Some Quinoline Azo- and Diazoamino Compounds

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Amino- and mono-C-methylaminoquinolines couple with benzenediazonium chloride to give phenylazoaminoquinolines under conditions which would favor the formation of diazoamino compounds. 1-Phenyl-3-quinolyltriazenes are formed from the coupling reaction of aniline with quinolinediazonium chlorides. The triazenes undergo scission upon treatment with acid to give rearrangement products or the production of an aminoquinoline and phenol. Trapping experiments on the diazo compound formed during the scission reaction indicate that the only diazo compound formed is benzenediazonium chloride.

In the course of a program of synthesis relating chemical structure and carcinogenic activity of heterocyclic derivatives of some aromatic azo compounds it was necessary to investigate some phenylazo- and phenyldiazoaminoquinolines.

The coupling reaction of benezenediazonium chloride with aminoquinolines to yield phenylazoaminoquinolines has previously been investigated.[1-3] 1-Phenyl-3-quinolyltriazenes have not been previously investigated.

The coupling reactions of benzenediazonium chloride with the amino- and mono-C-methylaminoquinolines were performed under conditions favorable for the formation of diazoamino compounds.[4] In no case, however, were any diazoamino compounds observed, nuclear coupling being the only reaction. The position of coupling is shown in Table I.

TABLE I

COUPLING POSITION OF BENZENEDIAZONIUM CHLORIDE WITH AMINO- AND MONO-C-METHYLAMINOQUINOLINES

Substituent on quinoline nucleus	Coupling position
5-NH_2	8
8-NH_2	5
6-NH_2	5
5-NH_2, 6-Me	8
8-NH_2, 7-Me	5
5-NH_2, 8-Me	6
8-NH_2, 4-Me	7, 5

The products of the coupling reaction of 5- and 8-aminoquinoline with benzenediazonium chloride are consistent with those reported by Renshaw.[1] Knueppel[2] coupled 6-aminoquinoline with benzenediazonium chloride and obtained a diazoamino compound and Renshaw reported the same coupling product as the present authors but with a higher melting point. Infrared and nmr spectral data are consistent with the structures reported. Reduction of the coupling product with sodium hydrosulfite gave 5,6-diaminoquinoline and aniline as the only products. 5-Amino-6-methyl-8-phenylazoquinoline, from the coupling reaction with 5-amino-6-methylquinoline, gave 5,8-diamino-6-methylquinoline upon reduction with sodium hydrosulfite.[5] A monohydrochloride of the azo compound has been reported by Petrow and Sturgeon.[6]

ortho coupling was observed when the position *para* to the amino group on the quinoline nucleus was blocked by a methyl substituent. 5-Amino-8-methylquinoline coupled at the 6 position and upon reduction with sodium hydrosulfite gave 5,6-diamino-8-methylquinoline. This was confirmed by nmr spectra and a condensation with benzil, typical of *ortho* diamines. The 4-methyl group in lepidine apparently exerts a steric hindrance to coupling in the 5 position as coupling in the 7 position occurs in the ratio 5:1.

The amino- and mono-C-methylaminoquinolines were diazotized using standard procedures, and coupled with aniline under conditions favorable for the formation of diazoamino compounds.[4] In every case the expected diazoamino compound was isolated; the products are summarized in Tables II and III. None of the diazoamino compounds has been previously reported with the exception of 1-phenyl-3-(6-quinolyl)-triazene. The compound isolated by the present authors has a higher melting point than that reported by Knueppel,[2] but has the same chemical characteristics.

Rearrangement of the diazoamino compounds was carried out by a procedure similar to that used by Kidd.[7] After the rearrangement the reaction mixtures were neutralized with ammonium hydroxide and the products were isolated. The results of the rearrangements are shown in the Table III.

In every case in which rearrangement was observed there was a *para* position free on the quinoline nucleus. No rearrangement was observed to an *ortho* position when the position *para* to the diazoamino link was occupied. In VI and VII, the products were the corresponding aminoquinoline and phenol from the triazene. With II no reaction was observed. In none of the reactions were any quinolylazoanilines observed. In separate experiments swamped with aniline and aniline hydrochloride the same results were observed.

Decomposition of the diazoamino derivatives in the presence of β-naphthol[7] gave, in each case except II, the aminoquinoline and 1-phenylazo-2-naphthol.

