CONCLUSIONS

1. α-Methoxy(methylthio)-3-thenylidene-o-aminophenols and the corresponding 3-thienyl-2'-benzoxazoles, having fungicidal and fungistatic activity with respect to several inducers of acute mycoses, were synthesized.

2. Salts of (2-methoxy-5-methylthio-3-thenylidene)cyanoacetic acid with the corresponding amines were prepared by reaction of Schiff bases (derived from 2-methoxy-5-methylthio-3-thiophenecarboxaldehyde and aromatic amines (o-aminophenol, p-anisidine)), with cyanoacetic acid.

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PREPARATION OF SUBSTITUTED 2-PHENYLPYRIDINES BY HETEROCYCLIZATION OF ACETYLENE WITH BENZONITRILES

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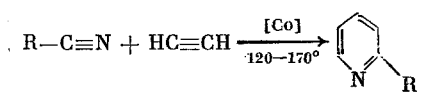
Two methods for the preparation of 2-phenylpyridines with substituents on the benzene ring are known: an organometallic synthesis [1, 2] and substitution of a diazo group on the benzene nucleus by pyridine [3, 4]. Reactions of pyridine with organolithium compounds give p- and m-tolyl- and p-methoxyphenylpyridines in yields of 40-60%. The method of substituting pyridine for a diazo group has been used for the preparation of compounds with various substituents on the benzene ring; Cl, Br, NO_2, AlkO, COOH, NH_2, etc., but difficultly separable mixtures of 2, 3, and 4 isomers (with predominance of the 2 isomer) are formed.

Some cobalt compounds that contain the metal in the lower oxidation state can be catalysts for the preparation of 2-substituted pyridines from acetylene and nitriles [5]:



In this work we used the catalyst η^5-dicyclopentadienylcobalt (cobaltocene). We assume the formation of a cobaltacyclopentadiene stabilized by a ligand as the active intermediate, the reaction of which with a nitrile leads to the formation of a substituted pyridine and with acetylene to benzene [6]:

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TABLE 1. Activity of Substituted Benzonitriles (I) in the Heterocyclization with Acetylene

R	H	*p*-CH_3	*m*-CH_3	*o*-CH_3	*p*-Cl	*o*-Cl	*o*-Br	*p*-OH	*p*-CH_3O	*p*-C_2H_5O	*p*-$(CH_3)_2N$	*p*-NO_2	*o*-NO_2
A, moles of product per g-atom Co	44	63–65	52–55	40–42	20–22	No reaction			75–82	70–75	45–46	No reaction	

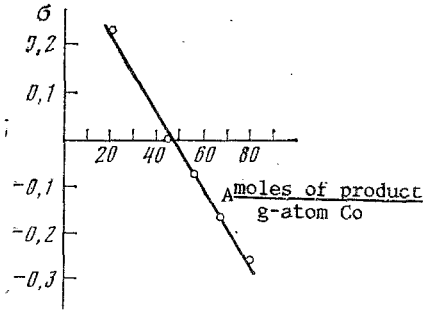
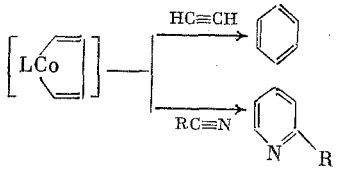
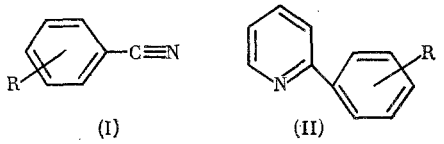


Fig. 1. Dependence of the activity of a substituted benzonitrile on the Hammett constant of the substituent.



(2)

On using benzonitriles with various substituents the corresponding 2-phenylpyridines can be prepared. We investigated the influence of the functional groups in the benzonitrile (I) on the activity in the formation of pyridines (II).



