the corresponding pyridine compounds. It might be that the third ring of the benzoquinolines would make them even more active. Haddow, Harris, Kon, and Roe[9] reported that 5-(*p*-dimethylaminostyryl)acridine, which may be thought of as 4-(*p*-dimethylaminostyryl)-2,3-benzoquinoline, had a slight but significant inhibitory effect on the growth of Walker 256 tumor in rats. When we attempted the synthesis of this compound, we obtained a product having the correct composition, but melting at 256° instead of 237–239°, the melting point reported by Porai-Koschitz[10] for his product.

All three benzoquinolines and most of the other compounds listed appeared active when tested against Lymphoma 8. There was a wide range, however, between 4-(*p*-dimethylaminostyryl)-3-methylquinoline and the relatively inactive 4-(*p*-dimethylaminostyryl)-6-iodoquinoline. Details of these tests, carried out at the Wistar Institute of Anatomy and Biology through the cooperation of Dr. Margaret Reed Lewis, Dr. Boland Hughes, and Mr. Aubrey Bates, and with the financial assistance of a grant from the National Cancer Institute, are to be reported elsewhere.

EXPERIMENTAL

The substituted lepidines used were prepared by reaction of substituted anilines with methyl vinyl ketone by the method of Campbell and Schaffner.[11] Methyl isopropenyl ketone furnished by the Celanese Corporation of America was used in place of methyl vinyl ketone to obtain lepidines containing a 3-methyl group.

The following method of preparing the styrylquinolines produced substantially improved yields with less inconvenience than the method we had used previously. Anhydrous zinc chloride, the lepidine, and *p*-dimethylaminobenzaldehyde were mixed in the proportion of 1 mole:2 moles:4 moles and heated 16 to 24 hr. at 110–120°. Water vapor was permitted to escape and the mixture was stirred at intervals. Chloroform, about 4 ml. per gram of starting materials, was added cautiously to the hot mass and boiled under a reflux condenser. The undissolved zinc salt was recovered by filtration, washed with more chloroform or ether, and dried. This dark red solid was triturated with excess 8*N* ammonium hydroxide and allowed to stand 1 hr. The yellow styrylquinoline liberated was washed with water and recrystallized from methanol, isopropanol, or ethyl acetate. Commercial methylpentanes were used in a Soxhlet extractor to separate the product from zinc salts and other insoluble impurities. An additional quantity of product was recovered from the chloroform solution by washing it with 8*N* sodium hydroxide until basic, then with water, drying over sodium sulfate, distilling off the solvent and excess aldehyde under vacuum, and recrystallizing the residue. The 3-methyl compounds were recovered solely from the chloroform solution, since they did not form insoluble zinc salts under the conditions employed.

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[10] A. Porai-Koschitz, *Centr.*, *II*, 1528 (1907).

[11] K. N. Campbell and I. J. Schaffner, *J. Am. Chem. Soc.*, **67**, 86 (1945).

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

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Studies[2,3] at the Wistar Institute of Anatomy and Biology and the Oak Ridge Institute of Nuclear Studies have shown that 4-(*p*-dimethylaminostyryl)quinoline (Ia)[4,5] and its methiodide (Ib)[6] administered in the diet of rats bearing Lymphoma 8 tumors brought about regression of the tumors, and that a number of related compounds showed different potencies in this respect. In order to learn the significance of structural relations, isoquinoline isomers of Ia and Ib, and other closely related isoquinoline derivatives were prepared for testing.

4-(*p*-Dimethylaminostyryl)quinazoline (III) combines structural features of Ia and IIa. Siegle and Christensen[7] were unable to isolate any 4-styrylquinazoline from the tar obtained by reaction of benzaldehyde with 4-methylquinazoline, but III was prepared readily by the method described below.

