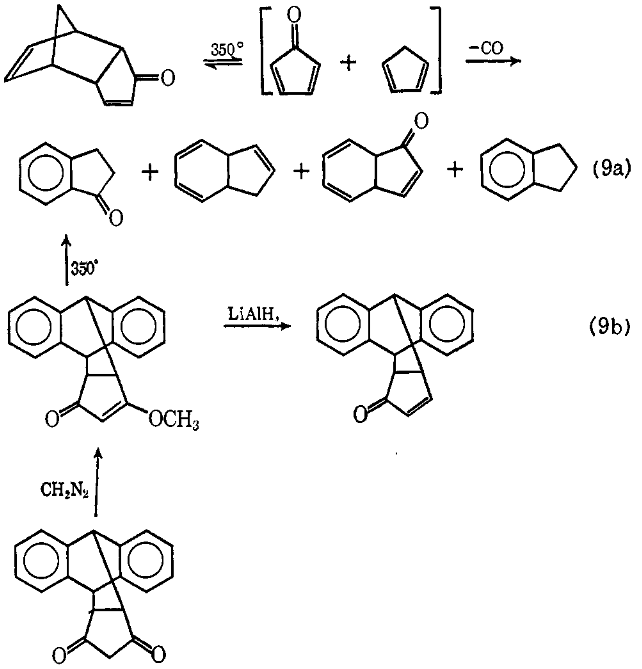
(68) D. M. Lemal, E. P. Grosselink, and S. D. McGregor, *J. Am. Chem. Soc.*, **88**, 582 (1966).

(69) D. M. Lemal, R. A. Lovald, and R. W. Harrington, *Tetrahedron Letters*, 2779 (1965).

(70) R. W. Hoffmann and C. Wunsche, *Ber.*, **100**, 943 (1967).

(71) K. Alder and F. H. Flock, *ibid.*, **87**, 1916 (1954).

bestos beads at 360–380° and aspirator vacuum, a mixture of 8,9-dihydroindene and 1-keto-8,9-dihydroindene was obtained as shown in eq 9a. This is best explained by decomposition into cyclopentadienone and cyclopentadiene followed by recombination of these addends in all possible ways. DePuy and Lyons[72] obtained the anthracene adduct of cyclopentadienone by adding cyclopentene-3,5-dione to anthracene; the product was converted to the enol ether with diazomethane and reduced with $LiAlH_4$, as indicated in eq 9b. It was hoped that the gain in resonance energy produced by anthracene formation would lower the temperature necessary for dissociation of the adduct, but it failed to do so; this adduct pyrolyzed at the same temperature as 1-ketodicyclopentadiene. This would indicate that the transition state for the Diels–Alder reaction is closer to the adduct than to the addends. Again the product obtained was 1-keto-8,9-dihydroindene.



(9a)

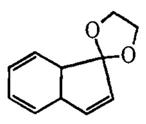
(9b)

The closest approach to cyclopentadienone is by bromination and dehydrobromination of 2-cyclopentenone. Photolytic bromination of this with N-bromosuccinimide gives a compound which was first identified by Hafner and Goliasch[73] as 2-bromo-4-cyclopentenone but was later shown to be 3-bromo-4-cyclopentenone.[74] Dehydrobromination of this with triethylamine at 5° gave dicyclopentadienone; only tar resulted when the temperature was raised to 20° or when 2-bromo-4-cyclopentenone was substituted for the 3-bromo compound. Hafner and Goliasch[73] claim to have obtained 2-phenylnorbornadien-7-one, which decomposed to biphenyl at 200°, by carrying out the dehydrobromination in the presence of phenylacetylene, but this is disputable; phenylnorbornadienone would be expected to decarbonylate even below room temperature.[74]

Cyclopentadienone could not be trapped with any other dienophile. This is not surprising in terms of molecular orbital theory referred to earlier.[54,55] The only reaction with a comparable energy difference between highest occupied and lowest unoccupied orbitals is the addition of cyclopentadiene to cyclopentadienone, with the latter acting as dienophile.

Hafner and Goliasch[73] found that pyrolysis of dicyclopentadiendione at 240° gave 1-indanone rather than the expected 1-keto-8,9-dihydroindene. Later work has shown that the product of decarbonylation is indeed the dehydroindene, but that any trace of acid or base causes a rapid isomerization to the indanone.[75] Pyrolysis of dicyclopentadienedione at 400° in a quartz apparatus, observing rigid exclusion of air, gave the expected 1-keto-8,9-dihydroindene uncontaminated by indanone.

The behavior of cyclopentadienone ketals is similar to that of cyclopentadienone itself. Vogel and Wyes[75] obtained **58** quantitatively by pyrolysis of **59** at 400°. This involves a Woodward–Katz[76] rearrangement (see also section VI), followed by decarbonylation. Compound **59** is itself obtained by reaction of ethylene glycol with dicyclopentadiendione. Reaction of **58** with dimethyl acetylenedicarboxylate gave the expected adduct, which decomposed at 160° to give dimethyl phthalate and **60** in 72% yield. Unlike cyclopentadienone, the ketal could be trapped with maleic anhydride to give **61**.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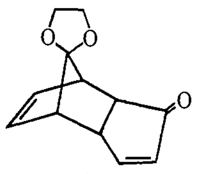
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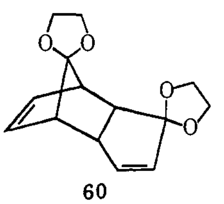
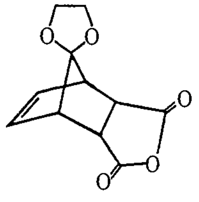

60


61

Fulvene epoxides also exist only as dimers. For instance, treatment[77] of dimethylfulvene with H_2O_2 gives **62**. Pyrolysis of **62** at 400° gives the cyclohexadienone (**63**), which itself decomposes at 550° to give *o*-cresol and 2,6-dimethylphenol. The cyclohexadienone

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(72) C. H. DePuy and C. E. Lyons, *J. Am. Chem. Soc.*, **82**, 631 (1960).

(73) K. Hafner and K. Goliasch, *Ber.*, **94**, 2910 (1961).

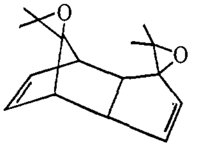
(74) C. H. DePuy, M. Isaks, K. L. Eilers, and G. F. Morris, *J. Org. Chem.*, **29**, 3503 (1964).

(75) E. Vogel and E. G. Wyes, *Ber.*, **98**, 3680 (1965).

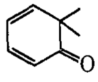
(76) R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

(77) K. Alder, F. H. Flock, and H. Lessenich, *Ber.*, **90**, 1709 (1957).

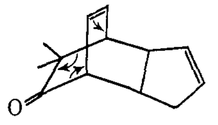
is isolable but dimerizes upon standing 1 day. The dimer may be cracked to monomer at 400°. Reaction of **63** with dimethyl acetylenedicarboxylate for 24 hr at 25° or for 4 hr in refluxing xylene affords the expected adduct. This undergoes the reverse Diels–Alder reaction at 500° to give dimethyl phthalate and dimethylketene. Unlike cyclopentadienone, cyclohexadienone reacts with cyclopentadiene as a diene to give **64**. This reaction may also be reversed by heat.



62



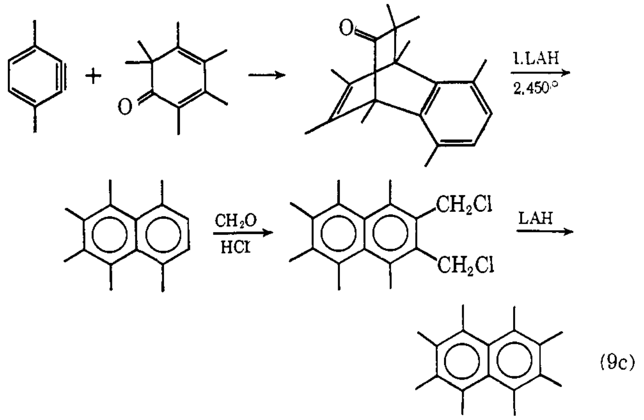
63



64

IV. CYCLOHEXADIENONES (NAPHTHALENE SYNTHESIS)

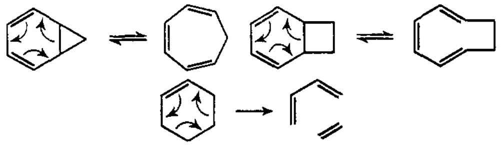
The reverse Diels–Alder reaction of cyclohexadienone adducts may also be used to prepare highly substituted naphthalenes.[78] Addition of 3,6-dimethylbenzyne to hexamethyl-2,4-cyclohexadienone, prepared by oxidation of hexamethylbenzene,[79] gave an adduct, which underwent reverse Diels–Alder reaction at 450° to give 17.8% 1,4,5,6,7,8-hexamethylnaphthalene and 80% recovered adduct. The very interesting and highly strained compound, octamethylnaphthalene, could be prepared from this by bischloromethylation and $LiAlH_4$ reduction. The general reaction sequence, as outlined in eq 9c, constitutes a versatile naphthalene synthesis which should receive wide application.



(9c)

V. INTERNAL DIELS–ALDER REACTION

Diels–Alder reactions in which the diene and dienophile are part of the same molecule are best known in the form of tautomerizations of medium-ring polyenes, for example, the interconversions of cycloheptatriene and norcardiene. The isomerization of norcaradiene to cycloheptatriene or of bicyclo[4.2.0]octa-2,4,7-triene to cyclooctatetraene can be considered retrodiene reactions. The same cyclic electron reorganization is involved in these tautomerizations as in the retrodiene reaction. This concept was first introduced by Cope.[8]



In reality, however, there is no more justification for considering this tautomerism in terms of the Diels–Alder reaction, in which two new σ bonds are formed, than for considering it in terms of the Cope rearrangement,[81] in which one bond is formed and one broken. Woodward and Hoffmann[7] have termed this tautomerism, in which one new bond is formed, an "electrocyclization." Electrocyclizations may involve any even number of π electrons and may occur either photochemically or thermally, but the thermal and photochemical reactions have different stereochemical results. The stereochemistry of the simplest 4π-electron electrocyclization, the ring closure of hextrienes to 1,3-cyclohexadienes, has recently been elucidated, and the results are in full agreement with the conclusions of Woodward and Hoffmann.[82,83]

Electrocyclization is a subject well worthy of review, but there is not space here to even begin to cover the subject. Our concern here is with reverse Diels–Alder reactions of adducts of medium-sized cyclopolyenes. These cyclopolyenes tend to undergo an electrocyclization just prior to or simultaneously with Diels–Alder addition, which leads to the production of a number of interesting small-ring compounds *via* retrodiene decomposition.

While the existence of monocyclic and bicyclic isomers of the C_7H_8 system is quite certain, the existence of a valence tautomerism between the two cannot be unequivocally demonstrated.[84] Nmr studies of tropilidene and eucarvone indicate that these compounds exist entirely in the monocyclic form. Appreciable quantities of the bicyclic isomer are definitely not present.[85] However, reaction of tropilidene with dienophiles gives adducts formally derived from norcaradiene; that is, they contain a three-membered ring.[86] Final proof of this is that the adduct of cycloheptatriene

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[78] A. Oku, T. Kakihana, and H. Hart, *J. Am. Chem. Soc.*, **89**, 4554 (1967).

[79] H. Hart, P. M. Collins, and A. J. Waring, *ibid.*, **88**, 1005 (1966).

[80] A. C. Cope, A. C. Haven, F. L. Ramp, and E. R. Trumbull, *ibid.*, **74**, 4867 (1952).

[81] W. von E. Doering and W. R. Roth, *Tetrahedron*, **18**, 67 (1962), and references therein.

[82] E. N. Marvell, G. Caple, and B. Schatz, *Tetrahedron Letters*, 385 (1965).

[83] E. Vogel, *ibid.*, 391 (1965).

[84] S. J. Rhoads in "Molecular Rearrangements," Part I, P. de Mayo, Ed., Interscience Publishers, 1963, Chapter 11, pp 701–703.

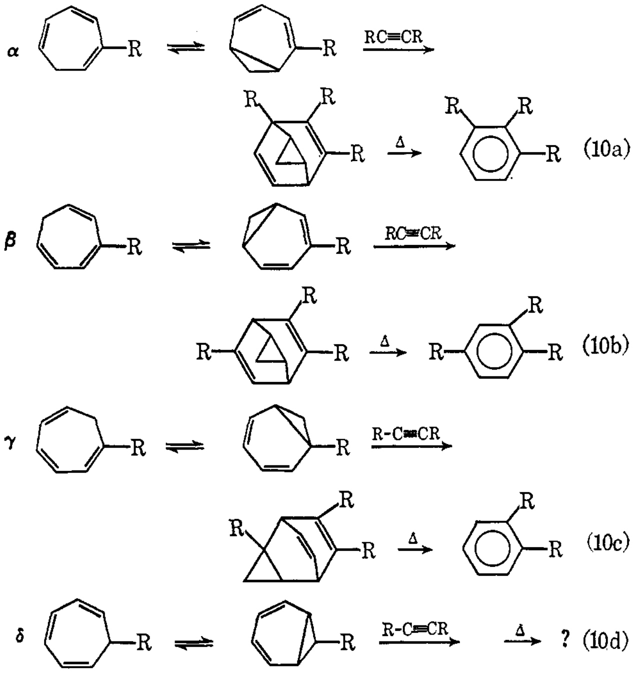
[85] E. J. Corey, H. J. Burke, and W. A. Remers, *J. Am. Chem. Soc.*, **77**, 4941 (1955).

[86] K. Alder and G. Jacobs, *Ber.*, **86**, 1528 (1953).

with acetylenedicarboxylic ester can be thermally cleaved to give phthalic ester quantitatively. The other product, cyclopropene, is obtained in only about 1% yield, the rest being polymer.[87] The polymerization of cyclopropene is well known;[88] this gas polymerizes even at its normal boiling point of −36°. Similarly[87] cleavage of the dimethyl acetylenedicarboxylate adduct of 1,1,4-trimethyl-2,4,6-cycloheptatriene, prepared[86] by $LiAlH_4$ reduction of eucarvone, gave dimethyl 4-methylphthalate. The other product, 3,3-dimethylcyclopropene, isomerized to isoprene. This may indicate that cycloheptatriene is in equilibrium with a small amount of norcaradiene, as has been claimed,[89] or that the cycloheptatriene isomerizes to norcaradiene under the influence of dienophiles. The problem of the existence of norcaradiene and its derivatives has recently been reviewed by Maier.[90]

The first introduction to the cycloheptatriene–norcaradiene problem came more than 60 years ago when Buchner[91,92] treated benzene with ethyl diazoacetate. The product of this reaction, ethyl norcaradienecarboxylate, can be isomerized to three different cycloheptatrienecarboxylic acids. Treatment of the norcaradiene ester with aqueous ammonia gives the corresponding amide. The oily norcaradiene acid can be obtained from this by dissolving in 30% sulfuric acid and steam distilling. However, refluxing the norcaradiene ester or amide in 10% NaOH gives the α acid, mp 71°. If the norcaradiene ester is heated above 150°, the ester of the β acid, mp 56°, is obtained. Continued refluxing of the α, β, or norcaradiene acids or esters with strong base gives the γ acid, which was obtained as an oil by Buchner[91] and by Grundmann[92] but as a solid, mp 63°, by Alder.[93] A fourth acid, δ, mp 31°, is obtained from the coca alkaloids. It is isomeric with the others but cannot be obtained from them. The δ acid isomerizes to the β on treatment with base.

The structure of these acids was determined independently by Alder[93] and Doering.[94] The method used was to identify the aromatic acids obtained by cleavage of the dimethyl acetylenedicarboxylate adducts. The α acid gave hemimellitic acid (benzene-1,2,3-tricarboxylic acid) and is assigned the 1,4,6-cycloheptatriene-1-carboxylic acid structure (eq 10a). The β acid gives trimellitic acid (benzene-1,2,4-tricarboxylic acid) and is assigned the 1,3,6-cycloheptatriene-1-carboxylic acid structure (eq 10b). The γ acid gave phthalic acid (eq 10c), and the δ acid (eq 10d) gave a mixture of phthalic and trimellitic acids. On the basis of spectral evidence Alder assigned the 1,3,5-cycloheptatriene-1-carboxylic acid structure to the γ acid and the 2,4,6-cycloheptatriene-1-carboxylic acid structure to the δ acid. Doering agreed with these assignments but concluded that the δ acid is actually a mixture of α and β. It would appear that in this case the two teams had different samples. The nmr spectra of all these acids are quite similar, showing great complexity in the vinyl region. Doering concludes from this that all the acids are monocyclic and planar. Thus, it is clear that there is no tautomerism in this case, for, if there were, the norcaradiene ester should give the δ ester (assuming the δ structure actually exists). Of course, the isomerization of the norcaradiene ester to the β ester may involve the δ ester as an intermediate, but this is just speculation.



