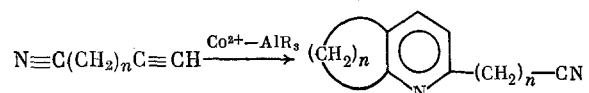


SYNTHESIS OF COMPLEX PYRIDINE BASES IN THE REACTION OF  
 $\alpha,\omega$ -NITRILEACETYLENES WITH ACETYLENE, CATALYZED BY  
 COBALT COMPLEXES

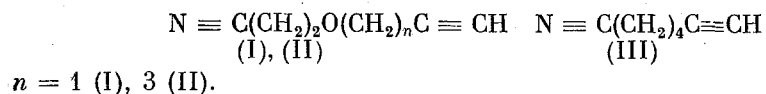
U. M. Dzhemilev, F. A. Selimov, and  
 V. R. Khafizov

UDC 542.97:547.339.2:547.314.2:547.82

It has been shown that  $\alpha,\omega$ -nitrileacetylenes under the action of homogeneous cobalt-containing catalysts undergo transformations into pyridine derivatives [1]:



In order to expand the scope of this method for synthesis of complex pyridine bases, for investigation of the reactivity of nitrileacetylenes of various structure in the reaction of cooligomerization with acetylene, as well as for the introduction to these reactions of new types of  $\alpha,\omega$ -nitrileacetylenes, containing in their molecules an oxygen atom, we studied in the present work the homo- and codimerization of  $\alpha,\omega$ -nitrileacetylenes with acetylene under the action of a  $\text{Co}(\text{2-ethyl hexanoate})_2\text{-AlR}_3$  catalyst in a toluene solution.



The  $\alpha,\omega$ -nitrileacetylenes were obtained by the cyanoethylation of propargyl alcohol and 4-pentyn-1-ol with acrylonitrile or by the reaction of 6-bromohex-1-yne with KCN [2].

Attempts to carry out the homodimerization of oxygen-containing nitrileacetylenes were unsuccessful. In all experiments, regardless of changes in the reaction conditions, as well as in the nature and concentration of the catalyst components, we obtained a small amount of products of homocyclotrimerization of the starting nitrileacetylenes to the corresponding trisubstituted benzenes. Apparently, the oxygen atom in the molecule of  $\omega,\alpha$ -cyanoacetylenes, using its lone electron pair, takes part in the formation of the coordination shell of the central atom of the catalysts, obstructing the approach and coordination of both the acetylene and nitrile groups in the starting monomers.

It is apparent that the oxygen-containing  $\alpha,\omega$ -nitrileacetylenes, in contrast to the simpler nitroacetylenes [1], do not form products of the intramolecular cyclization under the conditions of metal-complex catalysis leading to substituted pyridines.

Consequently, our further efforts were directed toward the investigation of the cyclo-dimerization of  $\alpha,\omega$ -nitrilacetylenes with acetylene on a catalytic system consisting of  $\text{Co}(\text{2-ethyl hexanoate})_2$  and  $\text{AlEt}_3$  in a toluene solution at 150°C and under an acetylene pressure of 10-15 atm.

Cyclocodimerization of (I) with acetylene under the above-mentioned conditions leads to a mixture of pyridines (IV) and (V) and the cyanoethylated derivative of benzyl alcohol (VI), as well as to the cyclotrimerization product of acetylene - benzene (5%). The yields of these products vary considerably with the nitrile/acetylene ratio. With an increasing acetylene content in the reaction mixture, the total yield of (IV)-(VI) increases to 98% at a (I):acetylene ratio equal to 1:10. At the same time, the (IV) and (VI) content decreases (Table 1).

TABLE 1. Codimerization of  $\beta$ -Propargyloxypropionitrile with Acetylene (150°C, 8 h)

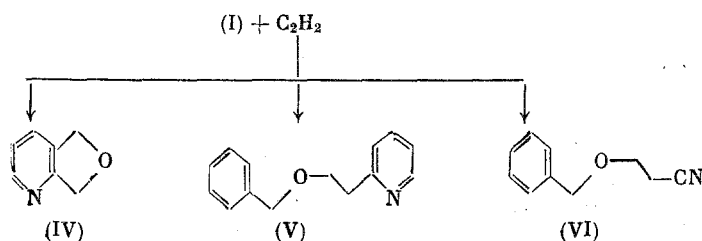
Molar ratio of the starting monomers		Conversion of the nitrile, %	Composition of the reaction products		
$\text{NC}(\text{CH}_2)_2\text{OCH}_2\text{C}\equiv\text{CH}$	$\text{HC}\equiv\text{CH}$		(IV)	(V)	(VI)
1	1	5	40	16	44
1	3	70	35	20	45
1	6	95	15	75	10
1	10	98	8	87	5