It has been reported that Ia was more effective than the corresponding 2-(*p*-dimethylaminostyryl)-quinoline compound, Ic, and Ib was more active than Id. The isoquinoline compound IIa resembles Ia in having the styryl group attached to the heterocyclic ring at a position adjacent to the benzene ring, but resembles Ic in having the styryl group attached to a carbon atom adjacent to the ring nitrogen. On the other hand IIc resembles Ic both in the fact the styryl group is attached to a carbon farther from the benzene ring and the fact that the styryl group is attached to a carbon adjacent to the ring nitrogen. Observations at the Wistar Institute of Anatomy and Biology,[8] to be

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[1] The organic syntheses reported here were supported in part by grants from the American Cancer Society, the Medical Research Foundation, and a Frederick Gardner Cottrell Grant from the Research Corporation to Carson-Newman College.

[2] B. Hughes, A. L. Bates, C. T. Bahner, and M. R. Lewis, *Proc. Soc. Exptl. Biol. Med.*, **88**, 230 (1955); M. R. Lewis, B. Hughes, C. T. Bahner, and A. L. Bates, *Growth*, **19**, 1 (1955); M. R. Lewis, B. Hughes, and A. L. Bates, *Growth*, **19**, 323 (1955).

[3] C. T. Bahner, *Cancer Research*, **15**, 588 (1955).

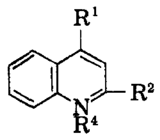
[4] H. Gilman and G. Karmas, *J. Am. Chem. Soc.*, **67**, 342 (1945).

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

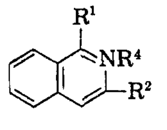
[6] C. T. Bahner, E. S. Pace, and R. Prevost, *J. Am. Chem. Soc.*, **73**, 3407 (1951).

[7] J. Siegle and B. E. Christensen, *J. Am. Chem. Soc.*, **73**, 5777 (1951).

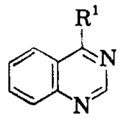
[8] These observations were made possible through the cooperation of Dr. Margaret Reed Lewis, Dr. Boland Hughes, and Mr. Aubrey Bates, and a grant from the National Cancer Institute.



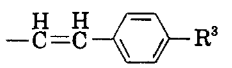
I



II



III



Y

	R^1	R^2	R^3	R^4
Ia	Y	H	$(CH_3)_2N—$	none
Ib	Y	H	$(CH_3)_2N—$	CH_3I
Ic	H	Y	$(CH_3)_2N—$	none
Id	H	Y	$(CH_3)_2N—$	CH_3I
IIa	Y	H	$(CH_3)_2N—$	none
IIb	Y	H	$(CH_3)_2N—$	CH_3I
IIc	H	Y	$(CH_3)_2N—$	none
IId	H	Y	$(CH_3)_2N—$	CH_3I
IIe	Y	H	$(CH_3CH_2)_2N—$	none
IIf	Y	H	$O(CH_2CH_2)_2N—$	none
III	Y	H	$(CH_3)_2N—$	none

published in detail elsewhere, indicated that the IIa, IIc, IIe and III were all less active than Ia against Lymphoma 8. The methiodides were less active than the corresponding free bases. The presence of the morpholino group, in IIf, in place of the dialkylamino group, reduced toxicity and activity against Lymphoma 8.

EXPERIMENTAL

3-(*p*-Dimethylaminostyryl)isoquinoline (IIc) was obtained readily from its methiodide (IId) by the method of Erlenmeyer, Baumann, and Sorkin[9] although 1-(*p*-dimethylaminostyryl)isoquinoline (IIa) was not so readily obtained from its methiodide (IIb), and 4-(*p*-diethylaminostyryl)-quinoline methiodide (Ib) decomposed to yield an unidentified liquid resembling lepidine in odor.

1-(p-Dimethylaminostyryl)isoquinoline (IIa). A mixture containing 15 g. (0.105 mole) of 1-methylisoquinoline purchased from Sapon Laboratories, 135 g. (0.90 mole) of *p*-dimethylaminobenzaldehyde and 5.3 g. (0.039 mole) of zinc chloride was heated 6 hr. at 200°, cooled somewhat and dissolved in 250 ml. of chloroform. The solution was washed with 150 ml. of 8*N* sodium hydroxide, then with water, and dried over sodium sulfate, and the solvent was removed by evaporation. Excess aldehyde was removed by distillation at an oil bath temperature of 220° and a pressure of 0.5 mm. The residue was dissolved in benzene and some impurities were thrown out by addition of isopropyl ether. The solvent was removed by distillation and the canary yellow product was crystallized four times from ethyl acetate; yield 3.0 g., 10%, m.p. 118°.[10]