Experimental Section

Microanalyses were performed by Crobaugh Laboratories, Charleston, W. Va., and by Mr. Daryl Sharp, University of Kentucky. Melting points were taken on a Fisher-Johns melting point block and are uncorrected. Infrared spectra were run on a Beckman IR-8 or a Perkin-Elmer Model 21 spectrophotometer. Nmr spectra were determined with a Varian A-60 spectrometer using tetramethylsilane as internal standard.

Aminoquinolines and Mono-C-methylaminoquinolines.—5-, 6-, and 8-aminoquinoline were prepared by low-pressure hydro-

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(3) B. W. A. Jacobs and M. Heidelberger, *J. Am. Chem. Soc.*, **42**, 2284 (1920).

(4) H. Zollinger, "Azo and Diazo Chemistry," Interscience Publishers, Inc., New York, N. Y., 1961, p 177.

(5) R. Long and K. Schofield, *J. Chem. Soc.*, 3161 (1953).

(6) V. Petrow and B. Sturgeon, *ibid.*, 570 (1954).

(7) H. V. Kidd, *J. Org. Chem.*, **2**, 198 (1937).

TABLE II

TRIAZENES PREPARED

Triazene	Yield, %	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
I	45	161.5–163	$C_{15}H_{12}N_4$	72.56	4.87	22.57	72.68	4.91	22.39
II	58	195–196	$C_{15}H_{12}N_4$	72.56	4.87		72.43	4.80	
III	60	133–135	$C_{15}H_{12}N_4$	72.56	4.87		72.52	5.05	
IV	62	131–134	$C_{16}H_{14}N_4$	73.26	5.38		73.23	5.32	
V	19	168–69	$C_{16}H_{14}N_4$	73.26	5.38	21.36	73.38	5.49	21.40
VI	53	149.5–151	$C_{16}H_{14}N_4$	73.26	5.38	21.36	73.22	5.51	21.49
VII	73	139–141	$C_{16}H_{14}N_4$	73.26	5.38		73.13	5.56	

TABLE III

REARRANGEMENT OF THE DIAZOAMINO COMPOUNDS

Triazene reacted (no.)	Products
1-Phenyl-3-(5-quinolyl)triazene (I)	5-Amino-8-phenylazoquinoline
1-Phenyl-3-(6-quinolyl)triazene (II)	Starting material
1-Phenyl-3-(8-quinolyl)triazene (III)	5-Phenylazo-8-aminoquinoline
1-Phenyl-3-[5-(6-methylquinolyl)]-triazene (IV)	5-Amino-6-methyl-8-phenylazoquinoline
1-Phenyl-3-[8-(7-methylquinolyl)]-triazene (V)	5-Phenylazo-7-methyl-8-aminoquinoline
1-Phenyl-3-[5-(8-methylquinolyl)]-triazene (VI)	5-Amino-8-methylquinoline
	Phenol
1-Phenyl-3-(8-lepidyl)triazene (VII)	8-Aminolepidine
	Phenol

genation (palladium–carbon) of the commercially available nitroquinolines. 5-Amino-6-methyl-, 5-amino-8-methyl-, 8-amino-7-methylquinoline, and 8-aminolepidine were prepared by the reduction of the nitro compounds, which were prepared by the nitration of the commercially available methyl compounds.

5-Amino-8-phenylazoquinoline.—A solution of 1.3 g of aniline in 10 ml of water and 3.3 ml of hydrochloric acid was cooled to 0°. A solution of 0.70 g of sodium nitrite in 3 ml of water was added dropwise with stirring, the temperature of the solution being kept below 5° with an ice bath. Stirring was continued for 30 min after the addition of sodium nitrite.

A solution of 3.4 g of sodium acetate in 20 ml of water was added and the solution was stirred for 10 min. A solution of 2 g of 5-aminoquinoline in 10 ml of ethanol was added dropwise and the mixture was stirred for 1 hr. The crude material which separated was filtered, washed with water, and dried. The crude azo compound was dissolved in 50 ml of benzene and chromatographed on an alumina column. The dye was recrystallized from ethanol to give 2.1 g (63.5%) of lustrous needles: mp 207.5–208°;[1,2] nmr (δ, ppm) 8.88 (2-H, q), 7.15 (3-H, q), 8.15 (4-H, q), 4.81 (5-NH_2, s), 6.78 (6-H, d), 7.98 (7-H, d); $J_{2,3}$ = 4.1 cps, $J_{2,4}$ = 1.8 cps, $J_{3,4}$ = 8.7 cps, $J_{6,7}$ = 8.3 cps.