TABLE 2. Codimerization of 1-Pentyne-4-hydroxypropionitrile with Acetylene (150°C, 8 h)

Molar ratio of the starting monomers		Conversion of the nitrile, %	Composition of the reaction products		
$\text{NC}(\text{CH}_2)_2\text{O}(\text{CH}_2)_3\text{C}\equiv\text{CH}$	$\text{HC}\equiv\text{CH}$		(VII)	(VIII)+(X)	(IX)
1	1	35	63	16	21
1	2,5	70	45	15	40
1	6	95	5	10	85
1	10	99	5	5	90

TABLE 3. Codimerization of Acetylene with  $\alpha,\omega$ -Nitrile-acetylene (150°C, 8 h)

Molar ratio of the starting monomers		Conversion of the nitrile, %	Composition of the reaction products, %				
$\text{NC}-(\text{CH}_2)_n-\text{C}\equiv\text{CH}$	$\text{HC}\equiv\text{CH}$		(XIV)	(XV)	(XVIII)	(XVI)	(XVII)
1	3	78	28	19	20	18	15
1	6	90	46	15	14	16	9
1	10	95	65	7	8	15	5



Analogous results were obtained in the reaction of nitrileacetylene (II) with acetylene, leading to a mixture of pyridines (VII)-(IX) and the monosubstituted benzene (X). As can be seen from Table 2, the selectivity toward the cyclocodimer (VII) drops considerably with an increasing concentration of acetylene in the catalyzate. The maximum content of (VII) in the mixtures of pyridines constitutes ~63% at a 1:1 (II):acetylene ratio. However, the conversion of the starting nitrileacetylene (II) under these conditions does not exceed ~35%.

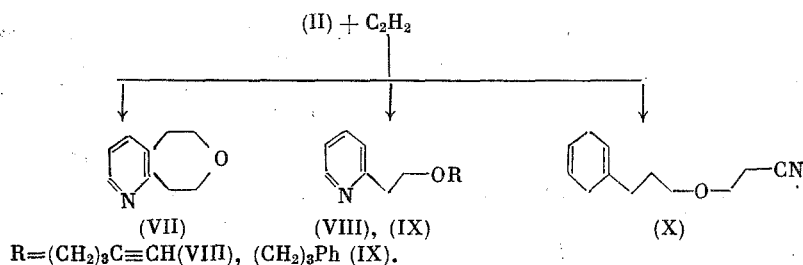
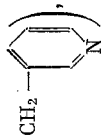
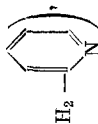


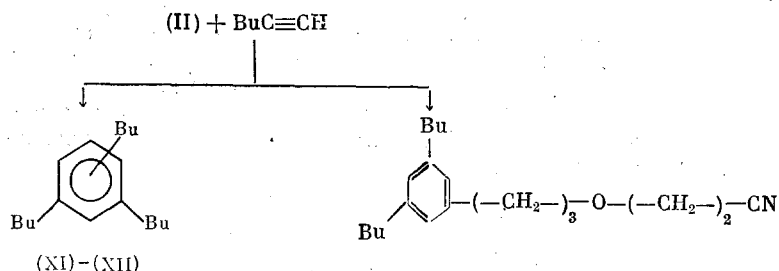
TABLE 4. Constants of the Obtained Compounds