(I) (II)

The results of the investigation are presented in Table 1. A comparison of the activity of the nitriles in the investigated reaction was carried out using the values of the efficiency of the catalyst. The nitriles whose activities were studied in the reaction with acetylene can be arranged in the series *p*-$CH_3O \approx$ *p*-$C_2H_5O >$ *p*-$CH_3 >$ *m*-$CH_3 >$ H $\approx$ *p*-$(CH_3)_2N \approx$ *o*-$CH_3 >$ *p*-Cl and, consequently, electron-donating groups increase the activity of the nitrile and electron-withdrawing groups lower it. The dependence of the activity (A) on the Hammett constants (σ) for p- and m-substituted benzonitriles is shown in Fig. 1. The values for σ were taken from [7]. As can be seen in Fig. 1, there is a linear relationship between the activity of the nitrile and σ. If we take into account only the electronic influence of the functional group, an increase in activity might be expected for σ-tolylnitrile because the influence of the CH_3 group (positive inductive effect) should be maximal, but this nitrile is as active as the unsubstituted benzonitrile. Obviously, the influence of the inductive effect of the CH_3 group is levelled out by the steric hindrance that emerges during the reaction of the intermediate cobalt complex with the nitrile group. The same hindrance arises when the heterocyclization is carried out with o-chloro- and o-bromobenzonitrile, and

the superimposed negative inductive effect of the halogen leads to complete inactivation of the nitrile group. These nitriles do not react with acetylene, while in the presence of o-chloro- and o-bromobenzonitrile the trimerization of acetylene (2) proceeds, i.e., the catalyst is not deactivated and so we can say these nitriles are inactive in the heterocyclization. p-Chlorobenzonitrile reacts with acetylene and forms the corresponding (II), although the electron-withdrawing effect of the chlorine lowers the activity of the nitrile group.

The dependence of the activity of the nitrile on the Hammett constants was observed for benzonitriles containing CH_3, Cl, and CH_3O groups. A deviation was found for p-dimethylaminobenzonitrile ($\sigma = -0.378$), the activity of which is close to that of unsubstituted benzonitrile. It is possible that this is related to the fact that amines, including tertiary amines, can form a complex with cobalt and thus can partially inactivate the catalyst. As regards the value of the Hammett constant for the nitrobenzonitriles ($\sigma = +0.778$) the efficiency of the catalyst should be low. On carrying out the heterocyclization of acetylene with p- and o-nitrobenzonitriles the pyridines are not formed, while in these cases only a trace of benzene is obtained, so it is obvious that nitrobenzonitriles deactivate the catalyst.

Benzonitriles with functional groups that contain active hydrogen, e.g., p-hydroxybenzonitrile, do not react with acetylene, and the formation of benzene has also not been found in that case and therefore complete deactivation of the catalyst takes place.

Thus, in the presence of η^5-dicyclopentadienylcobalt, acetylene heterocyclizes with benzonitriles that contain certain functional groups, on which 2-phenylpyridines are obtained in high yield (90-97% at a nitrile conversion of 100%) and with high selectivity (90-97%). The obtained pyridines are used as intermediate products for the synthesis of compounds with pesticidal activity.

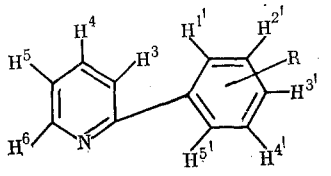
EXPERIMENTAL

Reactions were carried out for 2.5 h at 150-160°C in a 150-ml rotating steel autoclave at an initial acetylene pressure of 12-16 atm in THF solution. Reagents were added under Ar. The catalyst concentration was 1-2%. The conditions of the reaction were chosen in such a way that the conversion of the nitrile was not 100%, in which case the efficiency of the catalyst (A) characterizes the activity of the nitrile:

$$A = \frac{\text{moles of pyridine formed}}{\text{g-atom Co}}$$

The reaction mixture was analyzed by means of GLC on an LKhM-8MD chromatograph with a thermal-conductivity detector. Products were purified by crystallization from hexane or by fractional distillation. The structures of the compounds were confirmed by IR, NMR, and mass spectral data, and by elemental analysis. The IR spectra were taken on a Specord IR-75; the mass spectra, on a Varian CH-6 instrument. The NMR spectra were recorded on a Bruker WH-250 (operating at 250 MHz) in deuteroacetone.

