to a small extent with the dye and successfully competes with the dye for PNA sites. Actually the competition is slightly greater than shown in the table since the r/c for the PNA–adenylic acid system (D) is increased by an amount bound by the adenylic acid itself. The competitive effect persists in the presence of enzyme. For comparison, values of r at the same free dye concentration have been calculated (values in parentheses, Table VI). The per cent. drop in r resulting from the addition of adenylic acid is nearly identical for the PNA and PNA–RNAase systems (C–D and E–F). Since RNAase causes the same per cent. drop in r in the presence of adenylic acid (C–E and D–F)

it appears that the enzyme–substrate complex does not involve sites which combine with adenylic acid. Since the complex under discussion is probably the first of several formed during the course of the hydrolysis, it may be tentatively suggested that inhibition of the enzymatic action occurs during intermediate stages.

[CONTRIBUTION FROM THE CANCER RESEARCH LABORATORY, UNIVERSITY OF FLORIDA]

Diels–Alder Reactions of Maleimide[1]

BY FRANCIS EARL RAY, EUGENE SAWICKI AND OLIN H. BORUM

An attempt was made to condense acrolein, acrylonitrile and crotonic acid and its ester with 2,5-dimethyl-1,5-hexadiene-3-yne or with 1,1'-dicyclohexenylacetylene without success. In investigating the relative reactivity of maleic anhydride and maleimide, it was found that the latter was much more active in condensations with anthracene and 2,5-dimethylfuran This suggested that maleimide might react where the other compounds failed. Success was achieved in condensing 1,1'-dicyclohexenylacetylene with maleimide to yield $\Delta^{6a,7a,13a,13a}$-tetradecahydrochrysene-5,6,11,12-tetracarboxdiimide.

The determination of the spatial configuration of naturally occurring and synthetic steroids is a problem which requires much further research. Luttringhaus[2] has shown that it is possible to bridge the molecule by linking, for example, the 2,6-positions of naphthalene. The present work was undertaken in the hope of obtaining similar compounds from stereoisomeric forms of polynuclear substances.

In 1940 Butz, Gaddis, Butz and Davis[3] heated 2,5-dimethyl-1,5-hexadiene-3-yne with maleic anhydride and obtained 1,5-dimethyl-2,3,4,6,7,8-hexahydronaphthalene-3,4,7,8-tetracarboxylic acid (anhydride). Similarly, Joshel, Butz and Feldman[4] by treating 1,1'-dicyclohexenylacetylene and maleic anhydride obtained tetradecahydrochrysene-5,6,-11,12-dicarboxylicanhydride. It was not determined whether the anhydride groups were *cis* or *trans*.

Much time was spent in unsuccessful attempts at reaction of such dienophiles as acrolein, acrylonitrile or crotonic acid with dienynes. Under comparable conditions maleic anhydride readily formed an adduct. Maleimide was then investigated as a dienophile in the Diels–Alder reaction. The dipotassium salt of the adduct could then, conceivably, react with a polymethylene dihalide to form a large ring compound.

In the formation of 1,1'-dicyclohexanolacetylene, an ether-*insoluble* high melting by-product was obtained. Analyses and molecular weight determinations indicated the compound to be $C_{16}H_{24}O_2$. As the 1-cyclohexanolacetylene type of compound

is a known by-product in the Kazarian synthesis, it is possible that $C_{16}H_{24}O_2$ is a dimer of 1-cyclohexanolacetylene. A study is being made to elucidate the structure of this by-product.

Tuot and Guyard[5] attempted to prepare the dienyne from 2,5-diphenyl-3-hexyne-2,5-diol. They found that the diol was very sensitive to acids, only resins being obtained. We prepared 2,5-diphenyl-1,5-hexadiene-3-yne in rather poor yield by dehydration in an inert atmosphere.

Maleimide was prepared by a modification of the procedure of Plancher and Cattadori.[6] Blomquist and Winslow[7] and Harvey[8] were successful in bringing about its reaction with cyclopentadiene. A comparison of maleic anhydride and maleimide seemed to favor maleimide as the more active dienophile. For example, anthracene refluxed with maleic anhydride for 15 minutes gave a quantitative yield of the adduct as reported by Clar,[9] while the reaction of anthracene with maleimide in boiling xylene gave a violet exothermic reaction after two minutes of refluxing.

