Reaction of an Asymmetric Imidazolinium Compound with Nucleophiles

By **Isabel Perillo** * and **Samuel Lamdan**, Departamento de Química Orgánica, Facultad de Farmacia y Bioquímica, Universidad de Beunos Aires, Junín 956, República Argentina

1-Methyl-3-(*p*-nitrophenyl)-2-phenylimidazolinium iodide (2) reacts easily with nucleophiles to give addition products of various stabilities. In sodium hydroxide or a silver oxide suspension compound (2) reacted to give *N*-benzoyl-*N*-methyl-*N'*-(*p*-nitrophenyl)ethylenediamine (4), the structure of which was confirmed by synthesis from *N*-(2-bromoethyl)-*N*-methylbenzamide and *p*-nitroaniline. Treatment of compound (2) with IRA-400 resin (OH^-) afforded the imidazolinium hydroxide which rearranged to (4). Reaction of (2) with sodium methoxide in anhydrous methanol afforded 2-methoxy-1-methyl-3-(*p*-nitrophenyl)-2-phenylimidazolidine which was hydrolysed readily to (4). Sodium borohydride reduces (2) to 1-methyl-3-(*p*-nitrophenyl)-2-phenylimidazolidine.

ALTHOUGH the behaviour of symmetric 1,3-diarylimidazolinium salts, as models for tetrahydro-*N*(5),*N*(10)-methylidynefolic acid,[1,2] towards alkaline hydrolysis [1,3-5] and reduction [3] has been studied, asymmetric imidazolinium salts with different *N*-substituents have not been investigated. We now report the reaction of one such salt (2) with nucleophiles (OH^-, MeO^-, and H^-).

The carbocation form (I) of the resonance-stabilized imidazolinium ion would be expected to undergo nucleophilic attack as in simple ternary iminium compounds.[6,7] This proved to be the case with the imidazolinium iodide (2), which reacted in ethanol with 5% sodium hydroxide at room temperature during 30 min to give *N*-benzoyl-*N*-methyl-*N'*-(*p*-nitrophenyl)ethylenediamine (4), $\lambda_{max.}$ 386 nm, δ 4·0br (s, exchangeable), identical with material synthesized from *N*-(2-bromoethyl)-*N*-methylbenzamide (5) and *p*-nitroaniline. The insolubility of the product (4) in dilute acid,[8] even at 100°, and a negative Karl Fischer reaction,[9] proved the absence of the tautomeric pseudo-base (3), which may, however, be an intermediate. Accumulation of a tetrahedral intermediate of this type has been observed spectrophotometrically during the hydrolysis of 1,3-diphenylimidazolinium chloride above pH 11·6.[5] The existence of an open-chain structure as the only stable form has been observed with other pseudo-bases having a strongly electron-withdrawing group at the nitrogen atom.[8] The behaviour of (4) with dilute acids differs notably from that of the *NN'*-diaryl-*N*-formylethylenediamines arising from 1,3-diarylimidazolinium salts, which in acidic medium revert to the salts.[1,3] This difference can be partially explained by the stability conferred on the latter compounds by their symmetry.

Passage of the imidazolinium iodide (2) in anhydrous methanol through an IRA-400 resin (OH^-) column completely removed the iodide ion. T.l.c. analysis of the effluent showed the presence of a large amount of a polar product and traces of compound (4). The solution had pH 8·5 and u.v. absorption at 308 nm, characteristic of (2), indicating the presence of the imidazolinium hydroxide (6). The picrate of (6) was identical with that of (2). The ionic nature of compound (6), which is the ionic form of the carbinolamine (3) is enhanced by the polarity of the solvent, as seen with other pseudo-bases.[8] The hydroxide (6) is slowly transformed into compound (4), as shown by the decrease in both basicity and absorbance at 308 nm of the solution of (6) in methanol. This rearrangement was complete in about 7 days at room temperature (t.l.c.) and was accelerated by heating or by the presence of traces of water. It was instantaneous in the presence of alkali.