The following compounds of formula (II) were prepared:



(II)

2-phenylpyridine, bp 85°C (3 mm), mass spectrum: M^+ 155; NMR spectrum (δ, ppm: J, Hz): 8.68 d.t (1H, H^6, $J_{65} = 4.5$, $J_{64} = 1.0$, $J_{63} = 1.0$), 7.54 d.d (1H, H^3, $J_{34} = 7.8$, $J_{35} = 1.5$, $J_{36} = 1.0$), 7.50 t.d (1H, H^4, $J_{43} = 7.8$, $J_{46} = 1.0$, $J_{45'} = 7.8$), 7.08 m (1H, H^5, $J_{54} = 7.8$, $J_{56} = 4.5$, $J_{53} = 1.5$), 7.91 d (2H, $H^{1'}$, $H^{5'}$, $J_{1'2'} = J_{5'4'} = 8.0$), 7.30 t (3H, $H^{2'}$, $H^{3'}$, $H^{4'}$, $J_{2'1'} = J_{2'3'} = 8.0$).

2-(p-Tolyl)pyridine, bp 140°C (2 mm), mass spectrum: M^+ 1.77; NMR spectrum (δ, ppm; J, Hz): 8.66 d.d (1H, H^6, $J_{65} = 4.5$, $J_{64} = 1.0$), 7.54 d.d (1H, H^3, $J_{34} = 7.8$, $J_{35} = 1.5$), 7.52 t.d (1H, H_4, $J_{43} = 7.8$, $J_{45} = 7.8$, $J_{46} = 1.0$), 7.06 m (1H, H^5, $J_{54} = 7.8$, $J_{56} = 4.5$, $J_{53} = 1.5$), 7.90 d (2H, $H^{1'}$, $H^{5'}$, $J_{1'2'} = J_{5'4'} = 8.0$), 7.22 d (2H, $H^{2'}$, $H^{4'}$, $J_{2'1'} = J_{4'5'} = 8.0$), 2.32 s (3H, CH_3).

2-(m-Tolyl)pyridine, bp 126°C (2 mm), mass spectrum: M^+ 177; NMR spectrum (δ, ppm; J, Hz): 8.63 d.d (1H, H^6, J_{65} = 4.5, J_{64} = 1.0), 7.54 d.d (1H, H^3, J_{34} = 7.8, J_{35} = 1.5), 7.48 t.d (1H, H^4, J_{43} = 7.8, J_{45} = 7.8, J_{46} = 1.0), 7.01 m (1H, H^5, J_{54} = 7.8, J_{56} = 4.5, J_{53} = 1.5), 7.85 s (1H, $H^{1'}$), 7.76 d (1H, $H^{5'}$, $J_{5',4'}$ = 8.0), 7.28 t (1H, $H^{4'}$, $J_{4',5'}$ = $J_{4',3'}$ = 8.0), 7.14 d (1H, $H^{3'}$, $J_{3',4'}$ = 8.0), 2.46 s (3H, CH_3).

2-(o-Tolyl)pyridine, bp 150°C (22 mm), mass spectrum: M^+ 177; NMR spectrum (δ, ppm; J, Hz): 8.70 d.d (1H, H^6, J_{65} = 4.5, J_{64} = 1.0), 7.52 d.d (1H, H^3, J_{34} = 7.8, J_{35} = 1.5), 7.50 t.d (1H, H^4, J_{43} = 7.8, J_{45} = 7.8, J_{46} = 1.0), 7.21 t.d (1H, H^5, J_{54} = 7.8, J_{56} = 4.5, J_{53} = 1.5), 7.70 d (1H, $H^{1'}$, $J_{1',2'}$ = 7.8), 7.28 broad s (3H, $H^{2'}$, $H^{3'}$, $H^{4'}$), 2.36 s (3H, CH_3).

