HETEROAROMATIZATION OF ALIPHATIC IMINES IN THE PRESENCE OF AN ALUMINUM – POTASSIUM CATALYST*

G. Ya. Kondrat'eva, Yu. S. Dol'skaya,
E. A. Aleksandrova, and B. A. Kazanskii

UDC 542.97+547.821.4'831'833

A method for the catalytic synthesis of alkylpyridines by heteroaromatization of aliphatic imino compounds over an aluminum–potassium catalyst was found and investigated. Condensed heterocyclic systems – quinoline, isoquinoline, and pyridine – were obtained by heteroaromatization of imines of cyclic aldehydes or ketones.

Several types of catalytic transformations of unsaturated amines over an aluminum–potassium catalyst have been described: migration of the carbon–carbon double bond in N-alkylideneallylamines to give conjugated 2-aza-1,3-dienes [2], diene condensation of heterodienes with acrylonitrile and olefins [1,3,4], and heteroaromatization of imines to pyridine bases [5,6].

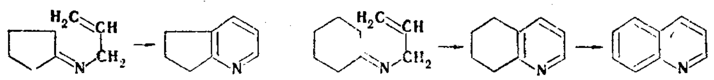
Our investigations have demonstrated that alkalized aluminum oxide is an active heteroaromatization catalyst with respect to aliphatic imines. Aliphatic imines of the RCH=NR' type, where R and R' are saturated or unsaturated hydrocarbon residues, are converted to the corresponding alkylpyridines on contact with K_2O/Al_2O_3.

A mixture of isomeric pyridine bases is obtained in the aromatization of imines whose molecules contain more than six atoms in the straight chain. The presence of a heteroatom creates greater possibilities for the formation of isomeric compounds than is observed in the analogous transformation of hydrocarbons: while dehydrocyclization of heptanes and heptadienes gives only toluene, catalytic conversion of an imine with a seven-membered chain gives α-, β-, and γ-picolines, depending on the form of the groups on both sides of the nitrogen.

The yields of the alkylpyridines formed depend primarily on the overall unsaturated character of the starting compounds. The most difficult heteroaromatization reactions were those involving RCH = NR' compounds with saturated R and R' groups. Pyridine bases are formed from such imines only at or above 400°C, and the yields are very low (see Table 1). Imines RCH = NR' in which R or R' contain a C=C bond are aromatized at lower temperatures in better yields: when the number and position of the atoms making up the imine molecule are held constant, an increase in the number of double bonds by one increases the yield of the corresponding alkylpyridines by a factor of 2-2.5 (see Table 1).

The position and number of multiple bonds in the starting molecule are of great importance. The difference in the yields of isomeric alkylpyridines obtained, for example, from N-crotylideneallylamine, is explained chiefly by the fact that carbon atoms with different degrees of unsaturation participate in closing of the six-membered ring.

Imino derivatives of cyclic aldehydes and ketones are converted to two-ring nitrogen-containing bases during heteroaromatization on K_2O/Al_2O_3. 2,3-Cyclopentenopyridine was thus obtained from N-cyclopentylideneallylamine, while cyclohexylideneallylamine gave a mixture of 5,6,7,8-tetrahydroquinoline and quinoline:



---

*Communication VII of the series "Investigation of Unsaturated Amines." See [1] for communication VI.

Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 970-974, July, 1972. Original article submitted June 22, 1971.

TABLE 1. Catalytic Dehydrocyclization of Imines at 350°C and a Space Velocity of 0.4 h^{-1}