Compound	bp, deg C (p, mm Hg)	$n_D^{20}$	IR spectrum, $\nu$ , $\text{cm}^{-1}$	NMR spectrum, $\delta$ , ppm	M+	Calculated, %				Found, %		
						C	H	N	O	C	H	N
(IV)	112-114(4)	1.5162	740, 870, 1110, 1450, 1580	2.87 t (2H, $\text{CH}_2\text{-C}_6\text{H}_4\text{N}$ ), 3.93-4.63 (4H, $\text{O}(\text{CH}_2)_2$ ), 7.16-8.33 (3H, $\text{C}_6\text{H}_5\text{N}$ )	135	71.1	6.7	10.4	11.8	71.3	6.8	10.5
(V)	145-147(3)	1.5363	750, 1110, 1370, 1595	3.0 t (2H, $\text{CH}_2\text{-C}_6\text{H}_4\text{N}$ ), 3.7-4.43 (4H, $\text{O}(\text{CH}_2)_2$ ), 7.23-8.5 (9H, $-\text{C}_6\text{H}_5$ , $\text{C}_6\text{H}_4\text{N}$ )	213	78.9	7.0	6.6	7.5	78.5	7.2	6.5
(VI)	130-132(4)	1.5241	745, 1110, 1370, 1600, 2260	2.4 t (2H, $\text{CH}_2\text{-CN}$ ), 3.5-4.47 (4H, $\text{O}(\text{CH}_2)_2$ ), 7.28 in (5H, $\text{C}_6\text{H}_5$ )	161	74.6	6.8	8.7	3.9	74.9	7.0	8.6
(VII)	125-130(4)	1.5295	770, 840, 1400, 1420, 1600	4.1 t (2H, $\text{CH}_2$ ), 2.3 d (2H,  ) 2, 8t (2H, $\text{CH}_2$ -  ) 3.8-4.55 (4H, $\text{O}(\text{CH}_2)_2$ ), 6.7-8.16 (3H, $\text{C}_6\text{H}_5\text{N}$ )	163	73.6	8.0	8.6	9.8	73.7	8.1	8.6
(VIII)	150-152(4)	-	770, 840, 1100, 1420, 1600, 2130	1.05 t (2H, $\text{CH}_2$ ), 2.2 t (3H, $-\text{C}\equiv\text{CH}$ ), $\text{CH}_2\text{-C}\equiv\text{C}$ ), 3.9-4.6 (4H, $\text{O}(\text{CH}_2)_2$ ), 7.2-8.3 (4H, $\text{C}_6\text{H}_4\text{N}$ )	189	76.2	7.9	7.4	8.5	76.4	0.1	7.5

(IX)	170-175(4)	1,4542	770, 1100, 1370, 1590	1,05 t (2H, -CH <sub>2</sub> ), 2,5 t (2H, -CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> ), 3,07 t (2H, CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> N), 3,83-4,47 (4H, O(CH <sub>2</sub> ) <sub>2</sub> ), 7,13-8,42 (4H, C <sub>6</sub> H <sub>4</sub> N)	241	79,7	7,9	5,8	6,6	C <sub>10</sub> H <sub>10</sub> NO	79,6	8,0	5,9
(X)	138-140(4)	-	780, 1100, 1365, 1590, 2270	1,05 t (2H, CH <sub>2</sub> ), 2,5 t (4H, -CH <sub>2</sub> -CN; -CH <sub>2</sub> -C <sub>6</sub> -C <sub>6</sub> H <sub>5</sub> ), 3,67-4,3 (4H, O-(CH <sub>2</sub> ) <sub>2</sub> ), 7,0 m (5H, -C <sub>6</sub> H <sub>5</sub> )	189	76,2	79,9	7,4	8,5	C <sub>12</sub> H <sub>15</sub> NO	76,0	7,8	7,6
(XI), (XII)	106-108(6)	1,4921	750, 1110, 1390, 1490, 1620	0,89 t (9H, -CH <sub>3</sub> ), 1,33 m (6H, CH <sub>3</sub> ), 2,42 d (6H, CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> ), 6,63-6,78 (3H, C <sub>6</sub> H <sub>5</sub> )	246	87,5	12,2	-	-	C <sub>18</sub> H <sub>30</sub>	88	11,7	-
(XIII)	190-193(5)	1,5095	760, 1150, 1600, 2270	0,9 t (9H, CH <sub>3</sub> ), 1,33 m (6H, CH <sub>3</sub> ), 2,42-2,5 (8H, CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> , CH <sub>2</sub> -CN), 3,67-4,3 (4H, O-CH <sub>2</sub> ) <sub>2</sub> , 6,63-6,8 (3H, C <sub>6</sub> H <sub>5</sub> )	301	79,7	10,3	4,7	5,3	C <sub>20</sub> H <sub>31</sub> NO	79,3	10,3	4,2
(XIV)	146-148(2)	1,5488	760, 1100, 1440, 1590	1,67 t (4H, CH <sub>2</sub> ), 2,38 (2H, CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> ), 2,7 t (2H, CH <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> N), 7,1-0,43 (9H, -C <sub>6</sub> H <sub>5</sub> , C <sub>6</sub> H <sub>4</sub> N)	211	85,3	8,1	6,6	-	C <sub>13</sub> H <sub>17</sub> N	85,6	8,0	6,5
(XV)	123-130(2)	1,5369	760, 1150, 1600, 2120	1,8 t (4H, CH <sub>2</sub> ), 2,25 m (3H, C≡CH), 2,76 t -CH <sub>2</sub> -C≡C), 2,76 t (2H, CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> N), 7,0-8,43 (4H, C <sub>6</sub> H <sub>4</sub> N)	159	83	8,2	8,8	-	C <sub>11</sub> H <sub>13</sub> N	83,1	8,3	8,7
(XVI)	88-90(2)	1,4900	745, 1440, 1580, 1610	1,67 m (3H, CH <sub>2</sub> ), 7,0-8,3 (3H, C <sub>6</sub> H <sub>5</sub> N)	133	81,2	8,3	10,5	-	C <sub>9</sub> H <sub>11</sub> N	81,0	8,5	10,2
(XVII)	94-96(1,5-2)	1,5320	735, 1580, 1610, 2270	1,5 m (8H, CH <sub>2</sub> ), 2,2 m (2H, CH <sub>2</sub> -CN), 2,5 (6H, (CH <sub>2</sub> ) <sub>3</sub> -C <sub>6</sub> H <sub>5</sub> N), 6,69-7,06 (2H, C <sub>6</sub> H <sub>5</sub> N)	214	78,5	8,4	13,1	-	C <sub>11</sub> H <sub>16</sub> N <sub>2</sub>	78,8	8,3	13,0
(XVIII)	112-114(2)	1,5089	770, 1440, 1590, 2270	1,67 t (4H, CH <sub>2</sub> ), 2,45 m (2H, CH <sub>2</sub> -CN), 2,38 (2H, CH <sub>2</sub> -C <sub>6</sub> H <sub>5</sub> ), 7,1 m (5H, C <sub>6</sub> H <sub>5</sub> )	159	83	8,2	8,8	-	C <sub>11</sub> H <sub>15</sub> N	88,3	8,1	8,5

