

# Organic Reactions

# Organic Reactions

## VOLUME IV

### EDITORIAL BOARD

ROGER ADAMS, *Editor-in-Chief*

WERNER E. BACHMANN

LOUIS F. FIESER

A. H. BLATT

JOHN R. JOHNSON

HAROLD R. SNYDER

### ASSOCIATE EDITORS

JAMES CASON

MILTON C. KLOETZEL

WILLIAM S. EMERSON

S. M. McELVAIN

H. L. HOLMES

ERICH MOSETTIG

WALTER S. IDE

DAVID TODD

NEW YORK

JOHN WILEY & SONS, INC.

LONDON: CHAPMAN & HALL, LIMITED

COPYRIGHT, 1948

BY

ROGER ADAMS

---

*All Rights Reserved*

*This book or any part thereof must not  
be reproduced in any form without  
the written permission of the publisher.*

PRINTED IN THE UNITED STATES OF AMERICA

## PREFACE TO THE SERIES

In the course of nearly every program of research in organic chemistry the investigator finds it necessary to use several of the better-known synthetic reactions. To discover the optimum conditions for the application of even the most familiar one to a compound not previously subjected to the reaction often requires an extensive search of the literature; even then a series of experiments may be necessary. When the results of the investigation are published, the synthesis, which may have required months of work, is usually described without comment. The background of knowledge and experience gained in the literature search and experimentation is thus lost to those who subsequently have occasion to apply the general method. The student of preparative organic chemistry faces similar difficulties. The textbooks and laboratory manuals furnish numerous examples of the application of various syntheses, but only rarely do they convey an accurate conception of the scope and usefulness of the processes.

For many years American organic chemists have discussed these problems. The plan of compiling critical discussions of the more important reactions thus was evolved. The volumes of *Organic Reactions* are collections of about twelve chapters, each devoted to a single reaction, or a definite phase of a reaction, of wide applicability. The authors have had experience with the processes surveyed. The subjects are presented from the preparative viewpoint, and particular attention is given to limitations, interfering influences, effects of structure, and the selection of experimental techniques. Each chapter includes several detailed procedures illustrating the significant modifications of the method. Most of these procedures have been found satisfactory by the author or one of the editors, but unlike those in *Organic Syntheses* they have not been subjected to careful testing in two or more laboratories. When all known examples of the reaction are not mentioned in the text, tables are given to list compounds which have been prepared by or subjected to the reaction. Every effort has been made to include in the tables all such compounds and references; however, because of the very nature of the reactions discussed and their frequent use as one of the several steps of syntheses in which not all of the intermediates have been isolated, some instances may well have been missed. Never-

theless, the investigator will be able to use the tables and their accompanying bibliographies in place of most or all of the literature search so often required.

Because of the systematic arrangement of the material in the chapters and the entries in the tables, users of the books will be able to find information desired by reference to the table of contents of the appropriate chapter. In the interest of economy the entries in the indices have been kept to a minimum, and, in particular, the compounds listed in the tables are not repeated in the indices.

The success of this publication, which will appear periodically in volumes of about twelve chapters, depends upon the cooperation of organic chemists and their willingness to devote time and effort to the preparation of the chapters. They have manifested their interest already by the almost unanimous acceptance of invitations to contribute to the work. The editors will welcome their continued interest and their suggestions for improvements in *Organic Reactions*.

## CONTENTS

CHAPTER	PAGE
1. THE DIELS-ALDER REACTION WITH MALEIC ANHYDRIDE— <i>Milton C. Kloetzel</i>	1
2. THE DIELS-ALDER REACTION: ETHYLENIC AND ACETYLENIC DIENOPHILES— <i>H. L. Holmes</i> . . . . .	60
3. THE PREPARATION OF AMINES BY REDUCTIVE ALKYLATION— <i>William S. Emerson</i> . . . . .	174
4. THE ACYLOINS— <i>S. M. McElwain</i> . . . . .	256
5. THE SYNTHESIS OF BENZOINS— <i>Waller S. Ide and Johannes S. Buck</i> . .	269
6. SYNTHESIS OF BENZOQUINONES BY OXIDATION— <i>James Cason</i> . . . . .	305
7. THE ROSENMUND REDUCTION OF ACID CHLORIDES TO ALDEHYDES— <i>Erich Mosettig and Ralph Mozingo</i> . . . . .	362
8. THE WOLFF-KISHNER REDUCTION— <i>David Todd</i> . . . . .	378
INDEX . . . . .	423