$R = -COOCH_3$

There is, however, no guarantee that Buchner's[91] "ethyl norcaradienecarboxylate" actually exists in the norcaradiene form. Reaction of tropylium bromide with potassium cyanide gives a nonionic nitrile which almost certainly has the 1-cyano-2,4,6-cycloheptatriene structure. This nitrile may be hydrolyzed to an amide identical with that obtained by Buchner from his ester.[95] On the other hand, Buchner's ester undergoes a Diels–Alder reaction with maleic anhydride at 5°, whereas cycloheptatriene, the hydrocarbon, does

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[87] K. Alder K. Kaiser, and M. Schumacher, *Ann.*, **602**, 80 (1957).

[88] K. B. Wiberg and W. J. Bartley, *J. Am. Chem. Soc.*, **82**, 6375 (1960).

[89] E. M. Mil'vitskaya and A. F. Plate, *Zh. Obsch. Khim.*, **32**, 2566 (1962); English transl., p 2531; *Chem. Abstr.*, **58**, 8927*e* (1963).

[90] G. Maier, *Angew. Chem. Intern. Ed. Engl.*, **5**, 402 (1967).

[91] W. Braren and E. Buchner, *Ber.*, **34**, 982 (1901), and earlier references cited therein.

[92] See also C. Grundmann and G. Ottmann, *Ann.*, **58 2**, 163 (1953).

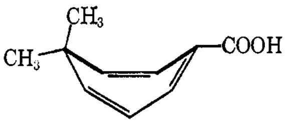
[93] K. Alder, K. Jungen, and H. Rust, *ibid.*, **602**, 90 (1957).

[94] W. von E. Doering, G. Laber, R. Vonderwahl, N. F. Chamberlain, and R. B. Williams, *J. Am. Chem. Soc.*, **78**, 5448 (1956).

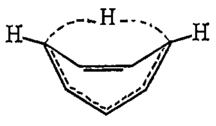
[95] W. von E. Doering and L. H. Knox, *ibid.*, **79**, 352 (1957).

not react except at much higher temperatures.[96] This should be compared to the results obtained by Cope with 1,3,5-cyclooctatriene.[80]

It is now known that cycloheptatriene and its derivatives are not planar. This was first proven by X-ray crystallography of thujic acid, which was found[97] to exist in the boat form **65a**. In the nmr spectrum of cycloheptatriene itself, the peak for the methylene protons splits into two peaks at very low temperatures.[98,99] In the boat conformation the two methylene protons must clearly be nonidentical, but rotation of the methylene group scrambles them at temperatures above −143°. Cycloheptatriene also undergoes a 1,5 hydrogen shift at higher temperatures, as shown by the nmr spectrum of monodeuteriocycloheptatriene;[100] see **65b**.



65a

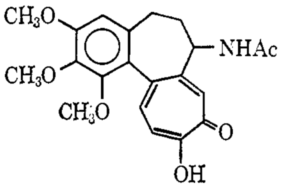


65b

The reverse Diels–Alder reaction has also been used to elucidate the structure of the products obtained by reaction of ethyl diazoacetate with a number of alkylbenzenes.[101] For example, photolysis of ethyl diazoacetate in toluene followed by Diels–Alder addition of acetylenedicarboxylic ester and retrodiene decomposition of the adducts gives 60% of 4-methylphthalic ester, 35% of 3-methyl phthalic ester, and 5% of phthalic ester. This implies that the photolysis products were 60% of **66** or **67**, 35% of **68** or **69**, and 5% of **70** or **71** (Chart I).

Treated in the same way *o*-xylene gives 40% of 4,5-dimethylphthalic ester, 40% of 3,4-dimethylphthalic ester, and 20% of 3-methylphthalic ester, implying structures **72–74** for the norcaradienes or **75–77** for the corresponding formulation as cycloheptatrienes. Notice that it is impossible by the Diels–Alder reaction to distinguish between norcaradienes and cycloheptatrienes since the latter undergo the Diels–Alder reaction as norcaradienes. Photolysis of ethyl diazoacetate in indan gives the two possible norcaradienes **78** and **79**, as proven by retrodiene decomposition of the acetylenedicarboxylic ester adducts. At 330° the maleic anhydride adducts of **78** and **79** undergo retrodiene exchange with 1,4-diphenylbutadiene followed by dehydrogenation to give the isomeric carbethoxyazulenes **80** and **81**.

Certain compounds can be shown unequivocally to exist in the norcaradiene form. The first example of this occurred during the synthesis of the alkaloid colchicine (**82**) by Eschenmoser and coworkers.[102] Since this synthesis involved as a key step the reverse Diels–Alder reaction, it will be discussed in detail. The starting material was purpurogallin (**83**), obtained by oxidation of pyrogallol (1,2,3-trihydroxybenzene). Hydrogenation of purpurogallin gave **84**, which upon treatment with methyl propiolate, HC≡CCOOMe, followed by ring closure with potassium *t*-butoxide and methylation with MeI, gave the pyrone **85**. *α*-Pyrones undergo Diels–Alder addition followed by, or, more often, simultaneously with, retrodiene decarboxylation. Thus, reaction of **85** with chloromethylmaleic anhydride at 175° gave **86** in 70% yield. Dehydrochlorination of **86** with KOBu gave the diester **87**, which was oxidized by OsO_4 to the tropone **88**. Decarboxylation of **88** was followed by conversion *via* the amine into desacetylaminocolchicine (**89**) identical with that obtained from the alkaloid.



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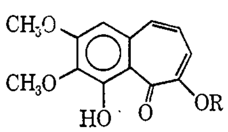

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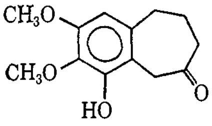

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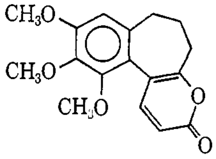

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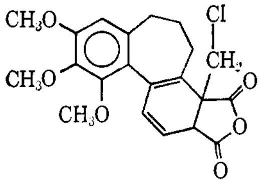

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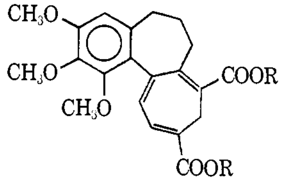
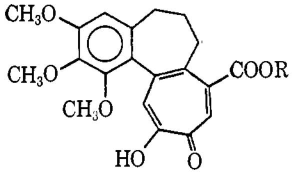


87

R = alkyl, H



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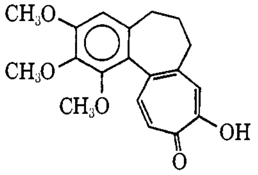

89

Retrodiene decarboxylation of adducts of *α*-pyrones with ethylenic dienophiles leads to a cyclohexadiene, which can add another mole of dienophile. With 3- or 6-substituted pyrones such a reaction leads to bridge-

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[96] H. L. Dryden and B. E. Burgert, *J. Am. Chem. Soc.*, **77**, 5633 (1955).

[97] R. E. Davis and A. Tulinsky, *Tetrahedron Letters*, 839 (1962).

[98] F. A. L. Anet, *J. Am. Chem. Soc.*, **86**, 458 (1964).

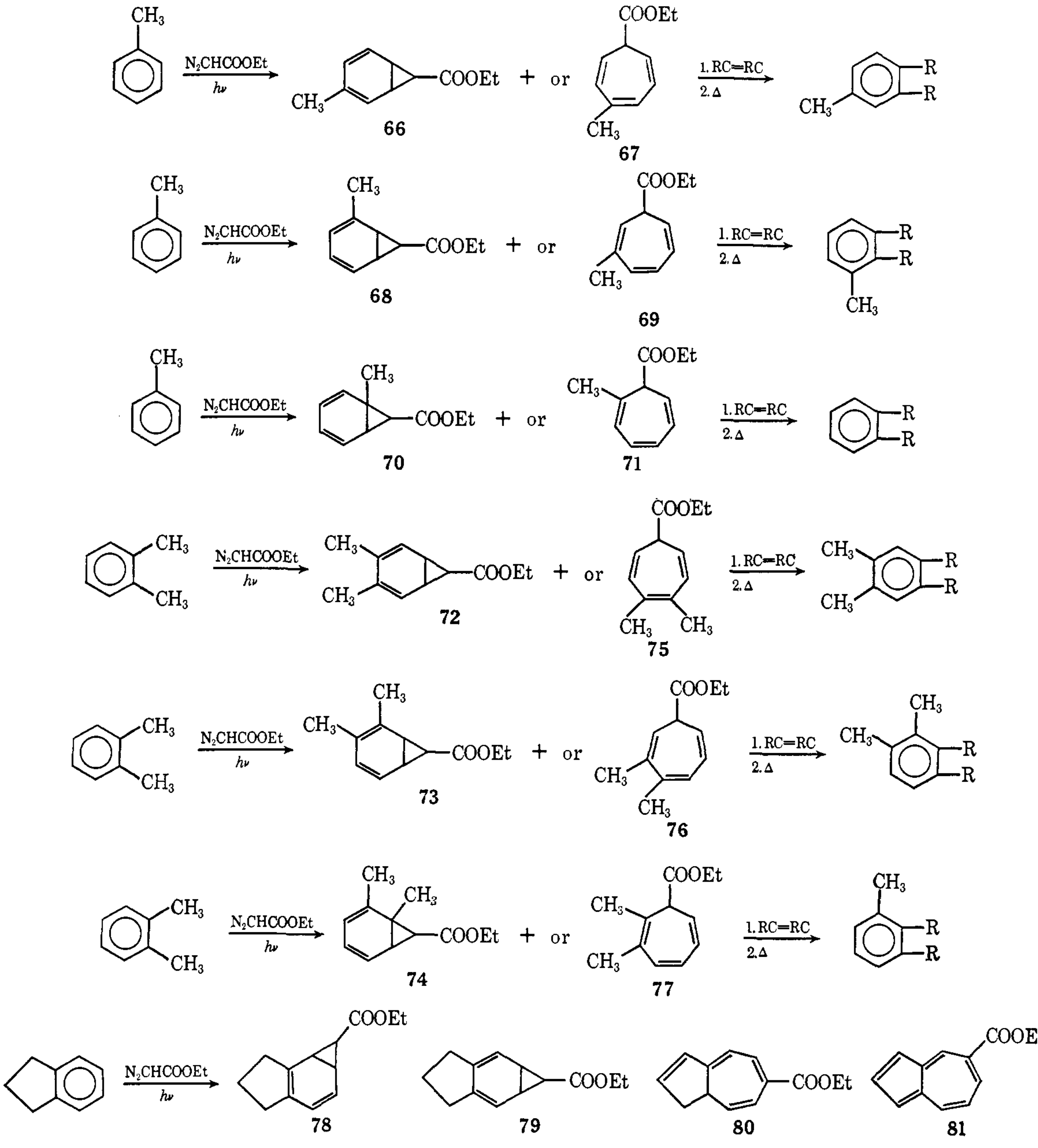
[99] F. R. Hensen and L. A. Smith, *ibid.*, **86**, 956 (1964).

[100] A. P. terBorg, H. Kloosterziel, and N. vanMeurs, *Rec. Trav. Chim.*, **82**, 717 (1963).

[101] K. Alder, R. Muders, W. Krane, and P. Wirtz, *Ann.*, **627**, 58 (1959).

[102] A. Eschenmoser, J. Schreiber, W. Leimgruber, M. Pesaro, P. Schudel, and T. Threlfall, *Helv. Chim. Acta*, **44**, 540 (1961).

CHART I



R = –COOCH$_3$

head-substituted bicyclo[2.2.2]octenes.[103] Similarly, reaction of α-pyrone with 2 moles of methyl vinyl ketone gives 2,6-diacetylbicyclo[2.2.2]oct-7-ene, from which was synthesized the interesting hydrocarbon barrelene, bicyclo[2.2.2]octa-2,5,7-triene.[104]

The diacid of **87** exists in the cycloheptatriene form, but dehydration with acetic anhydride converts it to an anhydride, **90**, which was shown to exist in the norcaradiene form. Also **87** showed a large pK_a difference between the two ionizable hydrogens, indicating intramolecular H bonding. However, the parent compound, **91**, did not show[105] this large pK_a difference and gave only tar when treated with acetic anhydride. Upon mixing this tar with unreacted **91** and subliming at 150° (0.5 mm), the very unstable norcaradiene anhydride **92** could be isolated. This indicates that steric strain due to the bridging five-membered anhydride ring cannot be the whole story. Another example[106] of a bridged norcaradiene is **93** prepared by dehydrobromination of **94**. The structure of **93** was

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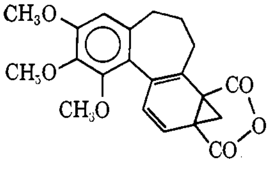
(103) J. C. Kauer, French Patent 1,472,947 (1965); British Patent 1,066,005 (1967).

(104) H. E. Zimmermann and R. M. Paufler, *J. Am. Chem. Soc.*, **82**, 1514 (1960).

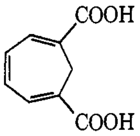
(105) A. Eschenmoser, M. Pesaro, T. Threlfall, and R. Darma, *Helv. Chim. Acta*, **46**, 2893 (1963).

(106) E. Vogel, W. Wiedemann, H. Kiefer, and W. F. Harrison, *Tetrahedron Letters*, 673 (1963).

proven by nmr. Unlike cycloheptatriene, which requires fairly vigorous conditions, **93** formed an adduct with maleic anhydride at room temperature.



90



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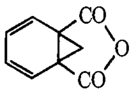

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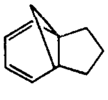

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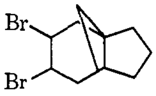
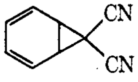


94

Compounds **90**, **92**, and **93** are forced into the norcaradiene form by steric factors. But electronic factors should also stabilize the norcaradiene structure. The best example of this has been provided by Ciganek.[107] He reported that 7,7-dicyanonorcaradiene (**95**), prepared by reaction of benzene with dicyanodiazomethane, existed almost entirely in the norcaradiene form. Heating isomerizes **95** to **96** and **97**, the ratio of these depending on solvent. In cyclohexane at 143° the ratio of **96** to **97** is 5:1 and the kinetic parameters for formation of **96** are $\Delta H^{\ddagger} = 30.7$ kcal and $\Delta S^{\ddagger} = -2.9$ eu. Reaction of dicyanodiazomethane with naphthalene gave a mixture of **98**, **99**, and **100** of which only one had the norcaradiene structure. It should be noted, however, that the latter structures cannot tautomerize without destroying the resonance of the benzene ring. But even more interesting was the reaction of benzene with $N_2C(CN)CF_3$. The product of this reaction was shown by studies of the proton and F^{19} resonance spectra at temperatures from 25 to −85° to be an equilibrating mixture of cycloheptatriene and norcaradiene forms, with the cycloheptatriene form predominating.



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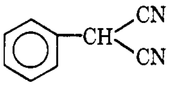

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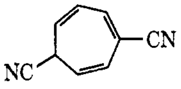

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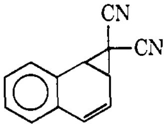

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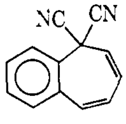

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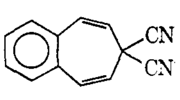

100

Ciganek[107] suggests that the thermodynamic preference for the norcaradiene form **95** is due to dipole-dipole interactions between the cyano groups which increase the NC–C–CN bond angle at the expense of the C(1)–C(7)–C(6) angle. This naturally favors formation of a three-membered ring, in which this latter angle is only 60°.

All products of addition of carbenes to the C(1)–C(2) bond of naphthalene are also stable norcaradienes, since electrocyclic ring opening here would destroy the resonance of the benzene ring. As might be expected these compounds are nonplanar.[108]

The only real evidence for the existence of norcaradiene itself is found in the thermal rearrangement of cycloheptatriene to toluene.[109] The reaction occurs above 350°, and the rate is insensitive to added nitric oxide. The reaction is first order even at very low pressures. Since these results exclude a free-radical chain, we are naturally drawn to consideration of norcaradiene as an intermediate. Thermodynamic calculations by Klump and Chesick[109] indicate that the free-energy difference between norcaradiene and cycloheptatriene is about 11 kcal/mole. Since the enthalpy of activation for the isomerization to toluene is 51.1 kcal/mole, the activation energy for breaking the C(1)–C(7) bond of norcaradiene must be at least 40 kcal/mole. This should be compared to the activation demand for the isomerization of **95** to **96** and **97**.

