[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Acridizinium Ion Chemistry. II.[1] The Diels–Alder Reaction

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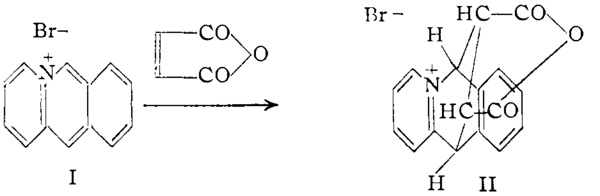
Acridizinium bromide (I) has been found to undergo the Diels–Alder reaction when heated with maleic anhydride, maleate or fumarate esters or acrylonitrile. Ethyl maleate and fumarate yield the same product, which appears to be best explained by a preliminary rearrangement of maleate to fumarate ester. Esterification of the acid III obtained by ring opening of the anhydride adduct II yielded esters unlike those obtained directly in the Diels–Alder reaction.

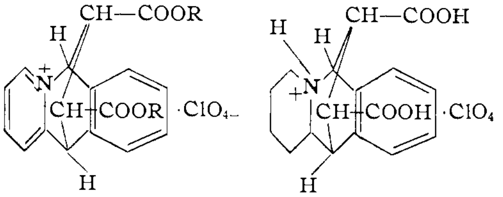
The acridizinium ion (I) is a new heterocyclic system, yet one which can be prepared conveniently on a large scale.[3] In the previous communication of this series[1] it was shown that like anthracene, acridizinium bromide undergoes photodimerization. This observation suggested that the acridizinium ion might also resemble anthracene[4] in functioning as the diene component in the Diels–Alder reaction.



I II

When acridizinium bromide was heated on the steam-bath with an excess of maleic anhydride, in the presence of acetic acid, a good yield of a colorless non-fluorescent salt was obtained. The adduct II had the expected composition, showed the characteristic (anhydride) double absorption[5] in the carbonyl region of the infrared spectrum, and had an ultraviolet absorption spectrum resembling that of the acridizinium photodimer[1] in that absorption was confined to the 263 mμ region.[6] The anhydride ring was opened by the action of dilute perchloric acid at room temperature, yielding what must be the *cis*-dicarboxylic acid III. As would be predicted from the formula the acid III absorbs three moles of hydrogen at atmospheric pressure yielding VIII.

Either ethyl fumarate or ethyl maleate when heated with the acridizinium ion in the presence of acetic acid yielded the same product, which we believe to be the *trans*-ester IV. While it seemed probable that the isomerization of the maleate ester to fumarate would not be a serious problem if acetic acid were omitted,[7] no conditions were found for carrying out the reaction in this way. By esterification of the *cis*-dicarboxylic acid an isomeric diethyl ester VI, believed to be *cis*, has been obtained. In the same way methyl maleate with the acridizinium ion in acetic acid gave a dimethyl ester V differing from that (VII) obtained by direct esterification of the *cis*-acid III. Unfortunately the instability of the aromatic quaternary ammonium ion in the presence of bases made it impossible to carry out the usual isomerization of the *cis*-esters by the action of alkoxide ion. Because of the unsymmetrical nature of the acridizinium ion maleic anhydride could theoretically produce two adducts, one with the anhydride ring inclined in the general direction of the benzenoid ring and the other in the direction of the pyridinum ion. Since the course of the reaction in this respect is not known, it is impossible to write the exact stereochemical structural formulas for our products.



III, R = H *cis*
IV, R = C_2H_5 *trans*
V, R = CH_3 *trans*
VI, R = C_2H_5 *cis*
VII, R = CH_3 *cis*

VIII

Although the acridizinium ion failed to give an adduct with quinone, it did yield a mixture of products with the unsymmetrical dienophile acrylonitrile. From the mixture there was obtained a compound having the composition of a Diels–Alder adduct, but it was not determined which structural isomer this was.

On the basis of our observations, the earlier opinion that ". . . it is always found that heterocyclic dienes which contain nitrogen as a member of the ring show abnormal diene reactions"[8] must be revised. Further, on the basis of reviews on the subject[9] of the Diels–Alder reaction, it

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[1] For the preceding communication of this series see *J. Org. Chem.*, **22**, 1740 (1957).

[2] Taken in part from a thesis to be submitted in partial fulfillment of the requirements for the Ph.D. degree, Duke University. This research was supported by a research grant (NSF-G2364) of the National Science Foundation.

[3] C. K. Bradsher and L. E. Beavers, THIS JOURNAL, **77**, 453 (1955). In recent experiments, as much as 60 g. of product I have been prepared at one time.

[4] *E.g.*, O. Diels and K. Alder, *Ann.*, **486**, 191 (1931); W. E. Bachmann and M. C. Kloetzel, THIS JOURNAL, **60**, 481 (1938); E. Clar, *Ber.*, **64**, 2194 (1931); Ch. Dufraisse, L. Velluz and L. Velluz, *Bull. soc. chim. France*, [5] **5**, 1073 (1938).

[5] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co., London, 1954, p. 109.

