SYNTHESIS OF HETERYLAMINES

B. A. Tertov, V. V. Burykin, and A. V. Koblik

UDC 547.78+547.789.6+547.821+542.957

N-Substituted (CH_3, $CH_2C_6H_5$, C_6H_5) 2-aminoimidazoles, 2-aminobenzothiazoles, and 2-aminopyridine were obtained by cleavage of heterylphenyltriazenes formed from organolithium and organosodium compounds of heterocycles and phenyl azide.

Methods for the preparation of primary amines of the aliphatic, alicyclic, and aromatic series from organometallic compounds that are based on the direct replacement of the metal by an amino group do not always give good results when they are used for the synthesis of heterylamines. Thus, for example, we were unable to isolate 2-amino-1-methylimidazole from the products of the reaction of 2-lithio- and 2-sodio-1-methylimidazole with chloramine and α-methylhydroxylamine. It therefore seemed of interest to open up the possibility for the synthesis of heterylamines by cleavage, with some mineral acid, of heterylphenyltriazenes, which are readily formed from active organometallic compounds of heterocycles and phenyl azide.

It is obvious that, in the absence of rapid side processes, the composition of the mixture of major products of the cleavage of the triazenes depends on the ratio of the amounts of tautomeric forms I and II.

$$\underset{\text{I}}{R{-}NH{-}N{=}N{-}R'} \rightleftarrows \underset{\text{II}}{R{-}N{=}N{-}NH{-}R'}$$

Since equilibrium in solution is usually shifted to favor form I, the more electronegative R is as compared with R' [1-3], it might have been assumed that many heterylphenyltriazenes (R is heteryl and R' is phenyl) obtained from heterocycles having higher acidities* than R'H will exist predominantly in form I, which also should form precisely the heterylamine on cleavage. In the case of triazenes that contain nitrogen heterocycle groupings, a factor that also promotes the conversion of form II to form I is protonation of the ring nitrogen atoms in acidic media, which leads to an increase in the electronegativity of these groupings. If there is an intramolecular hydrogen bond that stabilizes form II in the triazene, this bond is undoubtedly destroyed in the presence of acids.

We accomplished the following synthesis of heterylamines:

$$RM \rightarrow RNH{-}N{=}N{-}C_6H_5 \xrightarrow{HCl} RNH_2 \cdot HCl.$$

It should be noted that no other methods for the introduction of an amino group into the 2 position of the heterocyclic ring of an N-substituted imidazole have been reported. Several N-substituted 2-aminoimidazoles were previously synthesized by condensation of α-aminoaldehydes or their acetals with cyanamide [4,5].

EXPERIMENTAL

2-Amino-1-methylimidazole Hydrochloride Monohydrate. A solution of 8.8 g (0.064 mole) of butyl bromide in 15 ml of ether was added at 0° with stirring under nitrogen to 0.9 g (0.129 g-atom) of small

*Here we have in view the thermodynamic acidities of RH and R'H as C–H acids.

Rostov State University, Rostov-on-Don. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1552-1554, November, 1972. Original article submitted March 24, 1971.

pieces of lithium in 30 ml of ether. The butyl bromide was added in the course of 45 min, and the mixture was then stirred for another 15 min, after which a solution of 3 g (0.036 mole) of 1-methylimidazole in 20 ml of ether was added in the course of 40 min. A solution of 6 g (0.05 mole) of phenyl azide in 15 ml of ether was then added gradually in the course of 30 min to the resulting 2-lithio-1-methylimidazole. After 1 h, the lithium salt of the triazene was decomposed with 15 ml of water, and 20% acetic acid was then added until the mixture was neutral. The yellow precipitate was removed by filtration, washed with water, and added in portions to 50 ml of cold 15% hydrochloric acid, after which the mixture was held at 80-90° until nitrogen evolution had ceased. The phenol was extracted with ether, and the aqueous layer was boiled with activated charcoal and filtered. The filtrate was evaporated to dryness, and the 2-amino-1-methylimidazole hydrochloride was dissolved in 20 ml of alcohol. The product was precipitated by the addition of ether or ethyl acetate to give 3.9 g (70%) of a substance with mp 83-84°, in agreement with the literature data [4,5].

2-Amino-1-methylimidazole. The 2-amino-1-methylimidazole hydrochloride was dissolved in 25 ml of water, and the solution was treated with 5 g of potassium carbonate and extracted repeatedly with chloroform. The chloroform extract was dried with sodium sulfate, the chloroform was removed by distillation, and the residue was vacuum distilled to give a product with bp 136-137° (5 mm) and mp 81.5-82.5°. Found,%: C 49.7; H 7.5; N 43.4. $C_4H_7N_3$. Calculated,%: C 49.5; H 7.3; N 43.3. IR spectrum,* cm^{-1}: 930, 1315, 1472, 1510, 1560 (imidazole [6]); 3320, 3369 (NH_2 group).

