INVESTIGATIONS IN THE IMIDAZOLE SERIES

LXXVI.* CATALYTIC DECHLORINATION OF CHLORO DERIVATIVES OF IMIDAZOLE

P. M. Kochergin, M. A. Klykov, and I. S. Mikhailova

UDC 547.781.1.4:542.944.7

The catalytic dechlorination of 1-alkyl-5-chloro-, 1-alkyl-4-chloro-, and 1-alkyl(aralkyl)-2-alkyl(aryl)-5-chloroimidazoles in the presence of Raney nickel, which makes it possible to simplify the synthesis of a number of 1-alkyl- and 1-alkyl(aralkyl)-2-alkyl(aryl)imidazoles, was investigated.

Considering the accessibility of 1-alkyl(aryl)-5-chloro-, 1-alkyl(aryl, aralkyl)-2-alkyl(aryl)-5-chloroimidazoles [2-17], and some 1-alkyl(1,2-dialkyl)-4-chloroimidazoles [18-20], a number of investigators have attempted to use them for the synthesis of alkyl derivatives of imidazole by reduction with hydriodic acid in the presence of phosphorus [5, 8, 21, 22] with sodium amalgam [8, 21], sodium [4, 16, 18, 19, 21], magnesium [21], and aluminum [21] in alcohol, or with hydrogen in the presence of a palladium catalyst [23, 24]. However, because of their inconvenience and the low yields of 1-alkyl(1,2-dialkyl)imidazoles they afford, these methods have not found preparative application.

*See [1] for communication LXXV.

TABLE 1. Synthesized Compounds

Compound	R	Empirical formula	Found			Literature data		Yield, %
			bp, °C (mm)	n_D^{20}	mp of the picrate, °C	bp, °C (mm)	mp of the picrate, °C	
I	H	$C_4H_6N_2$	82—84 (12)	1,4948	158—159	94—95 (14—15)[26]	158—159[26, 27]	76—99
II	CH_3	$C_6H_{10}N_2$	95—96 (1—1,5)	1,4879	168—169	212—213 (760)[8]	168—169[19]	90
III	C_2H_5	$C_8H_{14}N_2$	92—94 (5—6)	1,4787	135—136	229—230 (760)[8]	138,5—140,5[16]	74
IV	C_3H_7	$C_{10}H_{18}N_2$	112—114 (5—6)	1,4740	108—109	242—245 (728)[28]	108,5—109,5[16]	82
V	C_4H_9	$C_{12}H_{22}N_2$[a]	90—91 (1—2)	1,4708	—	—	—	72
VI	i-C_4H_9	$C_{12}H_{22}N_2$	98—100 (1—2)	1,4748	—	261—262 (737)[29]	—	90
VII	C_6H_5	$C_{16}H_{14}N_2$[b]	mp 57—58	—	148—149[c]	—	—	94

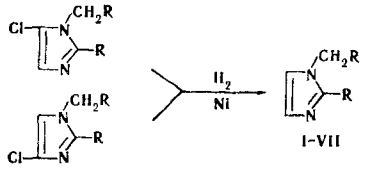
[a] Found: C 73.9; H 11.7; N 14.8%. Calculated: C 74.2; H 11.4; N 14.4%. [b] Found: C 82.3; H 6.0; N 11.7%. Calculated C 82.0; H 6.0; N 12.0%. [c] Found: N 15.2%. Calculated: N 15.1%.

S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 820-822, June, 1972. Original article submitted March 4, 1971.

Side reactions in the reaction of the reagents indicated above with chloroimidazoles have been observed in several studies, and it has also been found that it is impossible to use them for dechlorination. Thus replacement of Cl by I is possible when 1,2-dialkyl-5-chloroimidazoles are heated with HI [8]. A mixture of 1-benzyl-2,3-diphenylimidazolidine and phenylbenzylethylenediamine is obtained instead of the expected 1,2-diphenylimidazole in the reduction of 1,2-diphenyl-5-chloroimidazole with sodium in alcohol [13]. The chlorine atom in the 5 position is not involved in the reaction of sodium in alcohol or of zinc in acetic acid with 1-methyl-2-chloromethyl(cyanomethyl)-5-chloroimidazoles, and 1-methyl-2-methyl(aminomethyl)-5-chloroimidazoles are isolated [23]. The Wurtz reaction to give the corresponding 5,5'-diimidazoles occurs when sodium in petroleum ether acts on 1-alkyl(1,2-dialkyl)-5-chloroimidazoles [3, 8].

Continuing the research we began in [25], we have made a detailed study of the catalytic hydrogenation of 1-alkyl-5-chloro-, 1-alkyl-4-chloro-, and 1-alkyl(aralkyl)-2-alkyl(aryl)-5-chloroimidazoles. It was found that this reaction proceeds best in an organic solvent (lower alcohols) in the presence of Raney nickel and an equivalent amount of alkali or sodium alkoxide, which is necessary to tie up the HCl evolved in the reaction.

The dechlorination of chloroimidazoles to the corresponding imidazoles (I-VI, Table 1) occurs at 40-100° C and a hydrogen pressure of 50-100 atm.



Side reactions – debenzylation and reduction of the phenyl group to a hexahydrophenyl group to form 2-cyclohexylimidazole (VIII) – occur along with dechlorination in the hydrogenation of 1-benzyl-2-phenyl-5-chloroimidazole at 100° and 100 atm. The reaction must therefore be carried out at temperatures no higher than 20-25° in order to obtain 1-aralkyl-2-arylimidazoles, particularly VII.

EXPERIMENTAL

1-Alkyl- and 1-Alkyl(aralkyl)-2-alkyl(aryl)imidazoles (I-VII). A 0.1-mole sample of 1-alkyl(1,2-dialkyl)-5-chloroimidazole [14] or 1-alkyl-4-chloroimidazole [20] in 100-250 ml of ethanol in the presence of an equal amount (by weight) of an alcohol paste of Raney nickel and 0.1 mole of NaOH was hydrogenated at 98-100° at an initial hydrogen pressure of 90-100 atm until hydrogen absorption ceased (~3-5 h). The mixture was cooled and filtered, the alcohol was removed from the filtrate by distillation, and the residual crude I-V were vacuum-distilled. Compound VI was similarly obtained with the difference that the reaction was carried out at 38-40° in the presence of sodium ethoxide, while VII was obtained at a reaction temperature of 20° and 80 atm (in the presence of NaOH). Compound VII was purified for analysis by crystallization from petroleum ether. The picrates of bases I-IV and VII were obtained by the usual method and were recrystallized from ethanol, aqueous ethanol, or water.

2-Cyclohexylimidazole (VIII). This compound was isolated in 13% yield under the conditions of the synthesis of I-V and had mp 178-179°. The picrate had mp 191-192° (from water). According to [30], VIII has mp 178-179°, and its picrate has mp 191-192°.

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