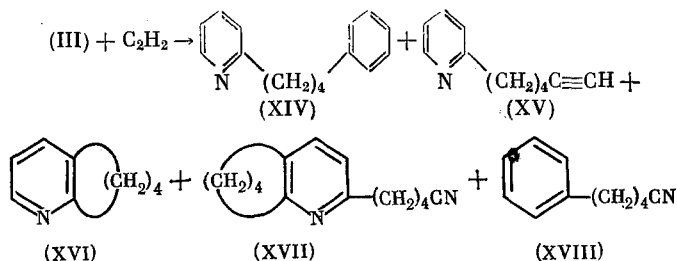
Thus, investigation of the cyclocodimerization of  $\alpha,\omega$ -nitrileacetylenes (I) and (II) with acetylene allowed us to achieve a regioselective synthesis of new types of bicyclic nitrogen- and oxygen-containing heterocycles of the pyridine series, as well as 2-substituted pyridines in sufficiently high yields.

Usage of alkylacetylenes instead of acetylene leads to the formation of benzene derivatives exclusively. Particularly, from (I) and 1-hexyne a mixture of benzenes (XI)-(XII) in a 1:1 ratio was obtained with a total yield >50%.



In order to compare the reactivity of oxygen-containing nitrileacetylenes (I) and (II) with  $\alpha,\omega$ -nitrileacetylene (III) in the reaction with acetylene, we studied the cyclocodimerization of (III) under the action of  $\text{Co(2-ethyl hexanoate)}_2\text{-AlEt}_3$ , under the above-mentioned conditions.

We obtained a mixture of 2-substituted (XIV) and (XV) and bicyclic pyridines (XVI) and (XVII), as well as monosubstituted benzene (XVIII). In contrast to (I) and (II), the nitrileacetylene (III) forms with acetylene the homocyclocodimerization product (XVII); the yield of the latter does not exceed 12%. Pyridine (XVII) was obtained in high yield during homocyclocodimerization of (III) [1]:



Thus, the reaction of nitrileacetylenes with acetylenes proceeding under the action of low-valence cobalt complexes can serve as a convenient and effective synthetic method for new types of mono- and bicyclic functionally substituted pyridine derivatives.

#### EXPERIMENTAL

The  $\alpha,\omega$ -nitrileacetylenes used in this work were obtained according to [2, 3] and were 99% pure. Oligomeric mixtures were analyzed on a Chrom 41 gas chromatograph with a flame-ionization detector using a 1.2-m column packed with 15% of Apiezon on Celite-545 and nitrogen as the carrier gas. The NMR spectra were recorded on a Tesla BS-467 instrument in  $\text{CCl}_4$ . The IR spectra were taken on a UR-20 spectrometer (film); the mass spectra, on an Mkh-13-06 instrument with an ionization chamber temperature of 200°C.