2-Amino-1-benzylimidazole Hydrochloride. A solution of 4.8 g (0.04 mole) of phenyl azide in 10 ml of toluene was added to 2-sodio-1-benzylimidazole in toluene, obtained from 4.8 g (0.032 mole) of 1-benzylimidazole via the method in [7]. The reaction was carried out for 1 h, and the triazene was isolated and cleaved with hydrochloric acid, as described above. The resulting hydrochloride was purified by dissolving in alcohol and precipitating with ether to give 4.7 g (63.5%) of a product with mp 185-186°. Found,%: C 57.5; H 6.0; Cl 17.2; N 20.4. $C_{10}H_{11}N_3 \cdot HCl$. Calculated,%: C 57.3; H 5.8; Cl 16.9; N 20.0.

2-Amino-1-benzylimidazole. The 2-amino-1-benzylimidazole hydrochloride was dissolved in the minimum amount of water and treated with 10% sodium hydroxide solution. The resulting base was removed by filtration and recrystallized from water to give a product with mp 139-140°. Found,%: C 69.2; H 6.6; N 24.6. $C_{10}H_{11}N_3$. Calculated,%: C 69.5; H 6.4; N 24.3. IR spectrum, cm^{-1}: 929, 1313, 1472, 1560 (imidazole); 770, 1590, 1613, (C_6H_5); 3315, 3412 (NH_2 group).

2-Amino-1-phenylimidazole Hydrochloride. A sample of 2-sodio-1-phenylimidazole, obtained from 5.8 g (0.04 mole) of 1-phenylimidazole [7], and 6 g (0.05 mole) of phenyl azide in 15 ml of toluene were allowed to react as described above. Cleavage of the triazene gave 3.4 g (43%) of the hydrochloride with mp 206-207°. Found: C 55.2; H 4.7; Cl 18.2; N 21.8. $C_9H_9N_3 \cdot HCl$. Calculated,%: C 55.2; H 5.2; Cl 18.1; N 21.4.

2-Amino-1-phenylimidazole. This compound was obtained by treatment of an aqueous solution of 2-amino-1-phenylimidazole hydrochloride with 10% sodium hydroxide solution. The product had mp 125-126° (hexane). Found,%: C 67.7; H 5.8; N 26.5. $C_9H_9N_3$. Calculated,%: C 67.9; H 5.7; N 26.4. IR spectrum, cm^{-1}: 929, 1322, 1474, 1506, 1560 (imidazole); 780, 1585 (C_6H_5); 3296, 3457 (NH_2 group).

2-Aminobenzothiazole. A 4-g (0.03 mole) sample of benzothiazole was converted to the lithium derivative in ether by the method in [8], and the 2-lithiobenzothiazole was then treated with a solution of 4.8 g (0.04 mole) of phenyl azide in 10 ml of ether. After 1 h, the mixture was treated with water and neutralized with 20% acetic acid. The ether layer was separated, the major portion of the ether was removed by distillation, and the triazene was precipitated with petroleum ether. Decomposition of the triazene gave 2.3 g (52%) of 2-aminobenzothiazole with mp 129-130° (water) (mp 130-131° [9]).

2-Aminopyridine Hydrochloride Dihydrate. A solution of 4.7 g (0.03 mole) of 2-bromopyridine in 15 ml of ether was added at −78° to butyllithium, prepared from 0.7 g (0.1 g-atom) of lithium and 6.6 g (0.048 mole) of butyl bromide in 40 ml of ether. After 20 min, 5 g (0.042 mole) of phenyl azide in 10 ml of ether was added to the resulting 2-lithiopyridine. The reaction was carried out for 1 h, after which the triazene was isolated and cleaved to give 1.9 g (38.5%) of the dihydrate with mp 85-86° (mp 86° [10]).

2-Aminopyridine. This compound had mp 57-58° (octane), in agreement with the melting point indicated in [10].

*The IR spectra of samples of this and other compounds in mineral oil suspensions were recorded with a UR-20 spectrophotometer.

LITERATURE CITED

1. A. P. Ershov and I. S. Ioffe, Zh. Obshch. Khim., 9, 2211, 2219 (1939).
2. T. W. Campbell and B. F. Day, Chem. Rev., 48, 299 (1951).
3. V. Ya. Pochinok, Triazenes [in Russian], Izd. Kievsk. Univ. (1968), p. 106.
4. A. Lowson, J. Chem. Soc., 307 (1956).
5. B. T. Storey, W. W. Sullivan, and C. L. Moyer, J. Org. Chem., 29, 3118 (1964).
6. D. Garfinkel and J. T. Edsall, J. Am. Chem. Soc., 80, 3807 (1958).
7. B. A. Tertov and V. V. Burykin, Khim. Geterotsikl. Soedin., 1554 (1970).
8. H. Gilman and J. A. Beel, J. Am. Chem. Soc., 71, 2328 (1949).
9. A. H. Corwin and G. R. Jackson, J. Am. Chem. Soc., 71, 3698 (1949).
10. Dictionary of Organic Compounds, Vol. 1, Oxford University Press (1966).