With the eight-membered rings, the situation is not nearly so ambiguous. When cyclooctatetraene is reduced[80] with sodium in ammonia, the product is an equilibrium mixture consisting, at 100°, of 85% of 1,3,5-cyclooctatriene and 15% of bicyclo[4.2.0]octa-2,4-diene. The monocyclic tautomer can be isolated as its silver nitrate complex. Bicyclooctadiene reacts with maleic anhydride at 10°. Cyclooctatriene does not react with maleic anhydride at 25° and upon heating gives the adduct derived from bicyclooctadiene. Decomposition at 200° of the dimethyl acetylenedicarboxylate adduct gives dimethyl phthalate and cyclobutene cleanly. Since the free-energy difference between the two isomers is small, substituent effects should be able to entirely eliminate one or the other of the two isomers. Thus, when the adduct[110] from butadiene and 1,2-dicarbomethoxy-1-cyclobutene is brominated and dehydrobrominated, the product is entirely 1,6-dicarbomethoxy-1,3,5-cyclooctatriene. However, when this ester is saponified and the resulting acid treated with acetic anhydride, the bicyclic anhydride results, from which the monocyclic acid can be regenerated by addition of water at 15°.

The properties of cyclooctatetraene have been extensively studied by Reppe,[111] once it became available in quantity from acetylene. This hydrocarbon

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[107] E. Ciganek, *J. Am. Chem. Soc.*, **89**, 1454, 1458 (1967).

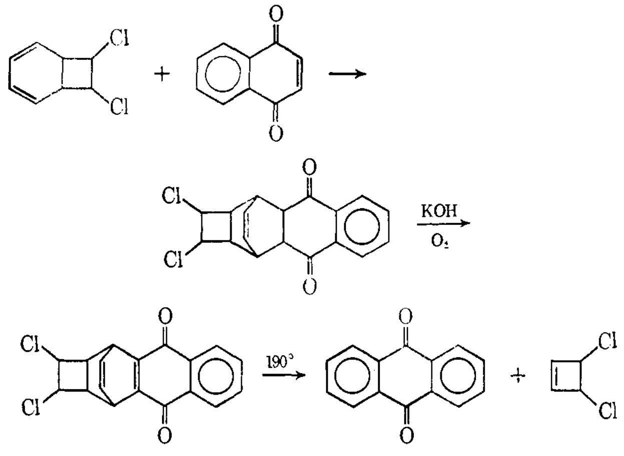
[108] E. Vogel, D. Wendisch, and W. R. Roth, *Angew. Chem. Intern. Ed. Engl.*, **3**, 443 (1964).

[109] K. N. Klump and J. P. Chesick, *J. Am. Chem. Soc.*, **85**, 130 (1963).

[110] E. Vogel, O. Roos, and H. Disch, *Angew. Chem.*, **73**, 342 (1961).

[111] W. Reppe, O. Schlichtung, K. Klager, and T. Toepel, *Ann.*, **560**, 1 (1948).

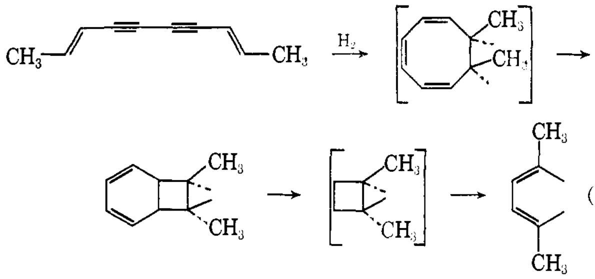
exists entirely in the monocyclic form but reacts with halogen and with dienophiles in the form of bicyclo[4.2.0]octa-2,4,7-triene. When 1 equiv of chlorine is added to cyclooctatetraene, the product is 7,8-dichlorobicycloocta-2,4-diene. The adduct of this with dimethyl acetylenedicarboxylate can be decomposed at 220° to give dimethyl phthalate and 3,4-dichlorocyclobutene. Similarly, the adduct with naphthoquinone can be cleaved, after oxidation by air, at 190° to give dichlorocyclobutene and anthraquinone (eq 11). Dichlorobicyclooctadiene reacts with dienophiles at room temperature; cyclooctatetraene requires temperatures greater than 100°. Cleavage of the cyclooctatetrane–dimethyl acetylenedicarboxylate adduct gives dimethyl phthalate and tar. The tar formation is not surprising since the other expected product, cyclobutadiene, is known to be unstable.



(11)

The isolation of cyclobutenes from retrodiene decomposition of adducts of acetylenic dienophiles with cyclooctatrienes appears doubtful since the cyclobutenes will probably undergo electrocyclic ring opening under the pyrolysis conditions. Thus, it has been shown that decomposition of the adduct of dimethyl acetylenedicarboxylate and 7,8-dichlorobicyclo[4.2.0]octa-2,4-diene gives 1,4-dichlorobutadiene[112] rather than 3,4-dichlorocyclobutene as claimed by Reppe.[111] The retrodiene reaction was carried out by distilling the adduct at 140° (17 mm). Correspondingly, 1,4-diacetoxybutadiene is obtained from 7,8-diacetoxybicyclooctadiene. Cope[80] claims isolation of cyclobutene in 95% yield by trapping the volatile material from retrodiene decomposition of the dimethyl acetylenedicarboxylate–cyclooctatriene adduct in a liquid nitrogen trap. On the other hand, heating the adduct of cyclooctatriene and dicyanoacetylene in a sealed tube at 185° for 40 min gives phthalonitrile and butadiene.[113]

This reaction has also been used to determine the stereochemistry of the electrocyclization products of 2,4,6,8-decatetraene.[114] When *trans*-2,*trans*-8-decadiene-4,6-diyne is partially hydrogenated over Lindlar catalyst, the main product is *trans*-7,8-dimethylbicyclo[4.2.0]octa-2,4-diene in 50% yield. This stereochemistry was determined by reacting the bicyclooctadiene with dimethyl acetylenedicarboxylate and subjecting the adduct to retrodiene decomposition at 200°; the product is 2,6-dimethyl-*trans*,*trans*-2,4-hexadiene in 57% yield (eq 12). On the other hand, when the *cis*-2,*trans*-8-decadiene-4,6-diyne is subjected to the same series of reactions, the final product is *cis*-3,4-dimethylcyclobutene (eq 13).



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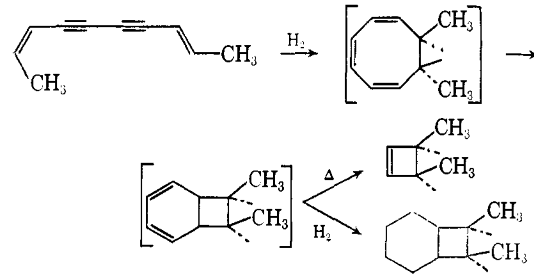

(13)

It is surprising that this did not open to the *cis*,*trans*-2,4-hexadiene. The bicycloctadiene formation evidently involves 7,8-dimethyl-1,3,5-cyclooctatriene as intermediate. This was proven by stopping the hydrogenation over Lindlar catalyst and then hydrogenating completely; 12% 1,2-dimethylcyclooctane was found. The results of the retrodiene reaction prove that the initial ring closure to the cyclooctatriene was conrotatory, as predicted by the Woodward–Hoffman rules.[7] The stereochemistry of electrocyclization will be discussed further in section VIII.

The reverse Diels–Alder reaction has also been used[115] to study the methylation of cyclooctatetraene dianion with 2 moles of methyl iodide. Treatment of the methylation product with dimethyl acetylenedicarboxylate at 200° gives dimethyl phthalate and dimethyl 4-methylphthalate in 1:9 ratio. This shows that 1,4 alkylation is preferred to 1,2 alkylation, but that both do occur. The position of the double bonds cannot be exactly specified because of the possibility

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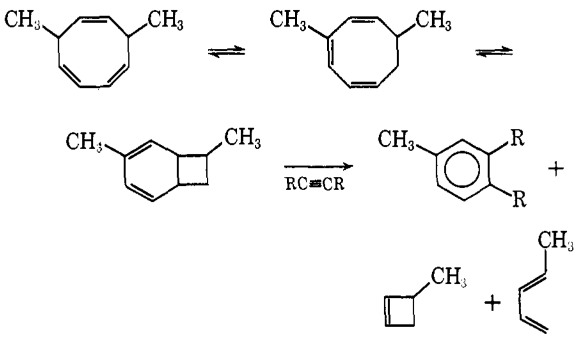
(112) R. Criegee, W. Horauf, and W. D. Schellenberg, *Ber.*, **86**, 126(1953).

(113) C. D. Weis, *J. Org. Chem.*, **28**, 74 (1963).

(114) E. N. Marvel and J. Seubert, *J. Am. Chem. Soc.*, **89**, 3377 (1967).

(115) D. A. Bak and K. Conrow, *J. Org. Chem.*, **31**, 3958 (1966).

of 1,5-hydrogen shifts in the dimethylcyclooctatrienes. Both cyclobutenes and butadienes result from the retrodiene reaction (see eq 14 and 15).



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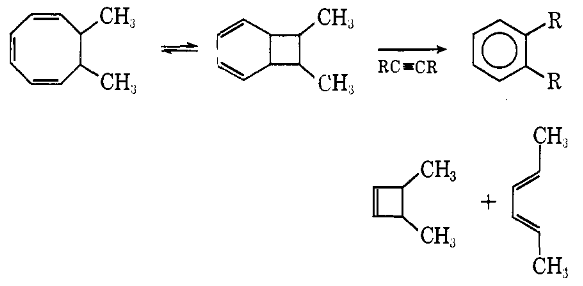
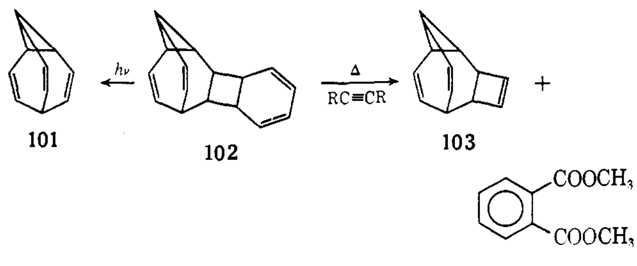


(15)

R = -COOCH$_3$

In this connection, it would not be proper to omit mention of Schröder's elegant synthesis of bullvalene[116] (**101**), by photolysis of the cyclooctatetraene dimer (**102**). Simultaneous Diels–Alder addition and retrodiene reaction of **102** with dimethyl acetylenedicarboxylate at 160° gives **103**, a hydrocarbon similar to bullvalene but containing a cyclobutene ring. The chemistry of bullvalene and its derivatives has been recently reviewed by Schröder and Oth.[117]

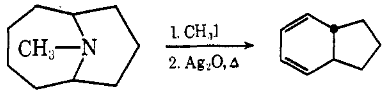


101 **102** **103**

R = COOCH$_3$

With the seven- and eight-membered rings, the problem has been to prove the existence of a bicyclic isomer, the product of an internal Diels–Alder reaction. This is due to Baeyer strain which destabilizes the bicyclic isomer. With the nine-membered ring, however, the problem is of just the opposite nature. Here electrocyclization would give an indene derivative, which has no strain.

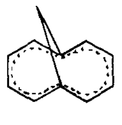
Thus when Alder and Dortmann[118] tried to prepare 1,3,5-cyclononatriene by removing the bridge nitrogen from homopseudopelleterine by decomposition of the dimethylammonium hydroxide, the only product found was *trans*-8,9-dihydroindane (eq 16). The only example

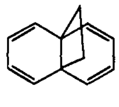


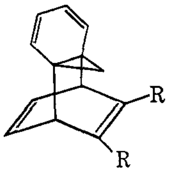
(16)

of a macrocyclic polyene which does not exist in the bicyclic form is Vogel's[119] 1,6-methano[10]annulene (**104a**). This 10-π-electron system would be expected to be aromatic by the Hückel rule, and it is this aromaticity which hinders electrocyclization. The [10]-annulene itself, cyclodecapentaene, has two interior hydrogens, the steric interaction of which would force the compound into the bicyclic form, 9,10-dihydronaphthalene. Similar strains[120] in 1,6-ethano[10]annulene preclude the existence of this compound except in the bicyclic form **104b**.

However, even 1,6-methano[10]annulene undergoes Diels–Alder reaction in the bicyclic form. Reaction[121] of **104a** with dimethyl acetylenedicarboxylate at 120° for 24 hr gives the adduct **105** which undergoes retrodiene decomposition at 400° (1 mm) to give benzocyclopropene (**106**) in 45% yield. This highly strained compound is stable at room temperature and may be distilled at 35° (30 mm) but decomposes upon atmospheric distillation. This decomposition must be bimolecular, thus permitting isolation of benzocyclopropene by reverse Diels–Alder reaction at low pressure.


104a


104b



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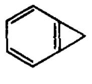
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VI. *endo–exo* ISOMERIZATION

Ever since the formulation of the Alder rule in 1937 it has been assumed that cyclic dienes react with ethylenic dienophiles to give predominantly *endo* adducts.[122] It is now known that this rule of maximum accumulation of unsaturation is rigorously obeyed only in the very simplest cases.[123] Although reaction of cyclopentadiene with monosubstituted and *cis*-1,2-disubstituted ethylenes leads predominantly, often exclusively, to the *endo* adduct, the preference for *endo* is very slight with

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(116) G. Schröder, *Ber.*, **97**, 3131 (1964).

(117) G. Schröder and J. F. M. Oth, *Angew. Chem. Intern. Ed. Engl.*, **5**, 402 (1967).

(118) K. Alder and H. A. Dortmann, *Ber.*, **87**, 1905 (1954).

(119) E. Vogel and W. R. Roth, *Angew. Chem.*, **76**, 145 (1964).

(120) E. Vogel, W. Maier, and J. Eimer, *Tetrahedron Letters*, 655 (1966).

(121) E. Vogel, W. Grimme, and S. Korte, *ibid.*, 3625 (1965).

(122) K. Alder and G. Stein, *Angew. Chem.*, **50**, 510 (1937).

(123) J. G. Martin and R. K. Hill, *Chem. Rev.*, **61**, 537 (1961).

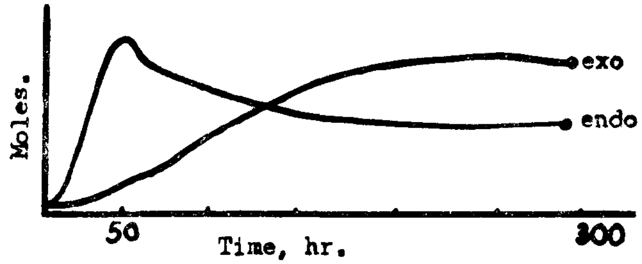

Figure 1.

trans-1,2-disubstituted ethylenes, and 1,1-disubstituted ethylenes such as methacrylonitrile sometimes give exclusively *exo* adduct. Berson has found that a high *endo*/*exo* ratio is often favored by polar solvents and suggests that the transition state for the formation of *endo* adduct has a higher dipole moment than that for the formation of *exo*.[124]

All these cases are kinetically controlled, so the retrodiene reaction is not involved. There are, however, cases where the preference for *exo* adduct involves an equilibrium between forward and reverse Diels–Alder reactions. When furan reacts with maleic anhydride in ether, almost entirely *exo* adduct is obtained.[125] By using nmr spectroscopy to follow the reaction in acetonitrile at 25°, Anet has found that the formation of *exo* adduct is initially twice as fast as that of *endo*, and that the *endo* adduct then isomerizes to the *exo*.[126] After 1 day there is no *endo* left. Since both adducts undergo the retrodiene reaction extremely readily, their isolation is difficult; they have recently been isolated by recrystallization from acetone at low temperature using petroleum ether as precipitant. The *endo* adduct is stable as a solid but undergoes retrodiene decomposition rapidly in solution at room temperature or at its melting point of 70°. The *exo* adduct decomposes only slowly in solution at room temperature and melts with decomposition at 110°. On the other hand, the maleimide adducts are much more stable.[127] Reaction of furan with maleimide in water or ether at 90° gave *exo* adduct; the *endo* could be obtained after 4 days of reaction in darkness at room temperature. Both adducts would be isolated in pure form. The *endo* adduct could be isomerized to the *exo* by boiling for 15 min in ethyl acetate or benzene. This ease of decomposition of the furan–maleimide adducts has been recommended as the basis of an efficient method of preparing maleimide.[25]

When furan is shaken with an aqueous solution of maleic acid, the initial formation of *endo* adduct is four times as fast as *exo*-adduct formation. The difference between this and the results in ether and acetonitrile is in line with Berson's suggestion that the transition state for *endo* formation has a higher dipole moment than that for *exo* formation.[124] When this solution is allowed to stand for several days, isomerization of *endo* adduct to *exo* takes place.

