BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 826—828 (1971)

Syntheses of 1,2,3-Trisubstituted 4-Aminoimidazolium Salts[1]

Akiko Chinone, Sigeru Sato,* and Masaki Ohta
Department of Chemistry, Faculty of Science, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo

(Received September 14, 1970)

The salts of new mesoionic compounds of imidazole ring system having imino group at 4 position were synthesized by the reaction of amidines with haloacetonitriles. The resulting 4-amino-1,2,3-triphenylimidazolium salt was treated with sodium hydroxide to give an intermediate, *N*-cyanomethyl-*N*,*N'*-diphenylbenzamidine, which gave the salt of mesoionic imidazole with dry hydrogen bromide. 1,2,3-Trisubstituted 4-aminoimidazolium salts were treated with acetic anhydride or with picric acid or with silver perchlorate to give acetylated derivative, picrates and perchlorates, respectively.

Of the mesoionic imidazoles with an exo-imino group, only fused ring compounds have been reported.[2] We wish to report here the preparation of salts of 4-iminoimidazole.

As a possible route towards a synthesis of mesoionic 3,4-dihydro-4-iminoimidazole (anhydro-4-aminoimidazolium hydroxide), we tried the reaction of *N*-methyl-*N'*-phenylbenzamidine (Ia) with bromoacetonitrile (IIa) anticipating the formation of an intermediate V. When the reaction was carried out in toluene, V was not isolated, but 4-amino-3-methyl-1,2-diphenylimidazolium bromide (IVa) was obtained. Attempts to isolate the intermediate, *N*-cyanomethyl-*N*-phenyl-*N'*-methylbenzamidine, were unsuccessful even in the presence of triethylamine or sodium acetate. The structure of the salt of mesoionic compound is most likely to be IVa instead of IVa', since the alkylation of amidine occurs preferentially at the doubly-linked nitrogen atom. It is known that *N*-methyl-*N'*-phenylbenzamidine reacts preferably in form A rather than in form B.[3,4] When the diphenylbenzamidine (Ib) was treated with IIa in xylene, corresponding triphenyl substituted derivative (IVb) was obtained. By the same method, *N*-phenyl-*N'*-*p*-tolylbenzamidine (Ic) was reacted with IIa to give IVc. Considering the influence of the groups R_1 and R_3 in Ic on the basicity of the nitrogen atom, IVc seems to be preferable to IVc'.[3] In the reaction of *N*-*p*-nitrophenyl-*N'*-phenylbenzamidine (Id) with IIa, it was found that the influence of the nitro group in Id was such that no reaction occurred with IIa under the same conditions. Although the isolation of the salt III was not successful, these ring formations seem to proceed through salts III, followed by interaction of two groups, with a mechanism similar to that of sydnone imine salts formation.[5] The structure of these products was established by elementary analyses and infrared spectra, which showed bands at 3380—3100 cm^{-1} corresponding to N–H stretching vibration, and at 1650—1645 cm^{-1} due to imidazole ring.

The reaction of amidines (Ia—Ic) with chloroacetonitrile (IIb) did not take place. However, amidines (Ia—Ic) reacted with IIb and equimolar amount of potassium iodide to give corresponding imidazolium iodides (IVd—IVf) in an ethanol solution. The mechanism of formation of the imidazolium iodides seems to proceed *via* halogen exchange followed by nucleophilic attack as mentioned above. Treatment of IVa with sodium bicarbonate or triethylamine did not give free base, but resulted in recovery of starting material. This indicates that the free base of IVa is stronger than the bases. No reaction was observed also in the treatment of IVb with sodium bicarbonate or triethylamine. Treatment of IVb with sodium hydroxide did not give the free base but afforded the intermediate Va, IR spectrum of which did not show C≡N stretching vibration as in the case of *O*-cyanomethyl-*N*-phenylbenzimidate.[6] On treating Va with dry hydrogen bromide, IVb was obtained. Treatment of IVa or IVc with sodium hydroxide gave oily substance which could not be purified. Treatment of IVa with acetic anhydride gave the *N*-acetyl derivative VI. The infrared spectrum was consistent with that expected for VI, showing a weak band at 3190 cm^{-1} resulting from N–H stretching vibration, and a strong band at 1697 cm^{-1} resulting from carbonyl group. On the other hand, treatment of IVb with acetic anhydride gave hygroscopic product which could not be identified. On treating IVa or IVb with picric acid, the picrates VIIa and VIIb were obtained respectively. On treating the iodides IVd—IVf with silver perchlorate, stable perchlorates VIIIa—VIIIc were obtained in good yield. Treatment of the perchlorate with acetic anhydride resulted in the recovery of starting material instead of acetylated product.