6-Amino-5-phenylazoquinoline.—A diazotized solution of 6.5 g of aniline was coupled with 6-aminoquinoline as in the procedure above. The crude product was chromatographed in Skelly B on an alumina column and the solid was recrystallized from ethanol. The yield of bright orange needles was 10.7 g (62%): mp 144–146°; nmr (δ, ppm) 8.58 (2-H, q), 7.31 (3-H, q), 9.03 (4-H, q), 7.40 (6-NH_2, s), 6.90 (7-H, d), 6.90 (8-H, d); $J_{2,3}$ = 4.0 cps, $J_{2,4}$ = 2.0 cps, $J_{3,4}$ = 9.0 cps, $J_{7,8}$ = 8.5 cps.

Anal. Calcd for $C_{15}H_{12}N_4$: C, 72.56; H, 4.87. Found: C, 72.77; H, 5.14.

Sodium hydrosulfite reduction of the azo compound in water gave only aniline and 5,6-diaminoquinoline as products upon isolation.

8-Amino-5-phenylazoquinoline.—A solution of 6.5 g of aniline was diazotized in the normal manner and coupled with 10 g of 8-aminoquinoline to yield the crude dye. The azo compound was recrystallized from 50% ethanol to give 6.8 g (41%) of bright needles: mp 133–134°; nmr (δ, ppm) 8.88 (2-H, q), 7.50 (3-H, q), 9.28 (4-H, q), 7.90 (6-H, d), 6.8 (7-H, d), 5.50 (8-NH_2, s); $J_{2,3}$ = 4.5 cps, $J_{2,4}$ = 2.0 cps, $J_{3,4}$ = 8.5 cps, $J_{6,7}$ = 7.5 cps.

5-Amino-6-methyl-8-phenylazoquinoline.—A diazotized solution of 2.3 g of aniline was coupled with 4 g of 5-amino-6-methylquinoline in the normal manner. Recrystallization of the crude product from ethanol yielded 4.2 g (64%) of the azo dye. An analytical sample chromatographed on an alumina column in benzene yielded a product: mp 106–107°; nmr (δ, ppm), 8.91 (2-H, q), 7.25 (3-H, q), 8.18 (4-H, q), 5.00 (5-NH_2, s), 2.25 (6-CH_3, s), 7.85 (7-H, s); $J_{2,3}$ = 3.4 cps, $J_{2,4}$ = 2.2 cps, $J_{3,4}$ = 8.5 cps. The infrared and nmr spectra are consistent with the present structure. An independent synthesis of the monohydrochloride by the method of Petrow and Sturgeon[6] and treatment of the hydrochloride with dilute ammonium hydroxide yielded a product identical with the one reported above.

Reduction of the azo compound with sodium hydrosulfite yielded aniline and 5,8-diamino-6-methylquinoline as the only products.

8-Amino-7-methyl-5-phenylazoquinoline.—A solution of 5.9 g of aniline was diazotized and coupled with 10 g of 7-methyl-8-aminoquinoline in the normal manner. The azo compound was recrystallized from ether to yield long, red needles, mp 147–148°, which weighed 12.3 g (75%): nmr (δ, ppm) 8.58 (2-H, q), 7.20 (3-H, q), 9.10 (4-H, q), 7.73 (6-H, s), 2.12 (7-CH_3, s), 5.10 (8-NH_2, s); $J_{2,3}$ = 3.8 cps, $J_{2,4}$ = 2.0 cps, $J_{3,4}$ = 8.3 cps. Reduction of the azo compound with stannous chloride–hydrochloric acid gave a compound identified as 5,8-diamino-7-methylquinoline by independent synthesis.

Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38. Found: C, 73.12; H, 5.46.