The curve of *endo* and *exo* obtained *vs.* time has been plotted by Berson and Swidler.[128] Qualitatively the shape of this curve is as expected (Figure 1); the *endo* isomer is kinetically favored, but long times or high temperatures favor the thermodynamically more stable *exo* isomer. However, if the isomerization occurs entirely by dissociation and recombination, then the slopes, $d(endo)/dt$ and $d(exo)/dt$, should both have maxima at $t = 0$. But the fact that $d(exo)/dt$ does not have a maximum at $t = 0$ could also be due to preferential losses of the *exo* isomer during work-up. That such is the case is indicated by the following attempt to determine the equilibrium constant for the *endo–exo* rearrangement.[128] *exo* adduct was dissolved in water with excess maleic acid and allowed to stand. The recovery of *endo* and *exo* isomers was as follows.

Days	*exo*, mole	*endo*, mole	Total % recovery
0.9	0.180	0	88
11	0.135	0.013	72
54	0.114	0.024	67

At the end of the period of study the solution was quite dark, evidently owing to acid-catalyzed decomposition of the furan. Since the material balance was so poor, an equilibrium constant could not be obtained. However, an upper limit can be set for one as $0.180/0.024 = 7.55$. This gives a free-energy difference between the two isomers of 1.2 kcal/mole, a reasonable value.

The lability of furan adducts is proven by the inability of furan to react with dimethylmaleic anhydride, even though this somewhat hindered dienophile does react with cyclopentadiene and with butadiene. This lack of reaction prevents the direct synthesis of cantharidin (**107**), a vesicant in the terpene series isolated from a species of beetle, which is formally the hydrogenated adduct of furan and dimethylmaleic anhydride.[129] However, the reverse Diels–Alder reaction has been used as a structure proof for cantharidin; dehydrogenation over palladium asbestos at 280° gives furan and dimethylmaleic anhydride cleanly, accompanied only by unreacted starting material[130] (eq 17). Stereospecific syntheses of cantharidin utilizing the Diels–Alder but not the reverse Diels–Alder reaction were accomplished separately by Stork and by Schenck.[131,132]

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(124) J. A. Berson, Z. Hamlet, and W. A. Mueller, *J. Am. Chem. Soc.*, **84**, 297 (1962).

(125) R. B. Woodward and H. Baer, *ibid.*, **70**, 1161 (1948).

(126) F. A. L. Anet, *Tetrahedron Letters*, 1219 (1962).

(127) H. Kwart and I. Burchuk, *J. Am. Chem. Soc.*, **74**, 3094 (1952).

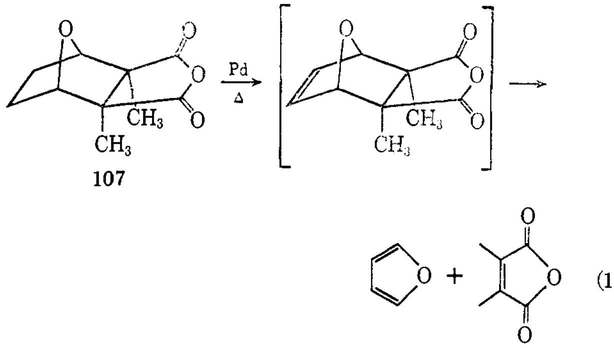
(128) J. A. Berson and R. Swidler, *ibid.*, **75**, 1721 (1953).

(129) L. F. Fieser and M. Fieser, "Topics in Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1963, p 179.

(130) F. von Bruchhausen and H. W. Bersch, *Arch. Pharm.*, **266**, 697 (1928).

(131) G. Stork, E. E. Van Tamelen, L. J. Friedman, and A. W. Burgstahler, *J. Am. Chem. Soc.*, **75**, 384 (1953).

(132) G. O. Schenck and R. Wirtz, *Naturwissenschaften*, **40**, 581 (1953).



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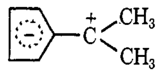
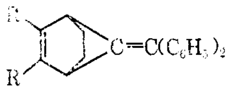
(17)

Fulvene adducts are also labile, and therefore the *exo* adduct is obtained under mild conditions. Woodward and Baer[133] report that reaction of 6,6-pentamethylenefulvene with maleic anhydride in benzene at room temperature gives the *endo* adduct, which rearranges to the *exo* on standing for several weeks. In solvents such as benzene or ethyl acetate, the *endo* adduct dissociates immediately as noted by the appearance of the colored fulvene; the *exo* adduct is more stable,[133,134] dissociating only above its melting point of 93°. Dimethylfulvene gives a mixture of *endo* and *exo* on reaction with maleic anhydride. As expected the ratio of *exo* to *endo* varies with temperature,[135,136] being 1.1 at 15° and 1.3 at 80°. When the *exo* adduct is heated to 80° for 3 hr, it gives an equilibrium mixture of 85% *exo* and 15% *endo*. It should be noted that, due to resonance forms such as



in the fulvene, the transition state for *exo* adduct is more favorable than it is with, say, cyclopentadiene. Evidently the position of equilibrium corresponds to the relative stabilities of the two transition states.

Adducts of aromatic fulvenes are more stable. Thus, when diphenylfulvene reacts with maleic anhydride in refluxing benzene, only the *endo* adduct is obtained.[137] When the reaction is carried out in xylene at 140°, a mixture of 71% *exo* and 29% *endo* is obtained. Another example of the stability of aromatic fulvenes is the dissociation of hydrogenated dimethyl acetylenedicarboxylate adducts.[138] As expected, adducts of fulvenes with dimethyl acetylenedicarboxylate are themselves stable, but, when the adducts are hydrogenated so as to remove the endocyclic double bond, the product should be able to decompose in the same manner as other hydrogenated dimethyl acetylenedicarboxylate adducts. This has been observed for diphenylfulvene (**108**), giving **109** and ethylene in diethyl malonate at 195°. However, **110**, derived from dimethylfulvene, gives only tar under the same conditions.



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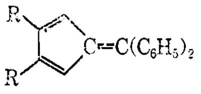

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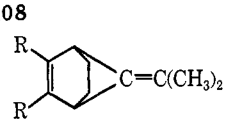
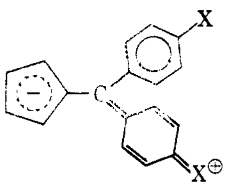


110

The equilibrium constants for the reactions of a number of fulvenes with tetracyanoethylene have been measured.[139] The adducts, obtained by reacting the fulvene with tetracyanoethylene in toluene at room temperature, are unstable to light and air, but last several hours in darkness under nitrogen. The adducts are completely dissociated in methanol and benzene but only partially so in chloroform, ethyl acetate, and dioxane. The equilibrium constants in chloroform at 20° were measured spectrophotometrically in the 400-mμ region. The results are shown in Table I. Electron-withdrawing groups on the benzene rings of aromatic fulvenes should destabilize resonance forms such as



thereby stabilizing the adduct relative to the fulvene reactant. This, however, is not observed; electron-withdrawing groups reduce the electron density in the cyclopentadiene ring, consequently making the fulvene less reactive to tetracyanoethylene.[139]

When the diene and dienophile are both active, the reverse Diels–Alder reaction occurs only at much higher temperature than the forward reaction. Under these conditions *endo–exo* isomerization often occurs. For instance, the adduct of cyclopentadiene and maleic

TABLE I
EQUILIBRIUM CONSTANTS

Fulvene dienophile	K(adduct)/(fulvene) (TCNE)
6,6-Di(*p*-methoxyphenyl)	325×10^3
6,6-Diphenyl	11
6,6-Di(*p*-bromophenyl)	3.3
6,6-Di(*p*-chlorophenyl)	2.6
6,6-Di(*p*-nitrophenyl)	0.1
6,6-Dimethyl	32.0
6-Methyl-6-ethyl	70
6,6-Pentamethylene	130

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[133] R. B. Woodward and H. Baer, *J. Am. Chem. Soc.*, **66**, 645 (1944).

[134] E. P. Kohler and J. Kable, *ibid.*, **57**, 917 (1935).

[135] D. Craig, J. J. Shipman, J. Kiehl, F. Widmer, R. Fowler, and A. Hawthorne, *ibid.*, **76**, 4573 (1954).

[136] K. Alder and R. Rahmann, *Ann.*, **566**, 1 (1950).

[137] K. Alder, F. W. Chambers, and W. Trimborn, *ibid.*, **566**, 28 (1950).

[138] K. Alder and W. Trimborn, *ibid.*, **566**, 58 (1950).

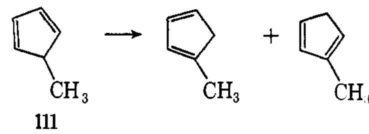
[139] G. Kresze, S. Rau, G. Sabelus, and H. Goetz, *ibid.*, **648**, 57 (1961).

anhydride, which is exclusively *endo*, rearranges at its melting point of 165° to give the *exo* adduct, mp 143°. This reaction is not catalyzed by acids or bases and does not take place with the hydrogenated adduct (norbornane-2,3-dicarboxylic acid). In this case, where the adduct is so stable, it is possible to conceive of an internal pathway for this rearrangement, one that does not involve dissociation into and recombination of the original addends. Berson, Reynolds, and Jones[140] obtained radioactive *endo* adduct by treating cyclopentadiene with maleic anhydride labeled with C^{14} in the carbonyl carbons. When this labeled adduct was refluxed in decalin with an equimolar quantity of unlabeled maleic anhydride, the *exo* adduct so obtained had an activity consistently higher than could be accounted for solely by dissociation into free addends and recombination of these. This would seem to indicate that about half of the *exo* adduct formed through an internal pathway.

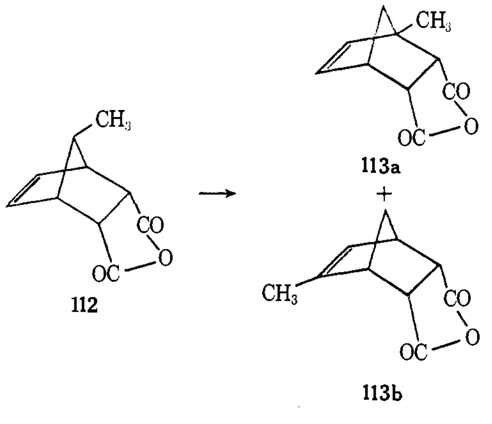
In subsequent studies Baldwin and Roberts[141] rearranged the *endo* isomer in the presence of tetracyanoethylene. The ratio of tetracyanoethylene adduct to *exo*-5-norbornene-2,3-dicarboxylic anhydride was found to be markedly temperature dependent: 1.72 at 185°, 0.63 at 160°. This would indicate that the internal and external pathways involve completely different reactions. On the assumptions that tetracyanoethylene reacts with cyclopentadiene under these conditions much faster than maleic anhydride and that the only source of cyclopentadiene is the *endo* isomer, the rate data[141] were calculated as: internal, $\log A = 8.3$, $\Delta H^{\ddagger} = 25$ kcal/mole; external, $\log A = 16.0$, $\Delta H^{\ddagger} = 42$ kcal/mole. It was also found that hydrogenated adduct, norbornane-2,3-dicarboxylic anhydride, rearranged from *endo* to 22% *exo* when heated 24 hr at 250°. It is unlikely that this reaction bears any similarity to that of the unsaturated adduct.

However, recent evidence indicates that the internal pathway, in fact, does not exist. It has been found[141] that above 150° maleic anhydride reacts with cyclopentadiene at almost the same rate as does tetracyanoethylene. As for the earlier results,[140] it appears that the maleic anhydride was not completely dissolved in the decalin.[142,143] With less unlabeled maleic anhydride available for the cyclopentadiene to react with, the *exo* adduct would have a higher activity than expected. When the isotopic exchange experiment was repeated in *t*-amylbenzene, in which solvent the maleic anhydride is completely soluble, the activity of the *exo* adduct obtained is very close to that calculated for the external path alone.[143] Berson,[144] however, has suggested that complexing between maleic anhydride and the aromatic solvent may eliminate the diene–dienophile complex and, thus, the internal path.

There is another line of evidence against the internal pathway; this involves the use of methylcyclopentadiene. Methylation of cyclopentadienyl Grignard at low temperature gives 1-methylcyclopentadiene (**111**) which isomerizes at temperatures above 25° to an equilibrium mixture containing approximately equal amounts of 2- and 3-methylcyclopentadiene and a small amounts of the 1-methyl isomer[145] (see eq 18a). This is a thermal hydrogen shift similar to that which occurs in the cycloheptatriene system.[96] The rate of this reaction is slower than that of Diels–Alder addition to active dienophiles such as maleic anhydride. As a result, the position of the methyl group can be "frozen" by Diels–Alder addition. However, in refluxing tetralin (207°) the maleic anhydride adduct **112** is converted to an equilibrium mixture (see eq 18b), containing approximately equal amounts of 1- and 5-methyl-5-norbornene-2,3-dicarboxylic acids (**113a** and **113b**, respectively) and a small amount of the 7-methyl isomer.[146] This is the mixture which would form from reaction of the equilibrium mixture of methylcyclopentadienes with maleic anhydride, and it occurs under conditions similar to those under which Berson first obtained evidence for the internal pathway.[140]



(18a)



(18b)

Berson and coworkers have made further attempts to find examples of an internal pathway.[147,148] In the case

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(140) J. A. Berson, R. D. Reynolds, and W. A. Jones, *J. Am. Chem. Soc.*, **78**, 6049 (1956).

(141) J. E. Baldwin and J. D. Roberts, *ibid.*, **85**, 115 (1963).

(142) V. Scheidegger, unpublished work reported in ref 144.

(143) J. D. Roberts, C. Ganter, and V. Scheidegger, *J. Am. Chem. Soc.*, **87**, 2771 (1965).

(144) J. A. Berson, private communication to Roberts, Ganter, and Scheidegger.[143]

(145) V. A. Mironov, E. V. Sobolev, and A. N. Elizarova, *Izv. Akad. Nauk SSSR*, 1607 (1963); English transl., p 1467; *Tetrahedron*, **19**, 1939 (1963).

(146) V. A. Mironov, T. M. Fadeeva, A. V. Stepaniantz, and A. A. K. Akhrem, *Tetrahedron Letters*, 5823 (1966).

(147) J. A. Berson and W. A. Mueller, *J. Am. Chem. Soc.*, **83**, 4940 (1961).

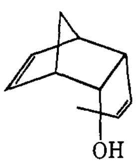
(148) J. A. Berson and A. Remanick, *ibid.*, **83**, 4947 (1961).

of 9-phenylanthracene the *endo–exo* isomerization becomes merely a racemization.[147] The rates of racemization and of exchange of labeled 9-phenylanthracene–maleic anhydride adduct with unlabeled maleic anhydride were measured and found to be about equal. It is also possible to determine whether the *endo–exo* isomerization involves breaking one C–C bond, as suggested by Craig,[135] or two bonds, as in a retrodiene reaction, by using optically active adducts of cyclopentadiene with the methyl esters of acrylic and methacrylic acids.[148] In this case optically active *exo* adduct was allowed to rearrange to the equilibrium mixture of *endo* and *exo* adducts in decalin at 170°. If one bond is broken, the starting isomer will be more completely racemized than the product; if two bonds are broken, the opposite situation will result. In this case the *endo* isomer was found to be completely racemized and the *exo* isomer only slightly. Consequently, in this case at least, isomerization of the adduct must involve complete dissociation either to a complex or to free addends. Unfortunately, it is not possible to distinguish between the complex (internal pathway) and free addends without using isotopic exchange experiments, which could not be performed because of the high rate of polymerization of methyl methacrylate under these conditions.

There are cases, however, where rearrangement of Diels–Alder adducts is known to proceed by an internal pathway. Best known in this area is the work of Woodward and Katz who found[76] that α-1-hydroxydicyclopentadiene (**114**) rearranged at 140° to *syn* 7-hydroxydicyclopentadiene (**115**) and β-1-hydroxydicyclopentadiene (**116**) to *anti*-7-hydroxydicyclopentadiene (**117**). Apparently the reaction proceeds with complete retention of stereochemistry and of optical activity.

A similar case is provided by the work of Yates and Eaton[149] who obtained **118** *via* sulfuric acid hydrolysis of the adduct of cyclopentadiene with the diethyl ketal of tetrachlorocyclopentadienone. Unlike most cyclopentadienone adducts, **118** did not lose CO on heating but instead rearranged smoothly and completely at 135° to **119**. This same reaction could be carried out at room temperature under $AlCl_3$ catalysis. Evidently coordination of the carbonyl group by the $AlCl_3$ facilitates bond breaking. A similar instance[150] of such catalysis is afforded by the case of 7-ketodicyclopentadiene, which undergoes rapid and complete conversion to the 1-keto isomer at room temperature in the presence of traces of BF_3 or HCl.

