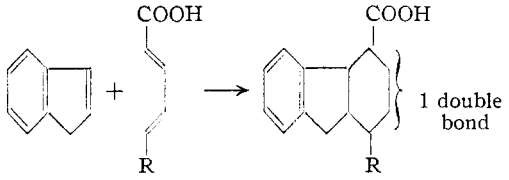
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY]

The Diels–Alder Reaction with $\alpha,\beta,\gamma,\delta$-Unsaturated Acids

BY N. C. DENO

In the usual Diels–Alder reaction, a polarizable diene reacts with an olefin which is strongly electrophilic due to substituents. A second type of Diels–Alder reaction has been postulated in which the roles of diene and olefin have been interchanged.[1] To further extend this second type, four olefins conjugated to aryl rings have been chosen as examples which should be readily polarizable to give a negative center on the carbon *beta* to the aryl group. Sorbic and muconic acids were employed as the dienes.

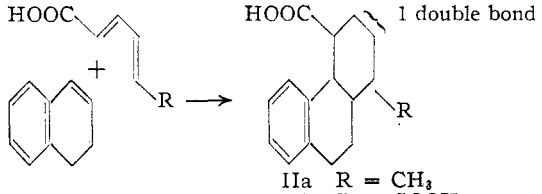
Both dienes reacted with indene to give the tetrahydrofluorene derivatives Ia and Ib in yields of



Ia, R = CH_3
Ib, R = COOH

24 and 13%. The ring structures were demonstrated by decarboxylation and dehydrogenation to 1-methylfluorene and fluorene.

Both dienes also reacted with 1,2-dihydronaphthalene to yield the hexahydrophenanthrenes IIa and IIb in yields of 18 and 12%. Although IIa was not obtained crystalline, the facts that



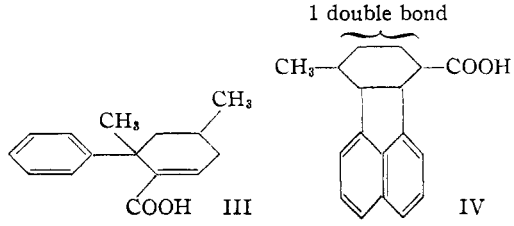
IIa R = CH_3
IIb R = COOH

the distilled yellow gum gave the correct neutral equivalent and that decarboxylation and dehydrogenation gave a 25% yield of 1-methylphenanthrene shows that the product consists principally of compounds of structure IIa. The crystalline adduct IIb was converted to phenanthrene in 40% yield.

With all four of these adducts one double bond remains to be placed to complete the structure. The three crystalline adducts failed to decolorize neutral permanganate, but readily decolorized permanganate at a *p*H of 10. This indicated that the double bond has migrated to a position in conjugation with a carboxyl group during the Diels–Alder reaction. The ultraviolet spectrum of Ia (Table I) indicated that it was not an indene derivative, and that the double bond was probably not conjugated to the benzene ring.

(1) Bachmann and Deno, THIS JOURNAL, **71**, 3062 (1949).

Sorbic acid was added to α-methylstyrene to give 4,6-dimethyl-6-phenylcyclohexene-1-carboxylic acid (III) in 19% yield. The biphenyl type of structure was shown by oxidation to



benzoic acid. The position of the carboxyl group was shown by conversion of III to 4-methyl-2-phenylbenzoic acid. Although this acid was previously unknown, it could be converted to the known 3-methylfluorenone, thus establishing its identity. The ability of III to slowly decolorize permanganate at a *p*H of 10, but fail at a *p*H of 7, suggests that the position of the double bond is that shown in structure III.

The addition of sorbic acid to acenaphthylene gave a tetrahydro-7-methylfluoranthene-10-carboxylic acid (IV). The ring system was shown by oxidation of IV to naphthalic anhydride. This acid (IV) immediately decolorized permanganate at a *p*H of 7 or 10. The ultraviolet absorption spectrum (Table I) indicated that IV is not an acenaphthalene derivative and that the double bond is probably not conjugated to the naphthalene ring.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA

Compound Ia		Compound IV	
λ, mμ	Log E^a	λ, mμ	Log E^a
220	4.00	222	4.68
255 min.	2.82	227 max.	4.84
259 max.	2.88	248 min.	3.75
262 min.	2.85	260 max.	3.81
266 max.	3.02	264 min.	3.80
270 min.	2.70	272 infl.	3.83
273 max.	3.04	280 max.	3.92
280	1.60	284 min.	3.89
		289 max.	3.94
		297 infl.	3.79
		320	3.00
		330	1.60

[a] E = log I_0/I/molarity × cell width (this same quantity was ambiguously labelled ϵ in a previous paper, ref. 1). The spectra were recorded on a Beckmann spectrophotometer with absolute ethanol as the solvent (these same conditions were also used in ref. 1).