Diaryl substituted imidazolium salts (IVa, IVd, and VIIIa) show absorption maxima at about 290 mμ and triaryl substituted imidazolium salts (IVb, IVc, IVe, IVf, VIIIb, and VIIIc) show absorption maxima at about 300 mμ irrespective of the anion, which are suggestive of their heteroaromatic system. The NMR spectrum of IVd in $CDCl_3$–CD_3CN exhibits two singlets at τ 6.40 (3H, methyl protons at 3-position) and at τ 3.03 (1H, a proton at 5-position) and multiplet at τ 2.4—2.8 (10H, protons of phenyl groups). Methyl protons of IVd are shielded to a greater extent as compared with those attached to sydnone and sydnone imine ring.[7,8] The proton at 5-position is deshielded

---

1) Studies of mesoionic compounds. XXXIV. Part XXXIII: A. Shaikh, A. Chinone, and M. Ohta, This Bulletin, 453 **43**, (1970).

* Present address: Mitsubishi Chemical Industries Ltd., Central Research Laboratory, 290 Isamoto, Kamoicho, Kawasaki.

2) N. W. Bristow, P. T. Charlton, D. A. Peak, and W. F. Short, *J. Chem. Soc.*, **1954**, 616.

3) F. L. Pyman, *ibid.*, **1923**, 3359.

4) C. G. Raison, *ibid.*, **1949**, 3319.

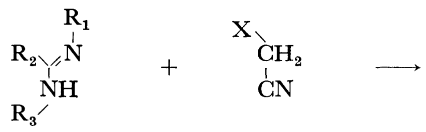
5) P. Brookes and J. Walker, *ibid.*, **1957**, 4409.

6) A. Chinone, S. Sato, T. Mase, and M. Ohta, This Bulletin, **42**, 2310 (1969).

7) K. D. Lawson, W. S. Brey, Jr., and L. B. Kier, *J. Amer. Chem. Soc.*, **86**, 463 (1964).

8) H. U. Daeniker and J. Druey, *Helv. Chim. Acta*, **45**, 2441 (1962).

as compared with imidazole. The NMR spectrum of IVe exhibits a multiplet at τ 2.40—2.95, and IVf exhibits a singlet at τ 7.65 (3H, methyl protons of p-tolyl group) and a multiplet at τ 2.4—3.0.



I II

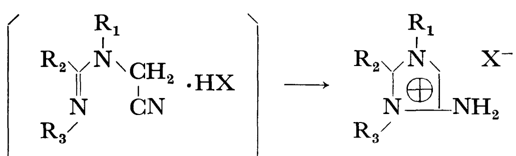
Ia: $R_1=R_2=C_6H_5$, $R_3=CH_3$ IIa: X=Br

IIb: X=Cl

Ib: $R_1=R_2=R_3=C_6H_5$

Ic: $R_1=R_2=C_6H_5$, $R_3=p\text{-}CH_3C_6H_4$

Id: $R_1=R_2=C_6H_5$, $R_3=p\text{-}NO_2C_6H_4$



III IV

IVa: $R_1=R_2=C_6H_5$, $R_3=CH_3$, X=Br

(IVa′: $R_1=CH_3$, $R_2=R_3=C_6H_5$, X=Br)

IVb: $R_1=R_2=R_3=C_6H_5$, X=Br

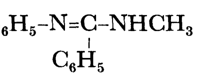
IVc: $R_1=R_2=C_6H_5$, $R_3=p\text{-}CH_3C_6H_4$, X=Br

(IVc′: $R_1=p\text{-}CH_3C_6H_4$, $R_2=R_3=C_6H_5$, X=Br)

IVd: $R_1=R_2=C_6H_5$, $R_3=CH_3$, X=I

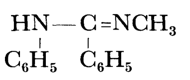
IVe: $R_1=R_2=R_3=C_6H_5$, X=I

IVf: $R_1=R_2=C_6H_5$, $R_3=p\text{-}CH_3C_6H_4$, X=I



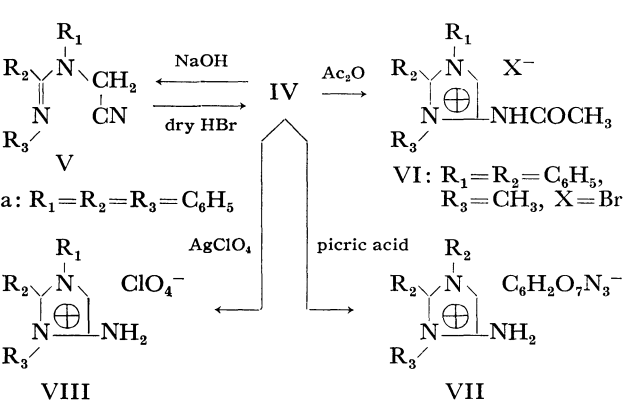
$C_6H_5\text{-}N{=}C(C_6H_5)\text{-}NHCH_3$

