Chemistry of Heterocyclic Compounds, Vol. 33, No. 10, 1997

TRANSFORMATIONS OF QUINOLINE-3-CARBOXYLIC ACID BY THE BACTERIUM *Rhodococcus opacus*

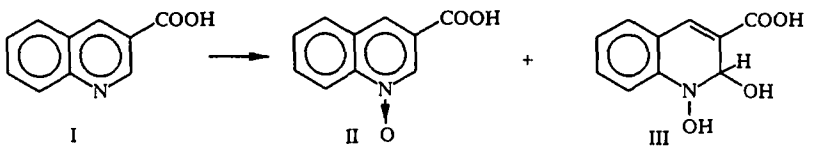
M. R. Duduchava, P. B. Terent'ev, N. F. Piskunkova, and G. A. Bulakhov

Biotransformation and biodegradation of quinolinecarboxylic acids is very important in view of the possibility of their use as intermediates for the synthesis of medicinals [1, 2] and also as intermediates in the course of degradation of toxic materials which are difficult to decompose [3].

We have investigated the transformation of quinoline-3-carboxylic acid (I) by the bacterium *Rhodococcus opacus*.

It has been shown previously that this culture transforms nicotinic acid by oxidative decarboxylation to give 3-hydroxypyridine, which was further oxidized to give 2,3-dihydroxypyridine [4].

In distinction from nicotinic acid, quinoline-3-carboxylic acid did not undergo decarboxylation: only the N-oxide II and the product of its hydration III were identified in the culture liquid:



The product yield was noticeably affected by the presence of glucose in the transformation medium. In the absence of glucose, only part of the substrate (about 65%) was transformed in 48 h, whereas all of the substrate was transformed in the presence of glucose. The presence of a sugar appears to stimulate hydroxylation, because oxidation of glucose generates reduced pyridinenucleotides which are necessary for the function of oxygenases which hydroxylate the substrate [2].

A museum culture of the bacterium *Rhodococcus opacus* VKM Ac-1333D was grown initially on Shukla synthetic medium [6], modified by Korostyleva [7], using twice distilled water and 0.15% pyridine.

The transformation substrate consisted of a suspension of nonreproducing bacteria in 10 cm^3 of 50 mmol dm^{-3} phosphate buffer of pH 7.0 at 28°C, to which was added acid I (the substrate to be transformed) (1 mmol dm^{-3}) and glucose (10 g dm^{-3} of medium). Transformation was continued for 48 h, with samples withdrawn periodically for HPLC analysis (Merck Hitachi chromatograph, reverse-phase column packed with 5 μ LiChrospher, L-4200, UV-vis detector, λ 210 nm). Water–methanol–phosphoric acid (80:20:1), rate of flow 2 cm^3/min (the UV spectrum of each compound was recorded in parallel), after which the transformation medium was centrifuged, evaporated, and analyzed.

TLC on Kieselgel 60 F 254 (Merck) strips with chloroform–methanol (1:2) and UV exposure was used to identify the transformation products. Mass spectra were recorded with an MX-1321A machine with an ionization voltage of 70 eV and direct injection into the ion source.

Quinoline-3-carboxylic Acid (I). R_f 0.56. Retention time 5.59 min. UV spectrum: λ_{max} 204, 243, 320 nm (lit data [8]: 204, 243, 320 nm). Mass spectrum:* 173 (100) (M), 156 (23) (M-OH), 155 (27) (M-H_2O), 145 (5) (M-HCN), 129 (17) (M-CO_2), 128 (41) (M-CO_2H), 127 (33) (M-CO_2H–H), 101 (18) (M-CO_2H–HCN).

*Here and below: *m/z* (rel. intensity) (route to formation of the ion).

Chemical and Biological Faculties, M. V. Lomonosov Moscow State University, Moscow 119899. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1418-1419, October, 1997. Original article submitted June 23, 1997.

 0009-3122/97/3310-1236$18.00

Quinoline-3-carboxylic Acid N-oxide (II). Yield 90%. Retention time 1.40 min, UV spectrum: λ_{max} 212, 259, 308 nm. Mass spectrum: 189 (72) (M), 173 (22) (M-O), 172 (11) (M-OH), 145 (100) (M-CO_2), 144 (17) (M-CO_2H), 129 (30) (M-CO_2−O), 102 (12) (M-CO_2−O−HCN).

1,2-Dihydroxy-1,2-dihydroquinoline-3-carboxylic Acid (III). Yield 10%. Retention time, 1.59 min. UV spectrum: λ_{max} 301 nm. Mass spectrum: 207 (35) (M), 189 (67) (M-H_2O),.178 (66) (M-CHO), 173 (100) (M-H_2O−O) (A), 156 (30) (A-OH), 155 (32) (A-H_2O), 150 (23) (M-CHO−CO), 145 (15) (A-CO_2), 144 (28) (A-CO_2H).

Under the TLC conditions, compounds II and III have the same mobility, R_f = 0.7, and were not separated.

We have developed optimum conditions for carrying out this reaction by changing the conditions for the biotransformation (temperature, pH, substrate and glucose concentration, optical density of the medium, etc.). The investigation is continuing.

REFERENCES

1. D. Dexter, Cancer Res., **45**, 5563 (1985).
2. Sung-Kee Chung and J. W. Lee, Bioorg. Med. Chem. Letters, **6**, 1309 (1996).
3. E. H. Weyand, J. Defauw, C. A. Mcqueen, C. L. Mestcher, S. K. Meegalla, and E. J. Lavoje, Food and Chem. Toxicol., **31**, 707 (1993).
4. N. S. Zefirov, L. V. Modyanova, A. Oyuuntsétség, N. F. Piskunkova, P. B. Terent'ev, V. V. Bagrov, and V. V. Ovcharenko, Khim. Geterotsikl. Soedin., No. 6, 847 (1993).
5. V. G. Debabov, Zh. V. Kh. O., **35**, 755 (1990).
6. O. P. Shukla, Indian J. Biochem. Biophys., **11**, 192 (1974).
7. L. A. Korostyleva, A. N. Kost, L. I. Borob'eva, L. V. Modyanova, P. B. Terent'ev, and N. S. Kulikov, Prikladnaya Biokhimiya i Mikrobiologiya, No. 3, 380 (1981).
8. E. Fehnel, J. Org. Chem., **23**, 1999 (1958).