[6] This observation is consistent with the assumption that the absorbing groups are isolated pyridine and benzene systems. If one assumes reaction in one of the terminal rings the absorbing group would be of the naphthalene or isoquinoline type with absorption to be expected at longer wave lengths; *cf.* R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Organic Compounds," John Wiley and Sons, Inc., Co., New York, N. Y., 1951.

[7] An attempted reaction using maleic acid in acetic acid gave no adduct and fumaric acid was recovered from the reaction mixture.

[8] J. A. Norton, *Chem. Revs.*, **31**, 319, 478 (1942).

[9] *E.g.*, ref. 8, M. C. Kloetzel, "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 1; H. L. Holmes, *ibid.*, p. 60; L. W. Butz, *ibid.*, Vol. V, p. 136; K. Alder, "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 381.

appears that there is no previous instance of the reaction in which the diene is a quaternary salt.

Experimental[10]

Spectroscopy.—All ultraviolet spectra were determined in 95% ethanol solution, using the Warren Spectracord recording spectrophotometer and 1-cm. matched silica cells. The infrared data were determined by the potassium bromide plate method using the Perkin–Elmer model 21 infrared spectrophotometer.

6,11,12,15-Tetrahydro[6,11,3′,4′]furanoacridizinium-13,-15-dione Bromide (II).—Fifteen grams of maleic anhydride 3.78 g. of acridizinium bromide[3] and 10 ml. of glacial acetic acid were placed in a 100-ml. flask equipped with a magnetic stirrer and reflux condenser and the mixture heated on the steam-bath for 13 hours. The reaction mixture, a light tan suspension, was poured into 150 ml. of boiling ether and the mixture cooled. The precipitate was collected and washed first by boiling in 25 ml. of ethyl acetate and then in 50 ml. of boiling acetone. The dry product consisted of a light tan powder, m.p. 202–215° (previous decomposition starting at 178°), yield 4.53 g. (87%). The analytical sample was a colorless microcrystalline powder, m.p. 244–246°. The ultraviolet absorption spectrum showed a maximum at 263 mμ and a minimum at 241.5 mμ with a value of 3.62 and 3.38, respectively, for log ε. Infrared absorption peaks in the 5–6 μ region were found at 5.34(w), 5.60, 5.68(w) and 5.82 μ.

Anal. Calcd. for $C_{17}H_{12}BrNO_3$: C, 57.00; H, 3.80; N, 3.91. Found: C, 56.59; H, 3.54; N, 4.02.

cis-**12,13-Dicarboxy-6,11-dihydro-6,11-ethanoacridizinium perchlorate** (III) was prepared in 66% yield by dissolving the adduct II in warm water (35°) and adding perchloric acid, m.p. 298–300°. The analytical sample was obtained as small colorless blunt needles from acetone, m.p. 299.5–300.5°. The ultraviolet absorption spectrum showed a maximum 263 mμ (log ε 3.58) and a minimum at 241.5 (log ε 3.33). The infrared spectrum in the 5–6 μ region showed a single peak at 5.77 μ.

Anal. Calcd. for $C_{17}H_{14}ClNO_8$: C, 51.59; H, 3.57; N, 3.55. Found: C, 51.74; H, 3.70; N, 3.81.

12,13-Dicarboxy-6,11-ethanobenzo[b]quinolizidine Hydroperchlorate (VIII).—One gram of the dicarboxylic acid III was dissolved in 50 ml. of methanol, 50 mg. of platinum oxide added, and the mixture hydrogenated at room temperature and at a pressure of one atmosphere. After four hours, three moles of hydrogen per mole of adduct had been taken up and hydrogen absorption had ceased. The catalyst was filtered off, the methanol evaporated and the residue allowed to crystallize. The crystalline residue was dissolved in the minimum quantity of hot water, 1 ml. of perchloric acid added and the solution cooled. Four recrystallizations of this type yielded transparent needles, m.p. 236–237°.

Anal. Calcd. for $C_{17}H_{20}ClNO_8$: C, 50.94; H, 5.03; N, 3.50. Found: C, 50.58; H, 5.03; N, 3.53.

trans-**12,13-Dicarbethoxy-6,11-dihydro-6,11-ethanoacridizinium Perchlorate** (IV). (a) **From Diethyl Maleate.**—One gram of acridizinium bromide, 15 ml. of diethyl maleate[11] and 15 ml. of glacial acetic acid were mixed and stirred for 48 hours at 95°. Water was added to the reaction mixture and the aqueous solution was washed well with ether. The aqueous solution was evaporated (30 mm. pressure) until the volume was only 15 ml., and 5 drops of perchloric acid was added. The colorless crystals were collected and dried in a desiccator over calcium chloride; yield 1.0 g. (59%), m.p. 176–180°. Four recrystallizations yielded the analytical sample as very small but well-formed elongated prisms, m.p. 182.5–183.5°.