## CHAPTER 1

### THE DIELS-ALDER REACTION WITH MALEIC ANHYDRIDE

MILTON C. KLOETZEL

*DePauw University \**

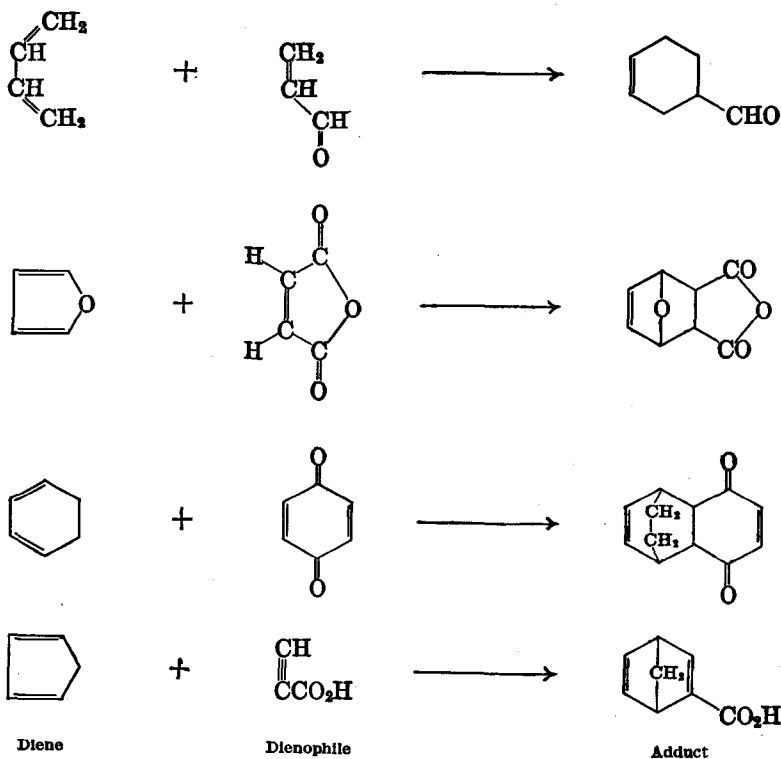
#### CONTENTS

	PAGE
NATURE OF THE REACTION . . . . .	2
Table I. Dienophiles in the Diels-Alder Reaction . . . . .	4
Reaction Mechanism . . . . .	8
Reversibility of the Reaction . . . . .	9
Stereochemical Selectivity of the Reaction . . . . .	10
Side Reactions . . . . .	12
SCOPE AND LIMITATIONS OF THE REACTION . . . . .	14
Reaction with Acyclic Compounds . . . . .	15
Reaction with Alicyclic Compounds . . . . .	22
Reaction with Aromatic Compounds . . . . .	28
Wholly Aromatic Systems . . . . .	28
Table II. Equilibrium Mixtures from Polycyclic Hydrocarbons and Maleic Anhydride in Boiling Xylene . . . . .	28
Aromatic-acyclic and Aromatic-alicyclic Systems . . . . .	32
Reaction with Heterocyclic Compounds . . . . .	35
Diene Analysis . . . . .	39
EXPERIMENTAL CONDITIONS AND PROCEDURES . . . . .	40
With Butadiene . . . . .	41
With 1-Phenyl-1,3-butadiene . . . . .	41
With 1,2-Diphenyl-1,3-pentadiene . . . . .	42
With Cyclopentadiene . . . . .	42
With 9-Methylantracene . . . . .	42
With 1,2-Benzanthracene . . . . .	42
With Isoeugenol Methyl Ether . . . . .	42
With Furan . . . . .	43
SURVEY OF THE DIELS-ALDER REACTION INVOLVING MALEIC ANHYDRIDE . . . . .	43
Table III. Adducts from Acyclic Compounds . . . . .	44
Table IV. Adducts from Alicyclic Compounds . . . . .	47
Table V. Adducts from Aromatic Compounds . . . . .	50
Table VI. Adducts from Heterocyclic Compounds . . . . .	53
Table VII. Adducts from Dienophiles Related to Maleic Anhydride . . . . .	54

\* Present address, University of Southern California, Los Angeles, California.

## NATURE OF THE REACTION

The Diels-Alder reaction (diene synthesis) consists in the addition of a compound containing a double or triple bond (usually activated by additional unsaturation in the  $\alpha,\beta$ -position) to the 1,4-positions of a conjugated diene system, with the formation of a six-membered hydro-aromatic ring. The following additions of various diene systems to dienophiles are typical examples of the Diels-Alder reaction.



A noteworthy feature of the Diels-Alder reaction is the great variety of the compounds which may serve as the dienophile. With a few exceptions, the compounds that have been employed as dienophiles fall into one of the following categories.

1.  $\text{CH}_2=\text{CHA}$ .

A = CHO, CO<sub>2</sub>H, CO<sub>2</sub>CH<sub>3</sub>, CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>, COCl, COCH<sub>3</sub>, COC<sub>6</sub>H<sub>5</sub>, CN, NO<sub>2</sub>, C<sub>6</sub>H<sub>5</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>X, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CN, CH<sub>2</sub>CO<sub>2</sub>H, CH<sub>2</sub>NCS, OCOCH<sub>3</sub>, SC<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>, SO<sub>2</sub>R, X, H.



2.  $C_6H_5CH=CHA$ . $A = CHO, CO_2H, CO_2CH_3, CO_2C_2H_5, COCH_3, COC_6H_5$ .3.  $CH_2=CA_2$ . $A = CO_2C_2H_5, CN, COCH_3, X$ .4.  $ACH=CHA$ . $A = CO_2H, COCl, CO_2CH_3, CO_2C_2H_5, COCH_3, COC_6H_5, X$ .

## 5. Quinones.

6.  $AC\equiv CA$ . $A = CO_2H, CO_2CH_3, CO_2C_2H_5, COC_6H_5, C_6H_5, H$ .

