and shaken at constant temperature until no further drop in hydrogen pressure was noted.

The reaction mass was filtered to remove the catalyst and the liquid product was carefully fractionated or recrystallized. (See Table I for the data.) The fractionizations were carried out with a 10-plate, glass helices-packed column. A Corad head was used with the column.

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NORTH TEXAS STATE COLLEGE
DENTON, TEX.

## Analogs of 4-(*p*-Dimethylaminostyryl)-quinoline[1]

CARL TABB BAHNER AND ROBERT NEELY

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The anti-tumor activity of 4-(*p*-dimethylaminostyryl)quinoline(I)[2-5] and 1-(*p*-dimethylaminostyryl)naphthalene[6] encouraged us to synthesize several analogous compounds in which a nitrogen atom occupies the place of one of the carbons in the ethylene bridge. *N*-(*p*-Dimethylaminophenyl)quinoline-4-aldimine did not produce regression or significant inhibition of the growth of Lymphoma 8 tumors in rats, either when the compound was mixed in the diet or administered by subcutaneous injection of a solution in vegetable oil, although identical concentrations of I brought about prompt regression of similar tumors.[7] The following new compounds have not yet been tested against tumors.

### EXPERIMENTAL

*N*-(*p*-Dimethylaminophenyl)naphthalene-1-aldimine. A mixture of 22 g. of *p*-aminodimethylaniline and 24.8 g. $\alpha$-naphthaldehyde was heated 5 hr. at 135°. The product was recrystallized from ethyl acetate, from isohexane, and four times from isopropyl ether to yield 7.4 g. (17%) dark yellow crystals, m.p. 77–79°.

*Anal.*[8] Calcd. for $C_{19}H_{18}N_2$: C, 83.20; H, 6.57. Found: C, 83.08, 82.82; H, 6.57, 6.76.

*N*-(*p*-Dimethylaminophenyl)pyridine-4-aldimine. A mixture of 8.6 g. of pyridine-4-aldehyde and 10.9 g. of *p*-dimethylaminoaniline was heated 45 min. at 105°. The dirty green crystals were recrystallized twice from isopropyl ether to give 8.5 g. (47%) of light yellow crystals, m.p. 195°.

(1) The research was aided by a grant from the American Cancer Society.

(2) H. Gilman and G. Karmas, *J. Am. Chem. Soc.*, **67**, 342 (1945).

(3) M. R. Clapp and R. S. Tipson, *J. Am. Chem. Soc.*, **68**, 1332 (1946).

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(7) We are indebted to Dr. Margaret Reed Lewis, Dr. Boland Hughes, and Mr. Aubrey L. Bates for testing the compounds at the Wistar Institute of Anatomy and Biology, with the aid of a grant from the National Cancer Institute.

(8) Analyses by Drs. G. Weiler and F. B. Strauss, Oxford, England.

*Anal.* Calcd. for $C_{14}H_{15}N_3$: C, 74.68; H, 6.71. Found: C, 74.75; 74.75; H, 6.79, 6.59.

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CARSON-NEWMAN COLLEGE
JEFFERSON CITY, TENN.

## 4-[4-(*p*-Dimethylaminophenyl)-1,3-butadienyl]quinoline[1]

CARL TABB BAHNER AND JOHN N. FAIN

*Received January 14, 1957*

The activity of 4-(*p*-dimethylaminostyryl)quinoline[2,3] and 4-(*p*-dimethylaminostyryl)quinoline methiodide[4] in causing regression of Lymphoma 8[5] tumors in rats encouraged the authors to synthesize the corresponding compounds in which the ethylene bridge is replaced by a butadiene bridge. The antitumor activity of the compounds has been investigated at the Wistar Institute of Anatomy and Biology through the cooperation of Dr. Margaret Reed Lewis, Dr. Boland Hughes, and Aubrey L. Bates, with the assitance of a grant from the National Cancer Institute. 4-[4-(*p*-Dimethylaminophenyl)-1,3-butadienyl]quinoline did not seem exceptionally toxic but had little or no effect on Lymphoma 8 when fed at a concentration of 0.03% in the diet. The methiodide, however, seemed more toxic than 4-(*p*-dimethylaminostyryl)quinoline methiodide.

