EXPERIMENTAL

The IR spectra were obtained on a UR-20 spectrometer as a thin layer.

1, 3-Dichloroisopropoxydimethylethynylsilane (I). A mixture of 6.3 g of 1, 3-dichloroisopropanol, 8 g of dimethylethynylmethoxysilane, and 0.05 g of p-toluenesulfonic acid was refluxed in the pot of a fractionating column, and the liberated methanol and excess dimethylethynylmethoxysilane were distilled off. Distillation of the residue gave 7.0 g (66.5%) of (I) (Table 1).

Compounds (II)-(VII) were obtained in a similar manner (Table 1).

CONCLUSIONS

Some ethynyl(organoxy)silanes were obtained by the transetherification of $CH_3O(CH_3)_2SiC \equiv CH$ with 1, 3-dichloroisopropanol, 4-iodophenol, and 3, 5-xylenol, of $CH_3O(CH_3)Si(C \equiv CH)_2$ with ethanol, of $CH_3O(CH_3)Si(CH = CH_2)(C \equiv CH)$ with ethanol and propanol, and of $CH_3(CH_3O)_2SiC \equiv CH$ with butanol.

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ELECTROPHILIC REACTIONS OF 3-HYDROXYISONICOTINIC ACID

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A study of the electrophilic substitution of hydroxypyridine acids is of interest for elucidating the effect of the COOH group on the reactivity of the hydroxypyridine ring and the direction of electrophilic reactions. The data given in [1-6] testify to a different reactivity of the α-, β-, and γ-hydroxypyridinecarboxylic acids. Besides this, the position of the COOH group also exerts a substantial effect on the ease with which electrophilic substitution progresses. Thus, the electrophilic reactions of 5-hydroxynicotinic acid proceed only in the 6 position [5]. At the same time, 5-hydroxypicolinic acid also forms the bis-substituted derivatives when iodinated [6].

We studied the electrophilic reactions of 3-hydroxyisonicotinic acid (I) and its ethyl ester (II). The halogenation of (I) was studied on the example of iodination, which was run in the presence of bases.

It proved that, depending on the reaction conditions and ratio of the reactants, either the mono- or diiodo derivatives of (I) can be formed. Thus, the iodination of (I) at ~20°C in aqueous ammonia solution leads mainly to iodide (III). 2, 6-Diiodo-3-hydroxyisonicotinic acid (IV) is formed in high yield when (I) is heated in Na_2CO_3 solution with excess I_2 and KI. The iodination of (II) under these conditions is accompanied by saponification of the ester group. The structure of iodo derivatives (III) and (IV) was established via the NMR spectra.

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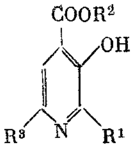
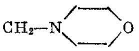
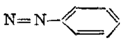
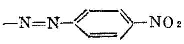
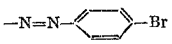
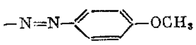
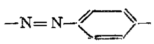
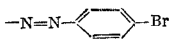
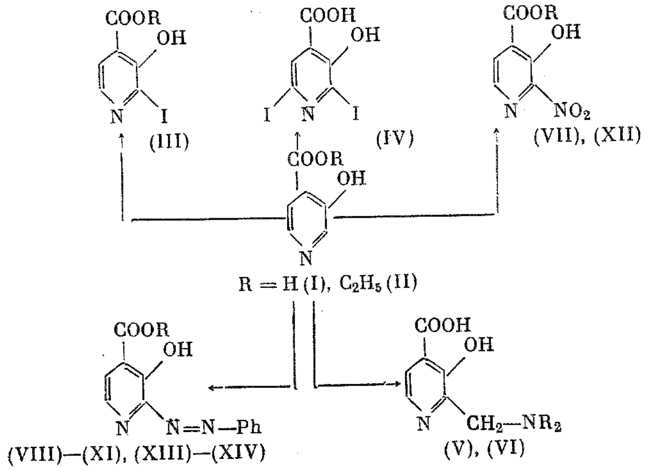
TABLE 1



Compound	R¹	R²	R³	Yield, %	mp.° C	Found, % C	Found, % H	Empirical formula	Calculated, % C	Calculated, % H	NMR spectrum, δ, ppm H²	H⁵	H⁶	other groups	SSCC J_{56}, Hz
(I)	H	H	H	–	312	—	–	$C_6H_5O_3N$	—	–	8,12 s	7,54 d	7,99 d		5,0
(II)	H	C_2H_5	H	42	35	57,88	5,46	$C_8H_9O_3N$	57,48	5,38	8,17 s	7,40 d	7,70 d	CH_3 1,38 t CH_2 4,35 q	5,0
(III)	I	H	H	74	242–243	27,55	1,93	$C_6H_4O_3NI$	27,16	1,51	–	7,04 d	7,37 d	—	4,5
(IV)	I	H	I	53	158–159	18,84	0,97	$C_6H_3O_3NI_2$	18,41	0,77	–	7,84 s	–	—	–
(V)	$CH_2—N(CH_3)_2$	H	H	95	230–231	57,03	6,48	$C_9H_{12}O_3N_2$	56,77	6,25	–	7,17 d	7,06 d	$N(CH_3)_2$ 2,27 s CH_2 3,60 s	5,0
(VI)		H	H	96	259–260	55,81	6,12	$C_{11}H_{14}O_4N_2$	55,50	5,88	–	7,06 d	7,51 d	$N{<}^{CH_2}_{CH_2}$ 2,61 m $O{<}^{CH_2}_{CH_2}$ 3,68 m CH_2 3,63 s	5,0
(VII)	NO_2	H	H	26	181–182	39,35	2,42	$C_6H_4O_5N_2$	39,10	2,17	–	7,54 d	7,64 d	—	5,0
(VIII)		H	H	97	229–230	59,56	4,12	$C_{12}H_9O_3N_3$	59,30	3,70	–	—	–	—	–
(IX)		H	H	95	219–220	50,45	2,96	$C_{12}H_8O_5N_4$	50,00	2,78	–	–	–	—	–
(X)		H	H	96	195–196	45,00	2,83	$C_{12}H_8O_3N_3Br$	44,70	2,48	–	–	–	—	–
(XI)		H	H	97	163–164	57,45	4,28	$C_{13}H_{11}O_4N_3$	57,14	4.03	–	–	–	—	–
(XII)	NO_2	C_2H_5	H	25	52,0–52,5	45,55	3,92	$C_8H_8O_5N_2$	45,28	3,79	–	7,28 d	7,45 d	CH_3 1,14 t CH_2 3,58 q	4,0
(XIII)		C_2H_5	H	98	69–70	62,15	4,54	$C_{14}H_{13}O_3N_3$	62,00	4,79	–				
(XIV)		C_2H_5	H	97	85–86	48,43	3,62	$C_{14}H_{12}O_3N_3Br$	48,00	3,43	–				



