[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF COLORADO]

Diels-Alder Reactions of 9-Substituted Anthracenes.[1] I. Some Reactions of 9-Anthraldehyde

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In the condensation of a monosubstituted diene with a monosubstituted dienophile, two or more isomeric adducts may be formed. As a continuation of our studies to see which adduct formed preferentially, 9-anthraldehyde has been condensed with acrylic acid, acrylonitrile, allyl alcohol and maleic anhydride. In the first three cases, it has been shown that the major product was an ortho type adduct.

In the Diels-Alder condensation of a 1-substituted butadiene with a monosubstituted dienophile, positional, geometrical and optical isomerism are possible in the resulting adducts. In an effort to obtain more examples on which to base predictions as to which positional isomer predominates in a given reaction, it was decided to study 9-substituted anthracenes. Here, a large variety of groups could be used and the compounds would be readily available. The driving force with anthracene compounds in the Diels-Alder reaction is generally good. The resulting adducts would not possess *cis-trans* isomerism nor would double bond migration be possible to complicate structure proofs of the adducts. In addition, anthracene adducts are solids and the separation, purification and identification of the isomers would be facilitated. Furthermore, the adducts would possess a variety of interestingly substituted bridgehead carbon atoms which would be of use for other studies.

The first 9-substituted anthracene chosen for study was 9-anthraldehyde (I) since the electron-attracting aldehyde group has not yet been studied on dienes and the compound is readily prepared from anthracene.

Solid adducts were readily obtained with maleic anhydride, acrylic acid, acrylonitrile and allyl alcohol. Since our work was started, the condensation of I with quinone has been reported.[3]

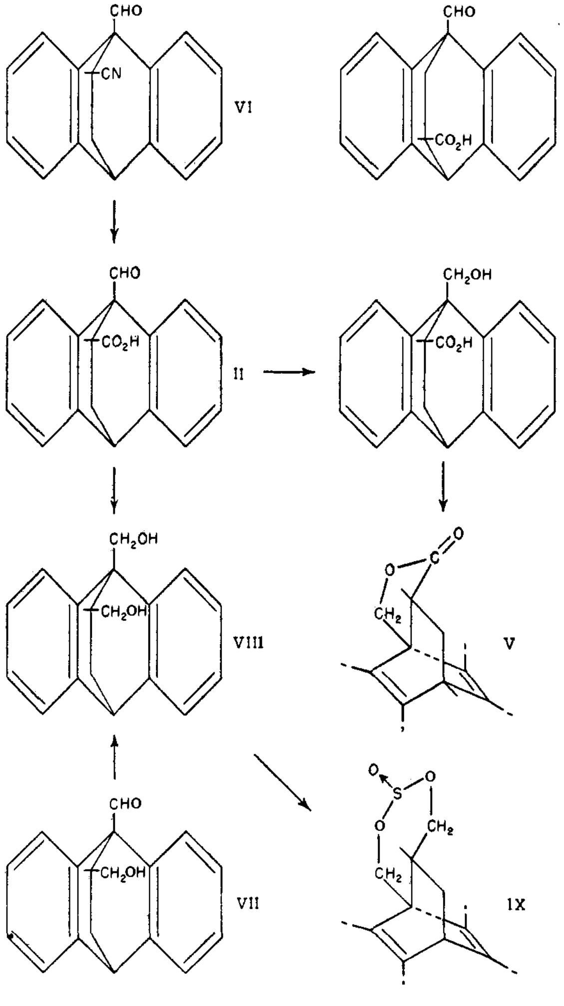
Attempts to oxidize the acrylic acid adduct to a dibasic acid so as to prepare an anhydride so far have been unsuccessful. The bridgehead aldehyde group of 1-aldehydotriptycenehydroquinone has been reported to be stable to sodium bromate in acetic acid.[3]

The reduction of the bridgehead aldehyde group was accomplished by the use of Raney nickel and hydrogen at room temperature in a solution of potassium hydroxide. The resulting hydroxy acid (IV) upon melting evolved water and gave a solid lactone (V). Molecular weight determinations showed that the product was a monomer rather than a linear polyester. The infrared absorption spectrum of the lactone was consistent with that of a five-membered lactone ring. This showed that the adduct was II rather than III. A Fisher-Hirschfelder-Taylor model of the hydroxy acid derived from III is sterically incapable of forming a lactone ring due to the rigidity of the bicyclic system.