Attempts to obtain the hydroxide (6) by stirring the iodide (2) in a suspension of silver oxide in methanol or methylene chloride, as described by Smith *et al.* for benzimidazolium compounds,[10] resulted instead in the formation of compound (4). The tendency of the benzimidazolium ion to maintain aromaticity accounts for the difference in results.

Treatment of the imidazolinium iodide (2) with sodium methoxide in anhydrous methanol afforded a yellow solid, $C_{17}H_{19}N_3O_3$, m.p. 158°, after immediate crystallization from anhydrous methanol. The structure of the product varied according to the nature of the solvent. The u.v. absorbance showed that the covalent form, 2-methoxy-1-methyl-3-(*p*-nitrophenyl)-2-phenylimidazolidine (7b), was present in non-polar or weakly

[1] M. May, T. J. Bardos, F. L. Barger, M. Lansford, J. M. Ravel, G. L. Sutherland, and W. Shive, *J. Amer. Chem. Soc.*, 1951, **73**, 3067.
[2] D. R. Robinson and W. P. Jencks, *J. Amer. Chem. Soc.*, 1967, **89**, 7098.
[3] L. Jaenicke and E. Brode, *Annalen*, 1959, **624**, 120.
[4] D. R. Robinson and W. P. Jencks, *J. Amer. Chem. Soc.*, 1967, **89**, 7088.
[5] D. R. Robinson, *J. Amer. Chem. Soc.*, 1970, **92**, 3138.
[6] C. R. Hauser and D. Lednicer, *J. Org. Chem.*, 1959, **24**, 46.
[7] N. J. Leonard and A. S. Hay, *J. Amer. Chem. Soc.*, 1956, **78**, 1984.
[8] D. Beke, *Adv. Heterocyclic Chem.*, 1963, **1**, 167.
[9] D. Beke, Cs Czántay, and M. B. Bárczai, *Periodica Polytech.*, 1960, **4**, 329.
[10] C. W. Smith, R. S. Rasmussen, and S. A. Ballard, *J. Amer. Chem. Soc.*, 1949, **71**, 1082.

polar solvents: solutions in n-hexane, benzene, or chloroform showed a strong absorbance at a similar wavelength to compounds (4), (8), and (9), suggesting the presence of the group p-$NO_2 \cdot C_6H_4 \cdot \dot{N}<$. In methanol the substance showed absorption at 307 nm, similar to compounds (2) and (6), which indicated the presence of the ionic form (7a). The i.r. spectrum of (7) in KBr did not show a strong absorption at 1660 cm^{-1} observed in the spectrum of (2) (CN str. of N ⋯ C^+ ⋯ N); this indicates that in the solid state the covalent form (7b) prevails.

nitrophenyl)-2-phenylimidazolidine (8), along with traces of (4) and N-methyl-N'-(p-nitrophenyl)ethylenediamine (9). Structure (8) was confirmed by the n.m.r. [δ 4·85 (s, benzylic H-2)] and i.r. spectra (C–H stretch at 2772 cm^{-1}) and by hydrolysis at room temperature with dilute acids to give compound (9),[13] identical with that obtained by hydrolysis of (4) with concentrated hydrochloric acid.

EXPERIMENTAL

M.p.s were taken with a Büchi capillary apparatus. I.r. spectra were recorded with a Beckman 20 A instrument for potassium bromide pellets. U.v. spectra were recorded with a Perkin-Elmer 202 spectrophotometer and extinction coefficients were calculated from readings on a Beckman DB-G grating spectrophotometer. N.m.r. spectra were obtained with a Perkin-Elmer R12 (60 MHz) spectrometer in deuteriochloroform, with tetramethylsilane as internal reference. The presence of exchangeable protons (NH) was confirmed by use of deuterium oxide. Protons *ortho* and *meta* to p-nitro-groups in p-$NO_2 \cdot C_6H_4$ are denoted as H_a and H_b, respectively. T.l.c. was carried out on 10 × 20 cm glass plates coated with Merck silica $HF_{254+366}$ and activated at 100° for 1 h. Non-activated plates were used to follow the hydrolysis of the methoxy-derivative (7). All solvents were purified by standard techniques.