### EXPERIMENTAL

*4-[4-(p-Dimethylaminophenyl)-1,3-butadienyl]quinoline.* A mixture of 10.3 g. (0.059 mole) of *p*-dimethylaminocinnamaldehyde,[6] 8.5 g. (0.059 mole) of lepidine, and 2.1 g. (0.03 mole) of anhydrous zinc chloride was heated 8 hr. at 120°. The resulting tar was washed thoroughly with concentrated ammonium hydroxide and crystallized from ethanol. The 7 g. of crude product was recrystallized twice from ethyl acetate to obtain 1.3 g. of brown crystals, 7%, m.p. 165–166°.

*Anal.*[7] Calcd. for $C_{21}H_{20}N_2$: C, 83.95; H, 6.77. Found: C, 83.74, 83.82; H, 6.59, 6.51.

*4-[4-(p-Dimethylaminophenyl)-1,3-butadienyl]quinoline methiodide.* A mixture of 15 g. (0.080 mole) of *p*-dimethylamino cinnamaldehyde and 22.5 g. (0.079 mole) of lepidine methiodide was poured into 500 ml. of boiling acetic an-

(1) This project was aided by a grant from the American Cancer Society.

(2) H. Gilman and G. Karmas, *J. Am. Chem. Soc.*, **67**, 342 (1945).

(3) M. A. Clapp and R. S. Tipson, *J. Am. Chem. Soc.*, **68**, 1332 (1946).

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(7) Analyses were carried out by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

hydride. The mixture was refluxed 30 min., cooled, and filtered after standing. The crystals were recrystallized repeatedly from methanol; m.p. 256°. They were slightly soluble in water, more soluble in alcohol. The water solution was cherry red. The alcohol solution was deep blue. The absorption spectra of these and other compounds are to be presented in a separate paper. Even though the analytical sample was dried 1 hr. at 95° at 0.05 mm. the analysis indicated that the compound was a monohydrate.

*Anal.* Calcd. for $C_{22}H_{25}IN_2O$: C, 57.39; H, 5.47; I, 27.57. Found: C, 57.06; H, 5.10; I, 27.43, 27.30. (Other samples: C, 57.45, 56.99, 57.68, 57.93; H, 4.96, 5.69, 5.48, 5.74.)

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JEFFERSON CITY, TENN.

## Quaternary Salts Similar to 4-(*p*-Dimethylaminostyryl)quinoline Methiodide[1]

CARL TABB BAHNER, JOHN DALE, JOHN FAIN, EDGAR FRANKLIN, J. C. GOAN, WILLIAM STUMP, MARY WEST, AND JOAN WILSON

*Received January 14, 1957*

Although 4-(*p*-dimethylaminostyryl)quinoline[2,3] was more potent than 4-(*p*-dimethylaminostyryl)-quinoline methiodide[4] in causing regression of Lymphoma 8 tumors in rats,[5] the latter was less toxic. For this reason a number of similar quaternary salts have been prepared for testing against this and other tumors.

Preliminary tests by Dr. Margaret Reed Lewis, Dr. Boland Hughes, and Aubrey L. Bates at the Wistar Institute of Anatomy and Biology[6] indicate that 4-(*p*-dimethylaminostyryl)quinoline propiodide shares the activity of the methiodide and ethiodide in producing regression of Lymphoma 8 tumors in rats, and that 2-(*p*-fluorostyryl)quinoline methiodide is inactive under the same conditions. Tests on the other compounds are not yet complete.

### EXPERIMENTAL

Most of the compounds were prepared by adding a mixture of equimolar amounts of the *p*-aminobenzaldehyde and the lepidine methiodide (or propiodide) to boiling acetic anhydride and refluxing 30 min. (Method A). After cooling, the crystals were recovered and recrystallized from methanol. A few of the preparations were carried out by refluxing the reactants 4 hr. in methanol with piperidine catalyst (Method B). The dialkylamino compounds were purple-black, except the brown-black 4-(*p*-dimethylaminostyryl)-3-methylquinoline. The *4-(p-acetamidostyryl)quinoline methiodide* was orange and the *p*-fluorostyryl compounds were tan. The compounds melted with decomposition. The melting points were determined by rapid heating.