The adduct (VI) of acrylonitrile was hydrolyzed to II.

Allyl alcohol and 9-anthraldehyde were found to condense readily, although in this case a negatively substituted diene and an electron-rich dienophile were used. The resulting adduct (VII) was reduced to a glycol (VIII) which was also obtained by the reduction of II.

This glycol was treated with thionyl chloride and a sulfite ester (IX) was obtained. Molecular weight studies showed the ester was a monomer. Fisher-Hirschfelder-Taylor models of this ester could be made only with a structure corresponding to IX and not from the model of a glycol derived from III. These results showed that VII was again an ortho type adduct.



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[2] American Cyanamid Fellow, 1950-1951.

[3] P. D. Bartlett, S. G. Cohen, J. D. Cotman, Jr., N. Kornblum, J. R. Landry and E. S. Lewis, THIS JOURNAL, **72**, 1003 (1950).

Experimental

9-Anthraldehyde.—9-Anthraldehyde was prepared from Reilly Coal Tar, 90–95% anthracene, according to the directions in "Organic Syntheses."[4] The N-methylformanilide used to formylate the anthracene in this preparation was prepared by refluxing 300 g. of 90–95% formic acid, 200 ml. of benzene and 321 g. of N-methylaniline in a round-bottomed flask fitted with an Ace Glass Barrett type moisture test receiver and a reflux condenser. When no more water was removed by the azeotropic distillation, the benzene was distilled and then the N-methylformanilide was purified by distillation *in vacuo*. Yields were the same as those reported by Fieser and Jones[5] whose directions call for the use of 1800 ml. of toluene and 5 to 6 hours of distilling the toluene to remove the water instead of using 200 ml. of benzene and a moisture receiver as noted above.

Maleic Anhydride Adduct.—To test the ease with which 9-anthraldehyde would undergo the Diels–Alder reaction, its condensation with maleic anhydride was studied. When one and three-hundredths grams (0.005 mole) of 9-anthraldehyde and 0.49 g. (0.005 mole) of maleic anhydride were refluxed in 10 ml. of xylene for 1 hour, 18.5% of the aldehyde could be recovered by extracting the mixture with base. When refluxing was maintained for 12 hours, less than 5% of the 9-anthraldehyde could be recovered. When the adduct itself was isolated from an hour run, the product melted at 238–239°, yield 0.87 g. (59%). Recrystallization of the 9-formyl-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylic anhydride from benzene failed to raise the melting point.

Anal. Calcd. for $C_{19}H_{12}O_4$: C, 74.99; H, 3.98. Found: C, 75.23; H, 3.91.

This product was white and indicated it was an ethanoanthracene derivative rather than (10-formyl-9-anthryl)-succinic anhydride which would be colored like other 9- and 9,10-substituted anthracenes. It is to be noted that a recent attempt to condense anthracene and *p*-quinone dibenzenesulfonimide in the Diels–Alder reaction gave cream-colored crystals of 2-(9-anthryl)-*p*-phenylenedibenzenesulfonamide.[6]