1-*Methyl*-3-(p-*nitrophenyl*)-2-*phenylimidazolinium Iodide*

When compound (7) was dissolved in dilute hydrochloric acid and picric acid was added, a precipitate of 1-methyl-3-(p-nitrophenyl)-2-phenylimidazolinium picrate, identical to that formed from compounds (2) and (6), was obtained.

During recrystallization from 96% ethanol, the methoxy-derivative (7) was easily hydrolysed to (4), in agreement with earlier reports.[11] When the hydrolysis in chloroform was followed by t.l.c., an intermediate, presumably the carbinolamine (3), was detected.

There are reports on the reduction of ternary iminium compounds with sodium borohydride,[12] but an attempt to reduce imidazolinium salts failed.[3] In our case the reduction was successful. Reaction of (2) with sodium borohydride in absolute ethanol gave 1-methyl-3-(p-

[11] B. Lachmann and H. W. Wanzlick, *Annalen*, 1969, **729**, 27.

[12] Among others (*a*) N. J. Leonard, P. D. Thomas, and V. W. Gash, *J. Amer. Chem. Soc.*, 1955, **77**, 1552; (*b*) W. M. Whaley and C. N. Robinson, *ibid.*, 1953, **75**, 2008.

[13] R. J. Ferm and J. L. Riebsomer, *Chem. Rev.*, 1954, **54**, 606.

(2).—A solution of 1-(*p*-nitrophenyl)-2-phenyl-Δ^2-imidazoline [14] (1) (1·5 g) in methylene chloride (15 ml) was refluxed with methyl iodide (3·5 ml) for 45 min. The solvent and the excess of methyl iodide were removed *in vacuo*. The residue crystallized, affording the *iodide* (2) (83%), m.p. 98° (from absolute ethanol) (Found: C, 46·9; H, 4·1; N, 10·0; I^-, 30·8. $C_{16}H_{16}IN_3O_2$ requires C, 46·9; H, 3·9; N, 10·3; I^-, 31·0%); $\lambda_{max.}$ (EtOH) 208, 221, and 308 nm; $\lambda_{max.}$ (MeOH) 207, 223, and 305 nm; $\lambda_{max.}$ ($CHCl_3$) 270 and 318 nm; $\nu_{max.}$ 1650, 1605, 1528, and 1350 cm^{-1}; δ 8·10—7·32 (9H, m, Ph and $C_6H_4{\cdot}NO_2$), 4·90—4·50 (4H, m, $CH_2{\cdot}CH_2$), and 3·25 (3H, s, Me); the *picrate* had m.p. 193° (from ethanol) (Found: C, 51·9; H, 3·8; N, 16·6. $C_{22}H_{18}N_6O_9$ requires C, 51·8; H, 3·5; N, 16·5%).

N-*Benzoyl*-N-*methyl*-N′-(p-*nitrophenyl*)*ethylenediamine* (4).—(*a*) A mixture of compound (2) (0·5 g) in ethanol (20 ml) and 10% sodium hydroxide (20 ml) was stirred for 1 h at 10—15°. The yellow solid was filtered off, washed with water, and crystallized giving *compound* (4) (92%), m.p. 149° (from methanol) (Found: C, 64·2; H, 5·7; N, 14·0. $C_{16}H_{17}N_3O_3$ requires C, 64·3; H, 5·9; N, 13·9%); $\lambda_{max.}$ (EtOH) 206 and 386 nm; $\lambda_{max.}$ (MeOH) 206 and 380 nm; $\lambda_{max.}$ ($CHCl_3$) 374 nm; $\lambda_{max.}$ (n-hexane) 347 nm; $\nu_{max.}$ 3263, 1624, 1592, and 1281 cm^{-1}; δ 8·16 (2H, d, H_a, *J* 9 Hz), 7·50 (5H, s, Ph), 6·62 (2H, d, H_b, *J* 9 Hz), 6·0br (1H, s, NH, exchangeable), 3·4—4·0 (4H, m, $CH_2{\cdot}CH_2$), and 3·09 (3H, s, Me); R_F (MeOH) 0·80.