(A)



$HN(C_6H_5)\text{—}C(C_6H_5){=}NCH_3$

(B)



V

Va: $R_1=R_2=R_3=C_6H_5$

VI: $R_1=R_2=C_6H_5$, $R_3=CH_3$, X=Br

VIII VII

VIIIa: $R_1=R_2=C_6H_5$, $R_3=CH_3$

VIIIb: $R_1=R_2=R_3=C_6H_5$

VIIIc: $R_1=R_2=C_6H_5$, $R_3=p\text{-}CH_3C_6H_4$

VIIa: $R_1=R_2=C_6H_5$, $R_3=CH_3$

VIIb: $R_1=R_2=R_3=C_6H_5$

Experimental

All melting points were determined on a micro hot stage and are not corrected. Infrared spectra were taken on KBr tablet.

4-Amino-3-methyl-1,2-diphenylimidazolium Bromide (IVa). A solution of 2.1 g of N-methyl-N'-phenylbenzamidine and 1.2 g of bromoacetonitrile (IIa) in 30 m*l* of toluene was refluxed for 3 hr. After cooling, the precipitates were collected and washed with benzene, and recrystallized from acetonitrile to give colorless prisms with a mp of 280—285°C.

Found: C, 58.24; H, 4.71; N, 12.50%. Calcd for $C_{16}H_{16}N_3Br$: C, 58.12; H, 4.85; N, 12.73%. IR: 3440, 3275, 3140, 1660, 1647 cm^{-1}. $\lambda_{\max}^{\text{EtOH}}$ 290 mμ (ε 7500).

4-Amino-1,2,3-triphenylimidazolium Bromide (IVb). (i) A solution of 2.7 g of diphenylbenzamidine and 1.2 g of IIa in 30 m*l* of xylene was refluxed for 4 hr. After cooling, the precipitates which separated out were collected and recrystallized from ethanol to give colorless prisms with a mp of 282—284°C (yield 60%).

Found: C, 64.05; H, 4.88; N, 10.60%. Calcd for $C_{21}H_{18}N_3Br$: C, 64.29; H, 4.59; N, 10.71%. IR: 3380, 3110, 1646 cm^{-1}. $\lambda_{\max}^{\text{EtOH}}$ 302 mμ (ε 7000).

(ii) To a solution of 0.1 g of N-cyanomethyl-N,N'-diphenylbenzamidine in 10 m*l* of benzene, 20 m*l* of benzene containing 0.05 g of gaseous hydrogen bromide was added dropwise. Precipitates which separated out were collected and recrystallized from ethanol. No depression of the melting point was observed on admixture with the product obtained by method (i).

*4-Amino-1,2-diphenyl-3-*p*-tolylimidazolium Bromide (IVc).* A solution of 2.86 g of N-phenyl-N'-p-tolylbenzamidine an 1.2 g of IIa in 30 m*l* of xylene for 40 min. After cooling, the precipitates were collected and reprecipitated from and ethanol solution with ether to give colorless prisms with a mp of 267—268°C (yield 58%).

Found: C, 64.88; H, 5.12; N, 10.52%. Calcd for $C_{22}H_{20}N_3Br$: C, 65.04; H, 4.93; N, 10.35%. IR: 3400, 3100, 1650 cm^{-1}. $\lambda_{\max}^{\text{EtOH}}$ 298 mμ (ε 6700).

4-Amino-3-methyl-1,2-diphenylimidazolium Iodide (IVd). A suspension of 2.1 g of N-methyl-N'-phenylbenzamidine and 0.8 g of chloroacetonitrile (IIb) and 1.7 g of potassium iodide in 50 m*l* of ethanol was refluxed for 5 hr, and after cooling the precipitates were filtered off. The filtrate was treated with activated charcoal and concentrated in a vacuum to give crude product, which was reprecipitated from an ethanol solution with ether to give colorless prisms with a mp of 205—206°C (yield 24%).

Found: C, 51.02; H, 4.48; N, 11.02%. Calcd for $C_{16}H_{16}N_3I$: C, 50.94; H, 4.25: N, 11.14%. IR: 3255, 3130, 1645 cm^{-1}. $\lambda_{\max}^{\text{EtOH}}$ 292 mμ (ε 7100).

4-Amino-1,2,3-triphenylimidazolium Iodide (IVe). A suspension of 1.36 g of diphenylbenzamidine and 0.38 g of IIb and 0.83 g of potassium iodide in 20 m*l* of ethanol was refluxed for 7 hr. After cooling, precipitates were collected and recrystallized from ethanol to give colorless needles with a mp of 280—283°C (yield 44%).