5-Amino-8-methyl-6-phenylazoquinoline.—A diazotized solution of 5.9 g of aniline was coupled with 10 g of 5-amino-8-methylquinoline in the normal manner. The crude dye which separated was recrystallized from ethanol to give 5.3 g (32%) of a red solid: mp 144–146°; nmr (δ, ppm) 8.82 (2-H, q), 7.18 (3-H, q), 8.10 (4-H, q), 6.2 (5-NH_2, s), 7.84 (7-H, s), 2.62 (8-CH_3, s); $J_{2,3}$ = 3.8 cps, $J_{2,4}$ = 2.0 cps, $J_{3,4}$ = 9.0 cps.

Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38. Found: C, 73.10; H, 5.33.

Sodium hydrosulfite reduction of the product gave aniline and a yellow solid melting over 285°. The solid was condensed with benzil by the procedure of Hall and Turner[8] to give a product, mp 218–220°. The infrared and nmr spectra confirm the structure of the product.

8-Amino-5-phenylazolepidine and 8-Amino-7-phenylazolepidine.—A solution of 6.5 g of aniline was diazotized in the normal manner and coupled with 11 g of 8-aminolepidine and allowed to stand. A dark red oil which solidified upon standing separated. The crude solid was dissolved in benzene and chromatographed on an alumina column to give two, bright red bands. The first fraction eluted with benzene was 5-phenylazo-8-aminolepidine weighing 1.3 g: mp 133–134°; nmr (δ, ppm) 8.13 (2-H, d), 6.78 (3-H, d), 2.55 (4-CH_3, s), 7.45 (6-H, d), 6.48 (7-H, d), 4.50 (8-NH_2, bs); $J_{2,3}$ = 4.2 cps, $J_{6,7}$ = 8.6 cps.

Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38. Found: C, 73.09; H, 5.23.

The second fraction was 7-phenylazo-8-aminolepidine weighing 6.7 g: mp 153–154°; nmr (δ, ppm) 8.12 (2-H, d), 6.79 (3-H, d), 2.14 (4-Me, s), 6.72 (5-H, d), 7.52 (6-H, d), 4.8 (8-NH_2, vb); $J_{2,3}$ = 4.2 cps, $J_{5,6}$ = 9.4 cps.

Anal. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38. Found: C, 73.30; H, 5.37.

Sodium hydrosulfite reduction of the 7-phenylazo isomer yielded 7,8-diaminolepidine, but no reduction product could be isolated from the 5 isomer.

1-Phenyl-3-quinolyltriazenes were prepared as illustrated by the following procedure.

1-Phenyl-3-(5-quinolyl)triazene (I) (Sample Procedure).—A solution of 2 g of 5-aminoquinoline in 3.5 ml of hydrochloric acid and 15 ml of water was cooled to 0°. A solution of 0.72 g of sodium nitrite in water was added dropwise with stirring over 20 min. A solution of 3.4 g of sodium acetate in 25 ml of water was added maintaining the temperature at 0–5° and stirring for 15 min. To this was added 1.3 g of aniline in 10 ml of ethanol

(8) D. M. Hall and E. E. Turner, *J. Chem. Soc.*, 699 (1945).

with stirring. The crude solid which separated was filtered, dissolved in benzene, and chromatographed on an alumina column. The eluted solid was recrystallized from a benzene–hexane mixture to yield 1.55 g (45%) of yellow needles, mp 161.5–163°. Sodium hydrosulfite reduction of the diazoamino compound yielded only aniline and 5-aminoquinoline as products. Analyses and melting points for the triazenes are in Table II.

Rearrangement of 1-Phenyl-3-(5-quinolyl)triazene in Hydrochloric Acid (Typical Procedure).—A solution of 2 g of the diazoamino compound in 40 ml of ethanol was added to 40 ml of 50% hydrochloric acid at 0°. The solution was maintained at the temperature for 3 hr with intermittent shaking and placed in a refrigerator for 3 days. The reaction mixture was poured on ice and neutralized with ammonium hydroxide. The solid which separated was dissolved in benzene and chromatographed on an alumina column to yield 5-amino-8-phenylazoquinoline as the only product.