General Method of Cyclocodimerization of  $\alpha,\omega$ -Nitrileacetylenes with Acetylene. To a solution of 3 moles ( $2.915 \cdot 10^{-3}$  g-atom Co) of  $\text{Co(2-ethylhexanoate)}_2$  in 10 ml of toluene at 0°C, in a stream of Ar, was added 9 moles of  $\text{AlEt}_3$ . The mixture transferred to a type B steel autoclave (1-liter capacity), where previously 0.14 mmole of an  $\alpha,\omega$ -nitrileacetylene (I)-(III) in 100 ml of toluene was placed. Then, a necessary acetylene pressure was applied (the pressure in the autoclave increased to 15 atm). The autoclave was heated for 8 h at 150°C. After cooling, the reaction mixture was treated with methanol and then filtered, vacuum distilled. The yields of the obtained products are shown in Tables 1-3, the

constants in Table 4 (the yield of pyridine derivatives on 1 g-atom of Co constitutes ~48 moles at an acetylene: $\alpha,\omega$ -nitrileacetylene ratio equal to 1:10).

## CONCLUSIONS

Cyclocodimerization of acetylene with  $\alpha,\omega$ -nitrileacetylenes, catalyzed by a  $\text{Co}(\text{2-ethyl hexanoate})_2\text{-AlEt}_3$  system gives new types of mono- and bicyclic pyridines.

## LITERATURE CITED

1. F. A. Selimov, V. R. Khafizov, and U. M. Dzhemilev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1885 (1983).
2. L. Brandsma, *Preparative Acetylenic Chemistry*, Amsterdam (1971), p. 164.
3. S. S. Nametkin, V. M. Radionov, and N. N. Mel'nikov, in: *Reactions and Methods of Investigation of Organic Compounds* [in Russian], Moscow (1952), p. 103.

## SYNTHESIS AND SOME CHEMICAL PROPERTIES OF 8-METHYL-3-HYDROXY-6-OXO-2H-3,4,5,6- TETRAHYDOPYRIMIDO[2,1-b][1,3]THIAZINES

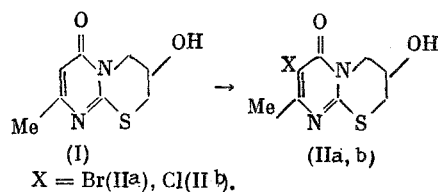
R. M. Faskhutdinov, N. G. Pashkurov,  
and V. S. Reznik

UDC 542.91:547.869:547.85

It was shown earlier that reaction of the sodium salt of 2-mercapto-6-methyluracil with glycerol 1,3-dichlorohydrin yields 8-methyl-3-hydroxy-6-oxo-2H-3,4,5,6-tetrahydropyrimido [2,1-b][1,3]thiazine (I), whereas reaction of 4,6-dimethyl-2-mercaptopyrimidine with glycerol dichlorohydrin leads to the formation of 1,3-bis(4',6'-dimethylpyrimidinyl-2'-thio)-2-hydroxypropane [1].

In the work described here we explore the possibility of synthesizing compound (I) by other methods and study its chemical properties. On using the 1,3-dibromo- instead of the 1,3-dichlorohydrin of glycerol the reaction proceeds faster, but it does not lead to a substantially increased yield. Next we have found that (I) is also formed in much higher yield on reacting the sodium salt of 2-mercapto-6-methyluracil with epichlorohydrin.

Reaction of (I) with bromo- and chlorosuccinimide gives the corresponding 7-halo compounds (II) in good yields:



In the IR spectra of these compounds the absorption band in the  $3000\text{-}3100\text{ cm}^{-1}$  region, characteristic of the C-H band at the 7 position of starting compound (I), has disappeared [2].

The OH group in the pyrimidothiazine (I) can be acylated with acid chlorides. Thus, from (I) and  $\text{PhCOCl}$  or p-toluenesulfonyl chloride in MeCN in the presence of  $\text{Et}_3\text{N}$  the corresponding derivatives (III) and (IV) are obtained.

---

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Branch of the Academy of Sciences of the USSR. Translated from *Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya*, No. 7, pp. 1634-1636, July, 1986. Original article submitted December 24, 1984.