Found: C, 57.12; H, 4.33; N, 9.73%. Calcd for $C_{21}H_{18}N_3I$: C, 57.42; H, 4.10; N, 9.57%. IR: 3400, 3140, 1645 cm^{-1}. $\lambda_{\max}^{\text{EtOH}}$ 300 mμ (ε 6300).

*4-Amino-1,2-diphenyl-3-*p*-tolylimidazolium Iodide (IVf).* This compound was prepared by a method analogous to that of IVd. Reprecipitation from an ethanol solution with ether gave colorless needles with a mp of 272—274°C (yield 36%).

Found: C, 58.04; H, 4.66; N, 9.34%. Calcd for $C_{22}H_{20}N_3I$: C, 58.29; H, 4.42; N, 9.27%. IR: 3400, 3150, 1650 cm^{-1}. $\lambda_{\max}^{\text{EtOH}}$ 300 mμ (ε 6600).

N-Cyanomethyl-N,N′-diphenylbenzamidine (Va). To a solution of 1 g of IVb in 20 m*l* of ethanol, 2 m*l* of 8% aqueous sodium hydroxide solution was added. Precipitates were collected and recrystallized from ethanol to give colorless prisms with a mp of 128—130°C (yield 60%).

Found: C, 80.96; H, 5.56; N, 13.40%. Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.50%. IR; 1615 cm^{-1}. NMR;

τ_{Me_4Si} ($CDCl_3$) 5.2 (2H, singlet), 2.7—3.4 (15H, multiplet).

N-*Acetyl-4-amino-3-methyl-1,2-diphenylimidazolium Bromide (VI).* A solution of 1 g of IVa in acetic anhydride was heated at 100°C for 5 min. After cooling, ether was added to the solution, and the precipitates were collected and recrystallized from acetonitrile to give colorless prisms with a mp of 270—273°C (yield 62%).

Found: C, 57.94; H, 4.72; N, 11.18%. Calcd for $C_{18}H_{18}N_3OBr$: C, 58.07; H, 4.83; N, 11.29%. IR: 3190, 3100, 1697, 1618 cm^{-1}.

Reaction of IVa or IVb with Picric Acid. To a solution of IVa in ethanol, a solution of picric acid in ethanol was added and refluxed for 2 min. After cooling the precipitates were collected and recrystallized from ethanol-ethyl acetate to give VIIa with a mp of 193—194°C.

Found: C, 54.96; H, 3.54; N, 17.71%. Calcd for $C_{22}H_{18}N_6O_7$: C, 55.23; H, 3.79; N, 17.57%.

By the same method as mentioned above, VIIb was obtained from IVb as yellow needles with a mp of 180—182°C.

Found: C, 59.46; H, 3.95; N, 15.27%. Calcd for $C_{27}H_{20}N_6O_7$: C, 60.00; H, 3.73; N, 15.55%.

1,2,3-Trisubstituted 4-Aminoimidazolium Perchlorates (VIIIa—VIIIc). To a solution of IVd (0.33 g) in acetonitrile-chloroform, a solution of 0.21 g of silver perchlorate in chloroform-ethanol was added dropwise. The precipitates were filtered off and filtrate was concentrated in a vacuum to give crude product, which was reprecipitated from a chloroform solution with ether to give VIIIa as colorless needles with a mp of 145—146°C (yield 69%).

Found: C, 54.73; H, 4.39; N, 12.06%. Calcd for $C_{16}H_{16}N_3O_4Cl$: C, 54.94; H, 4.61; N, 12.01%. IR: 3400, 3330, 1655 cm^{-1}. λ_{max}^{EtOH} 292 mμ (ε 6500).

By the same method as mentioned above, VIIIb was obtained from IVe as colorless needles with a mp of 254—256°C (yield 75%).

Found: C, 60.94; H, 4.60; N, 10.18%. Calcd for $C_{21}H_{18}N_3O_4Cl$: C, 61.22; H, 4.40; N, 10.21%. IR: 3425, 3330, 1650 cm^{-1}. λ_{max}^{EtOH} 302 mμ (ε 6600).

By the same method as mentioned above, VIIIc was obtained from IVf as colorless needles with a mp of 204—205°C (yield 59%).

Found: C, 62.14; H, 4.97; N, 9.89%. Calcd for $C_{22}H_{20}N_3O_4Cl$: C, 62.03; H, 4.73; N, 9.87%. IR: 3410, 3325, 1650 cm^{-1}. λ_{max}^{EtOH} 300 mμ (ε 6400).