When maleic anhydride was treated with 2,5-dimethylfuran in dry ether at 0°, an adduct started to separate after four to six hours standing.[10] For the same reaction with maleimide, crystals started to separate *immediately*. In all cases, however, a practically quantitative yield of adduct was obtained.

This evidence of the reactivity of maleimide suggested that it might be suitable for our purpose. It is of course less desirable than a monobasic com-

(1) Supported by Office of Naval Research, Contract NR-055-225-N9onr-97300.

(2) A. Luttringhaus, *Ann.*, **528**, 181, 206 (1937).

(3) L. W. Butz, A. M. Gaddis, E. Butz and R. E. Davis, *J. Org. Chem.*, **5**, 379 (1940).

(4) L. M. Joshel, L. W. Butz and J. Feldman, THIS JOURNAL, **63**, 3348 (1941).

(5) M. Tuot and M. Guyard, *Bull. soc. chim. France*, 1086 (1947).

(6) G. Plancher and F. Cattadori, *Atti accad. Lincei*, [5] **13**, I, 490 (1905); [5] **14**, I, 214 (1906).

(7) A. T. Blomquist and E. G. Winslow, *J. Org. Chem.*, **10**, 149 (1945).

(8) S. C. Harvey, THIS JOURNAL, **71**, 1121 (1949).

(9) E. Clar, *Ber.*, **65**, 503 (1932).

(10) L. W. Butz, THIS JOURNAL, **57**, 1315 (1935).

pound. The acidic hydrogen attached to the nitrogen, however, offers an unequivocal method of linking the opposite sides together. In conformity with our predictions, 1,1'-dicyclohexenylacetylene and maleimide when heated in xylene for 7 hours gave a good yield of tetradecahydrochrysene-5,6,11,12-tetracarboxdiimide. Only one stereoisomer could be isolated.
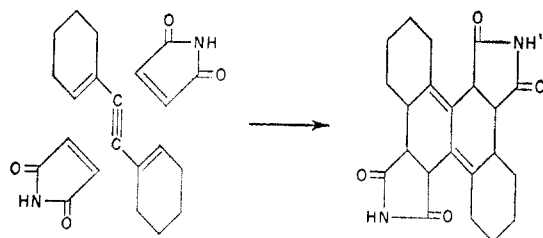
Unfortunately time did not permit us to carry out experiments to join the nitrogens and bridge the molecule.

Experimental

2,5-Dimethyl-3-hexyne-2,5-diol was prepared by a modification of the procedure of Kazarian.[11]

To a stirred solution of 112 g. of potassium hydroxide in 340 cc. of ether, 200 g. of calcium carbide was added. To this cooled (0-10°) and stirred mixture, acetone (116 g.) was added dropwise (1 hour). The temperature was allowed to rise to room temperature while the mixture was stirred seven more hours. The yellow mixture was allowed to stand overnight at room temperature. At this point it had solidified and was red-brown in color. Two hundred grams of ice was added and the solid was broken up. Then the ice cold mixture was stirred for one hour and finally poured into a 4-liter stainless steel beaker. While stirring the yellow mixture by hand, Dry Ice (660 g., 15 mole) was added in small pieces. The mixture soon solidified. Ether (100-200 cc.) was added. The contents were then thoroughly stirred. The ether was decanted into a liter erlenmeyer flask containing anhydrous calcium chloride. This process was repeated until 2 liters of ether had been thus used. The ether solutions were left overnight to dry, and then distilled off. A brown oil was obtained.

The oil was fractionally distilled under a vacuum. The fraction boiling at 65 to 135° under 1 to 2 mm. pressure was collected. Three hundred cc. of cold pentane was added to this half-crystallized mixture. The colorless crystals were filtered and rinsed with cold pentane. The yield of product melting at 95-96° was 47 g. The compound can be crystallized from heptane, benzene, toluene, xylene, carbon tetrachloride or chloroform.