2-(p-Chlorophenyl)pyridine, mp 51°C, mass spectrum: M^+ 189; NMR spectrum (δ, ppm; J, Hz): 8.48 d.t (1H, H^6, J_{65} = 4.5, J_{64} = 1.0, J_{63} = 1.0), 7.47 d.d (1H, H^3, J_{34} = 7.8, J_{35} = 1.5), 7.42 t.d (1H, H^4, J_{43} = 7.8, J_{45} = 7.8, J_{46} = 1.0), 6.96 m (1H, H^5, J_{54} = 7.8, J_{56} = 4.5, J_{53} = 1.5), 7.81 d (2H, $H^{1'}$, $H^{5'}$, $J_{1'2'}$ = $J_{5'4'}$ = 8.0), 7.30 d (2H, $H^{2'}$, $H^{4'}$, $J_{2'1'}$ = $J_{4'5'}$ = 8.0.

2-(p-Methoxyphenyl)pyridine, mp 53-54°C, mass spectrum: M^+ 185; NMR spectrum (δ, ppm; J, Hz): 8.50 d.d (1H, H^6, J_{65} = 4.5, J_{64} = 1.0), 7.51 d.d (1H, H^3, J_{34} = 7.8, J_{35} = 1.5), 7.43 t.d (1H, H^4, J_{43} = 7.8, J_{45} = 7.8, J_{46} = 1.0), 6.97 m (1H, H^5, J_{54} = 7.8, J_{56} = 4.5, J_{53} = 1.5), 7.85 d (2H, $H^{1'}$, $H^{5'}$, $J_{1',2'}$ = $J_{5',4'}$ = 8.0), 6.91 d (2H, $H^{2'}$, $H^{4'}$, $J_{2',1'}$ = $J_{4',5'}$ = 8.0), 3.66 s (3H, CH_3O).

2-(p-Ethoxyphenylpyridine, mp 72-74°C, mass spectrum: M^+ 199; NMR spectrum (δ, ppm; J, Hz): 8.48 d.d (1H, H^6, J_{65} = 4.5, J_{64} = 1.0), 7.53 d.d (1H, H^3, J_{34} = 7.8, J_{35} = 1.5), 7.45 t.d (1H, H^4, J_{43} = 7.8, J_{45} = 7.8, J_{46} = 1.0), 6.87 m (1H, H^5, J_{54} = 7.8, J_{56} = 4.5, J_{53} = 1.5), 7.85 d (2H, $H^{1'}$, $H^{5'}$, $J_{1',2'}$ = $J_{5',4'}$ = 8.0), 6.74 d (2H, $H^{2'}$, $H^{4'}$, $J_{2',1'}$ = $J_{4',5'}$ = 8.0), 3.92 q (2H, CH_2O, $J_{CH_2-CH_3}$ = 8.5), 1.33 t (3H, CH_3, $J_{CH_3-CH_2}$ = 8.5).

2-(p-Dimethylaminophenyl)pyridine, mp 94-95°C, mass spectrum: M^+ 146; NMR spectrum (δ, ppm; J, Hz): 8.47 d.d (1H, H^6, J_{65} = 4.5, J_{64} = 1.0), 7.71 d.d (1H, H^3, J_{34} = 7.8, J_{35} = 1.5), 7.63 t.d (1H, H^4, J_{43} = 7.8, J_{45} = 7.8, J_{46} = 1.0), 7.08 m (1H, H^5, J_{54} = 7.8, J_{56} = 4.5, J_{53} = 1.5), 7.85 d (2H, $H^{1'}$, $H^{5'}$, $J_{1',2'}$ = $J_{5',4'}$ = 8.0), 6.73 d (2H, $H^{2'}$, $H^{4'}$, $J_{2',1'}$ = $J_{4',5'}$ = 8.0), 2.32 s (6H, CH_3).

CONCLUSIONS

1. Heterocyclizations of acetylene with benzonitriles containing a CH_3, Cl, CH_3O, C_2H_5O, or $(CH_3)_2N$ group in the presence of η^5-dicyclopentadienylcobalt yield the corresponding 2-substituted pyridines in yields of about 90%.

2. Nitriles containing OH, NO_2, or halogen at the ortho position of the nitrile group do not react with acetylene.

3. For benzonitriles containing a CH_3, Cl, or CH_3O group in the ortho or para position, a relation between the activity of the nitrile and the value of the Hammett constant of the substituent was found for the investigated reaction.

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