The more reactive dienophiles usually contain the  $C=C-C=O$  or the  $C\equiv C-C=O$  system. Other unsaturated groups, such as  $CN$ ,  $NO_2$ , or  $SO_2$ , promote the addition. In some instances even substances with isolated double bonds have been found to add dienes, but these substances usually require more drastic reaction conditions. Ketenes do not react with dienes in the Diels-Alder fashion.<sup>1-4</sup>

Among those substances that have been employed most frequently as dienophiles are maleic anhydride and other closely related dicarboxylic acid derivatives (which are discussed in this chapter),  $\alpha,\beta$ -unsaturated carbonyl compounds and acetylenic compounds (which are discussed in Chapter 2), and quinones and other cyclic ketones (which will be discussed in Volume V). In Table I are listed some other compounds which have been employed successfully as dienophiles.

<sup>1</sup> Allen and Sheps, *Can. J. Research*, **11**, 171 (1934).

<sup>2</sup> Farmer and Farooq, *J. Chem. Soc.*, **1938**, 1925.

<sup>3</sup> Smith, Agre, Leekley, and Prichard, *J. Am. Chem. Soc.*, **61**, 7 (1939).

<sup>4</sup> Brooks and Wilbert, *J. Am. Chem. Soc.*, **63**, 870 (1941).

TABLE I

## DIENOPHILES IN THE DIELS-ALDER REACTION

Dienophile	Reference	Dienophile	Reference
Acrolein	5-21	Ethylenetetracarboxylic acid and ester	51
Crotonaldehyde	6, 12, 15, 16, 20-23	Azodicarboxylic ester	52, 53
Cinnamaldehyde	6, 24	Acrylonitrile	54
Acetylene (methyl vinyl ketone)	25	$\beta$ -Naphthol (keto tautomer)	55
Ethylidenacetone	9	Nitroalkenes	29, 56-59
Benzoylene (vinyl phenyl ketone)	26	$\alpha,\beta$ -Unsaturated sulfones	56
Benzalacetone and benzalacetophenone	27, 28	Cyclopentadiene	60-63
Dibenzalacetone	29	1,3-Cyclohexadiene	64
1-Cyclopenten-3-one and derivatives	30-33	Styrene	58, 65
1-Cyclohexen-3-one	34	Indenes	44, 65-69
<i>sym</i> -Diacetylene	35, 36	Acenaphthylene	69
<i>sym</i> -Diarylethylenes	27, 29, 37-41	Allyl compounds	70
Acrylic acids	8, 10, 18, 42	Vinyl halides, esters, and sulfides	56, 71, 72
Crotonic acid and crotonyl chloride	8, 43	Di- and poly-chloroethylenes	71, 73
Cinnamic acids and esters	24, 27, 44-47	4-Vinyl-1-cyclohexene	74
3,4-Dihydro-1-naphthoic acids and esters	48, 49	1-Methyl-1-cyclopentene	66
Coumarin	46	Unsaturated bicyclic compounds (such as dicyclopentadiene)	75, 76
$\beta$ -Aroylacrylic acids	27, 50	Ethylene	77, 78
Alkylidene-malonic, -acetoacetic, and -cyanoacetic esters	51		

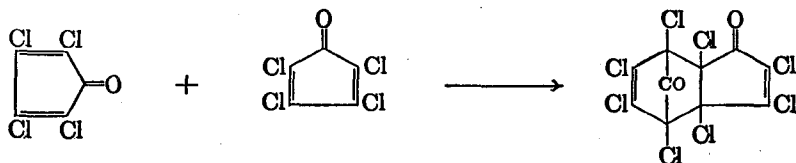
<sup>5</sup> Diels and Alder, *Ann.*, **460**, 98 (1928).<sup>6</sup> Diels, Alder, Lübbert, Naujoks, Querberitz, Röhl, and Segeberg, *Ann.*, **470**, 62 (1929).<sup>7</sup> Diels, Alder, Petersen, and Querberitz, *Ann.*, **478**, 137 (1930).<sup>8</sup> Alder, Stein, Liebmann, and Rolland, *Ann.*, **514**, 197 (1934).<sup>9</sup> Diels and Alder, U. S. pats. 1,944,731-2 [*C. A.*, **28**, 2016 (1934)].<sup>10</sup> Lehmann and Paasche, *Ber.*, **68**, 1146 (1935).<sup>11</sup> Kasansky and Plate, *Ber.*, **68**, 1259 (1935).<sup>12</sup> Arbuzov, *Ber.*, **68**, 1435 (1935).<sup>13</sup> Lehmann, *Ber.*, **69**, 631 (1936).<sup>14</sup> Dupont and Dulou, *Compt. rend.*, **202**, 1861 (1936).<sup>15</sup> Arbuzov, Zinov'eva, and Fink, *J. Gen. Chem. U.S.S.R.*, **7**, 2278 (1937) [*C. A.*, **32**, 507 (1938)].<sup>16</sup> Chayanov and Grishin, *Colloid J. U.S.S.R.*, **3**, 461 (1937) [*C. A.*, **32**, 6226 (1938)].<sup>17</sup> Chayanov, *J. Gen. Chem. U.S.S.R.*, **8**, 460 (1938) [*C. A.*, **32**, 7905 (1938)].

