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P. B. Terent'ev, A. N. Kost, A. A. Shchegolev

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Abstract

Full Text

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P. B. Terent' ev, A. N. Kost, A. A. Shchegolev
and Corresponding Member of the Academy of Sciences of the USSR **A. P. Terent' ev**

Synthesis and Some Reactions of Pyridylethynylcarbinols

Heterocyclic bases having a triple bond in the side chain have been studied very little. Yet such compounds may serve as starting materials for the synthesis of a whole series of new systems.

In studying the properties of the acetylene group attached to the pyridine nucleus, we carried out the condensation of 2-methyl-5-ethynylpyridine (I) ([1]) with aldehydes and ketones under the conditions of the Favorskii reaction. As in the case of other substituted acetylenes ([2]), the best yields of carbinols were achieved with the use of a 4-5-fold excess of alkali. Condensation of (I) with ketones proceeds readily and in good yields in anhydrous ether at 0°. At the same time, the reaction of I with aldehydes could be carried out only at −20, −40° and at high dilution, using tetrahydrofuran as the solvent.

$$\text{2-methyl-5-ethynylpyridine (I)} \quad + \quad \begin{matrix}\text{R}\\ \text{R}_1\end{matrix}\text{C=O} \xrightarrow{\text{KOH}} \text{2-methyl-5-pyridyl-C}\equiv\text{C}-\text{C(OH)(R)(R}_1\text{)}$$

The Kucherov reaction with the tertiary carbinols obtained does not take place in 15-20% sulfuric acid. Only by using 25% sulfuric acid were we able to obtain from carbinol II ($R = R_1 = CH_3$) the corresponding α-keto alcohol (III), the structure of which was proved by the infrared spectrum (the presence of a frequency at 1714 cm^{-1}, characteristic of a C=O group not conjugated with an aromatic nucleus) and by isolation from the products of its periodate oxidation of acetone (as the 2,4-dinitrophenylhydrazone).

$$\text{II} \xrightarrow[\text{H}^+,\,\text{Hg}^{++}]{\text{H}_2\text{O}} \text{III} \xrightarrow{\text{HIO}_4} [\text{2-methyl-5-pyridylacetic acid}] + (\text{CH}_3)_2\text{C=O}$$

Oxyketone III was subjected to the Fischer reaction by heating its phenylhydrazone with catalytic amounts of anhydrous zinc chloride at 190-210°. As a result, the sole product isolated was 2-(1-methyl-1-hydroxyethyl)-3-(6-methylpyridyl-3)-indole (V). It was identified by its IR spectrum (there is a frequency of N–H and OH vibrations in the region of 3200 cm^{-1}, and the vibration frequencies of an unsaturated bond in the region of 1640-1660 cm^{-1} are absent) and

by its UV spectrum (a maximum in the region of 267 mμ, characteristic of β-phenylindoles).

When an analogous reaction was carried out with oxyketone IV, in addition to 2-(1-hydroxycyclohexyl-1)-3-(6-methylpyridyl-3)-indole (VI), there was also isolated the pro-

product of its dehydration, 2-(cyclohexenyl-1)-3-(6-methylpyridyl-3)-indole (VII), in the IR spectrum of which there are vibration frequencies in the region of 1644 cm^{-1}.

(IV) $R + R_1 = -(CH_2)_5-$

$\xrightarrow[200^\circ]{ZnCl_2}$

(V) $R = R_1 = CH_3$

(VI) $R + R_1 = -(CH_2)_5-$

(VII)

Experimental Part

Condensation of I with ketones. To a mixture of 0.1 mole of I and 0.4 mole of powdered KOH in 25 ml of abs. ether at 0° and with stirring, 0.1 mole of ketone was added, the mixture was left overnight, saturated with carbon dioxide gas, and the carbinol was isolated (see Table 1).

Condensation of I with aldehydes. To a mixture of 0.05 mole of I and 0.25 mole of powdered KOH in 25 ml of abs. tetrahydrofuran, with stirring and cooling (−25, −40°), a solution of 0.1 mole of aldehyde in 20 ml of abs. tetrahydrofuran was slowly (1.5–2 hours) added, and the mixture was stirred for another 2 hours. On the following day it was acidified, extracted with ether, the aqueous solution was neutralized, extracted with ether, and the residue after removal of the solvent was chromatographed on alumina, eluting I with petroleum ether, and the carbinol with a mixture of benzene and acetone (1 : 1).

