FISCHER REACTION AND OTHER TRANSFORMATIONS OF ARYL- AND PYRIDYLHYDRAZONES UNDER THE INFLUENCE OF ALKALI METAL ALKOXIDES

M. F. Marshalkin and L. N. Yakhontov

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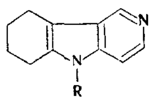
The closing of the indole ring to give a product in 40% yield on prolonged (16 h) heating of acetophenone phenylhydrazone with an alcohol solution of sodium ethoxide was described in [1]. We have made a more detailed study of the transformations of aryl- and pyridylhydrazones under the influence of alkali metal alkoxides and have found that the reaction of 21 mmole of cyclohexanone phenylhydrazone with 120 mmole of sodium ethoxide at 235°C for 40 min makes it possible to obtain 1,2,3,4-tetrahydrocarbazole (mp 115-116°) in 93.6% yield. Under similar conditions (for a reaction time of 15 min), 5,6,7,8-tetrahydro-γ-carboline (I) (mp 269°) was synthesized in 42% yield from cyclohexanone 4-pyridylhydrazone, and 4-aminopyridine (II) (5% yield) and 4-ethylaminopyridine (III) (35% yield) were isolated as side products; cyclohexanone 2,6-dimethyl-4-pyridylhydrazone with mp 165-176° (from 50% aqueous alcohol) (Found,%: C 71.5; H 8.7; N 19.5. $C_{13}H_{19}N_3$. Calculated,%: C 71.8; H 8.8; N 19.3) gave 2,4-dimethyl-5,6,7,8-tetrahydro-γ-carboline with mp 277-278° (from 50% aqueous methanol) (Found,%: C 78.2; H 8.2; N 13.7. $C_{13}H_{16}N_2$. Calculated,%: C 78.0; H 8.0; N 14.0) in 48% yield. The alkylation of 1 g (58 mmole) of I at the pyrrole nitrogen atom proceeds readily when 70 mmole of the appropriate alkyl halide is used in the presence of sodium amide (from 0.5 g of Na and 100 ml of liquid ammonia) in 30 ml of dimethylformamide at 80-85° for 3 h. For aryl- and pyridylhydrazones of aromatic aldehydes, in which the normal Fischer reaction is impossible and heating with alkali metal alkoxides is accompanied by cleavage of the N–N bond without the semibenzidine rearrangement [2], the chief direction of the process depends on the electromeric characteristics of both aromatic (or heteroaromatic) residues of the molecule. In contrast to benzaldehyde 4-pyridylhydrazone, for which the process gives 4-ethylaminopyridine (III) in 83% yield at 240° (15 min) and the mixture contains 2% II, according to gas-liquid chromatography [2], the chief product for benzaldehyde phenylhydrazone under the same conditions is aniline (IV) (86% yield), and the amount of N-ethylaniline (V) does not exceed 3%. Only IV (80% yield) is formed from p-nitrobenzaldehyde phenylhydrazone at 210° (15 min), while a mixture of IV and V in yields of 16 and 12%, respectively, is obtained from p-methoxybenzaldehyde phenylhydrazone at 255° (15 min). An uncontrollable exothermic reaction leading to ejection of the reaction mass ensues when benzaldehyde 2,4-dinitrophenylhydrazone is heated to 110° with sodium ethoxide.

TABLE 1. Yields and Properties of the Synthesized Compounds



Substituent in the 9 position (R)	mp of hydroch. °C	Empirical formula	Found, %				Calc., %				Yield, %
			C	H	Cl	N	C	H	Cl	N	
$-CH_2C_6H_5$	298—299	$C_{17}H_{25}N_2 \cdot HCl$	72,1	6,5	11,7	9,4	72,5	6,4	11,7	9,4	84
$-CH_2CH_2N(C_2H_5)_2$	256—257	$C_{17}H_{25}N_3 \cdot 2HCl$	59,2	7,9	20,7	12,0	59,3	7,9	20,6	12,2	85
$-CH_2CH_2CH_2N(CH_3)_2$	270—271	$C_{16}H_{23}N_3 \cdot 2HCl$	58,1	7,6	21,4	12,8	58,0	7,6	21,5	12,7	86
$-CH_2CH_2N(CH_3)_2$	282—283	$C_{15}H_{21}N_3 \cdot 2HCl$	57,2	7,5	22,4	13,3	57,0	7,3	22,4	13,3	83

S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, p. 1576, November, 1972. Original article submitted March 27, 1972.

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