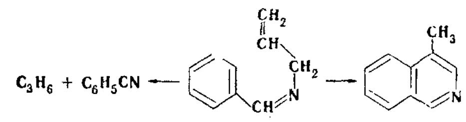
Starting imines	Material, g	Catalyzate yield, %	Dehydrocyclization products	bp, °C (mm)	Yield, % (GLC)	Picrate, mp, °C
$CH_3CH=NC_3H_7$ (I)*	20	7,2	Pyridine	114—115	4,4	163—164
$C_2H_5CH=NC_3H_7$ (II)*	24	18,4	β-Picoline	143—144	6,2	148—149
$(CH_3)_2C=NC_3H_7$ (III)*	20	12,5	α-Picoline	128—130	5,2	164—165
$CH_3CH=NCH_2CH=CH_2$ (IV)	26	20,6	Pyridine	114—115	11,7	163—164
			3,4-Dimethylpyridine [13]	178—179	20,0	162—163
			3-Ethylpyrid. [14]	164—165	14,3	128—130
			2-Ethylpyrid. [14]	149—150	5,0	107—108
$C_2H_5CH=NCH_2CH=CH_2$ (V)	20	17,6	β-Picoline	143—144	16,0	148—149
$(CH_3)_2C=NCH_2CH=CH_2$ (VI)	20	16,3	α-Picoline	128—129	10,2	163—164
			2-Methyl-3-isopropylpyridine	185—190[a]	16,0	
			2-Isobutylpyridine		6,0	
$C_3H_7CH=NCH_2CH=CH_2$ (VII)	25	19,5	3,4-Dimethylpyridine [13]	178—179	10,5	162—163
			3-Ethylpyrid. [14]	164—165	5,0	128—129
			2-Ethylpyridine		3,0	
$CH_3CH=CHCH=NCH_2CH=$ $=CH_2$ (VIII)	20	15,2	3,4-Dimethylpyridine [13]	178—179	20,0	162—163
			3-Ethylpyrid. [14]	164—165	14,0	128—129
			2-Ethylpyrid. [14]		5,0	
$CH_3CH=CHCH=NCH_3$ (IX)	21	14,5	Pyridine		1,7	
			3-tert-Butylpyridine [14][b]	194—195	56,0	153—154[c]
sym-Triallylhexahydrotriazine (X)	20	15,8	3,5-Dimethylpyridine [15]	169—170	31,0	237[d]
N-Cyclopentylideneallylamine (XI)	20	16,5	2,3-Cyclopentenopyridine [16]	135—140 (35)	38,0	182
N-Cyclohexylideneallylamine (XII)	23	17,3	5,6,7,8-Tetrahydroquinoline [16]	91—93 (12)	47,0	157—158
			Quinoline	116—120 (17)		201—202
N-Benzylideneallylamine (XIII)	20	15,9	4-Methylisoquinoline [17]	110—115 (6)	10,5	194—195

---

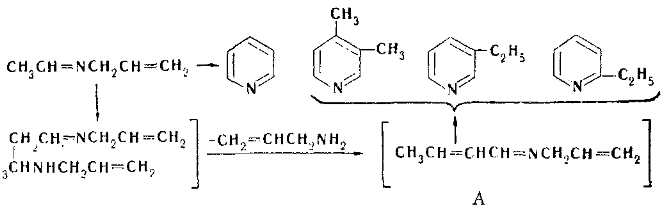
*The reaction temperature was 400°C.

[a] This fraction was oxidized with $KMnO_4$, and the pyridinecarboxylic acids isolated were identified by paper chromatography [12] with elution by $n-C_4H_9OH-CH_3COOH$–water (4 : 1 : 2) and subsequent treatment with a mixture of a 1% solution of Mohr's salt, 10% aqueous hydroxylamine hydrochloride solution, and pyridine in a ratio of 20 : 2 : 1. Only two acids – quinolinic and picolinic in a ratio of 3 : 1 – were found in the oxidation products. [b] Bands at 1250 and 1210 cm^{-1}, which are characteristic for groupings with a quaternary carbon atom, were observed in the IR spectrum of the alkylpyridine. The position of the substituent was proved by oxidation to the pyridinecarboxylic acid and determination of the melting point of a mixture of the product with genuine nicotinic acid. [c] Found: C 49.9, 49.7; H 4.2, 4.4%. $C_{15}H_{16}N_4O_7$. Calculated: C 49.5; H 4.4%. [d] Found: C 46.4, 46.2; H 3.5, 3.5%. $C_{13}H_{12}N_4O_7$. Calculated: C 46.4; H 3.6%.