In the three reactions where both olefin and diene were unsymmetrical (*i. e.*, sorbic acid plus indene, dihydronaphthalene, and α-methylstyrene), the structural isomer isolated was that

TABLE II[a]

YIELDS AND PROPERTIES OF PRODUCTS FROM THE DIELS–ALDER REACTIONS

	Reactants (M = moles)	Temp., °C.	Time, hr.	Product[b]
1	0.2 *M* Sorbic acid + 0.4 *M* indene	Reflux	100	Tetrahydro-1-methylfluorene-4-carboxylic acid (Ia)
2	0.025 *M* Muconic acid + 0.12 *M* indene	Reflux	75	Tetrahydrofluorene-1,4-dicarboxylic acid (Ib)
3	0.2 *M* Sorbic acid + 0.22 *M* 1,2-dihydronaphthalene[d]	200	120	Hexahydro-1-methylphenanthrene-4-carboxylic acid (IIa)[e]
4	0.05 *M* Muconic acid + 0.11 *M* 1,2-dihydronaphthalene	Reflux	30	Hexahydrophenanthrene-1,4-dicarboxylic acid (IIb)
5	0.2 *M* Sorbic acid + 0.5 *M* α-methylstyrene	Reflux	150	4,6-Dimethyl-6-phenylcyclohexene-1-carboxylic acid (III)
6	0.05 *M* Sorbic acid + 0.05 *M* acenaphthylene	200	20	Tetrahydro-7-methylfluoranthene-10-carboxylic acid (IV)

	M. p., °C.	Yield, % Crude	Pure	Formula	Neut. equiv. Calcd.	Found	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
1	197.6–199.2	50[c]	24	$C_{15}H_{16}O_2$	228.3	228.5	78.90	79.22	7.02	7.07
2	263.3–265.4		13	$C_{15}H_{14}O_4$	129.2	130.9	69.75	70.14 70.07	5.46	5.56 5.81
3		18		$C_{16}H_{18}O_2$	242	244				
4	263.5–265.5	33	12[f]	$C_{16}H_{16}O_4$	136.1	136	70.55	70.53 70.66	5.92	5.68 5.59
5	182.3–185	33[g]	19[g]	$C_{15}H_{18}O_2$	230.3	230.0	78.22	78.46	7.88	8.12
6	245–246.2	30[h]	14[h]	$C_{18}H_{16}O_2$	264.3	263	81.79	81.95 81.71	6.06	5.85 5.69

[a] The experimental conditions reported are those from a single experiment and do not necessarily represent optimum conditions for obtaining the products isolated. In all runs an atmosphere of carbon dioxide was employed. [b] The products were isolated by dissolving the reaction mixture in ether and extracting with dilute alkali. The 0.5 aqueous *M* solutions of the acids were precipitated with acetic acid. This procedure left most of the unreacted sorbic or muconic acid in solution. The precipitated product was crystallized from acetone unless otherwise noted. [c] After removing the 24% yield of pure product by crystallization from acetone, the residue was evaporatively distilled up to 250° at 1 mm. The yield of crude product includes this distillate which was crystalline, but of lower m. p. Recrystallization of this lower melting material failed to yield appreciable quantities of a pure product. [d] Prepared by the method of Strauss and Lemmel, *Ber.*, **54**, 32 (1941). [e] This product was obtained by evaporative distillation up to 250° at 1 mm. The clear yellow distilled gum could not be crystallized, but its correct neut. equiv. and conversion to 1-methylphenanthrene in 25% yield establishes that the gum is principally a mixture of isomeric hexahydro-1-methylphenanthrene-4-carboxylic acids (IIa). [f] Two-thirds of this was obtained by direct crystallization. The remaining third was obtained by evaporatively distilling the residue up to 300° at 1 mm. and crystallizing the distillate from acetone. [g] The product was distilled at 170–210° at 1 mm. before crystallization. [h] The product was evaporatively distilled up to 300° at 1 mm. before crystallization.

formed by linking the electrophilic *delta* carbon of the diene to the potentially nucleophilic *beta* carbon of the olefin. This result substantiates the picture of the Diels–Alder reaction previously presented.[1,2]

Experimental

The yields and properties of the Diels–Alder adducts are presented in Table II.