(*b*) A solution of silver nitrate (0·425 g) in water (2·1 ml) was treated with sodium hydroxide (0·112 g) in water (1 ml). The resulting silver oxide was filtered off, washed with water, and suspended in a solution of compound (2) (0·4 g) in methylene chloride (20 ml). After stirring for 1 h the silver iodide and the excess of silver oxide were filtered off. The filtrate gave a negative test for iodide ion and t.l.c. showed (4) as the only product. The solution was concentrated and the residue crystallized affording (4) (79%), m.p. 149.

(*c*) Benzoyl chloride (1·27 ml) was added to a solution of 2-bromo-*N*-methylethylamine hydrobromide [15] (2·19 g) in cold N-sodium hydroxide (23 ml). The mixture was vigorously shaken until the odour of benzoyl chloride had disappeared. The emulsion was extracted with chloroform and the extract was washed with 5% sodium hydroxide, 10% hydrochloric acid, and water, dried (Na_2SO_4), and evaporated. An intimate mixture of the crude amide (5) (2·42 g) and *p*-nitroaniline (2·76 g) was heated at 110° for 2 h. The crude product was washed three times with boiling water and the oil solidified after cooling. The solid was filtered off, pulverized, and washed with benzene to remove *p*-nitroaniline. Crystallization from methanol afforded compound (4), identical with the samples obtained from compound (2) (mixed m.p., t.l.c., and i.r.); this compound was insoluble in dilute acids and no reaction with the Karl Fischer reagent was observed.

1-*Methyl*-3-(p-*nitrophenyl*)-2-*phenylimidazolinium Hydroxide* (6).—A solution of compound (2) in anhydrous methanol was passed through an Amberlite IRA-400 (OH^-) column (20 × 2 cm). The effluent was alkaline (pH 8·5), contained no iodide ion, and absorbed strongly at 308 nm. T.l.c. in methanol showed considerable amounts of a polar compound (6) (R_F *ca.* 0) and traces of (4) (R_F *ca.* 0·8). Acidification and precipitation with aqueous picric acid gave the picrate corresponding to (6). When kept at room temperature for a week, the solution decreased in basicity as (6) rearranged completely to (4). The reaction required only 3 h for completion under reflux.

2-*Methoxy*-1-*methyl*-3-(p-*nitrophenyl*)-2-*phenylimidazolidine* (7).—Sodium methoxide [sodium (0·92 g) in absolute methanol (20 ml)] was added to compound (2) (4·09 g) in anhydrous methanol (30 ml) at 10°. After 45 min the precipitate was collected and recrystallized as quickly as possible to obtain *compound* (7), m.p. 158° (from anhydrous methanol) (Found: C, 65·2; H, 6·1; N, 13·4. $C_{17}H_{19}N_3O_3$ requires C, 65·4; H, 6·3; N, 13·2%); $\lambda_{max.}$ (MeOH) 206, 227, and 307 nm; $\lambda_{max.}$ ($CHCl_3$) 377 nm; $\lambda_{max.}$ (benzene) 365 nm; $\lambda_{max.}$ (n-hexane) 345 nm; $\nu_{max.}$ 1605, 1496, 1390, and 1306 cm^{-1}; δ 7·98 (2H, d, H_a, *J* 9 Hz), 7·31 (5H, s, Ph), 6·69 (2H, d, H_b, *J* 9 Hz), 3·0—3·97 (4H, m, $CH_2{\cdot}CH_2$), 3·14 (3H, s, MeO), and 2·01 (3H, s, MeN). Attempts to crystallize (7) from 96° ethanol afforded (4). Dissolution of (7) in 10% hydrochloric acid and precipitation with aqueous picric acid yielded a picrate identical with that obtained from (2) and (6) (mixed m.p.).