Determination of the Diazo Compounds Formed in the Rearrangement of 1-Phenyl-3-(5-quinolyl)triazene (Typical Trapping Procedure).—A solution of 2 g of the diazoamino compound in 25 ml of concentrated hydrochloric acid was allowed to stand at 0° for 1 hr. The mixture was then poured on ice and run slowly into a cold solution of naphthol in dilute sodium hydroxide and stirred for 1 hr at 0°. The mixture was then acidified and the precipitate was filtered and dried. The acid-insoluble product was 1-phenylazo-2-hydroxynaphthalene. When the solution was basified with sodium hydroxide 5-aminoquinoline was recovered.

Registry No.—I, 7771-16-6; II, 7731-50-2; III, 7775-90-8; IV, 7731-51-3; V, 7731-52-4; VI, 7731-53-5; VII, 7775-86-2; 5-amino-8-phenylazoquinoline, 7731-54-6; 6-amino-5-phenylazoquinoline, 7731-55-7; 8-amino-5-phenylazoquinoline, 7771-17-7; 5-amino-6-methyl-8-phenylazoquinoline, 7731-56-8; 8-amino-7-methyl-5-phenylazoquinoline, 7731-57-9; 5-amino-8-methyl-6-phenylazoquinoline, 7731-58-0; 8-amino-5-phenylazolepidine, 7731-59-1; 8-amino-7-phenylazolepidine, 7731-60-4.

Diels–Alder Reactions of Indene

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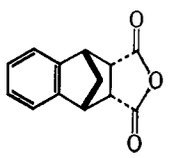
Details have been added to the indene–maleic anhydride reaction as well as a description of the *exo* adduct (II). The correct structure for the adduct with azodiformate is presented (VI). The reaction of indene with tetracyanoethylene leads to the cyclobutane (VIII) and pyrolysis of the latter is shown to lead, by a novel process, to the benzoquinoline (X). An interpretation of the reaction of indene and substituted indenes with two molecules of acetylene dicarboxylate is presented. The two different courses of the reaction are directed by a methyl substituent on the indene.

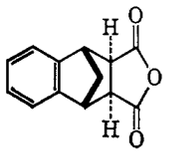
We have been interested for several years in the Diels–Alder reaction of indene. Our attention was drawn to this subject when it was found that the imide derived from the known maleic anhydride–indene adduct (I)[3] had strong sedative action of a



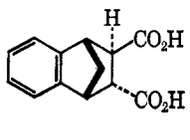
I

unique kind.[4] The reactions of indene with maleic anhydride,[3] dimethyl acetylenedicarboxylate,[3] and diethyl azodiformate[5,6] appear in the voluminous catalog of examples studied by Diels and Alder. Having already shown the structure of the acetylenedicarboxylate adduct to be XIa,[7] we now wish to comment on its chemistry, to add some details to the indene maleic anhydride reaction, to present the correct structure of the azodiformate adduct, and to describe the reaction of indene with tetracyanoethylene.

Alder and co-workers[3] have reported the preparation of both *endo* (I) and *exo* (II) isomers of the indene–maleic anhydride adduct. The former was prepared by a reaction of the olefin and the anhydride in benzene solution at 250°,[8] while the latter was obtained by esterification of I, alkaline epimerization to the *trans* diester, saponification, and pyrolysis of the resultant acid (III) at 260°. Repetition of these reactions indicated that the Alder *exo* compound (mp 159°) was a 1:1 mixture of I and II which could be separated by vapor phase chromatography. The actual *exo* isomer (until now not described) was shown to possess mp 252–253° and to be produced in small quantity in the preparation of the *endo* isomer. The formation of the *endo* compound (I) was improved in yield (42%) and in convenience by carrying out the Diels–Alder reaction in tetralin solution at 198° for 4.5 hr in the presence of a small amount of hydroquinone.



II



III

Resolution of the above problem of *endo–exo* isomerism was greatly aided by the use of proton magnetic resonance spectroscopy. In view of the difference of the magnetic environment of the hydrogens α to the carboxyl groups in *trans* diacid III, their pmr signals are distinct and characteristic of their stereochemical configuration. The spectrum of a solution of the acid in 1 *N* sodium deuterioxide in deuterium oxide revealed the *endo* hydrogen as a doublet of triplets at 3.03 ppm (from tetramethylsilane) and the

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(2) Indiana University, Bloomington, Ind.

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(8) *Cf.* J. A. Berson and G. B. Aspelin, *Tetrahedron*, **20**, 2697 (1964).