In contrast to iodination, both the aminomethylation and azo-coupling of (I) and (II) proceed only in the 2 position, i. e., all of the studied β-hydroxypyridinecarboxylic acids exhibit the same reactivity in these reactions [5, 6]. The structure of the end products was confirmed by the IR and NMR spectral data.

However, 3-hydroxyisonicotinic acid exhibits a greater reactivity in nitration. If 5-hydroxypicolinic acid fails to nitrate, while 5-hydroxynicotinic acid is nitrated under very drastic conditions to give the nitration product in low yield [5, 6], then the nitration of (I), and especially of (II), proceeds under less drastic conditions and gives a somewhat better yield of the nitro products when compared with the indicated acids. 2-Nitro-3-hydroxyisonicotinic acid (VII) and its ester (XII) are formed here, whose structure was confirmed by the IR and NMR spectral data.

As a result, a study of the electrophilic substitution of β-hydroxypyridinecarboxylic acids testifies to the fact that the electrophilic attack of all of the studied acids is initially directed to the o-position relative to the OH group. Substitution of the p-position relative to the OH group is possible only when the COOH group is located meta to the OH, and is observed only in the iodination reaction.

EXPERIMENTAL

The NMR spectra were taken on a HA-100 spectrometer at 29°. The compounds were studied as 5-8% solutions in 1 N NaOD solution; the internal standard was dioxane. The values of the chemical shifts are expressed on the δ scale, with an accuracy of ± 0.02 ppm. The IR spectra were taken on a UR-20 instrument.

Ethyl 3-Hydroxyisonicotinate (II). A solution of 0.036 mole of (I) in 35 ml of alcohol, 20 ml of conc. H_2SO_4, and 20 ml of benzene was heated for 4 h on the stream bath, cooled, poured on ice, neutralized with aqueous NH_3 to pH 3, extracted with ether, and the ether extract was dried, the solvent was removed in vacuo, and the residue was sublimed in a high vacuum.

Iodination. To a solution of 7.2 mmoles of (I) in 25 ml of 10% aqueous NH_3 solution was added a mixture of 0.8 g of I_2 and 0.9 g of KI in 5 ml of water, and the mixture was let stand overnight. The mixture was filtered, the mother liquor was neutralized with dilute H_2SO_4 solution, and the obtained precipitate was separated, washed with water, and recrystallized from water.

To a solution of 7.2 mmoles of (I) in 25 ml of 10% aqueous Na_2CO_3 solution was added a mixture of 1.6 g of I_2 and 1.8 g of KI in 10 ml of water, and the reaction mixture was refluxed on the water bath for 3 h, after which it was cooled, filtered, the mother liquor was neutralized with dilute H_2SO_4 solution, and the obtained precipitate was separated and recrystallized from water.

Aminomethylation. To a solution of 3.6 mmoles of (I) in 5 ml of water was added an equimolar amount of the secondary amine and 30% aqueous CH_2O solution. The mixture was heated for 4 h at 100-120°, and then the solvent was removed in vacuo. We obtained Mannich bases (V) and (VI).

Azo-Coupling. With stirring, to a solution of 7.2 mmoles of either (I) or (II) in 50 ml of 10% KOH solution, cooled to 5-10°, were added a solution of the diazo component (7.2 mmoles) and KOH solution in such manner that the pH of the medium remained in the range 8-9. The reaction mass was kept for 1 h, filtered, the mother liquor was neutralized with dilute H_2SO_4 solution, and the obtained precipitate was separated, washed with water, dried, and recrystallized from alcohol.

Nitration. To a solution of 3.6 mmoles of (I) in 3 ml of conc. H_2SO_4 was added a nitration mixture, composed of 0.25 g of HNO_3 (d = 1.5) and 0.25 g of conc. H_2SO_4. The reaction mass was stirred for 5 h at 100°, cooled, poured on ice, and the obtained precipitate was separated, washed with water, and recrystallized from water. Nitro derivative (VII) was obtained. The nitration of (II) was run in a similar manner, but at 50°.

The yields and constants of all of the obtained compounds are given in Table 1.

CONCLUSIONS

The aminomethylation, azo-coupling, and nitration of 3-hydroxyisonicotinic acid and its ester are directed to the 2 position, whereas their iodination proceeds with the formation of the 2-iodo and 2, 6-diiodo derivatives.

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