SYNTHESIS OF 3-ARYLAMINOINDAZOLES

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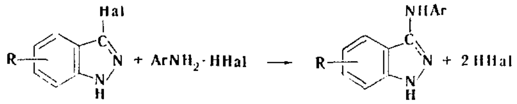
3-Chloro(bromo)indazoles do not react with aromatic amines even under severe conditions. It was found that the hydrochlorides (hydrobromides) of aromatic amines catalyze the exchange of a halogen atom by an arylamino group.

Halogen atoms bonded to the pyrazole ring are extremely inert with respect to nucleophilic agents [1]. In the 3-haloindazole series, the presence of activating electron-acceptor substituents in the benzene ring has almost no effect on the lability of the halogen. Only a certain increase in activity of the halogen in 3-bromo-5-nitroindazole was noted in the reaction with piperidine. An increase in the activity of halogen in nucleophilic substitution reactions is observed when the pyrazole ring is quaternized. For example, quaternary 3-halodimethylindazolium salts readily react with hydrazine and its substituted derivatives, hydroxyl amine, and aliphatic and aromatic amines [3, 4]. We have found that aromatic amines do not react with 3-haloindazoles even on heating above 200°C, and the halogen atom is replaced by an arylamine residue only on heating 3-haloindazoles with aromatic amine hydrohalides (or with mixtures of aromatic amines and their hydrohalides) in sealed tubes or in an autoclave.



$R = H$, CH_3, Br, Cl; Hal = Br, Cl;
Ar = phenyl, p-tolyl, m-tolyl, p-chlorophenyl

In this case, quite pure 3-arylaminoindazoles are obtained in almost quantitative yield. The ease of exchange of halogen provides a basis for assuming that, under the reaction conditions, the 3-haloindazole initially undergoes protonation to give the conjugate acid (I); a positive charge is thereby created to a sufficient degree on the carbon atom to which the halogen is attached, and this facilitates nucleophilic attack. The reactivities of chlorine and bromine are approximately the same, and the presence of substituents in the benzene ring of the 3-haloindazole does not have a substantial effect on the course of the reaction. The compositions and structures of the 3-arylaminoindazoles obtained were established on the basis of elementary analysis, IR spectra, and alternative synthesis, namely, by a reduction of 3-aryl-4-arylimino-3,4-dihydrobenzo-1,2,3-triazines via the method described in [5]. The synthesized 3-arylaminoindazoles are colorless crystalline substances, solutions of which have intense violet fluorescence. Reaction with p-dimethylaminobenzaldehyde is characteristic for them; in contrast to the usual yellow color observed for secondary arylamines [6, 7], an intense orange-red color is formed on paper in hydrogen chloride vapors.

Intense absorption bands at 3265-3420 cm^{-1} are present in the IR spectra of the 3-arylaminoindazoles. The high-frequency band apparently should be assigned to the stretching vibrations of the exocyclic amino

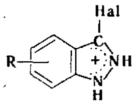


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TABLE 1. 3-Arylaminoindazoles

R	Ar	bp, °C	Empirical formula	Found, %			Calc., %			Yield, %
				C	H	N	C	H	N	
H	Phenyl	170—171	$C_{13}H_{11}N_3$	74,7	5,5	19,9	74,5	5,3	20,1	96[a]
H	p-Tolyl	179—180	$C_{14}H_{13}N_3$	75,4	5,9	18,7	75,3	5,9	18,8	98
H	m-Tolyl	140—141	$C_{14}H_{13}N_3$	75,2	6,0	18,8	75,3	5,9	18,8	91
5-CH_3	Phenyl	172—173	$C_{14}H_{13}N_3$	75,3	5,8	18,7	75,3	5,9	18,8	96
6-CH_3	Phenyl	195,5—196	$C_{14}H_{13}N_3$	75,4	5,9	18,7	75,3	5,9	18,8	92
5-CH_3	m-Tolyl	169—170	$C_{15}H_{15}N_3$	76,0	6,3	17,6	75,9	6,3	17,7	98
5-CH_3	m-Tolyl	126—127	$C_{15}H_{15}N_3$	75,8	6,2	17,6	75,9	6,3	17,7	92
H	p-Cl-phenyl	212,5—213,5	$C_{13}H_{10}ClN_3$[b]	64,0	4,1	17,3	64,1	4,1	17,2	94
5-Cl	Phenyl	188,5—190	$C_{13}H_{10}ClN_3$[c]			17,2	64,1	4,1	17,2	95[a]
5-CH_3	p-Cl-phenyl	201—202	$C_{14}H_{12}ClN_3$[d]			16,2			16,3	94[a]
5-Br	Phenyl	187—188	$C_{13}H_{10}BrN_3$[e]			14,5			14,6	95[a]
5,7-di-Cl	Phenyl	175—175,5	$C_{13}H_9Cl_2N_3$[f]			15,0			15,1	91[a]