Acrylic Acid Adduct.—Two and six-hundredths grams (0.01 mole) of 9-anthraldehyde and 12 g. (0.1 mole) of 60% technical acrylic acid and 0.5 g. of hydroquinone were heated under reflux for 12 hours. After cooling, 125 ml. of water was added and then the mixture was extracted with three 100-ml. portions of benzene. The benzene solution was concentrated and allowed to stand overnight. White crystals were obtained, yield 1.71 g. (62%), m.p. 205.5–206.5°. Recrystallization from benzene did not raise the melting point. This adduct, as well as that of allyl alcohol and acrylonitrile, dissolved very slowly in benzene and, on cooling, crystal deposition required several hours of standing. It was found advantageous to use an excess amount of benzene to dissolve the adducts and to concentrate the benzene solution before recrystallization. Drying at room temperature raised the melting point to 211.5–212°. When the two forms were mixed, the melting point was 211–212°. The structure assigned was that of 9-formyl-9,10-dihydro-9,10-ethanoanthracene-12-carboxylic acid rather than a pseudo-acid since the material readily dissolved in 5% sodium bicarbonate and was regenerated with no apparent change upon acidification of the ice-cold bicarbonate solution. Titration of II with both sodium and barium hydroxide gave neutralization equivalents consistent with a free carboxyl group. The infrared absorption spectrum of II in nujol showed a peak at 5.90 μ and an indistinct one at 3.86 μ. This is consistent with what one would expect for II rather than a lactol form.[7,8,9] The carbonyl group in a lacto would have a band at 5.6 to 5.7 μ.

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07; neut. equiv., 278. Found: C, 77.76; H, 5.34; neut. equiv. (NaOH), 277, 274, 273; ($Ba(OH)_2$), 268, 269.

9,10-Dihydro-9-methyl-9,10-ethanoanthracene-12-carboxylic Acid (IV).—To about 0.5 g. of potassium hydroxide in 30 ml. of water was added 0.83 g. (0.03 mole) of the adduct of 9-anthraldehyde and acrylic acid and a small amount of Raney nickel. This mixture was then shaken under an atmosphere of hydrogen at room temperature and pressure. After 3 hours, approximately 0.03 mole of hydrogen had been adsorbed. The catalyst was removed by filtration and the filtrate was acidified with concentrated hydrochloric acid. The solution was extracted with benzene and the benzene was evaporated in a jet of air leaving a residue of 0.84 g. of crude product which melted at 148–149° when a slow rate of heating was used. The recrystallized product melted at 149.0–149.2°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 77.12; H, 5.75. Found: C, 77.27; H, 5.52.

9,10-Dihydro-9-methylol-9,10-ethanoanthracene-12-carboxylic Acid Lactone (V).—When 1.00 g. (0.036 mole) of the hydrogenated adduct in a test-tube was placed in an oil-bath and the bath then heated at 160–195° for 25 minutes, water condensed at the top of the test-tube. Upon cooling, 0.92 g. (98%) of a white solid was obtained, m.p. 190–191°. Recrystallization from benzene raised the melting point to 191–192°. Infrared spectra showed a band at 5.55 μ in carbon disulfide, one at 5.65 μ in chloroform and one at 5.55 μ in carbon tetrachloride. This is comparable to the band reported at 5.65 μ for the carbonyl group of a five-membered lactone ring.[10,11]

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38; mol. wt., 262. Found: C, 82.33; H, 5.54; mol. wt. (Rast), 240 and 256.

Acrylonitrile Adduct (VI).—A mixture of 10.31 g. (0.05 mole) of 9-anthraldehyde, 22.50 g. (0.424 mole) of acrylonitrile and 0.15 g. of hydroquinone was heated in a sealed tube at 125–130° for 24 hours. The mixture was washed out of the tube with benzene and was then placed in a beaker under a jet of air. Additional amounts of benzene were added from time to time to facilitate evaporation of unreacted acrylonitrile. The resulting solid was filtered and washed with benzene, yield 10.1 g. (78%), m.p. 172°. Recrystallization gave 7.49 g. of white material, m.p. 179–182°. The analytical sample of 12-cyano-9,10-dihydro-9,10-ethanoanthracene-9-carboxaldehyde melted at 181.5–182°.

Anal. Calcd. for $C_{18}H_{13}NO$: C, 83.38; H, 5.05. Found: C, 83.23; H, 4.95.

Hydrolysis of VI.—To a mixture of 10 ml. of sulfuric acid and 10 ml. of water was added 0.21 g. of VI, m.p. 181.5–182°. The solution was heated to 105–110° for one-half hour and then heated to 155° for 3 minutes before cooling to room temperature. The sulfuric acid solution was poured slowly into water and was allowed to stand overnight. The mixture was made alkaline, filtered and extracted with benzene. The alkaline solution was then acidified and 0.18 g. (85%) of a white solid was obtained, m.p. 205–206°. A mixed melting point with II obtained from acrylic acid and 9-anthraldehyde melted at 207–208°.