1-Methylfluorene from Tetrahydro-1-methylfluorene-4-carboxylic Acid (Ia).—A mixture of 2.95 g. of the acid and 0.3 g. of 15% palladium–carbon catalyst was heated in a small distilling flask at 280° for forty-five minutes. The bath temperature was raised to 370° to effect distillation. The crystalline product weighed 2.02 g. and melted at 69–81°. One recrystallization from methanol gave 1.7 g. (74%) of glistening prisms, m. p. 85.5–86.6°, which agrees with the m. p. of 1-methylfluorene previously reported.[3]

Fluorene from Tetrahydrofluorene-1,4-dicarboxylic Acid (Ib).—By the method used above, a 23% yield of fluorene (m. p. 111.5–112.5°, no depression when mixed with an authentic sample) was obtained.

1-Methylphenanthrene from Hexahydro-1-methylphenanthrene-4-carboxylic Acid (IIa).—A mixture of 1 g. of the gummy adduct from sorbic acid plus 1,2-dihydronaphthalene was heated with 150 mg. of 15% palladium–carbon catalyst for ninety minutes at 310°. Evaporative distillation up to 220° at 1 mm. gave 410 mg. of partly crystalline distillate. Crystallization from methanol gave 100 mg. of 1-methylphenanthrene (m. p. 117.6–119.2°, no depression when mixed with an authentic sample). Treatment of the filtrate with picric acid gave an additional 260 mg. of the picrate of 1-methylphenanthrene (m. p. 135–139°). The total yield of hydrocarbon was thus 220 mg. (25%).

Phenanthrene from Hexahydrophenanthrene-1,4-dicarboxylic Acid (IIb).—By the method used above 100 mg. of crystals (m. p. 89–95°) was obtained from 0.3 g. of the acid (IIb). One recrystallization from methanol gave 80 mg. (40%) of phenanthrene (m. p. 98.2–99°, no depression when mixed with an authentic sample).

3-Methylfluorenone from 4,6-Dimethyl-6-phenylcyclohexene-1-carboxylic Acid (III).—A mixture of 2.1 g. of the acid and 0.62 g. of sulfur was heated at 235–245° for two hours. The mixture was evaporatively distilled up to 230° at 1 mm. The distillate was partitioned between ether and sodium bicarbonate solution. Acidification of the aqueous solution with acetic acid and ether extraction gave 0.62 g. of yellowish prisms (m. p. 135–160°). One recrystallization from methanol–water gave 0.32 g. (17%) of colorless granules of 4-methyl-2-phenylbenzoic acid, m. p. 161–166°, raised to 166.5–166.9° by recrystallization.[4]

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 79.24; H, 5.70. Found: C, 79.29; H, 5.62.

A mixture of 160 mg. of the acid and 20 cc. of concentrated sulfuric acid gave a deep purple solution. After one hour at 25°, the solution was added to ice and the product extracted with ether. The ether solution was washed with dilute alkali and evaporated to dryness. Crystallization of the residue from ethanol–water gave 110 mg. (71%) of yellow prisms of 3-methylfluorenone, m. p. 67–68°. The m. p. agreed with that previously reported.[5]

(2) Hudson and Robinson, *J. Chem. Soc.*, 715 (1941).

(3) Lothrop and Goodwin, THIS JOURNAL, **65**, 363 (1943).

(4) Although the nitrile of this acid has been prepared (Ghosh, Pascal and Todd, *J. Chem. Soc.*, 1118 (1940)), no reference to the free acid could be found.

(5) Ullmann and Mallet, *Ber.*, **31**, 1694 (1898).

Naphthalic Anhydride from Tetrahydro-7-methylfluoranthene-10-carboxylic Acid (IV).—A solution of 0.2 g. of the acid (IV) in 30 cc. of hot acetic acid and a solution of 2 g. of potassium dichromate in 20 cc. of water plus 0.5 cc. of concentrated sulfuric acid were mixed and heated twenty-four hours at 100°. After adding 30 cc. of water and 10 cc. of sulfuric acid, the cooled solution was extracted with three 50-cc. portions of ether. The ether was removed and the residue sublimed up to 250° at 30 mm. Recrystallization of the sublimate from ethanol gave 14 mg. (9%) of creamy-white needles of naphthalic anhydride, m. p. 271.5–272°, no depression when mixed with an authentic sample.