1-*Methyl*-3-(p-*nitrophenyl*)-2-*phenylimidazolidine* (8).—Sodium borohydride (3·8 g) was added to a solution of compound (2) (4·0 g) in anhydrous ethanol (60 ml). When the evolution of gas had ceased, water was added. The yellow precipitate was collected and crystallized, affording *compound* (8) (58%), m.p. 81—83° (from a small volume of methanol) (Found: C, 67·8; H, 6·0; N, 14·8. $C_{16}H_{17}N_3O_2$ requires C, 68·5; H, 6·3; N, 14·8%); $\lambda_{max.}$ (EtOH) 204 and 386 nm; $\lambda_{max.}$ (MeOH) 205 and 380 nm; $\lambda_{max.}$ ($CHCl_3$) 385 nm; $\lambda_{max.}$ (benzene) 377 nm; $\lambda_{max.}$ (n-hexane) 355 nm; $\nu_{max.}$ 1600, 1486, 1304, and 1110 cm^{-1}; δ 8·10 (2H, d, H_a, *J* 9 Hz), 7·10 (5H, s, Ph), 6·51 (2H, d, H_b, *J* 9 Hz), 4·86 (1H, s, benzylic H), 4·0—3·5 (4H, m, $CH_2{\cdot}CH_2$), and 2·40 (3H, s, Me). The crude product contained small amounts of (4) and (9) (t.l.c.).

N-*Methyl*-N′-(p-*nitrophenyl*)*ethylenediamine* (9).—(*a*) Compound (4) (0·5 g) in concentrated hydrochloric acid was refluxed for 6 h. After cooling and diluting with water, benzoic acid was filtered off. The solution was made alkaline with 20% sodium hydroxide. *Compound* (9) separated as a yellow oil which slowly solidified; m.p. 84° (from cyclohexane) (Found: C, 55·5; H, 7·0; N, 21·8. $C_9H_{13}N_3O_2$ requires C, 55·5; H, 6·8; N, 21·6%); $\lambda_{max.}$ (EtOH) 204 and 386 nm; $\lambda_{max.}$ (MeOH) 204 and 380 nm; $\lambda_{max.}$ ($CHCl_3$) 370 nm; $\lambda_{max.}$ (benzene) 368 nm; $\lambda_{max.}$ (n-hexane) 343 nm; $\nu_{max.}$ 1610, 1480, and 1315 cm^{-1}; δ 8·07 (2H, d, H_a, *J* 9 Hz), 6·53 (2H, d, H_b, *J* 9 Hz), 5·25br (1H, s, $NO_2{\cdot}C_6H_4{\cdot}NH$, exchangeable), 2·74—3·44 (4H, m, $CH_2{\cdot}CH_2$), 2·45 (3H, s, Me), and 1·26 (1H, s, MeN*H*, exchangeable). The *chloroplatinate* had m.p. 205° (Found: C, 27·3; H, 3·6; Cl, 26·8; N, 10·8. $C_{18}H_{28}Cl_6N_6O_4Pt$ requires C, 27·0; H, 3·5; Cl, 26·6; N, 10·5%).

(*b*) Compound (8) (0·5 g) was stirred with 10% hydrochloric acid for 1 h. The mixture was filtered and (9) was isolated from the solution, as above.

Financial support of this investigation was given by the Consejo Nacional de Investigaciones Cientificas y Técnicas and Universidad de Buenos Aires. We thank Dr. B. B. de Deferrari for microanalyses and Miss M. Esteve for technical collaboration.

[4/1816 *Received*, 3rd *September*, 1974]

[14] I. Perillo and S. Lamdan, *J. Heterocyclic Chem.*, 1970, **7**, 791.
[15] L. Knorr and G. Mayer, *Ber.*, 1905, **38**, 3133.