Allyl Alcohol Adduct (VII).—A mixture of 10.31 g. (0.05 mole) of 9-anthraldehyde and 11.21 g. (0.193 mole) of allyl alcohol and no inhibitor was heated at 195–202° for 12 hours in a sealed tube. The product was worked up as before with VI. The first crop of white crystals weighed 8.25 g. (63%) and melted at 170–171°. A second crop of 0.27 g., m.p. 169–170° was also obtained. Subsequent recrystallization from benzene failed to raise the melting point of the 9,10-dihydro-12-methylol-9,10-ethanoanthracene-9-carboxaldehyde above 170–171°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.64; H, 5.69.

Reduction of VII and II to VIII.—The reduction of VII and II was patterned after a procedure of Nystrom and Brown[12] for the reduction of slightly ether-soluble carbonyl compounds.

One hundred milliliters of anhydrous ether and 0.23 g. (0.0061 mole) of lithium aluminum hydride were placed in a flask attached to a soxhlet extractor in which was placed 1.33 g. (0.005 mole) of VII. The ether was refluxed for 10 hours

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[4] L. F. Fieser, J. L. Hartwell, J. E. Jones, J. H. Wood and R. W. Bost, *Org. Syntheses*, **20**, 11 (1940).

[5] L. F. Fieser and J. E. Jones, *ibid.*, 66 (1940).

[6] R. Adams and C. R. Walter, Jr., THIS JOURNAL, **73**, 1152 (1951).

[7] R. B. Barnes, R. C. Gore, U. Liddel and U. Z. Williams, "Infrared Spectroscopy," Reinhold Publishing Corp., New York, N. Y., 1944.

[8] H. W. Thompson, *J. Chem. Soc.*, 328 (1948).

[9] J. F. Grove and H. A. Willis, *ibid.*, 877 (1951).

[10] R. S. Rasmussen and R. R. Brattain, THIS JOURNAL, **71**, 1073 (1949).

[11] R. B. Woodward, *ibid.*, **72**, 3328 (1950).

[12] R. F. Nystrom and W. G. Brown, *ibid.*, **69**, 1197 (1947).

to extract the alcohol adduct, allowed to stand overnight and then was stirred for 24 hours. Water was then added, the ether layer removed, and the aqueous solution was extracted with more ether. The combined ether solutions yielded 1.21 g. of white material (90%), m.p. 164–166°. If the material was worked up immediately after addition was complete, some unreduced starting material was obtained.

An analytical sample of 9,10-dihydro-12-methylol-9,10-ethano-9-methanol (VIII) after recrystallization from benzene melted at 163–163.5° and a mixed melting point with the starting adduct was depressed.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.31; H, 6.86.

The acrylic acid 9-anthraldehyde adduct was reduced with lithium aluminum hydride in a similar fashion as above but was stirred only 3 hours following extraction of the adduct from the soxhlet extractor. From 0.65 g. of adduct, there was obtained 0.56 g. of crude alkali insoluble product, m.p. 154–157°. Recrystallization from benzene led to 0.34 g. of the glycol, m.p. 163–166°. There was no mixed melting point depression with VIII prepared from the allyl alcohol adduct and both gave the same sulfite ester.

Sulfite Ester of VIII.—Two milliliters (0.028 mole) of thionyl chloride was added to 0.20 g. (0.00075 mole) of VIII in 20 ml. of benzene and the solution was heated for 30 minutes. The mixture was evaporated to dryness and 0.20 g. of product, m.p. 209–213°, was obtained. Recrystallization from benzene gave 0.11 g. of white solid, m.p. 223–224°.