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JEFFERSON CITY, TENN.

TABLE I

QUATERNARY SALTS

| Compound | Method | Yield, % | M.P., °C. | Analyses[a] Calcd. C | Calcd. H | Found C | Found H |
|---|---|---|---|---|---|---|---|
| **Methiodides** | | | | | | | |
| 4-(*p*-Dimethylaminostyryl)-6-iodoquinoline[b] | A | 21 | 307–308 | | [c] | | |
| 4-(*p*-Dimethylaminostyryl)-3-methylquinoline | A | 72 | 284–285 | 58.61 | 5.39 | 58.75, 58.85 | 5.25, 5.23 |
| 4-(*p*-Dimethylaminostyryl)-8-methylquinoline | A | 68 | 272 | 58.61 | 5.39 | 58.62, 58.36 | 5.36, 5.28 |
| 4-(*p*-Dimethylaminostyryl)-8-phenylquinoline | A | 15 | 231–232 | 63.42 | 5.12 | 63.44, 63.28 | 5.05, 5.21 |
| 4-(*p*-Dimethylaminostyryl)-5,6-benzoquinoline[d,e] | B | 36 | 241 | 59.51[f] | 5.20 | 59.38, 59.55 | 4.97, 5.07 |
| 2-(*p*-Dimethylaminostyryl)-5,6-benzoquinoline[d] | A | 39 | 253 | 59.51 | 5.20 | 59.33, 59.14 | 5.01, 4.90 |
| 4-(*p*-Acetamidostyryl)quinoline[g] | B | 45 | 320 | 55.82 | 4.45[h] | 55.70, 55.81 | 4.55, 4.53 |
| 4-(*p*-Nitrostyryl)quinoline | B | 79 | 260 | 51.69 | 3.62 | 51.76, 51.55 | 4.18, 4.12 |
| 4-(*p*-Fluorostyryl)quinoline | B | 4 | 237 | | [i] | | |
| 2-(*p*-Fluorostyryl)quinoline | B | 50 | 249 | 55.25 | 3.84 | 55.16, 54.98 | 4.00, 3.98 |
| 2-(*p*-Dimethylaminostyryl)-5-methylpyrazine[j] | B | | 237–238 | 50.40 | 5.29[k] | 50.25, 50.43 | 5.44, 5.22 |
| **Propiodide** | | | | | | | |
| 4-(*p*-Dimethylaminostyryl)quinoline | A | | 226 | | [l] | | |

[a] Carbon, hydrogen, and nitrogen analyses were carried out by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Iodine was determined by the Volhard Method. [b] Recrystallized from 50% methanol. [c] Calcd.: I, 46.82; Found: (Carius Method) I, 46.95, 46.78. [d] Monohydrate. [e] Recrystallized from methanol and from isopropyl alcohol. [f] Calcd.: I, 26.20; Found; I, 26.01, 26.28. [g] Crude product was dissolved in hot 8*N* acetic acid and precipitated by neutralizing with ammonia. Recrystallized from methanol. [h] Calcd.: N, 6.51; Found: N, 6.54. [i] Calcd.: I, 32.44; Found: I, 32.50. [j] Recrystallized from methanol and from isopropyl alcohol. 2,5-Dimethylpyrazine was donated by Wyandotte Chemicals Corp., Wyandotte, Mich. [k] Calcd.: N, 11.02; Found: N, 10.59. [l] Calcd.: I, 28.56; Found: I, 28.7, 28.9.

(1) Aided by grants from the Research Corporation, the Medical Research Foundation, and the American Cancer Society.

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(3) M. A. Clapp and R. S. Tipson, *J. Am. Chem. Soc.*, **68**, 1332 (1946).

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(6) Assisted by a grant from the National Cancer Institute.