On the other hand, 1-acetoxydicyclopentadiene dissociated on heating to cyclopentadiene and 1-acetoxycyclopentadiene.[76] This could best be shown by carrying out the reaction in the presence of ethylene, in which case the products were norbornene and 7-acetoxynorbornene. Obviously this reaction cannot proceed by dissociation and recombination. However, if we redraw **114** as **120** we can see that the reaction involves merely a shift of bond a from C(3)–C(8) to C(5)–C(10) while bond b is held fixed. One may visualize **120** passing to **122** through the transition state **121**. To use the terminology of Woodward and Hoffmann,[7] this is a (3,3) sigmatropic shift or simply a Cope rearrangement. The identity of the Woodward–Katz and Cope rearrangements has been pointed out by many authors.[5] However, Woodward and Katz[76] themselves do not consider their reaction to be a Cope rearrangement but instead propose that **121**, the transition state for this reaction, is also the transition state for the Diels–Alder dissociation. They leave open the question of whether the Diels–Alder reaction involves an intermediate diradical or zwitterion; they merely say that in the transition state one bond is more broken than the other. The question of whether the Diels–Alder transition state involves equal weakening of the two bonds to be broken or formed is very much undecided. Therefore, although it is clear that this reaction is a Cope rearrangement, it is by no means clear what relationship there may be between it and the reverse Diels–Alder reaction.



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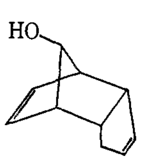

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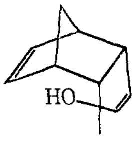

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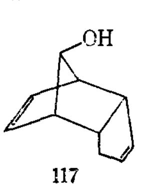

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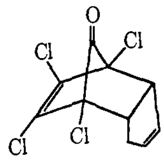

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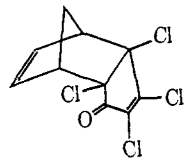

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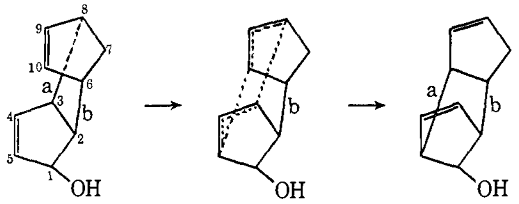

120 **121** **122**

Some evidence that the two reactions are related is provided by the work of Lutz and Roberts[151] who found that monodeuterated methacrolein dimer **123** underwent Cope rearrangement (see eq 19) at 171° to give **124** while giving substantial amounts of methacrolein. First-order rate constants for the two reactions at 180°

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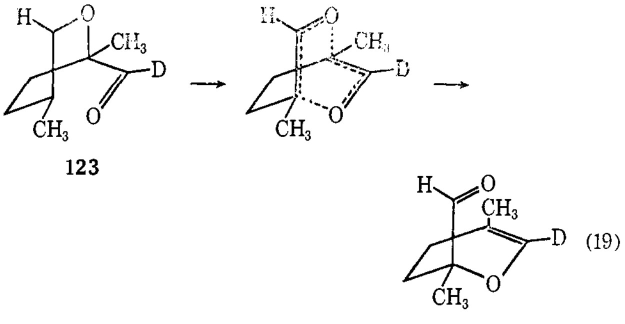
(149) P. Yates and P. Eaton, *Tetrahedron*, **12**, 13 (1961).

(150) R. C. Cookson, J. Hudec, and R. O. Williams, *Tetrahedron Letters*, **122**, 29 (1960).

(151) R. P. Lutz and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 2198 (1961).

were estimated as 1.8×10^{-3} min^{-1} for rearrangement and 5.2×10^{-4} min^{-1} for dissociation. This means that the difference in the free energy of activation for the two reactions is only about 1.1 kcal/mole. Such a result would seem to indicate that the two transition states are fairly similar but does not by any means prove they are identical. The Cope rearrangement here proceeds with retention of optical activity, which excludes a diradical intermediate.



123

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(19)

Hydrocarbons also undergo the Woodward-Katz rearrangement. Thus 1-methyldicyclopentadiene, if heated for 2 hr at 145°, is converted to a mixture of 44% 7-methyldicyclopentadiene and 56% starting material.[152] Had retrodiene dissociation to methylcyclopentadiene occurred, the facile double-bond migration of this monomer would have produced many other isomeric dimers.

VII. KINETIC CONSIDERATIONS

In principle, determination of the activation parameters for the forward and reverse Diels–Alder reaction should enable us to determine the geometry of the transition state in relation to that of the adduct and addends. The results of kinetic studies of a number of Diels–Alder reactions are given in Table II.[153–160]

Experimental errors in the determination of activation parameters are usually quite high, so the absolute values given in Table II do not have much meaning. Where the entropies of activation were not given, they were calculated[154] from the experimental values of log A by the simple relation $\Delta S^{\ddagger}/R = \ln A - \ln (kT/h)$. The reverse reactions are all unimolecular, and the forward reactions generally show good second-order kinetics, at least at low per cent conversions. At high conversions, free-radical polymerization, particularly with butadiene and isoprene, may lead to significant errors. It is generally said that the Diels–Alder reaction shows very little sensitivity to solvent and catalysts, but this generalization is not always safe to make, as can be seen from the various examples of the cyclopentadiene–quinone reaction. In fact, the initial rates of this reaction in benzene were third order when a little trichloroacetic acid was added; in the gas phase the reaction was heterogeneous.[161,162] In this case, of course, the dienophile is rather polar, but even in the retrodiene cracking of dicyclopentadiene, a heterogeneous reaction becomes superimposed on the unimolecular homogeneous one when certain heavy metal sulfides are added.[163]

TABLE II

ACTIVATION PARAMETERS FOR TYPICAL FORWARD AND REVERSE DIELS–ALDER REACTIONS

Reaction[a]	Solvent	Temp, °C	Log A	$\Delta H^{\ddagger}$, kcal	Ref	$\Delta S^{\ddagger}$, eu
1f	HOAc	18–30	7.5	11.0	153	−24.1
	EtOH	2–39	7.0	12.7	153	−26.4
	$PhNO_2$	21–42	7.0	11.1	153	−26.4
	Hexane	20–40	6.5	12.1	153	−28.7
	Benzene	8–50	6.5	11.6	153	−28.7
	CCl_4	2.49	4.5	9.12	153	−37.7
	CS_2	3.39	4.0	8.5	153	−40.1
1r	Benzene	55–79	12.6	29.0	153	−0.8
2f	Benzene	11–51	4.8	10.0	153	−36.4
	CCl	12–54	5.2	10.6	153	−34.6
2r	Benzene	49–79	12.1	27	153	−3.46
3f	Gas	80–150	6.1	16.7	153	−31.0
	Gas	...	7.3	14.9	154	−26
3r	Paraffin	135–75	13.0	34.2	153	0.5
	Neat liq	100–55	13.0	34.5	153	0.5
	Gas	27–111	13.1	35.	153	0.9
	Gas	~185	13.0	33.7	154	0
4f	Gas	108–210	6.2	15.2	153	−30.6
4r	Gas	192–242	12.3	33.6	153	−2.7
5f	Gas	170–390	9.9	23.7	155	−13.9
	Gas		10.67	25.3	154	−13.
	Gas	400–600	11.14	26.8	156	−9.2
5r	Gas	750	15.20	62.0	169	8.4
6f	Gas	400–600	10.48	27.5	156	−12.2
6r	Gas	485–565	12.95	57.5	157	−1.4
	Gas	700	12.09	55.1	158	−5.5
	Gas	500	17.1	72.7	166	17.3
	Gas	541–629	15.16	66.2	167	8.0
	Gas	750	15.00	66.6	169	7.5
7r	Gas	300–450	13.8	42.7	159	2.8

[a] Reactions (f = forward; r = reverse): (1) cyclopentadiene + quinone, (2) cyclopentadiene + naphthoquinone, (3) cyclopentadiene dimerization, (4) cyclopentadiene + acrolein, (5) butadiene dimerization, (6) butadiene + ethylene (cyclohexene pyrolysis), (7) norbornene pyrolysis (cyclopentadiene + ethylene).

Recently the rates of retrodiene decomposition of *endo-* and *exo-*dicyclopentadiene have been measured.[164]

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(152) V. A. Mironov, T. M. Fadeeva, A. V. Stepaniantz, and A. A. Akhrem, *Izv. Akad. Nauk SSSR*, 434 (1967).

(153) A. Wassermann, *Trans. Faraday Soc.*, **34**, 128 (1938), and references therein.

(154) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1961, pp 104–110.

(155) G. B. Kistiakowsky and W. W. Ransom, *J. Chem. Phys.*, **7**, 725 (1939).

(156) D. Rowley and H. Steiner, *Discussions Faraday Soc.*, **10**, 198 (1951).

(157) L. Kuchler, *Trans. Faraday Soc.*, **35**, 874 (1939).

(158) M. Kraus, M. Vavruska, and V. Bazant, *Collection Czech. Chem. Commun.*, **22**, 484 (1957).

(159) W. C. Herndon, W. B. Cooper, and M. J. Chambers, *J. Phys. Chem.*, **68**, 2016 (1964).

(160) J. H. Birely and J. P. Chesick, *ibid.*, **66**, 568 (1962).

(161) A. Wassermann, *J. Chem. Soc.*, 623 (1942).

(162) A. Wassermann, *ibid.*, 1089 (1946).

(163) A. Wassermann and B. S. Khambata, *ibid.*, 1090 (1946).

(164) W. C. Herndon, C. R. Grayson, and J. M. Manion, *J. Org. Chem.*, **32**, 526 (1967).

The results were log $A = 13.01$ and $\Delta H^{\ddagger} = 33.97$ for *endo*, and log $A = 13.72$ and $\Delta H^{\ddagger} = 38.49$ for *exo*. These data prove that the *exo*-dicyclopentadiene formed (along with polymer) when the *endo* isomer is heated in a sealed tube at 200° does not do so by an internal pathway. Under steady-state conditions, a plot of the ratio of *endo*- plus *exo*-dicyclopentadiene to monomer *vs.* flow rate should give a straight line whose intercept is the rate of internal isomerization. This intercept was found to be zero. The same thing was proven by Baldwin, who prepared *endo*-dicyclopentadiene labeled with deuterium in one ring and showed that heating this at 196° gave complete scrambling of the deuteriums.[165]

Attempts to determine the equilibrium constant for the *endo–exo* isomerism gave poor results, but it does appear that the free energy of isomerization is approximately zero.[164] It would seem that the transition state for retrodiene decomposition of the *exo* adduct is of higher energy than that for decomposition of the *endo* adduct and that the slower decomposition of the *exo* adduct is due to something more than the greater thermodynamic stability of the *exo* isomer.

Some kinetic data for *endo–exo* isomerism have been reported. Mironov and coworkers measured the rate of formation of 4- and 5-methyl-5-norbornene-2,3-dicarboxylic anhydride from the 7-methyl isomer and showed that the reaction occurs entirely by dissociation and recombination.[146] The kinetic parameters were: log $A = 16.73$, $\Delta H^{\ddagger} = 41.3$. It is interesting to note the close agreement of the kinetic parameters for the external pathway as calculated by Baldwin and Roberts[141] with those calculated by Mironov and coworkers[146] for the isomerization of methylcyclopentadiene adducts. Assuming steady-state conditions, it is easily calculated that $k = k_1k_3/k_2$ for the system

$$\textit{endo} \underset{2}{\overset{1}{\rightleftharpoons}} \text{addends} \xrightarrow{3} \textit{exo}$$

Unfortunately, the rate of formation of the *exo* adduct is not known, but it is certainly less than k_2. Thus the rate of the retrodiene (k_1) reaction is somewhat greater than k as calculated above.

Smith and Gordon studied the pyrolysis of cyclohexene and claim that it involves three paths.[166] The first of these is the normal retrodiene reaction to give butadiene and ethylene, while the second involves loss of hydrogen to give cyclohexadiene; the third is a free-radical chain mechanism to give methane, butene, and many other products. The first two paths are intramolecular in that deuterium was not incorporated into the products, and, most amazing of all, they had the same activation parameters, within experimental error. Smith and Gordon suggest that the observed activation enthalpy of 72.7 kcal/mole is the energy required to break one C–C bond to form the linear biradical, which can decompose to butadiene and ethylene or lose hydrogen and cyclize to cyclohexadiene.[166] Later work gives vastly different and probably more definitive results. Uchiyama, Tomioka, and Amano[167] pyrolyzed cyclohexene in a flow system at intermediate temperatures (550–630°). The yield of ethylene was 96% and the butadiene yield slightly less, but less than 3% cyclohexadiene was found. It should be noted in passing that this reaction is a standard laboratory preparation for butadiene.[168] An Arrhenius plot of the rates at these temperatures plus the lower temperature data of Smith and Gordon[166] and the high-temperature (800°) rates found by Kraus, Vavruska, and Bazant[158] gave log $A = 15.16$ and $\Delta H^{\ddagger} = 66.2$ kcal/mole. A least-squares analysis of the data of Smith and Gordon gives log $A = 15.14$ and $\Delta H^{\ddagger} = 65.9$ kcal/mole, quite different from the results stated.[167] The results of Uchiyama *et al.*, however, are in good agreement with those of Tsang,[169] who followed the cyclohexene pyrolysis by a shock-tube technique with temperatures calculated to be on the order of 750°. Further evidence in favor of these values is obtained by using the data of Rowley and Steiner[156] on the forward reaction to calculate the equilibrium entropy and enthalpy. These are $\Delta S°_{(800°\text{K})} = 44.7$ eu and $\Delta H°_{(800°\text{K})} = 40.1$ kcal/mole, in good agreement with literature.[167]

A similar situation arises in the pyrolysis of norbornadiene, first studied by Birely and Chesick.[160] At about 350°, norbornadiene decomposes by three paths: the first, a retrodiene reaction to give cyclopentadiene and acetylene; the second, a rearrangement to cycloheptatriene; and the third, reaction to give toluene. The toluene was considered to arise from the cycloheptatriene, which is known to rearrange to toluene under these conditions. Cyclopentadiene and cycloheptatriene formation were found to have very similar activation parameters as given in Table III. Set A was reported by Birely and Chesick[164] and set C by Herndon and Lowry.[170] Set B is the result of a least-squares

TABLE III

	Log A	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	Ref set
Cyclopentadiene	14.72	50.5	7.2	A
	13.64	50.4	2.3	B
	14.62	50.2	6.7	C
Cycloheptatriene	14.91	51.6	8.0	A
	13.44	50.4	1.2	B
	14.68	50.6	7.0	C

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(165) J. E. Baldwin, *J. Org. Chem.*, **31**, 2441 (1966).

(166) S. R. Smith and A. S. Gordon, *J. Phys. Chem.*, **65**, 1124 (1961).

(167) M. Uchiyama, T. Tomioka, and A. Amano, *ibid.*, **68**, 1878 (1964).

(168) E. B. Hershberg and J. R. Ruhoff, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p 102.

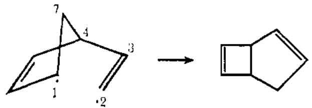
(169) W. Tsang, *J. Chem. Phys.*, **42**, 1805 (1965).

(170) W. C. Herndon and L. L. Lowry, *J. Am. Chem. Soc.*, **86**, 1922 (1964).

analysis on the data of Birely and Chesick performed by Herndon and Lowry.

This was considered evidence for a common intermediate, probably a biradical, in the formation of these products. However, it has been demonstrated[170] not to be the case since it can be proven that, if a common intermediate is involved, the ratio of the two products is also the ratio of the rate constants for the two decomposition modes of the intermediate. Then a plot of this ratio *vs.* $1/T$ should give the difference in activation enthalpies for the two decay modes of the intermediate. This difference was found to be zero.

The common intermediate must have the structure **125**. The two reactions of this intermediate are cleavage of the C(3)–C(4) bond to give the Diels–Alder addends and rotation of the *vinyl* group followed by attack on C(7) to give **126**, which undergoes thermal decyclization to cycloheptatriene with an activation energy of 39.5 kcal/mole.[171] It is unlikely that these two reactions would have the same activation energies. On the other hand, if we assume the isomerization occurs through these intermediates while the reverse Diels–Alder reaction does not, then the observed rate of isomerization is a function of three rates, thereby permitting greater latitude for coincidence. Also, if there is an intermediate formed in the process, then reaction of cyclopentadiene with acetylene should produce cycloheptatriene as well as norbornadiene. At 200 psi and 180°, these two hydrocarbons gave a 20% yield of norbornadiene and no other products. Apparently then, none of the kinetic results have to be interpreted in terms of a diradical intermediate.



125 **126**

Walling and Schugar[172] have also studied the pressure dependence of the rearrangement of 1-hydroxydicyclopentadiene, the Woodward–Katz[76] adduct. The entropy of activation of this reaction was only 2 eu, and the volume of activation is probably low because the plot of ln *k* *vs.* *P* was curved. These are the results expected for a retrodiene reaction and not for a Cope rearrangement, for which the entropy[173] and volume of activation[174] are large and negative. However, all the cases of the Cope rearrangement studied kinetically have involved acyclic reactants and products. Since the transition state for the reaction is cyclic, large negative entropies and volumes of activation would be expected. On the other hand, the Woodward–Katz rearrangement involves both a cyclic reactant and product as well as transition state, so the results obtained are not surprising.[175] The conclusion reached above that the Woodward–Katz rearrangement is not necessarily related to the retrodiene reaction is therefore still valid.