Anal. Calcd. for $C_{18}H_{16}O_3S$: C, 69.21; H, 5.16; S, 10.26; mol. wt., 312. Found: C, 69.24; H, 5.04; S, 10.14; mol. wt. (Rast), 315 and 338.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY]

N-Acyl-β-phenethylamines, and a New Isoquinoline Synthesis

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Several N-acyl-α-methyl-β-phenethylamines have been prepared by the reaction of allylbenzene with nitriles in the presence of concentrated sulfuric acid. Three 3,4-dihydroisoquinolines have been obtained by the reaction of methyleugenol with alkoxyaryl nitriles. This is a new synthesis of the isoquinoline ring system. One of these was dehydrogenated to the corresponding known isoquinoline. Amides or dihydroisoquinolines could not be obtained from safrol. A series of sixteen N-acyl-α,α-dimethyl-β-phenethylamines has been prepared from α,α-dimethyl-β-phenethyl alcohol and a group of nitriles.

It has been shown that the reaction of olefins with nitriles to yield N-alkyl amides may be extended to allylbenzene and acetonitrile.[2] Since the product of this reaction is an N-acyl-β-phenethylamine which may be cyclized to 1,3-dimethyl-3,4-dihydroisoquinoline[3] the reaction seemed to offer a new source of intermediates for synthesis of a variety of isoquinolines. Accordingly, the reaction of allylbenzene and substituted allylbenzenes, as safrol and eugenol ethers, with various nitriles was studied with the results reported herein.

TABLE I

N-ACYL-α-METHYL-β-PHENETHYLAMINES, $C_6H_5CH_2CH(CH_3)NHCOR$

					Analyses, %					
					Carbon		Hydrogen		Nitrogen	
R	Proc.	Yield, %	M.p., °C.	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found
C_6H_5	A	54	131–133[a]	$C_{16}H_{17}ON$	80.27	80.02	7.18	7.15	5.85	6.08
$C_6H_5CH_2$	A	53	113–115[b]	$C_{17}H_{19}ON$	80.57	79.91	7.58	7.70	5.53	5.40
$3,4\text{-}(CH_3O)_2C_6H_3$	B	53	114–120	$C_{18}H_{21}O_3N$	72.20	72.26	7.08	6.95	4.68	4.82
$3,4\text{-}(C_2H_5O)_2C_6H_3$	B	97	149–151	$C_{20}H_{25}O_3N$	73.34	73.41	7.71	7.71	4.28	4.58

[a] Dey and Ramanathan[4] report m.p. 128°, Kalish,[5] 134–135°. [b] Dey and Ramanathan[4] report m.p. 118°.

N-Benzoyl-α-methyl-β-phenethylamine was prepared from allylbenzene and benzonitrile, and N-phenylacetyl-α-methyl-β-phenethylamine from allylbenzene and benzyl cyanide, using concentrated sulfuric acid without a solvent. When the reaction was carried out under the same conditions with allylbenzene and veratronitrile no amide was obtained. The amide resulted in fair yield however when butyl ether was used as solvent in the reaction. The amide from 3,4-diethoxybenzonitrile was prepared in the same manner. Crystalline amides were not obtained from allylbenzene and 4-nitrophenylacetonitrile, diphenylacetonitrile, homoveratronitrile and β-phenylpropionitrile. The two procedures used in reactions carried out with allylbenzene are designated A and B, respectively (Experimental part) and amides so obtained appear in Table I.

One of the amides, N-benzoyl-α-methyl-β-phenethylamine, was cyclized to the dihydroisoquinoline in low yield.

Methyleugenol and benzonitrile seemed to react normally, but several attempts to obtain a crystalline reaction product were unsuccessful. However, when the oily reaction product was distilled *in vacuo* the corresponding dihydroisoquinoline could be isolated from the distillate as its hydrochloride, indicating that the amide had formed in the first step and had been at least partially dehydrated to the

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(1) Abstracted from the thesis presented by Francis X. Murphy in partial fulfillment of the requirements for the degree of Doctor of Philosophy, New York University, February, 1950.

(2) Ritter and Kalish, THIS JOURNAL, **70**, 4048 (1948).

(3) Hey, *J. Chem. Soc.*, **18** (1930).

(4) Dey and Ramanathan, *Proc. Natl. Inst. Sci. India*, **9**, 193 (1943).

(5) Kalish, M.S. Thesis, New York University, 1946.