The dibenzoate was prepared by the dropwise addition of 2.9 g. (0.02 mole) of benzoyl chloride to a stirred solution of 1.42 g. (0.01 mole) of the above-mentioned diol in 5 cc. of pyridine. The dibenzoate melted at 112-113° after recrystallization from alcohol.

Anal. Calcd. for $C_{11}H_{22}O_4$: C, 75.4; H, 6.29. Found: C, 75.41, 75.59; H, 6.23, 6.37.

2,5-Dimethyl-1,5-hexadiene-3-yne was prepared by the method of Mitchell and Marvel.[12]

2,5-Diphenyl-3-hexyne-2,5-diol.—The same procedure was followed as for the preparation of 2,5-dimethyl-3-hexyne-2,5-diol, except for the following modifications. Instead of acetone, 240 g. (2 moles) of acetophenone was used. The reaction took place readily at room temperature but not to any great extent at 0-10°. The ether extract of the reaction mixture contained a large amount of a yellow precipitate of the higher-melting stereoisomer. To the residual dark oil, obtained after the ether was distilled off, 200-300 cc. of pentane was added. The mixture was allowed to stand overnight. It was then filtered and

washed with pentane. The yield of yellow product was 130-150 g. (49-56%). Crystallization from 2250 cc. of xylene (charcoal) gave 120-140 g. (45-53%) of colorless crystals melting at 124-155° after washing with pentane. This is a mixture of the two stereoisomers. They can be separated by fractional crystallization from ether into an ether-insoluble product melting at 164-165.5° and an ether-soluble isomer melting at 124-127°.[13] Both of the isomers formed a violet solution in concentrated sulfuric acid.

2,5-Diphenyl-1,5-hexadiene-3-yne.—The procedure was patterned after that of 2,5-dimethyl-1,5-hexadiene-3-yne. 2,5-Diphenyl-3-hexyne-2,5-diol (m.p. 124-155°) (47.9 g., 0.18 mole) and 500 cc. of 60% phosphoric acid were refluxed for 90 minutes. Then the mixture was cooled. The phosphoric acid was poured off and the red-brown, brittle, resinous material was washed by decantation until the washings were neutral. This material was dried and dissolved in about 150 cc. of boiling benzene (charcoal) and filtered. On cooling, about 10 g. (24%) of yellow needles was obtained. Three recrystallizations from xylene gave light yellow needles melting at 240°. This compound was soluble in chloroform, carbon tetrachloride and acetophenone, and insoluble in alcohol and acetone.

Anal. Calcd. for $C_{18}H_{14}$: C, 93.9; H, 6.1. Found: C, 93.50, 93.78; H, 6.02, 6.11.

1,1'-Dicyclohexanolacetylene.—When the same procedure was used for the preparation of this compound as for 2,5-dimethyl-3-hexyne-2,5-diol, a yield of 25-30% of product was obtained. The procedure of Schwartzman[14] gave a higher yield. The compound was soluble in acetic acid, benzene, ether, acetone, alcohol and boiling heptane. One gram of the substance was soluble in approximately 125 cc. of boiling water. It formed a red-yellow solution in concentrated sulfuric acid. From aqueous acetic acid, water or heptane, long white needles were obtained melting at 109-110°; lit.[14] m.p. 109-110°. A by-product, $C_{16}H_{24}O_2$, was also obtained. In the first procedure after the ether extraction the mushy residue was filtered. The residue was suspended in 200-400 cc. of acetone and well stirred. The mixture was filtered. The filtrate was added to 2 liters of water and allowed to stand overnight. The precipitate was recrystallized from acetic acid. From 2 moles of cyclohexanone approximately 5-12 g. of white needles melting at 187-188° was obtained. Using Schwartzman's procedure in preparing the acetylene glycol it was found that when the benzene layer was evaporated carefully the same compound was obtained melting at 185-186°. The compound was not very soluble in cold ether or hot water but was soluble in benzene or acetic acid. It formed a yellow solution in concentrated sulfuric acid. On reaction with benzoyl chloride and pyridine it was recovered unchanged; on reaction with 2,4-dinitrophenylhydrazine only starting products were isolated. Refluxing one gram of this compound for one hour with 50 cc. of 50% sulfuric acid gave a violet oil, from which mixture a small amount of colorless oil could be separated by steam distillation. This latter product is being further investigated.