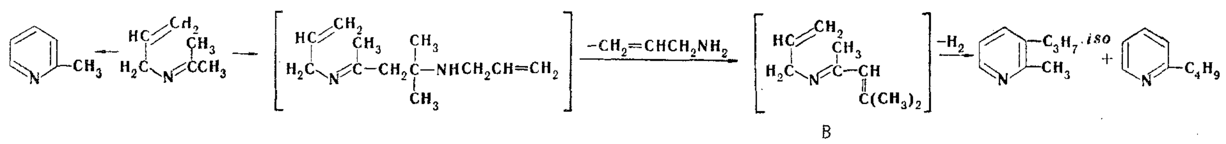
These transformations proceed in good yields and can be used in the synthesis of condensed nitrogen-containing cyclic systems of the quinoline type. Two-ring bases that contain an isoquinoline ring are formed during the dehydrocyclization of imino derivatives of aromatic aldehydes. The yields of aldimine aromatization products are, however, lower than in the case of derivatives of cyclic ketones. For example, N-benzylideneallylamine in contact with K_2O/Al_2O_3 is chiefly cleaved to give benzonitrile and propylene (50% yield); the dehydrocyclization product – 3-methylisoquinoline – was isolated in only 10% yield:



The high-boiling fractions of the catalyzates contain a considerable amount of pyridine bases of higher molecular weight than expected from the scheme of the usual dehydrocyclization. These compounds are also formed in the reaction mixture as a result of aromatization of more complex imines rather than of the starting imines. It is known [7,8] that heating of aliphatic imines gives their unstable dimers, which readily split out an RNH_2 molecule and are converted to new, more complex imino compounds. The new imines, which have high molecular weights and a high degree of unsaturation, are extemely active in ring closing; they also serve as a source for the formation of higher alkylpyridines – 3,4-dimethylpyridine and 2- and 3-ethylpyridines (39.3% yield) are formed along with pyridine (11.7% yield) from N-ethylideneallylamine:

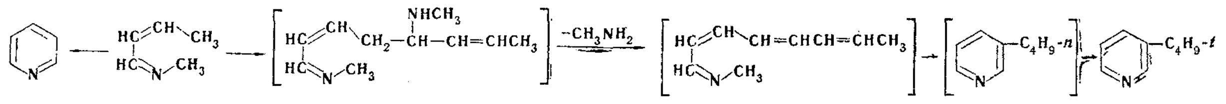


Under the same conditions, N-isopropylideneallylamine not only cyclizes to α-picoline, but, to a considerably greater degree, forms 2-methyl-3-isopropylpyridine and 2-isobutylpyridine:

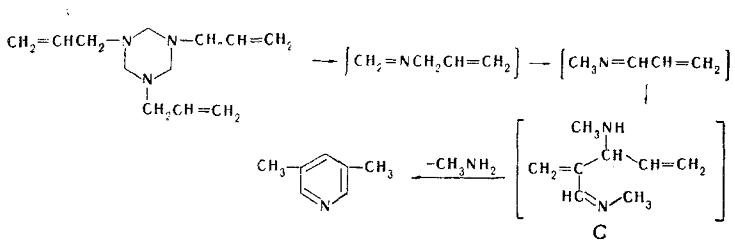


The proposed intermediate polyunsaturated imines A and B were obtained by condensation of the appropriate carbonyl compounds (crotonaldehyde and mesityl oxide) with allylamine; the heteroaroamatization of these imines give the same final products as indicated in the schemes presented above.

N-Crotylidenemethylamine, the molecule of which is a six-membered chain bounded by methyl groups of low activity, gives virtually no pyridine in the catalytic process but is converted to high yields of 3-tert-butylpyridine in high yields:



N,N',N"-Triallyl-sym-hexahydrotriazine reacts peculiarly over the aluminum–potassium catalyst to give 3,5-dimethylpyridine in 31% yield. The sequence of transformations of the starting triazine apparently includes steps involving depolymerization, migration of the C=N bond in the monomer, followed by dimerization of the monomer to imine C, and, finally, aromatization of the latter:



The last two examples – formation of tert-butylpyridine from N-crotylidenemethylamine and of 3,5-dimethylpyridine from triallyltriazine – are also of interest because of the fact that closure of the pyridine ring occurs without splitting out of hydrogen in these cases.