Anal. Calcd. for $C_{19}H_{18}N_2$: C, 83.17; H, 6.61. Found: C, 83.06, 82.95; H, 6.60, 6.77.[11]

1-(p-Diethylaminostyryl)isoquinoline (IIe). A mixture containing 10 g. (0.07 mole) of 1-methylisoquinoline, 23 g. (0.13 mole) of *p*-diethylaminobenzaldehyde, and 9.5 g. (0.07 mole) of anhydrous zinc chloride was heated 24 hr. at 115–120°. The mixture was extracted with chloroform. The chloroform solution was washed with 8*N* sodium hydroxide, then with water, and dried over sodium sulfate. Solvent and unreacted benzaldehyde were removed by vacuum distillation and the residue was dissolved in absolute ethanol. Addition of water and chilling several days produced yellow crystals which, after repeated recrystallization from ethanol and from isohexane, melted at 93°; yield 5 g., 24%.

Anal. Calcd. for $C_{21}H_{22}N_2$: C, 83.40; H, 7.33. Found: C, 83.39, 83.25; H, 7.11, 7.31.

1-(p-N-Morpholinostyryl)isoquinoline (IIf). A mixture of 1-methylisoquinoline 18.69 g. (0.131 mole) and 25 g. (0.131 mole) *p*-*N*-morpholinobenzaldehyde[12] was heated 2.5 hours at 270–275°, permitting water vapor to escape.[13] Repeated recrystallizations from ethyl acetate, from isopropyl ether, from isohexane, and from methanol yielded 5.86 g., 14%, 1-(*p*-*N*-morpholinostyryl)isoquinoline, dark yellow crystals, m.p. 149°.

Anal. Calcd. for $C_{21}H_{20}N_2O$: C, 79.72; H, 6.37. Found: C, 79.78, 79.52; H, 6.35, 6.43.

4-(p-Dimethylaminostyryl)quinoline (III). A mixture of 4.3 g. (0.030 mole) of 4-methylquinazoline,[14] 8.6 g. (0.058 mole) of *p*-dimethylaminobenzaldehyde and 2.2 g. (0.016 mole) of zinc chloride was heated 24 hr. at 120° in a glass stoppered bottle. Unreacted aldehyde was removed by extraction with boiling chloroform and the residue was treated with excess concentrated ammonium hydroxide to liberate the free base and dissolve zinc salts. The tarry material and ammonium hydroxide were kept in contact, with occasional stirring, over a period of four days. The residue was washed with water, allowed to dry at room temperature, then ground. The product was extracted with boiling methylpentanes in a Soxhlet extractor and recrystallized twice from methanol to give bright red crystals, m.p. 138°. Yield 12%.

Anal. Calcd. for $C_{18}H_{17}N_3$: C, 78.51; H, 6.22. Found: C, 78.35, 78.58; H, 6.32, 6.20.

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[9] H. Erlenmeyer, H. Baumann, and E. Sorkin, *Helv. Chim. Acta*, **31**, 1978 (1948).

[10] All temperatures recorded are corrected.

[11] Analyses were carried out by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

[12] E. I. du Pont de Nemours & Company, British Patent 607,920, Sept. 7, 1948.

[13] R. S. Tipson, *J. Am. Chem. Soc.*, **67**, 507 (1945).

[14] M. T. Bogert and F. P. Nabenhauer, *J. Am. Chem. Soc.*, **46**, 1932 (1924).

Some Tetrasubstituted Silanes Prepared by Free Radical Addition to Alkenes

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A recent communication from this laboratory[1] has described the benzoyl peroxide-catalyzed addition of triphenylsilane to long-chain terminal-unsaturated alkenes. We have extended this synthesis to the addition of triphenylsilane to the ethylenic linkages of allyltriphenylsilane and diallyldiphenylsilane. In both cases low yields of completely saturated crystalline compounds were isolated. Unsaturation tests with bromine and with aqueous

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[1] H. Merten and H. Gilman, *J. Am. Chem. Soc.*, **76**, 5798 (1954). This paper gives references to related free radical additions.