(b) **From Diethyl Fumarate.**—When the above procedure was carried out as described above except that diethyl fumarate[11] was used and heating was at 105° for ten hours, 0.92 g. (54%) of product, m.p. 175–175.5°, was obtained. The recrystallized sample, consisting of very small but well-defined elongated prisms, melted at 178.5–179.5° alone, and at 180–183.5° when mixed with the product obtained in (a). The infrared spectra of the two products were identical. The ultraviolet absorption spectrum showed a single maximum at 263 mμ (log ε 3.73) and a minimum at 242 mμ (lot ε 3.49). A strong infrared absorption peak was observed at 5.76 μ.

Anal. Calcd. for $C_{21}H_{22}ClNO_8$: C, 55.93; H, 4.92; N, 3.12. Found[12]: C, 55.96, 55.67; H, 4.98, 5.01; N, 3.29, 3.25.

trans-**12,13-Dicarbomethoxy-6,11-dihydro-6,11-ethanoacridizinium Perchlorate** (V).—Two grams of acridizinium bromide, 10 ml. of dimethyl maleate[13] and 15 ml. of acetic acid were heated, and the mixture worked up essentially as before. The product, thrice recrystallized from methanol consisted of colorless needles, m.p. 298.5–299° dec., yield 0.3 g.[14] (10%). An ultraviolet absorption maximum was observed at 264 mμ (log ε 3.60), minimum at 244 mμ (log ε 3.38). An infrared absorption peak was observed at 5.74 μ.

Anal. Calcd. for $C_{19}H_{18}ClNO_8$: C, 53.84; H, 4.28; N, 3.30. Found[15]: C, 53.68; H, 4.30; N, 3.27.

cis-**12,13-Dicarbethoxy-6,11-dihydro-6,11-ethanoacridizinium Perchlorate** (VI).—One gram of the dicarboxylic acid perchlorate III was esterified by refluxing it for 29 hours in 240 ml. of 1% ethanolic hydrogen chloride. The solvent was removed under vacuum and the residue crystallized from water as long, colorless rectangular prisms, m.p. 255.5–256.5°, yield 0.71 g. (62%). The analytical sample was crystallized from ethanol, m.p. 262–263°. An ultraviolet absorption maximum was observed at 262 mμ (log ε 3.78), minimum 241 mμ (log ε 3.51). Infrared absorption peaks were observed at 5.70 and 5.79 μ.

Anal. Calcd. for $C_{21}H_{22}ClNO_8$: C, 55.93; H, 4.92; N, 3.12. Found[15]: C, 55.55; H, 4.95; N, 3.19.

cis-**12,13-Dicarbomethoxy-6,11-dihydro-6,11-ethanoacridizinium Perchlorate** (VII).—One gram of the dicarboxylic acid perchlorate III was esterified in methanol essentially as in the case of the preparation of the homolog. The product crystallized from water upon addition of perchloric acid and was collected and recrystallized from methanol (Norite) as colorless crystals, m.p. 243–244°, yield 0.5 g. (47%). The analytical sample was crystallized from methanol as colorless irregular plates, m.p. 249–250°. An ultraviolet absorption maximum was observed at 263 mμ (log ε 3.76), minimum at 2.41 mμ (log ε 3.49). An infrared absorption peak was observed at 5.72 μ.

Anal. Calcd. for $C_{19}H_{18}ClNO_8$: C, 53.84; H, 4.28; N, 3.31. Found[15]: C, 53.79; H, 4.26; N, 3.35.

12- or 13-Cyano-6,11-dihydro-6,11-ethanoacridizinium Perchlorate.—Three grams of acridizinium bromide, 40 ml. of acrylonitrile and 5 ml. of acetic acid were refluxed for five days. At the end of this period nearly all of the low-boiling material was removed by distillation at 30 mm. pressure, the residue was dissolved in water, and perchloric acid added. The yellow-white gum gradually solidified and was collected, m.p. 176–180°, yield 2.00 g. (52%).

Best separation of this mixture was obtained by dissolving it in 150 ml. of boiling ethanol and allowing it to cool slowly to room temperature. In this way 0.58 g. of microscopic colorless rectangular plates was obtained, m.p. 204–204.5°. An ultraviolet absorption maximum was found at 261 mμ (log ε 3.68), minimum 239 mμ (log ε 3.41). Attempts to obtain a pure product from the mother liquors were unsuccessful.

Anal. Calcd. for $C_{16}H_{13}ClN_2O_4$: C, 57.65; H, 3.93; N, 8.42. Found: C, 57.38; H, 4.09; N, 8.33.

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(10) All melting points were determined on the Fisher–Johns block and are not corrected. Except as noted all analyses were by Micro-Tech. Laboratories, Skokie, Ill.

(11) Distillations Products Industries.

(12) In each the first value reported is for the product by procedure a and the second by procedure b.

(13) B.p. 100–101° (17 mm.), prepared by the silver salt method; *cf.* A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed., Longmans, Green and Co., London, 1956, p. 388.

(14) The low yield may be due in part to the formation of some of the *cis* isomer, but the yellow color and fluorescence of the crude product indicated that at least part of the starting material was unchanged.

(15) Analysis by Galbraith Laboratories, Knoxville, Tenn.