# Some Alkylidene Derivatives of Isonicotinyl Hydrazine

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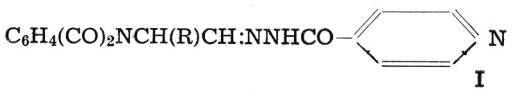
The remarkable *in vivo* activity of isonicotinyl hydrazine against *M. tuberculosis*[1,2] led to much searching for further tuberculoactive pyridine derivatives[3]. From these investigations it is evident, with regard to the hydrazides, that certain changes, such as the shifting of the hydrazide grouping from the gamma to the beta position resulted in total abolition of activity[4]. When further exploring this field it was found that a great number of alkylidene derivatives of the 1-isonicotinyl-2-alkylidene hydrazine type were tuberculostatic *in vivo*[5].

In the search for a powerful tuberculostatic drug with low toxicity we prepared the hitherto undescribed 2-alkylidene hydrazides Ia-d, by condensing the corresponding aldehydes with isonicotinyl hydrazine.



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a, R = H c, R = $CH(CH_3)_2$
b, R = $CH_3$ d, R = $CH_2CH(CH_3)_2$

## EXPERIMENTAL*

*1-Isonicotinyl-2-(2-phthalimidoethylidene)-hydrazine* [Ia].

To a suspension of phthalimidoglycine aldehyde (1.89 g., 0.01 mole) in methanol (10 ml.) a solution of isonicotinyl hydrazine (1.37 g., 0.01 mole) in methanol (10 ml.) was added, and the mixture refluxed on a water bath for three hours. On cooling, crystals of the crude *1-isonicotinyl-2-(2-phthalimidoethylidene)-hydrazine* separated from the reaction mixture. Yield 2.90 g. (94%), m. p. 187—197°. Several recrystallizations from ethanol yielded the pure compound in clusters of colorless needles, m. p. 196—197°.

*Anal.* 11.810 mg. subst.: 27.21 mg. $CO_2$, 4.22 mg. $H_2O$
$C_{16}H_{12}N_4O_3$ (308.28) calc'd: C 62.33; H 3.92%
found: C 62.88; H 4.00%

*1-Isonicotinyl-2-(2-phthalimidopropylidene)-hydrazine* [Ib].

A suspension of α-phthalimidopropionaldehyde prepared according to Balenović, Bregant, Cerar, Fleš and Jambrešić[6] (2.03 g., 0.01 mole) in ethanol (10 ml.) and a solution of an equimolar quantity of isonicotinyl hydrazide (1.37 g.) in ethanol (10 ml.) were treated in the same manner as described above. The crude *1-isonicotinyl-2-(2-phthalimidopropylidene)-hydrazine*, m. p. 160—165° was obtained. Several recrystallizations from methanol yielded crystals of the pure compound, m. p. 176.5—177.5°.

* Microanalyses were carried out by Dr. L. Filipović.
All melting points are uncorrected.

*Anal.* 6.100 mg. subst.: 14.28 mg. $CO_2$, 2.48 mg. $H_2O$
$C_{17}H_{14}N_4O_3$ (322.30) calc'd: C 63.35; H 4.37%
found: C 63.59; H 4.43%

*1-Isonicotinyl-2-(2-phthalimido-3-methylbutylidene)-hydrazine* [Ic].

A suspension of N-phthaloyl-valinealdehyde prepared according to Balenović, Bregant, Dvornik and Štimac[7] (2.31 g., 0.01 mole) in ethanol (10 ml.) and a solution of an equimolar quantity of isonicotinyl hydrazide (1.37 g.) in ethanol (10 ml.) were treated in the same manner as described above. The crude *1-isonicotinyl-2-(2-phthalimido-3-methylbutylidene)-hydrazine*, 3.1 g. (89%), m. p. 183—185° was obtained. Several recrystallizations from ethanol-water (1 : 1) yielded crystals of the pure compound, m. p. 185—186°.

*Anal.* 9.905 mg. subst.: 26.67 mg. $CO_2$, 4.70 mg. $H_2O$
$C_{19}H_{18}N_4O_3$ (350.35) calc'd: C 65.13; H 5.17%
found: C 65.22; H 5.39%

*1-Isonicotinyl-2-(2-phthalimido-4-methylpentylidene)-hydrazine* [Id].

A suspension of N-phthaloyl-leucinealdehyde[6] (2.45 g., 0.01 mole) in ethanol (10 ml.) and a solution of an equimolar quantity of isonicotinyl hydrazide (1.37 g.) in ethanol (10 ml.) were treated in the same manner as described above. The crude *1-isonicotinyl-2-(2-phthalimido-4-methylpentylidene)-hydrazine*, 1.3 g. (36%), m. p. 112—120° was obtained. Several recrystallizations from ethanol-water (1 : 1) yielded clusters of colorless needles of the pure compound, m. p. 146—147°.

*Anal.* 11.990 mg. subst.: 28.70 mg. $CO_2$, 6.09 mg. $H_2O$
$C_{20}H_{20}N_4O_3$ (364.37) calc'd: C 65.92; H 5.53%
found: C 65.31; H 5.68%

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## IZVOD

### Neki alkilidenski derivati hidrazida izonikotinske kiseline

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U traženju aktivnih tuberkulostatika male toksičnosti priređeni su — dosad neopisani — 2-alkilidenski derivati izonikotinilhidrazina [Ia—d], i to kondenzacijom odgovarajućih N-ftaloilaldehida s hidrazidom izonikotinske kiseline.

Tako su priređeni 1-izonikotinil-2-(2-ftalimido-etiliden)-hidrazin [Ia], t. t. 196—197°; 1-izonikotinil-2-(2-ftalimido-propiliden)-hidrazin [Ib], t. t. 176.5—177.5°; 1-izonikotinil-2-(2-ftalimido-3-metilbutiliden)-hidrazin [Ic], t. t. 185—186°; 1-izonikotinil-2-(2-ftalimido-4-metilpentiliden)-hidrazin [Id], t. t. 146—147°.

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