- <sup>18</sup> Lehmann, *Ber.*, **71**, 1874 (1938).  
<sup>19</sup> Dupont, Dulou, Desreux, and Picoux, *Bull. soc. chim. France*, [5] **5**, 322 (1938).  
<sup>20</sup> Langenbeck, Gödde, Weschky, and Schaller, *Ber.*, **75**, 232 (1942) [*C. A.*, **37**, 3746 (1943)].  
<sup>21</sup> Fiesselmann, *Ber.*, **75**, 881 (1942) [*C. A.*, **37**, 3417 (1943)].  
<sup>22</sup> Shorygin and Guseva, *J. Gen. Chem. U.S.S.R.*, **6**, 1569 (1936) [*C. A.*, **31**, 2184 (1937)].  
<sup>23</sup> Clar, *Ber.*, **72**, 1817 (1939).  
<sup>24</sup> Fujise, Horiuti, and Takahashi, *Ber.*, **69**, 2102 (1936).  
<sup>25</sup> Petrov, *J. Gen. Chem. U.S.S.R.*, **11**, 309 (1941) [*C. A.*, **35**, 5873 (1941)].  
<sup>26</sup> Allen, Bell, Bell, and Van Allan, *J. Am. Chem. Soc.*, **62**, 656 (1940).  
<sup>27</sup> Bergmann and Eschinazi, *J. Am. Chem. Soc.*, **65**, 1405 (1943).  
<sup>28</sup> Natsinskaya and Petrov, *J. Gen. Chem. U.S.S.R.*, **11**, 665 (1941) [*C. A.*, **35**, 6934 (1941)].  
<sup>29</sup> Bergmann, Eschinazi, and Neeman, *J. Org. Chem.*, **8**, 179 (1943).  
<sup>30</sup> Dane, Schmitt, and Rautenstrauch, *Ann.*, **532**, 29 (1937).  
<sup>31</sup> Dane and Schmitt, *Ann.*, **536**, 196 (1938).  
<sup>32</sup> Dane and Schmitt, *Ann.*, **537**, 246 (1939).  
<sup>33</sup> Dane and Eder, *Ann.*, **539**, 207 (1939).  
<sup>34</sup> Bartlett and Woods, *J. Am. Chem. Soc.*, **62**, 2933 (1940).  
<sup>35</sup> Goldberg and Müller, *Helv. Chim. Acta*, **21**, 1699 (1938).  
<sup>36</sup> Goldberg and Müller, *Helv. Chim. Acta*, **23**, 831 (1940).  
<sup>37</sup> Adams and Geissman, *J. Am. Chem. Soc.*, **61**, 2083 (1939).  
<sup>38</sup> Adams and Gold, *J. Am. Chem. Soc.*, **62**, 56 (1940).  
<sup>39</sup> Adams and Wearn, *J. Am. Chem. Soc.*, **62**, 1233 (1940).  
<sup>40</sup> Adams and Gold, *J. Am. Chem. Soc.*, **62**, 2038 (1940).  
<sup>41</sup> Adams, U. S. pat. 2,341,850 [*C. A.*, **38**, 4270 (1944)].  
<sup>42</sup> Komppa and Komppa, *Ber.*, **69**, 2606 (1936).  
<sup>43</sup> Komppa and Beckmann, *Ann.*, **523**, 68 (1936).  
<sup>44</sup> Weiss and Beller, *Monatsh.*, **61**, 143 (1932).  
<sup>45</sup> Weizmann, Bergmann, and Berlin, *J. Am. Chem. Soc.*, **60**, 1331 (1938).  
<sup>46</sup> Adams, McPhee, Carlin, and Wicks, *J. Am. Chem. Soc.*, **65**, 356 (1943).  
<sup>47</sup> Adams and Carlin, *J. Am. Chem. Soc.*, **65**, 360 (1943).  
<sup>48</sup> Fieser and Holmes, *J. Am. Chem. Soc.*, **58**, 2319 (1936).  
<sup>49</sup> Fieser and Holmes, *J. Am. Chem. Soc.*, **60**, 2548 (1938).  
<sup>50</sup> Fieser and Fieser, *J. Am. Chem. Soc.*, **57**, 1679 (1935).  
<sup>51</sup> Alder and Rickert, *Ber.*, **72**, 1983 (1939).  
<sup>52</sup> Diels, Blom, and Koll, *Ann.*, **443**, 242 (1925).  
<sup>53</sup> Diels, Schmidt, and Witte, *Ber.*, **71**, 1186 (1938).  
<sup>54</sup> Wolfe, U. S. pat. 2,217,632 [*C. A.*, **35**, 1069 (1941)].  
<sup>55</sup> Salfeld, *Ber.*, **73**, 376 (1940).  
<sup>56</sup> Alder, Rickert, and Windemuth, *Ber.*, **71**, 2451 (1938).  
<sup>57</sup> Allen and Bell, *J. Am. Chem. Soc.*, **61**, 521 (1939).  
<sup>58</sup> Allen, Bell, and Gates, *J. Org. Chem.*, **8**, 373 (1943).  
<sup>59</sup> Nightingale and Janes, *J. Am. Chem. Soc.*, **66**, 352 (1944).  
<sup>60</sup> Alder, Stein, and Finzenhagen, *Ann.*, **485**, 223 (1931).  
<sup>61</sup> Alder, Stein, Eckardt, Buddenbrock, and Schneider, *Ann.*, **504**, 216 (1933).  
<sup>62</sup> Alder and Stein, *Angew. Chem.*, **47**, 837 (1934).  
<sup>63</sup> Grummitt, Kloppe, and Blenkhorn, *J. Am. Chem. Soc.*, **64**, 604 (1942).  
<sup>64</sup> Alder and Stein, *Ann.*, **496**, 197 (1932).  
<sup>65</sup> Alder and Rickert, *Ber.*, **71**, 379 (1938).  
<sup>66</sup> Bergmann and Weizmann, *J. Org. Chem.*, **9**, 352 (1944).  
<sup>67</sup> Swain and Todd, *J. Chem. Soc.*, **1942**, 626.  
<sup>68</sup> Mameli, Pancotto, and Crestani, *Gazz. chim. ital.*, **67**, 669 (1937).  
<sup>69</sup> Diltthey, Henkels, and Schaefer, *Ber.*, **71**, 974 (1938).  
<sup>70</sup> Alder and Windemuth, *Ber.*, **71**, 1939 (1938).  
<sup>71</sup> Alder and Rickert, *Ann.*, **543**, 1 (1940).