Vaughan and Andersen have studied steric effects on the Diels–Alder reaction by reacting a number of monosubstituted maleic and fumaric acids with anthracene in refluxing propionic acid.[176] Rates of the forward and reverse reactions and the equilibrium constant were measured. As the steric requirements of the substituting group increase, the rate of the forward reaction decreases tremendously while that of the reverse reaction increases only slightly. This is in line with the differences in entropy of activation between forward and reverse Diels–Alder reactions. The high negative entropy of activation of the forward and the small activation entropy of the reverse reaction imply a cyclic transition state, one which is much closer to adduct than to addends. Increasing the steric requirements of diene or dienophile would make it more difficult for the addends to reach the cyclic configuration of the transition state, while the only effect on the decomposition of the cyclic adduct is a slight rate increase in going to the more open transition state.

The best way to decide between a cyclic or a linear transition state should be to calculate theoretically the entropies of activation for the two possible transition-state structures and compare the results with experiment. This has been done for the reaction of butadiene and ethylene, with results clearly favoring the cyclic transition state.[154] While this does not completely eliminate a biradical intermediate, it does make one rather improbable since it would require that the rate-determining (slow) step be cyclization of the biradical to cyclohexene. For the dimerization of butadiene, theoretical calculations may be made to favor either structure depending on whether or not one uses certain bending frequencies near 190 cm^{-1} for the cyclic transition state.[153,177]

The argument most used in favor of a diradical intermediate is that of product composition. For example, reaction of butadiene-1-carboxylic acid with acrylic acid gives the *ortho* isomer, 1,2,3,4-tetrahydrophthalic acid, rather than the *meta* isomer, tetrahydroisophthalic acid.[178] This does not necessarily mean, however, that there is an actual diradical intermediate, but merely that the transition state has diradical character.

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(171) M. R. Willcott and E. Goerland, *Tetrahedron Letters*, **6341** (1966).

(172) C. Walling and H. J. Schugar, *J. Am. Chem. Soc.*, **85**, 607 (1963).

(173) A. C. Cope, E. G. Foster, and F. Daniels, *ibid.*, **69**, 1893 (1947).

(174) C. Walling and M. Naiman, *ibid.*, **84**, 2628 (1962).

(175) S. W. Benson and J. A. Berson, *ibid.*, **86**, 259 (1964).

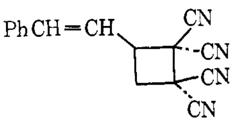
(176) W. R. Vaughan and K. S. Andersen, *J. Org. Chem.*, 21, 673 (1956).

(177) A. Wassermann, *J. Chem. Soc.*, 612 (1942).

(178) J. A. Berson and A. Remanick, *J. Am. Chem. Soc.*, 83, 4947 (1961).

Evidently there is no need to postulate any sort of intermediate in the Diels–Alder reaction.

Furthermore the high stereospecificity of the Diels–Alder reaction—the maintenance of configuration of the dienophile—argues against any sort of intermediate. This is especially evident when one compares the Diels–Alder reaction to the 1,2 cycloaddition of perhalogenated ethylenes to dienes. This latter reaction is known to involve a diradical intermediate.[179] This reaction is not stereospecific; in the addition of $Cl_2C{=}CF_2$ to 2,4-hexadiene, the configuration at the C-3 carbon of the diene is not maintained.[180] There are other differences between this reaction and the Diels–Alder. Butadiene reacts with $Cl_2C{=}CF_2$ faster than does cyclopentadiene, but with the latter diene a mixture of 1,2 and 1,4 cycloaddition products results.[181] A similar situation[182] occurs with tetracyanoethylene, which reacts rapidly and reversibly with 1,1-diphenylbutadiene to form the 1,2 cycloadduct **127** and slowly to form the Diels–Alder adduct **128**. Slow isomerization of **127** to **128** also occurs under the same conditions. These reactions almost certainly involve a biradical intermediate, but extension to other cases is doubtful. Exclusive 1,4 addition from a biradical intermediate seems unlikely since in its most favored (*trans*) configuration the two ends would be too far apart to react.



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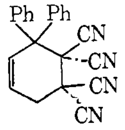

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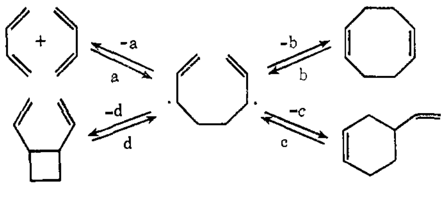
Nonetheless, the question of a biradical intermediate is still unsettled. Benson has recently argued in favor of such an intermediate based on the decomposition of 1,5-cyclooctadiene to butadiene and 4-vinylcyclohexene.[183,184] Benson assumed the scheme in eq 20 and used previously published data on the above reaction, the dimerization of butadiene, and the retrodiene reaction of 4-vinylcyclohexene to calculate kinetic parameters for each step in the scheme. These were used to calculate the equilibrium enthalpies and entropies for each step, which were found to be in good agreement with those calculated by the method of group contributions (see section VIII).

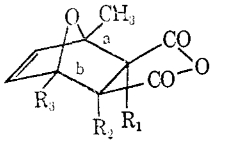


(20)

In this connection it is of interest to compare the decompositions of cyclohexene and 4-vinylcyclohexene. Note that the difference in activation enthalpies is only 4.7 kcal, using the data of Tsang.[169] If there is a biradical intermediate we should expect the two activation enthalpies to differ by the resonance energy of one allyl group, which is about 12 kcal.[185] In comparison the decompositions of methyl- and isopropenylcyclobutane, which do proceed *via* biradical intermediates, have a 10.2-kcal difference in activation energies.[186,187] Under steady-state conditions $k - k_ck_a/(k_{-c} + k_{-a}) \cong k_ck_a/k_{-c}$, where k is the over-all rate of the retrodiene reaction. Benson suggests that an decrease in the ratio k_a/k_{-c} could partially compensate for the increase in k_c in going from cyclohexene to 4-vinylcyclohexene, thus explaining the low over-all difference in activation energies. It would appear somewhat unlikely, however, that a decrease in k_a/k_{-c} would be enough to compensate since the increase in $\Delta H_a{}^{\ddagger}$ is probably no more than 2 kcal while the decrease in $\Delta H_c{}^{\ddagger}$ would be expected to be at least 10 kcal.[184]

Even if it were definitely proven that there is no intermediate in the Diels–Alder reaction, there still remains the question of whether both bonds are formed or broken equally in the transition state, *i.e.*, whether the reaction is two-stage as distinct from two-step. Two authors in two recent papers have reached exactly opposite conclusions on this matter.

Seltzer studied the secondary deuterium isotope effect in the retrodiene decomposition of the adduct of 2-methylfuran and maleic anhydride in isooctane at 50°.[188] The following isomers were prepared.



129, $R_1 = R_2 = H; R_3 = H$
130, $R_1 = R_2 = D; R_3 = D$
131, $R_1 = R_2 = H; R_2 = D$
132, $R_1 = R_3 = H; R_2 = D$
133, $R_2 = R_3 = H; R_1 = D$

It was found that $k_{129}/k_{130} = 1.16$, the value found for the secondary isotope effect per deuterium atom in alicyclic systems. This implies that either bond a or bond b is being weakened in the transition state but not both. In that case, $k_{129}/k_{131} = 1.16$ or 1.00 depending on which bond, a or b, is being broken. Instead it is found

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(179) J. D. Roberts and C. M. Sharts, *Org. Reactions*, **12**, 1 (1962).

(180) P. D. Bartlett, L. K. Montgomery, and K. Schueller, *J. Am. Chem. Soc.*, **86**, 622 (1964).

(181) P. D. Bartlett and L. K. Montgomery, *ibid.*, **86**, 628 (1964).

(182) J. J. Eisch and G. R. Husk, *J. Org. Chem.*, **31**, 589 (1966).

(183) R. Srinivasan and A. A. Levi, *J. Am. Chem. Soc.*, **86**, 3756 (1964).

(184) S. W. Benson, *J. Chem. Phys.*, **46**, 4920 (1967).

(185) R. W. Egger, D. M. Golden, and S. W. Benson, *J. Am. Chem. Soc.*, **86**, 5420 (1964).

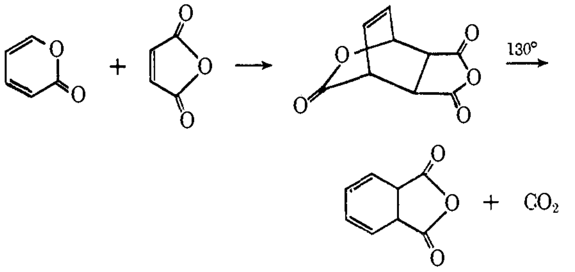
(186) M. N. Das and W. D. Walters, *Z. Physik. Chem.* (Frankfurt), **15**, 22 (1958).

(187) R. J. Ellis and H. M. Frey, *Trans. Faraday Soc.*, **59**, 2076 (1963).

(188) S. Seltzer, *J. Am. Chem. Soc.*, **87**, 1534 (1965).

that $k_{129}/k_{131} = 1.08$. This is best explained by the assumption that both bonds are being weakened equally and that the isotope effect per deuterium atom is only 1.08 for this system. That this assumption is correct is shown by the fact that $k_{132}/k_{133} = 1.00$. The secondary isotope effect in this case is due to the change in C–H bending frequency on going from adduct to transition state.[188] The difference in zero-point energies of the C–H and C–D bonds will affect this bending frequency and consequently the stability of the transition state. Since the secondary isotope effect is smaller than usual in this case, it is evident that the transition state must resemble the adduct.

Goldstein and Thayer studied primary C^{13} and O^{18} isotope effects in the retrodiene decarboxylation of the adduct of α-pyrone with maleic anhydride.[189] This reaction (eq 21) was first discovered by Diels and Alder.[190] The activation parameters for this reaction are $\log A = 13.94$, $\Delta H^{\ddagger} = 33.2$ kcal/mole, and $\Delta S^{\ddagger} = 2.7$ eu, in agreement with those for other retrodiene reactions. The solvent was dimethyl phthalate. The values of $k_{O^{12}}/k_{C^{13}}$ and $k_{O^{16}}/k_{O^{18}}$, studied by noting in the mass spectrometer how much less C^{13} and O^{18} were present in the evolved CO_2 than in a sample of naturally occurring CO_2, were found to be 1.03 and 1.04, respectively. Theoretical computation of the isotope effect in terms of normal vibrational modes could not give agreement with experiment unless it was assumed that in the transition state only the C–C bond is weakened; the C–O bond must remain unchanged. Using a simple three-center model for the transition state such as **134**, where Ⓟ is the pivot point and Ⓛ and Ⓢ are large and small masses, respectively, good agreement with experiment was obtained for the oxygen isotope effects, but the carbon isotope values were much lower than the experimental. Goldstein and Thayer suggest that this is due to a change in the force constant at the carbonyl carbon with respect to the reaction coordinate.



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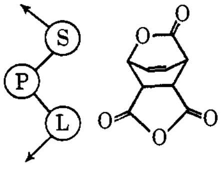

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It is becoming increasingly clear that there are very few generalizations which can be safely made about the over-all mechanism of the retrodiene, as well as the Diels–Alder reaction. Just as the polarity of the Diels–Alder can completely invert itself so that electron-deficient dienes such as hexachlorocyclopentadiene react faster with simple olefins such as cyclopentene than with the usual electron-deficient dienophiles[6,191] (the inverse electronic effect), so there may be a whole range of transition-state symmetries for the Diels–Alder reaction, ranging from completely symmetric, with both bonds equally formed, to completely asymmetric, with one bond much more fully formed or broken than the other. Even the rule that the Diels–Alder reaction is not sensitive to catalysts is not always valid. Thus, the reaction of anthracene with maleic anhydride undergoes a tremendous rate increase when conducted in the presence of 1 molar equiv of aluminum chloride.[192] In methylene chloride at room temperature the reaction is 95% complete in 48 hr without the catalyst, fully complete in 1.5 min with it. Other Friedel-Crafts catalysts such as $SnCl_4$ were found effective in the reactions of butadiene with acrolein, acrylic acid, and methyl vinyl ketone.[193] It should be noted, however, that in these cases the diene is very electron-rich and the dienophile very electron-poor. In fact, with anthracene and maleic anhydride there is preliminary formation of a charge-transfer complex. It is unlikely that such catalysis would be effective when there is very little difference in electron density at the reaction center between diene and dienophile.

VIII. THEORETICAL INTERPRETATIONS

The first attempt to explain the observed stabilities of Diels–Alder adducts was an empirical one, the so-called "double-bond rule" of Schmidt.[194] This rule merely states that in any olefin pyrolysis it is the bond β to the double bond which cleaves; a C–C single bond in this position appears to be weaker than a normal C–C single bond, while the position α to the double bond is one of strength. This need not be restricted to C–C bonds; the high lability of groups attached to allyl and benzyl systems is a clear example. In the case of Diels–Alder adducts the rule is quite useful. The adduct of furan with maleic anhydride, for example, is extremely labile while that with acetylenedicarboxylic acid is much more stable, since the latter has no single bonds β to a double bond which would be involved in a Diels–Alder reaction. In all cases adducts of acetylenic dienophiles seem to be more stable than corresponding adducts of ethylenic dienophiles.

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(189) M. J. Goldstein and G. L. Thayer, *J. Am. Chem. Soc.*, **87**, 1925, 1933 (1965).

(190) O. Diels and K. Alder, *Ann.*, **490**, 257 (1931).

(191) J. Sauer and H. Wiest, *Angew. Chem. Intern. Ed. Engl.*, 1, 269 (1962).

(192) P. Yates and P. Eaton, *J. Am. Chem. Soc.*, **82**, 4436 (1960).

(193) G. I. Fray and R. Roginson, *ibid.*, **83**, 249 (1961).

(194) O. Schmidt, *Z. Physik. Chem.*, **159**, 337 (1932).

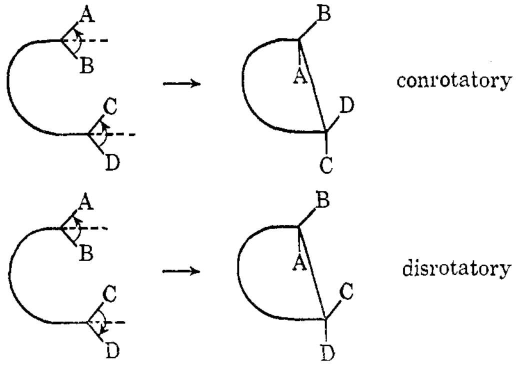
One way to explain the rule might be by hyperconjugation. Mulliken, Rieke, and Brown made simple HMO calculations of the magnitude of hyperconjugation by treating the methyl group as a heteroatom.[195] Later authors have elaborated the calculations but the results are qualitatively similar. To use Mulliken's own words, "Every C–C bond can act as hyperconjugation-donor wherever this is needed without appreciable cost." Thus 1,3-pentadiene, where the methyl group is conjugated with two double bonds, has a hyperconjugation energy of 0.112β, while isoprene, where the methyl group is α to one double bond and β to the other, has hyperconjugation energy of 0.114β. Thus hyperconjugation explains the strengthening of the α bond but does not explain the weakening of the β bond.

To explain the weakening of the β bond we must consider not the adduct but the transition state. If we break the β bond, we form an allylic radical (assuming homolytic cleavage), whereas if we break an α bond we place the odd electron on an sp^2 carbon, a very unfavorable situation. Since the resonance energy of the allyl radical is about 12 kcal, this might explain the statement of Smith and Gordon[166,185] that the β bond in cyclohexane is at least 15 kcal weaker than an ordinary carbon–carbon single bond. Of course, it is not at all likely that a radical intermediate is involved in the Diels–Alder reaction, but the very same considerations affecting radical stabilities will determine the stability of the transition state.

Because the Diels–Alder reaction has such a simple energy profile, with no intermediates, its treatment by MO theory will be simpler than for many other reactions. An early attempt along this line was that of Brown, who found that *para* localization energies correlated well with the equilibrium constants for the reaction of polycyclic aromatics with maleic anhydride.[196] The *para* localization energy, L_p, is the loss in π-bonding energy resulting from the removal of two carbons with a mutual *para* orientation from the π network.[197] For anthracene this is the difference between the π-bonding energy of anthracene and twice that for benzene, since the maleic anhydride adduct has two unconjugated benzene rings. It appears that a given aromatic system will not react with maleic anhydride if its L_p is greater than 3.6.[196] This treatment obviously cannot explain the stereochemistry observed in the reactions of simple dienes or the orientation observed in the reactions of monosubstituted dienophiles. Streitwieser, however, has suggested that this latter point can be explained by treating the transition state as a modified benzene.[197] For example, the reaction of 1-phenylbutadiene with acrolein could lead to two transition states, one corresponding to *o*-phenylbenzaldehyde and the other to *m*-phenylbenzaldehyde. The former is more stable and so it is the *ortho* adduct which is observed.

