ml. of water. The resulting precipitate was collected by filtration. The product was recrystallized from ethanol to afford 1.1 g. of 4-methylaminobenzonitrile, m.p. 86°. In the case of ethyl-, propyl-, and butylaminobenzonitrile, method B was better than method A.

4-Methylaminobenzothioamide (Table III).—4-Methylaminobenzonitrile (2 g.) was dissolved in a mixture of 10 ml. of pyridine and 5 ml. of triethylamine, and the solution was treated with H_2S for 4 hr. The reaction mixture was evaporated under reduced pressure and the residual product was triturated with water. The precipitated product was collected by filtration and purified by recrystallization from ethanol to yield 2 g. of pure product, m.p. 170°. Other alkylaminobenzothioamides were prepared by the same method.

TABLE III

4-ALKYLAMINOBENZOTHIOAMIDES: p-$RNHC_6H_4CSNH_2$

R	M.p., °C.	% calcd. C	% calcd. H	% found C	% found H
CH_3	170	57.80	6.06	58.14	6.06
C_2H_5	165	59.96	6.71	60.46	6.69
n-C_3H_7	164	61.81	7.26	61.84	7.43
i-C_3H_7	172	61.81	7.26	61.68	7.32
n-C_4H_9	131	63.42	7.74	63.42	7.96
i-C_4H_9·H_2O	183	58.37	8.02	58.45	7.96
n-C_5H_{11}	142	64.82	8.16	64.06	8.07
i-C_5H_{11}	154	64.82	8.16	64.61	8.31
$C_6H_5CH_2$	178	69.38	5.82	69.06	6.05
C_6H_5	174	68.39	5.30	68.77	5.71

4-Phenylaminobenzothioamide.—A solution of 10 g. of NaCN in 25 ml. of water was added to a solution of 8 g. of $CuSO_4$ in 50 ml. of water. A diazo solution was prepared from 9.5 g. of p-aminodiphenylamine, 45 ml. of 6% HCl, and 4 g. of $NaNO_2$. The diazo solution was added to the warm well-stirred CuCN solution in 10 min. After 15 min., the reaction mixture was extracted with ether. The ether was distilled, the resulting syrup (1.4 g.) was treated with H_2S as usual to afford 1.1 g. of the crude 4-phenylaminobenzothioamide. Recrystallization from ethanol gave 0.6 g. of pure substance, m.p. 174°.

Extinction Coefficient, E_{max}, in Infrared Absorption Spectra.—The CN stretching band (2215–2230 cm.$^{-1}$) was measured in KBr disks (10 μmoles in 1 g.).

In Vitro **Antituberculous Activity.**—The *in vitro* test against human-type tubercule bacilli, strain H37Rv, using Kirchner's medium was conducted according to the method described in a previous paper.[6] The minimum inhibitory concentrations (MIC) are shown in Table I.

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Antituberculous Compounds. XXIII.[1] Alkyl- and Acylisonicotinic Acid Hydrazides

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Among acyl derivatives of isonicotinic acid hydrazide (INH) Rieche, *et al.*,[2] reported that in the series having unbranched carbon chains from C_6 to C_{18}, the undecanoyl derivative was the most active and showed approximately the same activity as INH against tubercle bacilli.

Acetyl, propionoyl, and butyryl derivatives of INH have almost no activity. In the literature,[3] these substances are all described as anhydrous compounds, but we have found that they crystallize with water of crystallization from water or aqueous solvent. As alkyl derivatives of INH, N-isopropyl-N′-isonicotinoylhydrazine has been reported as a good antituberculous compound, but only a few other alkyl derivatives have been described with chemical data and biological activities. Fox and Gibas[4] reported the synthesis of monoalkyl derivatives of INH, and McMillan, *et al.*,[5] prepared some higher homologs.

We have prepared the ethyl, propyl, and butyl derivatives and have shown that these compounds are more active than the acyl derivative containing the same number of carbon atoms, as shown in Table I.

TABLE I

MINIMUM INHIBITORY CONCENTRATION OF ALKYL DERIVATIVES OF INH AGAINST H37Rv IN KIRCHNER'S MEDIUM (28 DAYS, 38°)

$C_5H_4NCONHNHR$

R	MIC, μmole/l.
H (INH)	1
$COCH_3$	400
C_2H_5	40
COC_2H_5	400
C_3H_7	40
COC_3H_9	400
C_5H_{11}	5

Experimental Section

N-Acyl-N′-isonicotinoylhydrazine.—The crude crystalline material obtained by the literature[3] methods was recrystallized from water or aqueous ethanol and acetone. The pure crystalline material contained solvate water as shown in Table II. Anhydrous substances were obtained by recrystallization from absolute ethanol or acetone and by drying under reduced pressure.

In Vitro **Antituberculous Activity.**—The *in vitro* test against human tubercule bacilli, strain H37Rv, using Kirchner's medium was conducted according to the method described in a previous paper.[6] The minimum inhibitory concentration (MIC) is shown in Table I.

TABLE II

$C_5H_4NCONHNHCOR$

R	Water of crystn., moles	M.p., °C.	Anhydrous m.p., °C.	% calcd. C	% calcd. H	% calcd. H_2O	% found C	% found H	% found H_2O
CH_3	2	76	158	44.64	6.09	16.75	44.48	6.38	16.61
C_2H_5	2	95	131.5	47.15	6.60	15.72	47.13	6.41	15.82
C_3H_7	1	84	139	53.32	6.71	8.00	53.32	6.81	7.76

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The Use of Substituent Constants in the Correlation of Demethylation Rates

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In continuing our study[1-4] of substituent effects on the biological activity of congeneric drugs we have in

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