The types of conjugated systems capable of undergoing the Diels-Alder reaction are equally diverse. These may be classified conveniently in the following manner.

1. Acyclic conjugates (butadiene, alkylbutadienes, arylbutadienes, conjugated polyenes, etc.).
2. Alicyclic conjugates.
  - a. Wholly alicyclic systems (cyclopentadiene, 1,3-cyclohexadiene, fulvenes).
  - b. Bicyclic systems (1,1'-bicyclohexenyl, etc.).
  - c. Alicyclic-acyclic systems (1-vinyl-1-cyclohexene, 1-vinyl-3,4-dihydronaphthalene).
3. Aromatic conjugates.
  - a. Wholly aromatic systems (anthracene, 9,10-dialkylantracenes, pentacene, etc.).
  - b. Aromatic-acyclic systems (isosafrole, 1-vinylnaphthalene, 9-vinylphenanthrene, etc.).
  - c. Aromatic-alicyclic systems (1- $\alpha$ -naphthyl-1-cyclopentene, etc.).
4. Heterocyclic compounds (furan, isobenzofurans,  $\alpha$ -pyrone).

The versatility of the Diels-Alder reaction was recognized primarily through the work of Diels and Alder, whose series of papers on this subject began to appear in 1928.<sup>5</sup> Isolated instances of the reaction were discovered, however, as early as 1893<sup>79</sup> and 1897<sup>80</sup> by Zincke,<sup>81, 82</sup> who subsequently formulated the reactions as additions which conform to the general scheme of the diene synthesis.



In 1906, Albrecht<sup>83</sup> described the addition products of *p*-benzoquinone with one and two molecules of cyclopentadiene, for which he suggested the erroneous formulas I and II. Staudinger<sup>84</sup> suggested formulas III

<sup>72</sup> Alder and Windemuth, *Ann.*, **543**, 41 (1940).

<sup>73</sup> Alder and Rickert, U. S. pat. 2,351,311 [*C. A.*, **38**, 5222 (1944)].

<sup>74</sup> Alder and Rickert, *Ber.*, **71**, 373 (1938).

<sup>75</sup> Alder, Stein, Reese, and Grassmann, *Ann.*, **496**, 204 (1932).

<sup>76</sup> Alder and Windemuth, *Ber.*, **71**, 2409 (1938).

<sup>77</sup> Joshel and Butz, *J. Am. Chem. Soc.*, **63**, 3350 (1941).

<sup>78</sup> Nudenberg and Butz, *J. Am. Chem. Soc.*, **66**, 307 (1944).

<sup>79</sup> Zincke and Günther, *Ann.*, **272**, 243 (1893).

<sup>80</sup> Zincke, Bergmann, Francke, and Prenntzell, *Ann.*, **296**, 135 (1897).

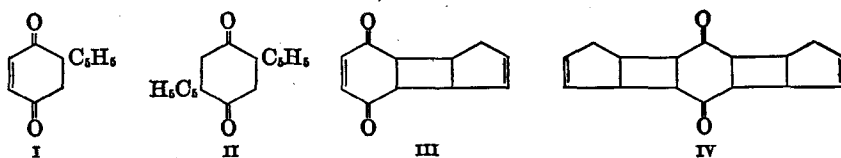
<sup>81</sup> Zincke and Meyer, *Ann.*, **367**, 1 (1909).

<sup>82</sup> Zincke and Pfaffendorf, *Ann.*, **394**, 3 (1912).

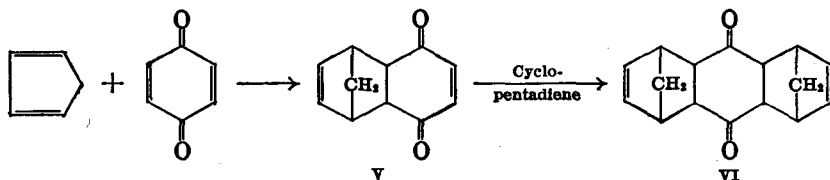
<sup>83</sup> Albrecht, *Ann.*, **348**, 31 (1906).

