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Received November 14, 1969.
Accepted for publication January 13, 1970.
Supported in part by Fellowship No. 1 FO1 GM-43160-01 for W.L.H. from the U.S. Public Health Service.

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Synthesis and Antibacterial Activity of 1-Styryl-3,4-dihydroisoquinolines

Keyphrases □ 1-Styryl-3,4-dihydroisoquinolines—synthesis □ Antibacterial activity—1-styryl-3,4-dihydroisoquinolines

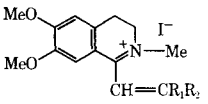
Sir:

So far, the synthesis of 1-styrylisoquinolines has been achieved either by the cyclization of the Schiff bases derived from cinnamaldehyde (1, 2) or by the condensation of 1-methylisoquinoline with aromatic aldehydes (3). In this communication, we wish to report a new procedure for the synthesis of 1-styryl-3,4-dihydroisoquinolines which were isolated as methiodide salts. The procedure involves the cyclodehydration of substituted β-phenethylamides to 3,4-dihydroisoquinolines through the Bischler-Napieralski reaction (4).

Details about the synthesis and characterization of 1-styryl-3,4-dihydroisoquinoline methiodides (Compounds 1–7) will be published (5).

The methiodide salts (Compounds 1–7) were subjected to *in vitro* screening for antimetabolites by a new method (6). In this method, the detection system utilizes the gram-positive *Bacillus subtilis* and gram-negative *Escherichia coli*. Both organisms were grown in two types of agar: nutrient agar and a completely synthetic medium with glucose as the only source of carbon.

Table I—Inhibition of *B. subtilis* Grown in Two Different Media[a]



Compound	R_1	R_2	Nutrient Agar	Synthetic Agar
1	Ph	Ph	24	35
2	Ph	*p*-Methylphenyl	25	36
3	*p*-Methylphenyl	*p*-Methylphenyl	29	35
4	*p*-Ethylphenyl	*p*-Ethylphenyl	36	39
5	*p*-Chlorophenyl	*p*-Chlorophenyl	28	35
6	Me	Ph	16	22
7	Me	Me	0	0

[a] The numbers in the body of the table are zones of growth inhibition in mm. around a 13-mm. paper disk.

These seven compounds were tested at concentrations of 1 mg./ml., and the results are presented in Table I.

The inhibition of test organism by Compounds 1–6 was stronger on synthetic agar than on nutrient agar. However, the difference was not large enough to suggest an antimetabolitelike mode of action (5). Compound 7 was essentially inactive against *B. subtilis*. None of the compounds inhibited the growth of *E. coli*. These results indicate that 1-styryl-3,4-dihydroisoquinoline methiodides possess some antibacterial activity.

A more extensive testing will be required before any structure–activity correlation can be drawn.

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Received November 24, 1969.
Accepted for publication February 3, 1970.
The work at Western Michigan University was supported by Grant CA-06140 from the National Cancer Institute. The work at The Upjohn Co. was in part supported by Contract PH 43-68-1023 with Chemotherapy, National Cancer Institute, National Institutes of Health, Bethesda, Md.