Epstein has found that 1,4 bond orders correlate well with Brown's *para* localization energies.[196,198] The 1,4 bond order, p_{14}, is a static reactivity index in contrast to L_p, which is a dynamic index; that is, p_{14} depends only on the properties of the diene while L_p is a characteristic of the transition state. Interpretation of bond orders between nonbonded atoms is difficult, particularly here where the values of p_{14} are all less than zero, but increasingly negative values of p_{14} do seem to correlate with increasing Diels–Alder reactivity of the diene.

The most promising work in this area is that of Woodward and Hoffmann, who in a recent series of communications brilliantly delineated the molecular orbital basis of all reactions involving merely electron shifts.[7,8] The first such reaction to be considered, and the easiest to treat by MO theory, is the electrocyclic reaction, which is defined as the formation of a single bond between the ends of a conjugated polyene. The cyclizations of butadienes to cyclobutenes and of hexatrienes to conjugated cyclohexadienes are well-known examples of this type of reaction. The reverse of this type of reaction is also known and is treated in the same way. The stereochemistry of an electrocyclic reaction may be either conrotatory, in which groups on opposite ends of the polyene chain rotate in the same direction, or disrotatory, in which they rotate in opposite directions. Which stereochemistry will occur is determined by the symmetry of the highest occupied π orbital or the open-chain polyene. In order for bonding to occur between the ends of the polyene chain; that is, for overlap between opposite lobes of the highest occupied orbital to occur, the two lobes which overlap must have the same sign. This requirement leads to the simple rule that all electrocyclic reaction involving systems of $4n$ π electrons will be conrotatory, while all



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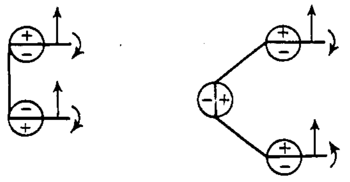
[195] R. S. Mulliken, C. A. Rieke, and W. G. Brown, *J. Am. Chem. Soc.*, 63, 41 (1941).

[196] R. D. Brown, *Quart. Rev.* (London), 6, 63 (1952).

[197] A. Streitwieser, Jr., "Molecular Orbital Theory," John Wiley and Sons, Inc., New York, N. Y., 1961, p 432.

[198] I. R. Epstein, *Trans. Faraday Soc.*, 63, 2085 (1967).

those involving systems of $(4n + 2)$ π electrons will be disrotatory. This applies only to those electrocyclic reactions brought about by heat alone; for those occurring photolytically, the reacting species is in the first excited state, so the opposite stereochemistries will occur.



The above is a direct illustration of the frontier electron method, which assumes that for any reaction the products will be determined solely by the properties of the highest occupied and lowest unoccupied orbitals of the reactants; the other orbitals can be neglected.[55] Fukui has used perturbation theory to show quantitatively that this is the case for electrocyclization.[199]

There are other ways in which the same stereochemical conclusions about electrocyclization may be reached. One of these has recently been suggested by Zimmerman.[200] He begins by considering the transition state for electrocyclization as a conjugated cyclopolyene; for instance, in the cyclization of butadiene the transition state would be a form of cyclobutadiene. It will be noted that all the conjugated cyclopolyenes have degenerate energy levels; this means that two orbitals of the polyene must become equivalent in the transition state. Clearly, the favored transition state will be the one with the lowest degenerate energy level. As an example of a more general method, Zimmerman solves the secular determinant for a cyclobutadiene of irregular geometry and variable resonance integrals and shows that there will be a degenerate energy level less than zero bonding provided the signs on the p orbitals of two adjacent atoms are reversed; this would give a cyclobutadiene with a Möbius structure—a twisted ring. Considering the lowest orbital of butadiene, we see that such a structure could be reached by a conrotatory ring closure. A mnemonic is presented for finding the energy levels of any cyclopolyene in normal (Hückel) and Möbius forms.[200] In general, those cyclopolyenes with $4n$ π electrons will have a lower degenerate energy level in the Möbius form, indicating consequently that systems of $4n$ π electrons will close conrotatory. The opposite result obtains for systems of $(4n + 2)$ π electrons; these prefer disrotatory ring closure to give the cyclopolyene of normal structure. Notice that this conclusion was reached without invoking frontier electron theory.

This implies that a disrotatory thermal electrocyclization reaction for systems of $4n$ π electrons is not impossible but merely of higher energy than the conrotatory process. Experimental evidence supports this.[201] Photochemical cyclization of 1,3-cycloheptadiene gives bicyclo[3.2.0]hept-6-ene. The presence of the seven-membered ring requires this process to be disrotatory, as do the Woodward–Hoffmann rules for photolytic electrocyclizations. The reverse of this process occurs thermally with an activation energy of 45.5 kcal/mole. Conrotatory ring opening, as required by the Woodward–Hoffmann rules, would give *cis,trans*-cycloheptadiene, which is sterically impossible; hence the ring opening can only take place disrotatory. The only other possibility is a biradical process, but this is claimed to require an activation energy of at least 55 kcal/mole.[201] Evidently p-orbital overlap does occur in the disrotatory mode though not as strongly as in the conrotatory. For comparison[202] the conrotatory ring opening of cyclobutene to butadiene has an activation energy of only 32.2 kcal/mole. Bicyclo[3.2.0]hepta-2,6-diene, which has been claimed as an intermediate in the isomerization of norbornadiene to cycloheptatriene, undergoes[171] disrotatory ring opening with an activation energy of 39.5 kcal/mole. Apparently decreased overlap in the disrotatory transition state has lowered the allylic resonance energy to 6 kcal.

A third method of studying electrocyclization is to use correlation diagrams, as has been done by Longuet-Higgins and Abrahamson.[203] Here we begin by classifying each orbital in reactant and product as symmetric or antisymmetric with respect to each element of symmetry in the transition state. For electrocyclization the conrotatory transition state has an axis of symmetry and the disrotatory a plane of symmetry. An energy-level diagram is then drawn. If the maintenance of symmetry throughout the reaction requires that a filled bonding orbital become antibonding, that reaction is quantum mechanically forbidden since it would involve a change in energy state. When this is done for the cyclization of butadiene to cyclobutene (or the reverse reaction), the disrotatory mode is found to require just such a transition from bonding to antibonding; therefore it is forbidden, in agreement with the Woodward–Hoffmann rule. On the other hand, the disrotatory mode is preferred photochemically since here we are dealing with the first excited state, where one of the electrons is already in an antibonding orbital.

The correlation diagram is also the method used by Woodward and Hoffmann in determining allowable

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(199) K. Fukui, *Tetrahedron Letters*, 2009 (1965); *Bull. Chem. Soc. Japan*, **39**, 498 (1966).

(200) H. E. Zimmerman, *J. Am. Chem. Soc.*, **88**, 1564, 1566 (1966).

(201) G. R. Branton, H. M. Frey, D. C. Montague, and I. D. R. Stevens, *Trans. Faraday Soc.*, **62**, 659 (1966).

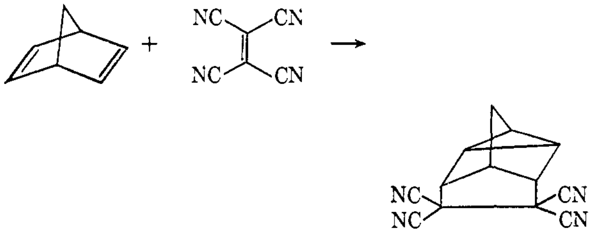
(202) R. W. Carr and W. D. Walters, *J. Phys. Chem.*, **69**, 1073 (1965).

(203) H. C. Longuet-Higgins and E. W. Abrahamson, *J. Am. Chem. Soc.*, **87**, 2045 (1965).

cycloaddition reactions. Consider the addition of two molecules of ethylene to form cyclobutane. Arranging the two ethylene molecules in parallel planes we find two elements of symmetry: (1) the plane bisecting the two molecules, and (2) the plane parallel to and midway between the planes framing the two molecules. Classifying each orbital in reactants and product with respect to these elements of symmetry we obtain the correlation diagram[7] in Figure 2. It will be seen that a filled bonding orbital must become antibonding, thus showing that the general case of 2 + 2 cycloaddition is thermally disallowed. The reaction is still allowable photochemically, since here there is no change in energy state. The reaction may still occur thermally, but here it involves a diradical intermediate, as in the 1 + 2 cycloaddition of dichlorodifluoroethylene to butadiene.[181] Hence the molecular orbital considerations discussed above do not apply.

The 4 + 2 cycloaddition, or familiar Diels-Alder reaction, involves only one element of symmetry: the plane parallel to and midway between the parallel planes containing the addends. Here the correlation diagram above shows no crossing of bonding and antibonding orbitals, so the reaction is allowed thermally in agreement with experiment (Figure 3).

Cycloaddition reactions may be defined generally as the coming together of *n* different addends, each containing *m* electrons to form a cyclic adduct containing *n* new σ bonds. Each addend need not have the same value of *m*. Those values of *m* for which the cycloaddition reaction is allowed are determined by use of correlation diagrams, as explained above. The values of *m* for which reaction is allowed will not be the same for thermal and for photochemical reactions since the latter involve excited states. Some of the thermally allowed reactions are: for $n = 2$, $m_1 = 4$, $m_2 = 2$ or $m_1 = 6$, $m_2 = 4$; for $n = 3$, $m_1 = 2m_2 = m_3$ or $m_1 = 2$, $m_2 = m_3 = 4$; and for $n = 4$, $m_1 = 4$, $m_2 = m_3 = m_4 = 2$. The most familiar 4 + 2 reaction, in which one addend contains 4 π electrons and the other 2 is of course the familiar Diels-Alder reaction. The 2 + 2 + 2 reaction, in which three olefins come together to form a cyclohexane ring, is important in connection with a possible mode of decomposition of 2,3-dicarbomethoxy-2-norbornene. Woodward and Hoffmann cite as an example of this reaction (see eq 22) the addition of dienophiles such as tetracyanoethylene to norbornadiene to give nortricyclene derivatives.[204,205] In all known cases of the 2 + 2 + 2 reaction, two of the three olefinic bonds involved are tied together into one molecule. The collision of three separate olefinic molecules to form a cyclohexane ring would be extremely unlikely on kinetic grounds. The reverse of the 2 + 2 + 2 reaction has not been experimentally observed, but there is no theoretical reason why it should not be possible.



(22)

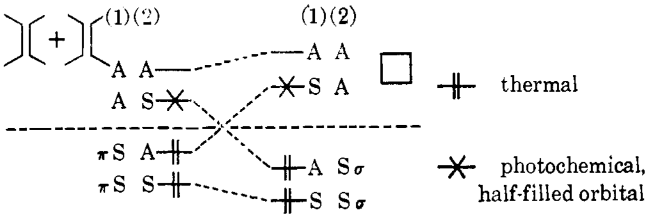


Figure 2.—Correlation diagram, where A and S are the abbreviations for symmetric and antisymmetric and π and σ have their usual orbital significance.

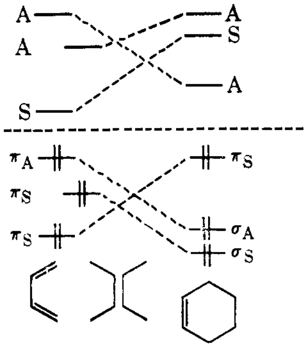


Figure 3.—Correlation diagram of 4 + 2 cycloaddition, where π_S = π orbital symmetric with respect to the parallel planes containing diene and dienophile; π_A = the corresponding antisymmetrical π orbital, σ_S = the σ orbital of cyclohexane symmetric with respect to the planes defined above, and σ_A = the corresponding antisymmetric σ orbital.

Correlation diagrams of this sort are also used to determine selection rules for allowed sigmatropic reactions. This type of reaction, which has already been discussed in connection with the Woodward-Katz experiment,[76] is defined as the migration of a σ bond along an extended polyene chain. The order of the reaction is defined as (*i,j*), where *i* and *j* are the numbers of atoms across which each terminus of the migrating bond pass in going from the old to the new position. The Cope rearrangement, probably the best known sigmatropic reaction, has order (3,3); that is, each terminus of the migrating C–C bond moves three atoms over. For hydrogen migrations one of the termini of the migrating bond does not change but remains on the migrating H, so that $i = 1$.

The stereochemistry of the sigmatropic reaction may be either suprafacial, in which the migrating group remains on the same face of the residual electron system, or antarafacial, in which it switches from one face to

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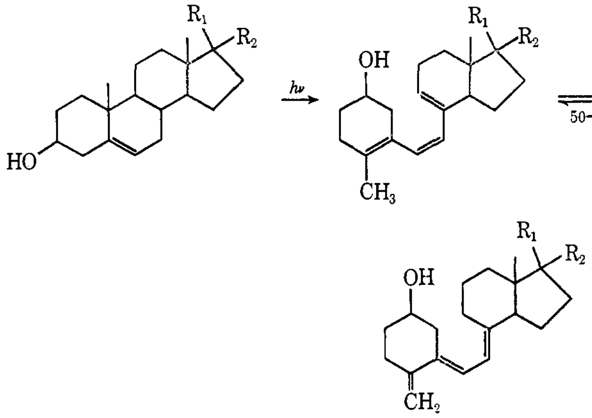
(204) A. T. Blomquist and Y. C. Meinwald, *J. Am. Chem. Soc.*, 81, 667 (1959).

(205) R. C. Cookson, J. Dance, and J. Hudec, *J. Chem. Soc.*, 5416 (1964).

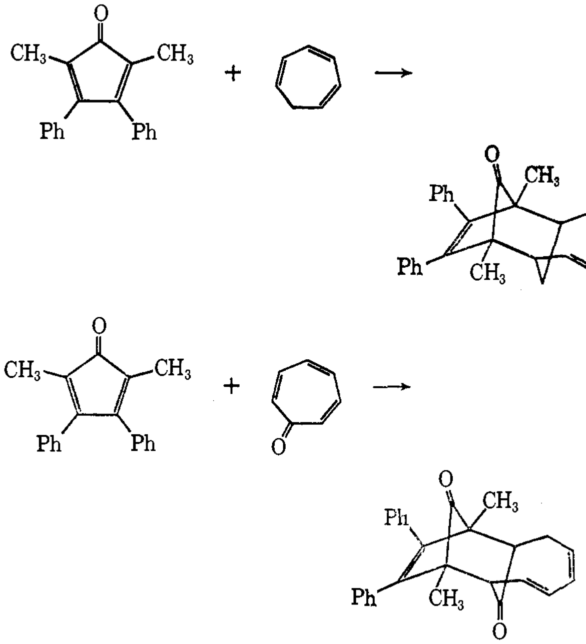
the other. The suprafacial transition state possesses a plane of symmetry and the antarafacial an axis of symmetry. The selection rules for the suprafacial process state simply that the reaction is allowed thermally whenever $i + j = 4n + 2$ and photochemically whenever $i + j = 4n$. The suprafacial process is far more important than the antarafacial since, whenever $i + j$ is small, or small or medium size rings are involved, the latter would require impossible distortions of the carbon framework. Thus, the thermal 1,7 hydrogen shift, which is permissible antarafacially, is known in the precalciferol–calciferol equilibrium (see eq 23) in the vitamin D series, but the 1,3 hydrogen shift, which is also theoretically allowable antarafacially, is "geometrically" impossible.[206]



(23)

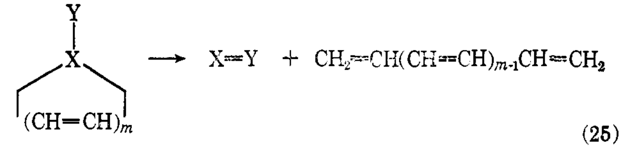
The above selection rules arise from orbital symmetry considerations similar to those used in the treatment of electrocyclization. Orbital symmetry arguments may also be applied to determine the stereochemical preferences of cycloaddition reactions. According to the treatment of Woodward and Hoffmann the preference for *endo*-adduct formation in the Diels-Alder reaction is due to symmetry-controlled overlap at secondary centers (atoms which do not become bonded in the adduct) between the highest occupied orbital of the diene and the lowest unoccupied orbital of the dienophile. However, the use of these frontier orbital symmetry arguments for other cycloadditions need not lead to the same preference for the transition state corresponding to *endo* product.