<sup>84</sup> Staudinger, *Die Ketene*, p. 59, F. Enke, Stuttgart, 1912.

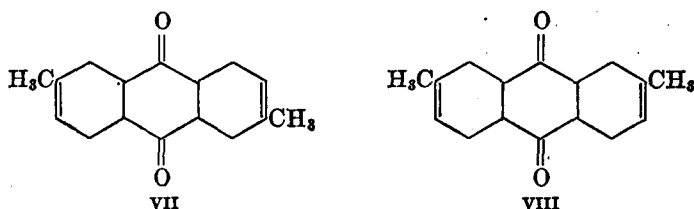
and IV for these compounds. That Albrecht's addition compounds



were actually the result (V and VI) of a typical diene synthesis was shown later by Diels and Alder.<sup>5, 85</sup> During the controversy concerning



the quinone-cyclopentadiene reaction, Euler and Josephson<sup>86</sup> reported that isoprene could be made to react with 1,4-benzoquinone to yield VII. Diels and Alder subsequently showed that this reaction product was actually a mixture of VII and VIII.



An indication of the generality of these addition reactions was given by the work of Diels, Blom, and Koll<sup>52</sup> on the reaction of azodicarboxylic ester with cyclopentadiene. The remarkably broad scope of the diene synthesis was then established by the papers of Diels and Alder, which appeared in rapid succession.

The development of the Diels-Alder reaction has been of inestimable value not only in synthesis but also for the light it has cast upon the mechanism of polymerization. Indeed, the discovery of certain dimerization processes that conform to the general scheme of the diene synthesis preceded the work of Diels and Alder. Among these may be mentioned the dimerization of butadiene to 4-vinyl-1-cyclohexene<sup>87, 88</sup>

<sup>85</sup> Diels, Alder, Stein, Pries, and Winckler, *Ber.*, **62**, 2337 (1929).

<sup>86</sup> Euler and Josephson, *Ber.*, **53**, 822 (1920).

<sup>87</sup> Lebedev, *J. Russ. Phys. Chem. Soc.*, **42**, 949 (1910) [*C. A.*, **6**, 2009 (1912)].

<sup>88</sup> Lebedev and Skavronskaya, *J. Russ. Phys. Chem. Soc.*, **43**, 1124 (1911) [*C. A.*, **6**, 855 (1912)].

and of isoprene to dipentene.<sup>89</sup> Discovery of the Diels-Alder reaction, however, gave impetus to the further investigation of these and other polymerization processes. Thus, the dimerizations of isoprene,<sup>90</sup> 3,4-dimethyl-2,4-hexadiene,<sup>91</sup> 1,3,5-hexatriene,<sup>92</sup> cyclopentadiene,<sup>60-62, 93, 94</sup> cyclohexadiene,<sup>64</sup> and dienecarboxylic acids<sup>95, 96</sup> were shown to be diene syntheses, as were the trimerization of butadiene<sup>74</sup> and the polymerization of cyclopentadiene.<sup>60, 61, 75, 93</sup> The dimerizations of such carbonyl compounds as acetylketene,<sup>97</sup> acrolein,<sup>98</sup> methyl vinyl ketone,<sup>99</sup> and *o*-methylenecyclohexanone<sup>100</sup> have also been shown to be additions of the Diels-Alder type.

**Reaction Mechanism.** The diene synthesis appears to be initiated by an ionic reaction involving electron transfer from the diene to the dienophile. This step is probably rapid and results in a complex that is held together by ionic forces.<sup>27, 29, 101-103</sup> Stereochemically, this complex may be visualized as two parallel charged (usually flat) surfaces, oriented in such a way as to take maximum advantage of electrostatic attractive forces.<sup>102, 103</sup> It has been postulated that this intermediate complex is in some instances an open-chain diradical, although kinetic studies of the association of butadiene and of other diene syntheses are not in harmony with this view.<sup>104-106</sup> The second, and probably rate-controlling, step in the reaction is a rearrangement of the ionic complex to yield the stabilized adduct.

Certain characteristics of the Diels-Alder reaction appear to support this mechanism.

1. The reaction usually (though not necessarily) is accompanied by the production of a transient color, which has been attributed to forma-

<sup>89</sup> Wallach, *Ann.*, **227**, 277 (1885).

<sup>90</sup> Wagner-Jauregg, *Ann.*, **488**, 176 (1931).

<sup>91</sup> vonRomburgh and vonRomburgh, *Proc. Acad. Sci. Amsterdam*, **34**, 224 (1931) [*C. A.*, **25**, 3309 (1931)].

<sup>92</sup> Kharasch and Sternfeld, *J. Am. Chem. Soc.*, **61**, 2318 (1939).

<sup>93</sup> Alder, Stein, and Grassmann, *Ann.*, **504**, 205 (1933).

<sup>94</sup> Pirsch, *Ber.*, **67**, 101 (1934).

<sup>95</sup> Kuhn and Deutsch, *Ber.*, **65**, 43 (1932).

<sup>96</sup> Farmer, *Trans. Faraday Soc.*, **35**, 1034 (1939).

<sup>97</sup> Hurd, Roe, and Williams, *J. Org. Chem.*, **2**, 314 (1937).