[a] 3-Chloro-substituted indazoles were used in these reactions, while 3-bromo-substituted indazoles were used in the remaining reactions. [b] Found,%: Cl 14.7. Calculated,%: Cl 14.6. [c] Found,%: Cl 14.4. Calculated,%: Cl 14.6. [d] Found,%: Cl 13.6. Calculated,%: Cl 13.8. [e] Found,%: Br 27.6. Calculated,%: Br 27.7. [f] Found,%: Cl 25.4. Calculated,%: Cl 25.5.

group, while the low-frequency band should be assigned to the −N−H− vibrations of the amino group of the indazole ring [8]. Only one intense broad band with a maximum at 3200 cm^{-1} is observed in the spectrum of unsubstituted indazole in these absorption ranges. 3-Phenyl(p-tolyl)aminoindazoles are identified by strong absorption at 1620, 1605, 1560, 1450, 1240, 900, 745, 655, and 435 cm^{-1}. The band at 1620 cm^{-1} should be assigned to the −C=N− vibrations of the indazole ring [8], while the closely situated band at 1600-1605 cm^{-1} should be assigned to the stretching vibrations of the bond of the nitrogen atom with the carbon of the aryl group (−N−Ar) [9].

EXPERIMENTAL

The IR spectra of KBr pellets were recorded with a UR-20 spectrophotometer. The 3-haloindazoles were obtained by known methods [10, 11] and had physical constants that were in agreement with those presented in the literature.

3-Phenylaminoindazoles. A mixture of 5.8 g (0.03 mole) of 3-bromoindazole and 7.8 g (0.06 mole) of aniline hydrochloride was heated in a sealed glass ampule in an oil bath at 170-175° for 8 h. The reaction mass was made alkaline with sodium hydroxide solution, and the unchanged aniline was removed by steam distillation. The residue was removed by filtration and washed with hot 3% sodium hydroxide solution to remove the unchanged 3-bromoindazole to give 6 g (96%) of product. Recrystallization from dilute alcohol gave silvery plates with mp 170-171°. Found,%: C 74.4; H 5.3; N 19.9. $C_{13}H_{11}N_3$. Calculated,%: C 74.5; H 5.3; N 20.1. No melting-point depression was observed for a mixture of this product with the preparation obtained by reduction of 3-phenyl-4-phenylimino-3,4-dihydrobenzo-1,2,3-triazine with stannous chloride. Comparable samples had identical IR spectra. The compounds presented in Table 1 were similarly obtained.

LITERATURE CITED

1. I. I. Grandberg, L. I. Gorbacheva, and A. N. Kost, Zh. Obshch. Khim., 33, 511 (1963); 34, 650 (1964).
2. J. M. Barclay, N. Campbell, and G. Dodds, J. Chem. Soc., 113 (1941).
3. R. Sureau, K. Gilbert, and V. Dupre, French Patent No. 1,297,123 (1962); Chem. Abstr., 58, 1467 (1963).
4. Neth. Appl., 6,616,531 (1967); Chem. Abstr., 68, 60,518 (1968).
5. M. W. Partridge and M. F. Stevens, J. Chem. Soc., 3663 (1964).
6. S. I. Burmistrov, Byul. VKhO im. D. I. Mendeleeva, 2, 14 (1942).
7. S. I. Burmistrov, Zh. Analit. Khim., 1, 265 (1946).
8. D. G. O'Sullivan, J. Chem. Soc., 3278 (1960).
9. L. A. Kazitsina and N. B. Kupletskaya, Application of UV, IR, and NMR Spectroscopy in Organic Chemistry [in Russian], Moscow (1971), p. 43.
10. F. T. Pozharskii, V. G. Sayapin, and B. K. Martsokha, Zh. Obshch. Khim., 34, 2777 (1964).
11. V. S. Belykh and S. I. Burmistrov, Zh. Organ. Khim., 7, 848 (1972).