Anal. Calcd. for $C_{16}H_{24}O_2$: C, 77.42; H, 9.68; mol. wt., 248. Found: C, 78.03, 77.80; H, 9.20, 9.42; mol. wt. (Rast, camphor), 253.

1,1'-Cyclohexenylacetylene was prepared by dehydration with 40% sulfuric acid[14] or potassium bisulfate.[15]

9,10-Dihydroanthracene-9,10-endo-α,β-succinimide crystallizes in a practically quantitative yield as colorless crystals from a solution of 1.0 g. of anthracene and 0.6 g. of maleimide in 6 cc. of xylene which has been gently refluxed for two to three minutes. After plunging in a bath at 320° it melts at 327-329°. It can be recrystallized from aqueous methyl cellosolve or xylene.

Anal. Calcd. for $C_{18}H_{13}NO_2$: N, 5.09. Found: N, 5.32, 5.27.

3,6-Dimethyl-3,6-endoxo-1,2,3,6-tetrahydrophthalimide was obtained in quantitative yield as colorless plates melting at 116-117° when 2.4 g. (0.025 mole) of freshly distilled 2,5-dimethylfuran was added to an ice-cold solution of 1.94 g. (0.02 mole) of maleimide (m.p. 113.5-114.5°) in 10 cc. of ether.

(11) L. Kazarian, *J. Gen. Chem. (U. S. S. R.)*, **4**, 1347 (1934); *C. A.*, **29**, 3978 (1935).

(12) D. T. Mitchell and C. S. Marvel, THIS JOURNAL, **55**, 4276 (1933).

(13) G. Dupont, *Ann. chim.*, [8] **30**, 485 (1913).

(14) L. H. Schwartzman, *J. Org. Chem.*, **15**, 520 (1950).

(15) I. N. Narazova and S. S. Bakhmutskaya, *Zhur. Obschei Khim.*, **19**, 1777 (1949); *C. A.*, **44**, 8907 (1950).

Anal. Calcd. for $C_{16}H_{11}NO_2$: N, 7.25. Found: N, 7.41, 7.27.

$\Delta^{6,7a,1a12a}$-Tetradecahydrochrysene-5,6,11,12-tetracarboxdiimide.—One gram (0.01 mole) of maleimide was suspended in a solution of 1.0 g. (0.0053 mole) 1,1'-dicyclohexenylacetylene and 15 cc. of xylene. A few crystals of hydroquinone were added and the mixture was refluxed for seven hours. On

cooling and filtering 1.0 g. of crude product was obtained. Recrystallization from aqueous methyl cellosolve gave 0.6 g. of colorless microcrystals melting at 357–358° with gas evolution (placed in bath at 350°).

Anal. Calcd. for $C_{22}H_{24}N_2O_4$: N, 7.36. Found: N, 7.25, 7.34.

GAINESVILLE, FLORIDA   RECEIVED APRIL 23, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Action of Aluminum Bromide on Allyl Phenyl Ether

BY JOHN C. PETROPOULOS[1] AND D. S. TARBELL

Both allyl phenyl ether (I) and o-allylphenol have been found to be converted very rapidly by aluminum bromide in chlorobenzene solution to 51 and 50%, respectively, of 1-(o-hydroxyphenyl)-1-(p-chlorophenyl)-propane (II). This compound (II) in the presence of aluminum bromide is converted at a slower measurable rate to 65–75% of phenol and a corresponding amount of ClC₆H₄CH(C₂H₅)C₆H₄Cl; in addition a side reaction occurs in which II is isomerized to 1-(o-hydroxyphenyl)-2-(p-chlorophenyl)-propane. The latter compound is not readily converted to phenol. The formation of II is thought to proceed by the intramolecular path, in which allyl phenyl ether is converted first to o-allylphenol; the latter is isomerized to the propenyl compound, which then adds chlorobenzene to form II.
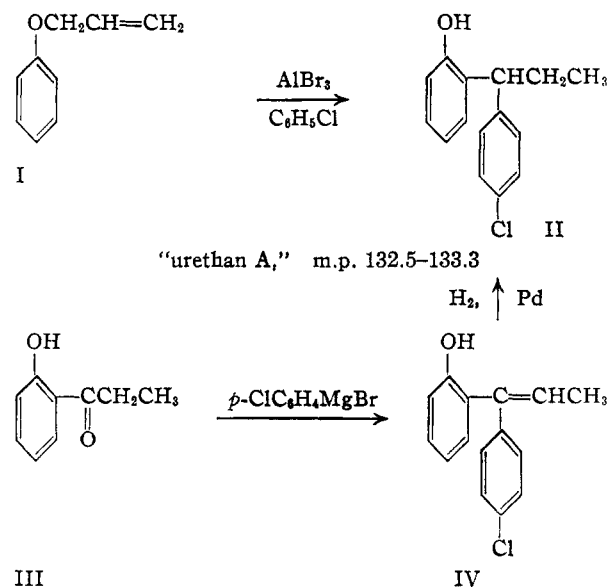
It was reported previously[2] that benzyl phenyl ether was converted by aluminum bromide in an extremely rapid intramolecular reaction to o-benzylphenol, with no evidence for the formation of p-benzylphenol.

