(1-Methyl-3-piperidylidene)di(2-thienyl)methane. 56.2 g II was carefully added to 110 ml 85% boiling formic acid and the flask heated for 10 min. 90 ml acid were vacuum-distilled off and the residue carefully poured into saturated Na_2CO_3. The oil which separated was extracted with ether. The ether is evaporated off till dryness and the residue vacuum-distilled. Yield 44.15 g I (83.7%) bp 178–180° (6 mm). Found: C 65.82, 65.55; H 6.54, 6.29%. Calculated for $C_{15}H_{17}NS_2$. C 65.40; H 6.22%; λ_{max} 247 (in EtOH) λ min 218 mμ.

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6 January 1966 Chernyshevskii Saratov State University

SYNTHESIS AND ANTITUBERCULAR ACTIVITY OF ISONIAZONES OF SOME ALDEHYDES IN THE FURAN AND THIOPHENE SERIES

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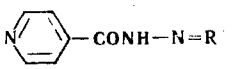
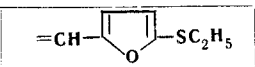
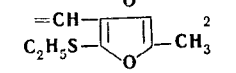
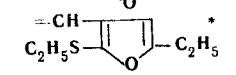
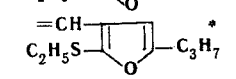
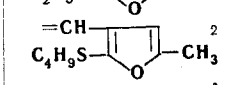
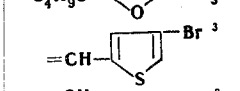
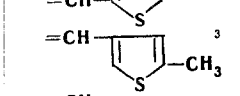
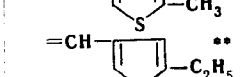
8 Isoniazones of aldehydes of the furan and thiophene series are synthesized; in vitro they all exhibited high antitubercular activity. Two compounds, 5-ethylmercaptofurfural and 2-ethylmercapto-5-n-propyl-3-furanaldehyde isoniazones showed the greatest activity.

At present the most widely used antitubercular preparations are isonicotinic acid hydrazide (isoniazid, tubazid), and its derivatives isoniazones): ftivazid, metazid, saluzid, and larusan.

The rather large number of isoniazones in practical use provides a basis for discovering other, even more effective isoniazid derivatives. In particular, it was of interest to synthesize and test for antitubercular activity, isoniazones of aldehydes of the furan

Isoniazone 

Compound number	R	Mp, °C	N, % Found	N, % Calculated	In vitro tuberculostatic activity, dilution 1 : X million: Academia strain without serum	Academia strain with serum	H 37 RV strain with serum
I		174—175	15.36	15.22	1 : 32	1 : 32	1 : 16
II		176—177.5	14.51	14.87	1 : 16	1 : 4	1 : 4
III		157—159	13.47	13.84	1 : 16	1 : 8	1 : 4
IV		113—115	13.29	13.23	1 : 32	1 : 16	1 : 16
V		129—130.5	13.13	13.24	1 : 16	1 : 8	1 : 2
VI		234—235.5	13.66	13.55	1 : 16	1 : 2	1 : 2
VII		175.5—176	16.74	17.17	1 : 16	1 : 8	1 : 8
VIII		185.5—186.5	16.24	16.20	1 : 16	1 : 8	1 : 4

*Prepared similarly to II.

**Prepared similarly to VII.

and thiophene series, recently synthesized in the heterocyclic compounds laboratory of the Institute of Organic Chemistry of the AS USSR, most of these aldehydes having a CHO group at the β position in the ring. According to some results [1], precisely such derivatives of thiophene or furan, with a functional group in the β position, have valuable pharmacological properties.

The isoniazones are obtained by refluxing together in ethanol solution, for 1–2 hr, equimolar amounts of isoniazid and aldehyde. The solution was left overnight, the isoniazone which crystallized out filtered off, and recrystallized from ethanol. If the isoniazone did not separate, the solution was evaporated, or, in some cases, diluted with water.

The compounds prepared were tested in vitro for antitubercular bacteriostatic activity on 2 strains of microbacteria of human type tuberculosis: Academia and H 37 RV. The tests were carried out using a semisynthetic nutrient medium, and the same medium plus 10% blood serum. All the compounds investigated were highly effective, stopping the growth of Academia strain at dilutions of 1 in 16–32 million (see table).

The activities of the compounds were cut 2–8-fold in nutrient containing blood serum, but activity was still at a high level.

Of the compounds investigated, the most effective were the isoniazones of 5-ethylmercaptofurfural (previously described and tested [5]) and 2-ethylmercapto-5-n-propyl-3-furanaldehyde. The in vitro effectiveness of these compounds considerably exceed that of the clinical antituberculosis compound larusan, furfurylidenacetone isoniazone [4].

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THE SCHMIDT REACTION WITH PYRIDINE CARBOXYLIC ACIDS

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UDC 547.826

The Schmidt reaction in oleum is used to prepare 2, 3-and 4-aminopyridines.

Up to the present a convenient method of preparing pyridine amines has not been available, since application of the Chichibabin reaction is limited to 2- and 2,6-amino derivatives [1]. The Hofmann and Curtius reactions are primarily used for preparing 3- and 4-aminopyridines [1]; but the starting materials are not very accessible. It was recently shown [2] that 100% sulfuric acid must be used to effect the Schmidt reaction successfully with benzoic acids containing electron-accepting substituents. However aminopyridines are not obtained even under those conditions.

We have now shown that all the monoaminopyridines can be prepared by the Schmidt reaction when 20–30% oleum is used.

EXPERIMENTAL

24 g NaN_3 was sprinkled into a solution of 38 g (0.3 mole) nicotinic acid in 165 ml 30% oleum at 0–5° over a period of 3 hr (faster addition is not recommended, because of risk of explosion). Then the temperature was gradually raised to 95° over a period of 6 hr, held there for 3 hr, cooled to 10°, and the products poured onto 500 g ice and neutralized with 40% NaOH, temperature not exceeding 30°. Seven extractions with ether (about 500 ml) gave 28.8 g moist product. Two recrystallizations from benzene gave 14.71 g (50.4%) 3-aminopyridine mp 61–62° (the literature gives [3] mp 62°), while the mother liquors gave 5.47 g (18.7%) material mp 53–57°. Mixed mps confirmed that the two materials were identical, and identical with authentic 3-aminopyridine. The picrate and perchlorate of 3-aminopyridine were prepared.

Under the above conditions the yields of 2- and 4-aminopyridine did not exceed 30%.

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