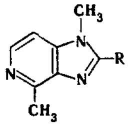
LETTERS TO THE EDITOR

HOMOLYTIC C-METHYLATION OF IMIDAZOLO[4,5-c]PYRIDINE DERIVATIVES

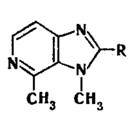
Yu. M. Yutilov and A. G. Ignatenko

UDC 547.785.5'821

For the first time we have demonstrated the possibility of C-methylation of imidazo[4,5-c]pyridine derivatives (I) under the conditions of silver ion-catalyzed oxidative decarboxylation of acetic acid with ammonium persulfate [1]. Methylation initially takes place in the 4 position of the imidazo[4,5-c]pyridine ring, after which the ring is methylated in the 2 position. Thus a mixture of 1,4-dimethyl-I (III) and 1,2,4-trimethyl-I (IV) is formed from 1-methyl-1H-imidazo[4,5-c]pyridine (II), whereas methylation of 3-methyl-3H-I (V) leads to 3,4-dimethyl-I (VI) and 2,3,4-trimethyl-I (VII). The 1,2- and 2,3-dimethyl derivatives of I were not detected in the reaction mixtures. In other words, the homolytic C-methylation of I derivatives proceeds quite selectively and can be used for the synthesis of difficult-to-obtain 4-methyl derivatives of imidazo[4,5]pyridine. The structures of the compounds obtained were confirmed by the results of elementary analysis and the PMR and mass spectra. The course of the reactions and the separation of the methylation products were monitored by gas–liquid chromatography (GLC) with a PAKhV-0.5 preparative chromatograph with a 2 m by 26 mm column filled with Apiezon L on Chromaton N-AW-DMCS and helium as the carrier gas.



III, IV



VI, VII

III, VI R = H; IV, VII R = CH_3

EXPERIMENTAL

Methylation of 1-Methyl- and 3-Methylimidazo[4,5-c]pyridines (II and V). A solution of 1.0 mmole of $(NH_4)_2S_2O_8$ in 0.5 ml of H_2O was added to a solution of 0.25 mmole of II or V and 0.05 mmole of $AgNO_3$ in a mixture of 1.0 mmole of acetic acid and 0.5 ml of 10% H_2SO_4 solution, and the mixture was stirred at 75° for 10 min, after which it was poured over a mixture of ice and ammonium hydroxide. The resulting mixture was extracted with chloroform, the extract was dried over Na_2SO_4, and the solvent was removed by distillation. Compound II yielded a mixture of III and IV, whereas V gave a mixture of VI and VII. The products were obtained in overall yields of 95 and 85%, respectively. The ratio of IV and V in the mixture was 0.95, as compared with a ratio of 1.95 for VI and VII.

1,4-Dimethyl-1H-imidazo[4,5-c]pyridine (III). The picture of this compound had mp 205-206° (from alcohol). PMR spectrum, δ: 3.23 (s, 4-CH_3), 4.26 (s, 1-CH_3), 8.16 (s, 2.H), 8.63 (d, 7-H, J = 7.4 Hz), and 9.40 ppm (d, 6-H, J = 7.4 Hz).

3,4-Dimethyl-3H-imidazo[4,5-c]pyridine (VI). This compound had mp 159° (from heptane). PMR spectrum, δ: 4.61 (s, 3-CH_3), 3.46 (s, 4-CH_3), 8.44 (d, 7-H, J = 6.0 Hz), 8.75 (d, 6-H, J = 6.0 Hz), and 9.78 ppm (2-H).

1,2,4-Trimethyl-1H-imidazo[4,5-c]pyridine (IV). The dihydrate of this compound had mp 119-120° (from heptane), and the picrate had mp 215-216° (from ethanol). PMR spectrum, δ: 3.13 (s, 2-CH_3), 3.23 (s, 2-CH_3), 4.20 (s, 1-CH_3), 8.21 (d, 7-H, J = 7.1 Hz), and 8.71 ppm (d, 6-H, J = 7.1 Hz).

Institute of Physical-Organic Chemistry and Coal Chemistry, Academy of Sciences of the Ukrainian SSR, Donetsk 340050. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, p. 993, July, 1977. Original article submitted July 13, 1976.

2,3,4-Trimethyl-3H-imidazo[4,5-c]pyridine (VII). This compound had mp 134-135° (from heptane). PMR spectrum, δ: 2.55 (s, 2-CH_3), 3.00 (s, 4-CH_3), 4.01 (s, 3-CH_3), 7.88 (d, 7-H, J = 7.2 Hz), and 8.28 ppm (d, 6-H, J = 7.2 Hz).

LITERATURE CITED

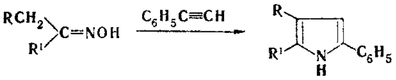
1. F. Minisci, Synthesis, No. 1, 1 (1973).

REACTION OF KETOXIMES WITH PHENYLACETYLENE – A ROUTE TO α-PHENYLPYRROLES

B. A. Trofimov, A. I. Mikhaleva,
S. E. Korostova, and G. A. Kalabin

UDC 547.748.07

The synthesis of pyrroles from ketoximes and acetylene [1] could not be extended to substituted acetylenes (for example, see [2]). However, we have demonstrated that phenylacetylene is capable of undergoing reaction with various ketoximes when the reagents are heated to 120-140°C with 30-50% KOH (based on the weight of the ketoxime) to give the expected α-phenylpyrroles.



R=H, CH_3, C_2H_5, n-C_3H_7; R' = CH_3, C_2H_5, C_6H_5

Thus we have demonstrated the possibility of the use of substituted acetylenes in the reaction; this makes the range of application of this synthesis considerably wider than it was prior to this research.

Thus 2-methyl-5-phenylpyrrole was obtained from acetone oxime in 21% yield. The product was isolated from the reaction mixture by steam distillation and was obtained as white crystals with mp 95°C (from 50% aqueous methanol). Its ^1H and ^{13}C NMR spectra and UV spectra were identical to those previously described, and the results of gas–liquid chromatography (GLC) and the PMR spectrum indicated that it was an individual substance. Similar reaction of acetophenone oxime gave 2,5-diphenylpyrrole (15% yield) as greenish crystals with mp 143°C [isolated by chromatography on Al_2O_3 by elution with petroleum ether–hexane–diethyl ether–alcohol (40 : 32.8 : 26.2 : 1)]. PMR spectrum (in CCl_4): singlet at 8.5 ppm (1-H), doublet at 6.3 ppm ($J_{CH-C-NH}$ = 2 Hz); 3-H and 4-H), and a multiplet of phenyl protons centered at 7.27 ppm. The results of elementary analysis of both compounds were in agreement with the empirical formulas, and the IR spectra contained the typical bands of pyrroles.

LITERATURE CITED

1. B. A. Trofimov, G. A. Kalabin, A. S. Atavin, A. I. Mikhaleva, and E. G. Chebotareva, Khim. Geterotsikl. Soedin., No. 3, 360 (1975).
2. L. V. Sokolyanskaya, A. N. Volkov, and B. A. Trofimov, Zh. Org. Khim., 12, 905 (1976).

Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Irkutsk 664033. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, p. 994, July, 1977. Original article submitted October 25, 1976; revision submitted January 1, 1977.