EXPERIMENTAL

The starting imines were obtained by known methods from the appropriate carbonyl compounds and amines. The method in [9] was used in the synthesis of imines I, II, IV, V, VII, VIII, and IX; imine XIII was obtained according to the directions in [10]; III, VI, XI, and XII were obtained by the method in [2, [11]; and imine X was synthesized by the method in [3]. The physical constants of all of the substances were in agreement with the values presented in the literature. The imine obtained from mesityl oxide had mp 180-185°. Found: C 78.4; H 11.0%. $C_9H_{15}N$. Calculated: C 78.8; H 11.0%.

A flow apparatus with 25 ml of aluminum–potassium catalyst (3% K_2O/Al_2O_3) from one batch of a preparation with 3-by-5-mm grains was used for the heteroaromatization of the imines. The imine was passed over the catalyst at 350° at a space velocity of 0.4 h^{-1} in a stream of nitrogen. The liquid catalyzate collected at 0° was dried with KOH and distilled. After each dehydrocyclization experiment (4-5 h), the system was flushed with nitrogen for 15 min, and the catalyst was regenerated in an air stream at 550° for 1.5 h. The activity of the catalyst was checked after each 25-30 h of operation from the degree of conversion of N-ethylideneallylamine.

The pyridine bases were identified from their physicochemical properties, by spectral methods (UV and IR spectroscopy), and from their retention times in a chromatographic column. The IR spectra were recorded with a PS-301 spectrophotometer, and the UV spectra of alcohol solutions were recorded with a Hitachi EPS-2 spectrophotometer. An LKhM-8 chromatograph with a flame-ionization detector and a 1.5-m-long stainless steel column filled with Apiezon L on Chromosorb W was used for the gas-liquid chromatography. The temperature was 150°, and the carrier gas was nitrogen.

In some cases, the position of the substituents in the alkylpyridines was proved by oxidation of them to known pyridinecarboxylic acids. Paper chromatography [12] was sometimes used to interpret the mixtures of acids. The chief experimental results of the present investigation are assembled in Table 1.

LITERATURE CITED

1. Yu. S. Dol'skaya and G. Ya. Kondrat'eva, Izv. Akad. Nauk SSSR, Ser. Khim., 2123 (1970).
2. G. Ya. Kondrat'eva and Yu. S. Dol'skaya, Izv. Akad. Nauk SSSR, Ser. Khim., 2045 (1967).
3. B. A. Kazanskii, G. Ya. Kondrat'eva, Yu. S. Dol'skaya, V. A. Petukhov, I. P. Yakovlev, and B. V. Lopatin, Zh. Organ. Khim., 6, 2197 (1970).
4. B. A. Kazanskii, G. Ya. Kondrat'eva, and Yu. S. Dol'skaya, Zh. Organ. Khim., 6, 2203 (1970).
5. Yu. S. Dol'skaya, Candidate's Dissertation [in Russian], Inst. Organ. Khim., Akad. Nauk SSSR (1968).
6. G. Ya. Kondrat'eva, Yu. S. Dol'skaya, and B. A. Kazanskii, USSR Author's Certificate No. 270,735 (1968); Byull. Izobr., No. 17 (1970).
7. G. Ya. Kondrat'eva and Yu. S. Dol'skaya, Izv. Akad. Nauk SSSR, Ser. Khim., 654 (1967).
8. R. Tiollais, Bull. Soc. Chim. France, 716 (1947).
9. R. Tiollais, Bull. Soc. Chim. France, 708 (1947).
10. M. Bergmann and A. Mieckely, Ber., 57, 662 (1924).
11. D. G. Norton, V. E. Haury, F. C. Davis, L. J. Mitchell, and S. A. Ballard, J. Org. Chem., 19, 1054 (1954).
12. J. Morimoto and K. Furuta, Anal. Chem., 34, 1033 (1962).
13. Y. Oshima and K. Ishibashi, J. Chem. Soc. Japan, 29, 445 (1926).
14. H. C. Brown and W. A. Murphey, J. Am. Chem. Soc., 73, 3308 (1951).
15. M. P. Oparina, Zh. Russk. Fiz.-Khim. Obshchestva, 61, 2001 (1929).
16. V. Prelog and S. Szpilfogel, Helv. Chim. Acta, 28, 1684 (1945).
17. M. Le Blanc, Ber., 21, 2299 (1888).