<sup>98</sup> Alder and Rüden, *Ber.*, **74**, 920 (1941).

<sup>99</sup> Alder, Offermanns, and Rüden, *Ber.*, **74**, 905 (1941).

<sup>100</sup> Mannich, *Ber.*, **74**, 557 (1941).

<sup>101</sup> Hudson and Robinson, *J. Chem. Soc.*, **1941**, 715.

<sup>102</sup> Woodward, *J. Am. Chem. Soc.*, **64**, 3058 (1942).

<sup>103</sup> Woodward and Baer, *J. Am. Chem. Soc.*, **66**, 645 (1944).

<sup>104</sup> Wassermann, *J. Chem. Soc.*, **1935**, 828.

<sup>105</sup> Benford and Wassermann, *J. Chem. Soc.*, **1939**, 362.

<sup>106</sup> Wassermann, *J. Chem. Soc.*, **1942**, 612.

tion of the complex.<sup>107-110</sup> Production of a color with maleic anhydride, however, should not be construed as a reliable test for a diene or a guarantee that a normal Diels-Alder reaction will ensue. Stilbene, for example, when mixed with maleic anhydride gives first a yellow color and then an amorphous substance having a high molecular weight.<sup>108</sup> In other instances a colored complex is formed, but no further reaction takes place.<sup>110</sup>

2. Ionic compounds actually have been isolated from the reaction of dimethyl acetylenedicarboxylate with such heterocyclic substances as pyridine,  $\alpha$ -picoline, quinoline, isoquinoline, and quinaldine.<sup>111-115</sup> Furthermore, the nature of the solvent affects not only the rate of reaction<sup>116-118</sup> but also in some instances (the aforementioned nitrogen heterocycles) the nature of the product.

3. The course of the reaction is sterically specific (see p. 10).

4. The tendency of a styrene to react with maleic anhydride is enhanced by an alkoxyl group *para* to the unsaturated side chain, but a similar group in the *meta* position has no such effect.<sup>101</sup>

5. Certain substances which may act as donor or acceptor molecules, but which cannot themselves take part in the diene reaction, have been found to catalyze diene syntheses. Among these are trichloroacetic acid, trimethylamine,<sup>118-120</sup> and possibly dimethylaniline and *sym*-trinitrobenzene.<sup>102</sup>

**Reversibility of the Reaction.** It has been observed repeatedly that adducts from the Diels-Alder reaction are thermally unstable. Dissociation takes place with varying facility, depending upon the nature of the adducts. Those which have an *endo* bridge, such as XXXIII, XLI, LXXXVII, and XCIII (pp. 22, 24, 35, 38), generally show a pronounced tendency to revert to their components.<sup>121</sup> The adduct from furan and maleic anhydride, for example, decomposes at its melting point (125°). When the adduct from cyclopentadiene and maleic anhydride is warmed,

<sup>107</sup> Kuhn and Wagner-Jauregg, *Helv. Chim. Acta*, **13**, 9 (1930).

<sup>108</sup> Kuhn and Wagner-Jauregg, *Ber.*, **63**, 2662 (1930).

<sup>109</sup> Littmann, *J. Am. Chem. Soc.*, **58**, 1316 (1936).

<sup>110</sup> Sandermann, *Seifensieder-Ztg.*, **65**, 553 (1938) [*C. A.*, **32**, 8698 (1938)].

<sup>111</sup> Diels, Alder, Friedrichsen, Klare, Winckler, and Schrum, *Ann.*, **505**, 103 (1933).

<sup>112</sup> Diels, Alder, Friedrichsen, Petersen, Brodersen, and Kech, *Ann.*, **510**, 87 (1934).

<sup>113</sup> Diels and Meyer, *Ann.*, **513**, 129 (1934).

<sup>114</sup> Diels and Pistor, *Ann.*, **530**, 87 (1937).

<sup>115</sup> Diels and Harms, *Ann.*, **525**, 73 (1936).

<sup>116</sup> Wassermann, *Ber.*, **66**, 1392 (1933).

<sup>117</sup> Wassermann, *J. Chem. Soc.*, **1936**, 1028.

<sup>118</sup> Wassermann, *J. Chem. Soc.*, **1942**, 623.

<sup>119</sup> Wassermann, *Fr. pat.* 838,454 (1939) [*C. A.*, **33**, 7818 (1939)].

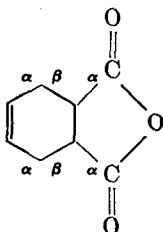
<sup>120</sup> Wassermann, *J. Chem. Soc.*, **1942**, 618.

<sup>121</sup> Diels, Alder, and Naujoks, *Ber.*, **62**, 554 (1929).

it likewise dissociates into its components. On the other hand, the adducts from cyclohexadiene and its derivatives are much more thermo-stable. Indeed, this difference in properties has been suggested as a means of differentiating between five- and six-carbon cyclic dienes<sup>122</sup> (compare Chapter 2).

The reactions between maleic anhydride and a number of polycyclic hydrocarbons containing the anthracene nucleus are truly reversible.<sup>123</sup> Identical mixtures of hydrocarbon, maleic anhydride, and adduct were obtained by heating xylene solutions of either the pure adduct or the components in equimolecular proportion. The quantitative results of this investigation are discussed in a later section (p. 28).