Anisole has been found not to undergo this type of reaction; it forms no detectable amount of o-cresol, although it is demethylated, as would be expected.[3] It appeared that, for the intramolecular rearrangement to occur, a group with greater tendency for carbonium ion formation than the methyl group was required. The present paper describes the behavior of allyl phenyl ether with aluminum bromide in chlorobenzene solution.

Treatment of the ether (I) with two moles of aluminum bromide in dilute solution in chlorobenzene, followed by immediate quenching with water, led to 51% of 1-(p-chlorophenyl)-1-(o-hydroxyphenyl)-propane (II); the remainder of the starting material was converted into a non-volatile neutral material (possibly a polymer of I) and an alkali-soluble polymer, possibly a polymer of 2-allylphenol. The structure of II was inferred from the fact that permanganate oxidation gave p-chlorobenzoic acid in 50% yield, and that the Liebermann nitroso reaction[4] was positive, indicating a free position *para* to the phenolic hydroxyl group. The structure of II was proved by synthesis as indicated below; the synthetic product was compared to the reaction product through the crystalline phenylurethan m.p. 132.5–133.3° ("urethan A").

It is noteworthy that in contrast to benzyl phenyl ether,[2] there was no initial formation of phenol itself; in analogy to the previous case, however, there was no isolatable amount of the para isomer of II.

In the presence of aluminum bromide in chlorobenzene, o-benzylphenol was quantitatively con-

(1) Abbott Laboratories Fellow, 1951–1952.
(2) D. S. Tarbell and J. C. Petropoulos, THIS JOURNAL, **74**, 244 (1952).
(3) P. Pfeiffer and E. Haack, *Ann.*, **460**, 156 (1928); P. Pfeiffer and W. Loewe, *J. prakt. Chem.*, **147**, 293 (1937); R. Adams and J. Mathieu, THIS JOURNAL, **70**, 2120 (1948).
(4) J. Houben, "Die Methoden der organischen Chemie," Georg Thieme, Leipzig, 1930, Vol. III, p. 30.

"urethan A," m.p. 132.5–133.3

verted at a measurable rate to phenol.[2] Similarly, II was converted to phenol. However, the reaction appeared not to be quantitative and ceased after a production of 65–75% of phenol. The data are listed in Table I.

These results implied that in addition to the reaction causing the phenol formation, a simultaneous isomerization reaction must be taking place. This was proved by an isolation run in which synthetic II was treated with aluminum bromide in chlorobenzene for three hours at 25°. It was found that the major portion of II was converted to phenol and 24% was converted to a mixture of isomers of II. This mixture was shown to contain some 1-(o-hydroxyphenyl)-2-(p-chlorophenyl)-propane (V), which was characterized through its crystalline phenylurethan, m.p. 93.5–94° ("urethan B"). In addition, a small amount of a phenylurethan ("urethan C," m.p. 148–149°) was obtained, which was probably derived from a para-substituted phenol, such as p-HOC₆H₄CH₂CH(C₆H₄Cl)CH₃.

The structure of V was established by synthesis from the readily available o-methoxyphenylacetic