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ON THE BIOSYNTHESIS OF THE 2-n-ALKYL-4-HYDROXYQUINOLINES OF PSEUDOMONAS AERUGINOSA (SCHROET.) MIGULA

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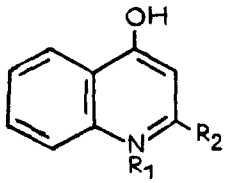
From certain strains of Pseudomonas aeruginosa (Schroet.) Migula a group of 2-n-alkyl-4-hydroxyquinolines and 2-n-alkyl-4-hydroxyquinoline-N-oxides (TABLE I) have been isolated (1-5). This paper deals with first results on the biosynthesis of these compounds.

By selection a strain of P. aeruginosa was obtained which produced in roundshaking cultures and an ammonium lactate - glucose or mannitol medium 5-15 mg 2-n-alkyl-4-hydroxyquinolines per liter. These alkaloids are mainly located in the cells. Addition of 10 mmol sodium acetate per liter or 2 mmol anthranilic acid per liter to the culture liquid gave a strong increase of the formation of these compounds.

Feeding of acetate-1-^{14}C, acetate-2-^{14}C and anthranilic acid-$^{14}COOH$ has shown incorporation of these compounds into the alkaloids. The specific incorporation rates given in TABLE II are calculated on the basis of 1 mol precursor per 1 mol formed alkaloid. Certainly there are incorporated more than 1 mol

acetate per mol alkaloid and the real incorporation rate of acetate therefore should be lower. The difference between the incorporation rates of acetate-1-^{14}C and acetate-2-^{14}C will be investigated further.

TABLE I



name	R_1	R_2
Pyo Ib	-	$-(CH_2)_6-CH_3$
Pyo Ic	-	$-(CH_2)_8-CH_3$
Pyo III	-	$-CH=CH-(CH_2)_6-CH_3$
2-n-heptyl-4-hydroxyquinoline-N-oxide	$\rightarrow O$	$-(CH_2)_6-CH_3$
2-n-octyl-4-hydroxyquinoline N-oxide	$\rightarrow O$	$-(CH_2)_7-CH_3$
2-n-nonyl-4-hydroxyquinoline-N-oxide	$\rightarrow O$	$-(CH_2)_8-CH_3$
2-n-undecyl-4-hydroxyquinoline-N-oxide	$\rightarrow O$	$-(CH_2)_{10}-CH_3$

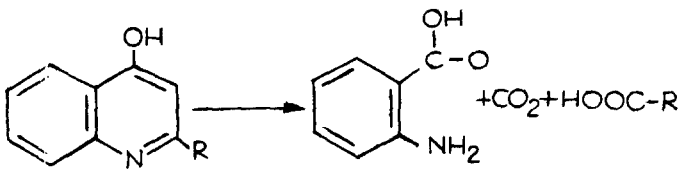
Degradation of the 2-n-alkyl-4-hydroxyquinolines by ozonisation and hydrolysis of the breakdown products gives anthranilic acid, CO_2 and fatty acids (6) (FIG. 1). In our experiments only anthranilic acid and CO_2 were isolated.

TABLE II

	precursors		isolated alkaloids		degradation products				
					anthranilic acid		CO_2		
	name/ amount	radio-activity c/min .µmol	radio-activity c/min .µmol	specific incor-poration rate	radio-activity c/min .µmol	% of the total incorp-orated radio-activity	radio-activity c/min .µmol	% of the total incorpo-rated radio-activity	% of the radio-activity in the not isolated fatty-acids
1	sodium acetate -2-^{14}C 10 mmol	$21,6.10^3$	$18,0.10^3$	83,3 %	425	2,3	4,2	0,025	97,7
2	"	$21,6.10^3$	$18,2.10^3$	84,5 %	274	1,4	4,2	0,025	98,6
3	"	$21,6.10^3$	$15,9.10^3$	73,4 %	329	2,4	5,1	0,042	97,6
4	sodium acetate -1-^{14}C 10 mmol	$35,0.10^3$	$6,4.10^3$	18,3 %	178	2,8	0,1	0,0022	97,2
5		$35,0.10^3$	$7,1.10^3$	22,3 %	233	3,3	0,6	0,0024	96,7
6		$35,0.10^3$	$6,6.10^3$	18,7 %	234	3,3	1,0	0,0026	96,7
7	anthra-nilic acid -^{14}COOH 2 mmol	450.10^3	$278,4.10^3$	62,0 %	$264,0.10^3$	94,9	938	0,35	5,8
8	"	450.10^3	$300,2.10^3$	66,7 %	$266,2.10^3$	88,8	416	0,31	11,0
9	"	450.10^3	$276,1.10^3$	56,9 %	$262,2.10^3$	95,2	899	0,35	4,5

The experiments No. 1-6 are carried out with the same cell suspension and under equal cultural conditions.

FIG. 1



2n-alkyl-4-hydroxy-quinoline | anthranilic acid | fatty acid

On the degradation of the radioactive labeled alkaloids, which are formed after feeding anthranilic acid-^{14}COOH, a very high percentage of the total radioactivity was found in the isolated anthranilic acid again (TABLE II).
After feeding acetate-^{14}C the anthranilic acid and the CO_2 obtained by degradation of the formed alkaloids were only low radioactive. Nearly all of the incorporated radioactivity in this case therefore must be localized in the not isolated fatty acids (TABLE II).
By reason of these results the quinoline nucleus of the alkaloids of P. aeruginosa may be formed from anthranilic acid and a second precursor not identified until now. The side chain in position 2 may be built up from acetate.

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