The course taken by dissociation of maleic anhydride adducts is in keeping with the thermal decomposition of other bicyclic compounds. It has been observed<sup>124-126</sup> that the bonds that undergo pyrolytic rupture are those once removed from unsaturation rather than those adjacent to unsaturation (the double bond rule). In a typical maleic anhydride



adduct the  $\alpha$ -bonds are strong, whereas the  $\beta$ -bonds are weak and subject to thermal cleavage.

**Stereochemical Selectivity of the Reaction.** The Diels-Alder reaction exhibits pronounced stereochemical selectivity. The configuration of a given adduct conforms to the following general principles,<sup>27,127</sup> commonly known as the Alder rules.

1. The addition of a dienophile to a diene is a purely *cis* addition. The relative positions of substituents in the dienophile are retained in the adduct. For example, maleic anhydride reacts with anthracene to yield the *cis*-anhydride adduct IX, while fumaric acid yields the *trans*-dicarboxylic acid adduct X.<sup>128a</sup>

<sup>122</sup> Alder and Rickert, *Ann.*, **524**, 180 (1936).

<sup>123</sup> Bachmann and Kloetzel, *J. Am. Chem. Soc.*, **60**, 481 (1938).

<sup>124</sup> Littmann, *J. Am. Chem. Soc.*, **57**, 586 (1935).

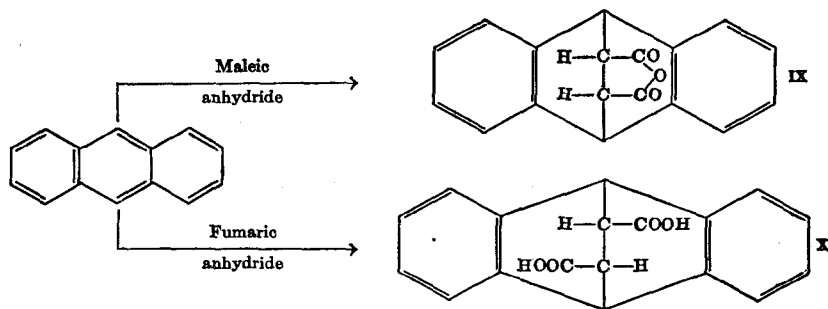
<sup>125</sup> Norton, *Chem. Revs.*, **31**, 387, 469 (1942).

<sup>126</sup> Allen and Van Allan, *J. Am. Chem. Soc.*, **65**, 1384 (1943).

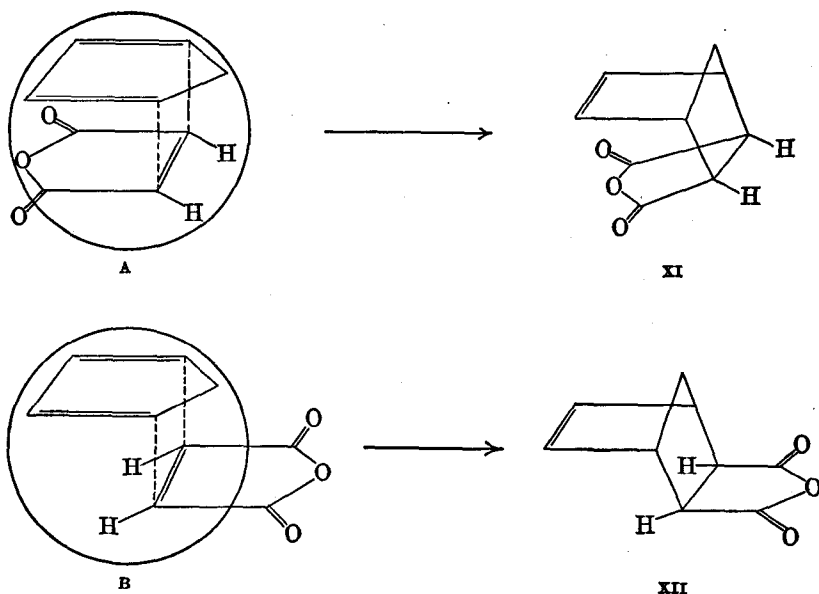
<sup>127</sup> Alder and Stein, *Angew. Chem.*, **50**, 510 (1937).

<sup>128</sup> (a) Bachmann and Scott, *J. Am. Chem. Soc.*, **70**, 1458, 1462 (1948); (b) Bachmann and Chmerda, *J. Am. Chem. Soc.*, **70**, 1468 (1948).





2. In the reaction of maleic anhydride with a cyclic diene, such as cyclopentadiene, two modes of addition are theoretically possible, leading to the formation of an “*endo*” configuration (XI) or an “*exo*” configuration (XII) respectively. Actually, the *endo* configuration (XI) is produced exclusively.<sup>127,129</sup> This “one-sided” addition indicates that immediately before combination the components must always be oriented in exactly the same manner with respect to each other; that is, of the two possible orientations, A and B, A is favored.



The favored orientation (A) corresponds to the maximum accumulation of double bonds (the double bonds of the carbonyl groups are in

<sup>129</sup> Alder, Stein, Buddenbrock, Eckardt, Freerks, and Schneider, *Ann.*, **514**, 1 (1934).