Summary

Indene and 1,2-dihydronaphthalene reacted with sorbic and muconic acids to give partially hydrogenated fluorene and phenanthrene derivatives. Sorbic acid also reacted with α-methylstyrene and acenaphthylene to give partially hydrogenated biphenyl and fluoranthene derivatives.

The structures of the products were proven by appropriate degradative experiments and add support to current electronic theories of the Diels–Alder reaction.

Although the yields were low (12 to 24% of pure product), the ease of isolation recommends these reactions as practical methods for the preparation of the above condensed ring systems.

COLUMBUS, OHIO RECEIVED FEBRUARY 6, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

Further Study of the Rearrangement Occurring during the Alkylation of 6-Methoxy-8-aminoquinoline with 1-Diethylamino-3-chloropentane[1]

BY ROBERT C. ELDERFIELD AND CHARLOTTE RESSLER

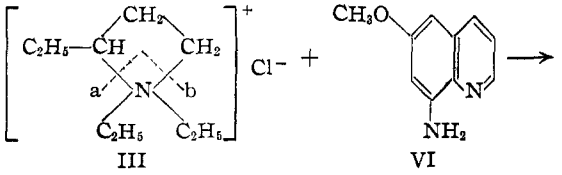
In a previous paper[2] in which the preparation of the antimalarial SN-13,431[3a] was described, the formation of isomeric substances was noted when the product of the reaction of 6-methoxy-8-aminoquinoline (VI) and 1-diethylamino-3-chloropentane (II) was examined by the Craig countercurrent distribution method. Two major components of the reaction product, present to the extent of 75–80% (compound A) and 20–25% (compound B) respectively, were partially characterized by unique distribution constants and by a citrate of B melting at 136–139°. The latter salt was identical with the citrate prepared from the major contaminant of commercial pamaquin and was given the trivial name of *iso*-pamaquin. Although no experimental evidence was offered, it was suggested that the isomeric bases might be formed by way of a cyclic intermediate (III)

$$C_2H_5CHOHCH_2CH_2Cl \longrightarrow C_2H_5CHOHCH_2CH_2N(C_2H_5)_2 \longrightarrow$$

I

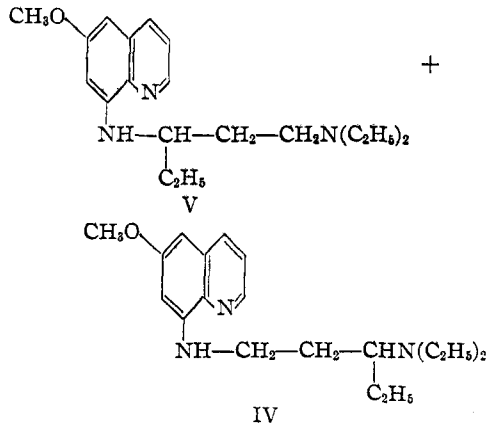
$$C_2H_5CHClCH_2CH_2N(C_2H_5)_2 \longrightarrow$$

II



III VI

Displacement by the base, VI, on bond "a" of III would lead to the isomer V while displacement on bond "b" of III would lead to the isomer IV. In the present investigation the structures previously tentatively assigned to Compounds A and B (IV and V) have been experimentally substantiated and the suggested mechanism accounting for their formation has been discussed.



IV

In addition to the above mechanism wherein the propylenimmonium ion, III, is regarded as the effective alkylating intermediate, the possibility exists that rearrangement may also have occurred during the preparation of the amino alcohol (I) from the precursor chloro alcohol, conceivably through an analogous trimethylene oxide intermediate. Evidence that a mixture of isomers did not result in the preparation of I was obtained by a close examination of several crystalline fractions of a salt obtained in good yield from I.

Rearrangement may have also occurred during the preparation of the chloroamine (II) either at the time of its liberation from its hydrochloride or

(1) This investigation was made possible by a grant-in-aid from the National Institutes of Health.

(2) Elderfield, Craig, Lauer, *et al.*, THIS JOURNAL, **68**, 1516 (1946).

(3) This Survey Number has been assigned according to the system used by Wiselogle, Survey of Antimalarial Drugs (1941–1945), J. W. Edwards, Ann Arbor, Michigan, 1946; (a) Vol. II, part 2, 1191; (b) *ibid.*, 1136.