At the time the Woodward–Hoffmann theory was published,[7] no examples of the 6 + 4 cycloaddition were known. More recently, however, Woodward and Houck[207] have obtained a 6 + 4 cycloadduct of 2,5-dimethyl-3,4-diphenylcyclopentadienone with cycloheptatriene and with tropone. As predicted by theory, the adduct formed is the *exo* isomer. A 6 + 4 cycloadduct of tropone with cyclopentadiene has also been prepared[208,209] (see eq 24).



(24)

The Woodward–Hoffmann theory has also been applied to the decarbonylation of cyclopentadienone adducts.[210] This reaction may be written in general form as in eq 25. Like the electrocyclic ring opening, the



$$\longrightarrow X{=}Y + CH_2{=}CH(CH{=}CH)_{m-1}CH{=}CH_2 \qquad (25)$$

reaction may be either conrotatory or disrotatory, although Lemal and McGregor[211] prefer to use the terms axisymmetric and sigmasymmetric, respectively, signifying symmetry of the transition state with respect to an axis or a plane of symmetry. By the use of correlation diagrams similar to those described above, it was shown[210] that the concerted thermal elimination should be disrotatory (sigmasymmetric) for n odd and conrotatory (axisymmetric) for n even. Baldwin[210] has determined the kinetic parameters for the decarbonylation of dicyclopentadiene-1,8-dione to 1-keto-8,9-dihydroindene at 100°. The enthalpy of activation is 34.5 kcal/mole and the entropy of activation −9.8 eu. Although there is no question that the reaction is concerted, the presence of the ring system enforces a disrotatory stereochemistry, thus preventing positive verification of the theoretical stereochemical predictions. This positive verification has been provided by Lemal and McGre-

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[206] J. L. M. A. Schlatmann, J. Pot, and E. Havinga, *Rec. Trav. Chim.*, **83**, 1173 (1964).

[207] R. B. Woodward and K. Houck, unpublished material presented by Woodward at a symposium on aromaticity held at Sheffield, England, July 8, 1966; Special Publication No. 21, The Chemical Society, London, 1967.

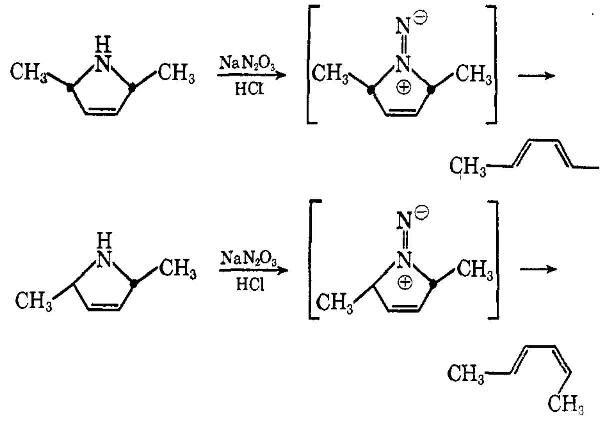
[208] R. C. Cookson, B. V. Drake, J. Hudec, and A. Morrison, *Chem. Commun.*, 15 (1966).

[209] S. Ito, Y. Fujise, T. Oduda, and Y. Inoue, *Bull. Chem. Soc. Japan*, **39**, 1351 (1966).

[210] J. E. Baldwin, *Can. J. Chem.*, 44, 2051 (1966).

[211] D. M. Lemal and S. D. McGregor, *J. Am. Chem. Soc.*, **88**, 1335 (1966).

gor,[211] who showed that the formation of dienes by deamination of 3-pyrrolines is disrotatory. Thus, from *trans*-2,5-dimethyl-3-pyrroline, there is obtained *cis,-trans*-2,4-hexadiene cleanly while *cis*-2,5-dimethyl-3-pyrroline gives the *trans,trans*-2,4-hexadiene (see eq 26).



(26)

Tyutyulkov and Markov[212] used Hückel MO theory to find the energy of the π complex between diene and dienophile in the anthracene cases. The reaction diagram (Figure 4) was assumed as a basis for this analysis. The secular determinant for the complex was solved on the assumption that the resonance integral between one atom of diene and another of dienophile was proportional to the corresponding overlap integral.[213] For the reactions of cyclopentadiene with itself, ethylene, acrolein, benzoquinone, and naphthoquinone, a plot of ΔE_π *vs.* activation energy was linear. In all cases the *exo* π complex and therefore the *exo* transition state was of higher energy. The secular determinant was also used to find the electron density of each atom of the π complex.[212] Summing up these electron densities established that the diene component acquires a net negative charge. The charge difference was greater in the *exo* π complex than in the *endo*.

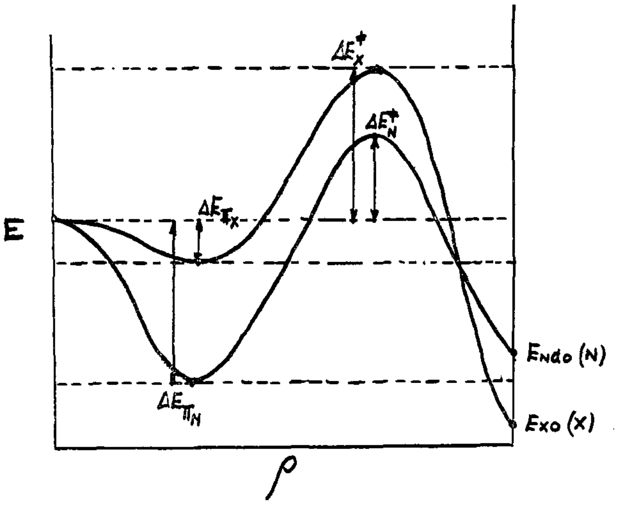
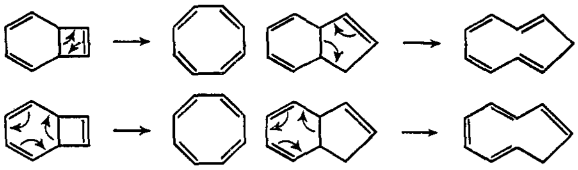


Figure 4.—Reaction diagram, where $E_{\pi X}$ = energy of the *exo* π complex, $E_{\pi N}$ = energy of the corresponding *endo* complex, and ‡ and ρ have their usual significance.

Most treatments of Diels–Alder stereochemistry have involved interactions at secondary centers. The fact that the much larger interactions at primary centers may also vary with stereochemistry is indicated by recent calculations of Herndon and Hall.[214] The transition state for the dimerization of cyclopentadiene was considered as a perturbation on the π orbitals of cyclopentadiene. For each combination of one atom from one cyclopentadiene ring and one atom from the other, the overlap integral was resolved into a sum of the form $S = aS_{\pi\pi} + bS_{\sigma\sigma}$, where a and b are trigonometric functions of an angle θ, which in turn depends on the assumed bond lengths and transition-state geometry. The $\pi\pi$ and $\sigma\sigma$ overlaps were determined from the tables of Mulliken, Rieke, Orloff, and Orloff.[215] Under these conditions, the overlap at primary (bond-forming) centers was found to be very much larger than the overlap at secondary centers and to vary considerably between *endo* and *exo* transition states. Since the resonance integral was again assumed proportional to the overlap integral,[213] and since the energy of the transition state involves a second-order perturbation (squared resonance integral), it is clear that the energy difference between the *endo* and *exo* transition states will be quite large even without taking secondary overlaps into account. Assuming β = 60 kcal, an *endo–exo* energy difference of 4.7 kcal/mole (90% of which was due to the primary overlaps) was found.[214] This is in good agreement with the observed difference in activation energies for the retrodiene decomposition of *endo* and *exo* dicyclopentadiene.[162]

It is of interest now to consider the internal Diels–Alder reaction in terms of the rules for electrocyclic reactions. The tautomerization of cyclooctatetraene to and from bicyclo[4.2.0]octa-2,4,7-triene and of cyclononatetraene to 8,9-dihydroindene can be considered as involving either four or six electrons. Since these are cyclic systems the tautomeric changes must be disrotatory; hence the six-electron process is the clear choice here. The cycloheptatriene–norcaradiene equilibrium is also disrotatory. Since all these processes (see eq 27 below) follow the Woodward–Hoffmann rules, they should, and do, take place under mild conditions.



(27)

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(212) M. Tyutyulkov and P. Markov, *Monatsh. Chem.*, **96**, 2030 (1965); **97**, 1229 (1966).

(213) R. S. Mulliken, *J. Phys. Chem.*, **56**, 295 (1952).

(214) W. C. Herndon and L. H. Hall, *Tetrahedron Letters*, 3095 (1967).

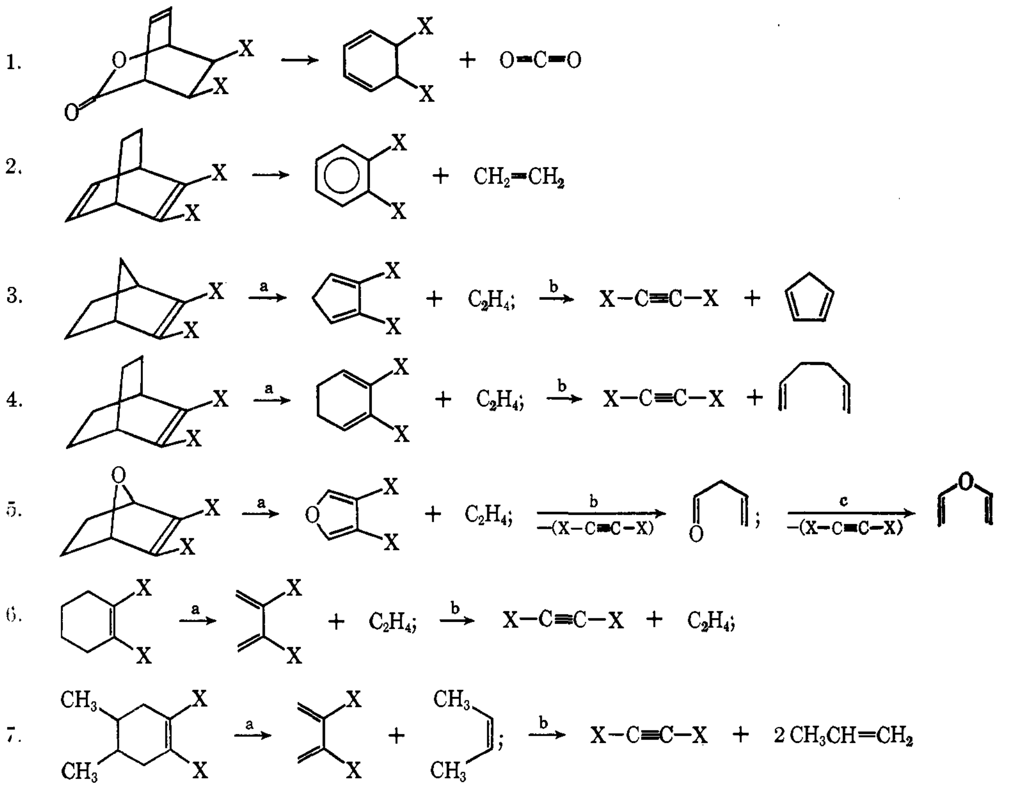
(215) R. S. Mulliken, C. A. Rieke, D. Orloff, and H. Orloff, *J. Chem. Phys.*, **17**, 1248 (1949).

TABLE IV

CALCULATED FREE ENERGIES OF RETRODIENE DECOMPOSITION (kcal/Mole)

Reaction[a]	300°K	500°K	600°K	700°K	800°K	1000°K	1100°K	1200°K
1	−6.2	−18.6	...	...	...	...	...	...
2	5.6	−4.0	...	...	...	...	...	...
3a	...	...	...	−0.8	...	−13.9	...	−22.5
3b	...	...	...	21.9	...	2.4	...	−10.5
4a	...	...	...	−0.3	...	−15.1	...	...
4b	...	...	...	26.7	...	5.2	...	...
5a	...	...	8.7	...	...	−11.3	...	...
5b	...	...	−10.1	...	...	−43.6	...	...
5c	...	...	15.7	...	...	−20.9	...	...
6a	...	...	...	16.0	...	3.0	−2.8	−5.6
6b	...	...	...	27.0	...	4.6	−5.9	−10.3
7a	...	...	...	...	2.9	−7.0	...	...
7b	...	...	...	...	3.6	−14.1	...	...

[a] The reactions are as follows where X = -COOCH$_3$.



Considering the decomposition of hydrogenated adducts of acetylenedicarboxylic acid, such as 3,4,5,6-tetrahydrophthalic acid, there is only one retrodiene reaction which this compound undergoes, and that gives butadiene-2,3-dicarboxylic acid. However, another possible mode of decomposition exists, namely, the reverse of the 2 + 2 + 2 cycloaddition, something which has never been observed. This would require cleavage of the C$_2$–C$_3$ and C$_6$–C$_1$ bonds, a violation of the double-bond rule and therefore kinetically unfavorable. The activation energy for this reaction would be expected to be at least 15 kcal higher than that for the retrodiene reaction. However, since the free-energy calculations discussed below show that the acetylenedicarboxylic acid formed in this reaction is much more stable than butadiene-2,3-dicarboxylic acid, its formation might perhaps outweigh the unfavorable kinetic factor at high enough temperature. To consider this possibility further, simple free-energy calculations have been made.

These calculations were carried out by the method of group contributions using the data of Van Krevelen and Chermin.[216,217] By this method $\Delta F_f = \Sigma A + 10^{-2}T\Sigma B + RT \ln \sigma$, where the summation is over all the groups which make up the compound and also includes corrections for ring formation and for substitution. Aromatic compounds and conjugated polyenes are considered to be composed of different groups from

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(216) D. W. Van Krevelen and H. A. G. Chermin, *Chem. Eng. Sci.*, 1, 66 (1951).

(217) G. J. Janz, "Estimation of Thermodynamic Properties of Organic Compounds," Academic Press Inc., New York, N. Y., 1958.

those in simple olefins, avoiding in this fashion the need for a resonance energy correction. From the formula given above, it is apparent that A is roughly equivalent to an enthalpy term and B to an entropy, but A is by no means equal to the enthalpy of formation. Since most of the thermochemical data available are for hydrocarbons, the results are quantitatively accurate only for this type of compound. Even though we are not concerned with only hydrocarbons, the results should still be qualitatively useful as an indication of whether a given reaction would be expected to occur easily. The results for a number of retrodiene reactions are given in Table IV.

Reactions 1 and 2 in Table IV were included merely as a test of how well these calculations agreed with experimental fact; it will be seen that the agreement is fair. Therefore, we can confidently use this method to draw conclusions about other reactions. The most noticeable thing about reactions 3a, 4a, 6a, and 7a is that all require a temperature between 700 and 800°K in order to occur. It is somewhat unlikely that the bicyclic systems in reactions 3a and 4a would be stable up to the temperature required for the retrodiene reaction. For this reason the decomposition of dimethyl 2-norbornene-2,3-dicarboxylate into tar at 433° as observed in these laboratories[47] is not surprising. Since the only other reverse cycloaddition which can occur (reaction 3b) is unfavorable, it is at once apparent that this decomposition must take place through a multistep process, possibly a radical chain. The same sort of thing would probably occur with the bicyclo[2.2.2]octyl system in reaction 4, although this has not been studied. The cyclohexene system in reactions 6 and 7, on the other hand, is quite a bit more stable. Thus, Barney and Stevenson[45] were able to obtain 2,3-dicarbomethoxybutadiene by reaction 6a at about 800°. Although the reverse $2 + 2 + 2$ cycloaddition, reactions 6b and 7b, is slightly more favorable thermodynamically, the high activation energy would prevent it from competing effectively with the retrodiene reaction.

The calculations for reaction 5a, however, are completely at variance with the experimental data. The favorable activation energy for the retrodiene reaction cannot possibly explain the difference since the calculations show the adduct to be much more stable than its dissociation products, 3,4-dicarbomethoxyfuran and ethylene, at 140°, the temperature at which the adduct decomposed experimentally. Clearly, the stability of 3,4-dicarbomethoxyfuran has been grossly underestimated. While Van Krevelen and Chermin included the 18-kcal resonance energy of furan in their compilation of group contributions, they evidently failed to include the increase in resonance energy on attaching carboalkoxyl groups to furan. The error experienced through such an omission can be seen in comparing the experimental ΔH_f for 2-furoic acid, -118.8 kcal, with that calculated[39,216] using the group contributions of Franklin, -69.4 kcal. Even if we include the 18-kcal resonance energy of furan, we are still left with a difference of 31.4 kcal. The same situation exists with pyrrole and the pyrrolecarboxylic acids, but here group contributions were not available for calculations to be made. The only possible reason that the retrodiene reactions of furan and pyrrole adducts occur so readily is that the dicarboxylic acids formed are highly stabilized by resonance.