2-Methyl-5-(3-methyl-3-oxobutyl)-pyridine (III). A solution of 8.7 g of 2-methyl-5-(3-methyl-3-hydroxybutyn-1-yl)-pyridine (II, $R = R_1 = CH_3$) in 50 ml of 25% sulfuric acid was boiled in the presence of 0.1 g of mercuric oxide for 10 hours, neutralized with soda, extracted with chloroform, and after removal of the solvent the residue was distilled in vacuum. Yield 50.5%, b.p. 158–162°/7 mm, m.p. 52–54°.

Found, %: N 6.95; 7.05

$C_{11}H_{15}O_2N$. Calculated, %: N 7.25

2-(1-Methyl-1-hydroxyethyl)-3-(6-methylpyridyl-3)-indole (V). 1.9 g of

III and 1 g of phenylhydrazine were heated (150°) for 0.5 hour, 0.2 g of anhydrous zinc chloride was added, and heating was continued for another 1.5 hours at 200-220°. The mixture was cooled, and the reaction mass was reprecipitated twice from an acidic solution. Yield 0.5 g (19%), m.p. 150-152° (from benzene + petroleum ether 1 : 1). λ_{max}267 mμ (lg ε 4.08) (from methanol).

Found, %: N 10.92; 10.81
$C_{17}H_{19}ON_2$. Calculated, %: N 10.53

2-Methyl-5-(2-(1-hydroxycyclohexyl-1)-2′-oxoethyl)-pyridine (IV). A solution of 4.3 g of II ($R + R_1 = -(CH_2)_5$) in 25 ml of 25% sulfuric acid with addition of 0.05 g of mercuric oxide was boiled for 7 hours, neutralized with soda, extracted with benzene, the extract was evaporated and chromatographed on alumina. 2.7 g (49%) of a substance with m.p. 64-65° was isolated.

Found, %: N 6.51; 6.15
$C_{14}H_{19}O_2N$. Calculated, %: N 6.00

2-(1-Hydroxycyclohexyl-1)-3-(6-methylpyridyl-3)-indole (V). 5.8 g of IV and 2.7 g of phenylhydrazine were heated (150°) for 0.5 hour, add-

Table 1

$CH_3-C_5H_3N-C\equiv C-C(OH)(R)(R_1)$

R	R_1	Yield, %	M.p., °C	B.p., °C mm	C, % found	C, % calculated	H, % found	H, % calculated	N, % found	N, % calculated
CH_3	CH_3	90	101–102	–	75,43	75,57	7,52	7,55	–	–
C_2H_5	CH_3	80	98–99	–	75,98	76,19	7,94	7,94	–	–
C_3H_7	CH_3	48	30–32	146–150°/2	76,53	76,85	8,46	8,37	–	–
$(CH_3)_3C$	CH_3	70	100–101	–	77,52	77,45	9,22	9,20	–	–
$(CH_2)_5$	$(CH_2)_5$	98	116–118		78,38	78,14	8,02	7,91	–	–

R	R_1	Yield, %	M.p., °C	B.p., °C mm	C, % found	C, % calculated	H, % found	H, % calculated	N, % found	N, % calculated
C_6H_5	CH_3	60	104 – 105		–	–	–	–	5,69	5,71
C_2H_5	H	38,7*	120 – 123**	165 – 167°/8	50,32	50,25	4,31	4,08	5,99	5,91
C_3H_7	H	20,0*	103 – 104***	182 – 184°/8	–	–	–	–	9,46	9,43
– C_4H_9	H	35,0*	112 – 114**	178 – 180°/6	52,37**	52,78	4,80	4,91	4,66	9,09***

* Based on pyridylacetylene charged.
** Picrate.
*** Phenylurethane.

0.2 g of anhydrous zinc chloride was added and the mixture was heated for another 2.5 hours at 175-190°. It was cooled, reprecipitated twice from an acidic solution, and the resulting oil was extracted with benzene. From the extract, 0.9 g (12%) of V was obtained, m.p. 152-154°, λ_{max}275 mμ ($\lg\varepsilon$4.01) (from methanol).

Found, %: N 9.03; 8.98
$C_{20}H_{22}ON_2$. Calculated, %: N 9.11

The residue insoluble in benzene was chromatographed on alumina. 0.3 g of VI was obtained, m.p. 70-71°.

Found, %: N 9.46; 9.33
$C_{20}H_{20}N_2$. Calculated, %: N 9.72

Moscow State University
named after M. V. Lomonosov

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Note: Figure translations are in progress. See original paper for figures.

Source: Math-Net.Ru and CyberLeninka. Machine translation. Verify with the original.