854. *Verda's Bromination Method*

By F. Bell and K. R. Buck

VERDA [1] described the use of a mixture of hydrobromic acid and nitric acid for the bromination of acetanilides, and his method was fully exemplified by Mannino and di Donato.[2] We now find that this process sometimes results in the replacement of the acetamido-group by bromine; thus *o*- and *m*-nitroacetanilide yield 2,5-dibromo-1-nitrobenzene, 4-acetotoluidide gives 2,4,5-tribromotoluene, 2-chloroacetanilide gives 1,4-dibromo-2-chlorobenzene, and 4-chloroacetanilide gives 1,2,3-tribromo-5-chlorobenzene. It is likely that these reactions involve the intermediate production of nitrosoacetanilides, by the action of nitrosyl bromide, and that these subsequently undergo typical diazo-acetate decompositions.[3]

It was incidentally observed that the addition of bromine to chloroform solutions of certain acetanilides resulted in the production of golden-yellow, highly crystalline addition compounds, which readily reverted to the starting materials when slightly heated.

Experimental.—Bromination method. The compound (3 g.) was warmed on a steam-bath with a mixture of hydrobromic acid (30 c.c.; *d* 1·48) and concentrated nitric acid (9 c.c.), until most of the fumes had been expelled. After cooling, the aqueous layer was decanted and the precipitate purified by crystallisation from ethanol.

(i) *m*-Nitroacetanilide gave 2,5-dibromo-1-nitrobenzene (0·5 g.), m. p. 82—84°, identified by infrared and n.m.r. spectra (2 protons at τ 2·42 and 1 proton at τ 2·05), some 4-bromo-3-nitroacetanilide, and a small amount of an unidentified acetanilide, m. p. 298°.

(ii) *o*-Nitroacetanilide gave a difficultly separable mixture, which did not yield pure individuals even after chromatography on alumina. The mixture was boiled with ethanolic hydrochloric acid for a few minutes and the product was then readily separated by use of acid into 2,5-dibromo-1-nitrobenzene (see i) and 4-bromo-2-nitroaniline, m. p. 108—110°.

(iii) *p*-Nitroacetanilide gave 1,2,3-tribromo-5-nitrobenzene (2·7 g.), m. p. 108—110° (lit., 112°).[4]

---

[1] A. Verda, *Gazzetta*, 1902, II, **32**, 20.

[2] A. Mannino and L. di Donato, *Gazzetta*, 1908, II, **38**, 24.

[3] H. France, I. M. Heilbron, and D. H. Hey, *J.*, 1940, 369.

[4] W. Korner, *Gazzetta*, 1874, **4**, 420.

(iv) *p*-Acetotoluidide gave 2,5,6-*tribromo*-4-*methylacetanilide* as prisms (0·2 g.), m. p. 205° (Found: C, 27·8; H, 1·9. $C_9H_8Br_3NO$ requires C, 28·0; H, 2·0%), and 2,4,5-tribromotoluene (0·8 g.), m. p. 112° (lit., 112°) [5] (n.m.r. showed 1 proton at τ 2·53 and 1 proton at τ 2·25).

(v) 2-Chloroacetanilide gave 4-bromo-2-chloroacetanilide, m. p. 151° (lit., 151°),[6] and 1,4-dibromo-2-chlorobenzene, m. p. 39—40° (lit., 40°).[7]

(vi) 4-Chloroacetanilide gave 1,2,3-*tribromo*-5-*chlorobenzene* as needles (0·7 g.), m. p. 98—100° (Found: C, 21·0; H, 0·9; N, 0·0. $C_6H_2Br_3Cl$ requires C, 20·6; H, 0·6%).

(vii) 4-Bromo-2-chloroacetanilide was partly unchanged and partly converted into 1,4-dibromo-2-chlorobenzene (0·5 g.), m. p. 36°, after crystallisation from light petroleum (lit., 40°) [7] (Found: C, 26·6; H, 1·1. Calc. for $C_6H_3Br_2Cl$: C, 26·6; H, 1·1%).

(viii) 3,4-Dimethylacetanilide gave a mixture of compounds from which was isolated the 2,5,6-*tribromo-derivative*, needles (1·0 g.), m. p. 251—253°, from acetic acid (Found: C, 30·3; H, 2·4. $C_{10}H_{10}Br_3NO$ requires C, 30·0; H, 2·5%) (n.m.r. shows no ring protons, *i.e.*, hexasubstitution).

(ix) 2,6-Dimethylacetanilide gave a mixture of products from which was isolated the 3,4,5-*tribromo-derivative*, needles (0·4 g.), m. p. 246°, from acetic acid (Found: C, 29·9; H, 2·9. $C_{10}H_{10}Br_3NO$ requires C, 30·0; H, 2·5%).

(x) *m*-Bromoacetanilide gave 2,4,5-tribromoacetanilide (3·8 g.), m. p. 186—189° (lit., 188—189°).[2]

(xi) 2-Acetamidobiphenyl gave the 3,5,4′(?)-*tribromo-derivative* as prisms (0·8 g.), m. p. 248—249° (Found: C, 37·5; H, 2·2; Br, 53·6. $C_{14}H_{10}Br_3NO$ requires C, 37·5; H, 2·4; Br, 53·6%).

(xii) 2-Acetonaphthalide (or 1-bromo-2-acetonaphthalide) gave a slightly impure tribromo-derivative as fine needles (2·5 g.), m. p. 260° (decomp.), from *o*-dichlorobenzene (lit., 250° decomp.).[2] Hydrolysis gave 1,4,6-tribromo-2-naphthylamine, as pinkish needles, m. p. 132—134°, from ethanol (lit., 125°); $\nu_{max.}$ 806s, 853, 869, 875, 933s, 1000, 1078, 1178, 1225w, 1257, 1320, 1337, 1375, 1475, 1580sh, 1620s, and 3450 cm.$^{-1}$. On acetylation it regenerated the pure acetyl derivative, m. p. 269°.

1,3,6-Tribromo-2-naphthylamine, m. p. 142—144° (lit., 143°) [8] was prepared by the hydrolysis of the corresponding toluene-*p*-sulphonamido-derivative; [9] it had $\nu_{max.}$ 766, 805s, 888s, 927s, 1010, 1065, 1185, 1230, 1350, 1370w, 1380w, 1440, 1470, 1545, 1590sh, 1610s, and 3280 cm.$^{-1}$. A mixture of these tribromo-bases melted below 110°.

(xiii) 2,5-Dimethyltoluene-*p*-sulphonanilide gave the 4-nitro-derivative, m. p. 183—184° (lit. 185°),[10] readily hydrolysed by solution in cold concentrated sulphuric acid to give 2,5-dimethyl-4-nitroaniline as needles, m. p. 144—146° (lit., 144°),[11] from ethanol. No bromo-derivatives were isolated.

Interaction of acetanilides with bromine. (i) Bromine (3·2 g.) was added to a suspension of 4-chloroacetanilide (3·4 g.) in chloroform (30 c.c.). On warming, a clear solution was obtained which on cooling deposited golden yellow crystals of the addition compound, m. p. 126—130° (Found: C, 30·8; H, 2·7. $C_8H_8Br_2ClNO$ requires C, 29·2; H, 2·4%); $\nu_{max.}$ 709, 830, 1090, 1310, 1365, 1390, 1490, 1540, 1600, 1660, and 3250 cm.$^{-1}$. On exposure to the atmosphere this product soon reverted to 4-chloroacetanilide.

(ii) 4-Bromoacetanilide similarly gave golden yellow crystals, m. p. 146—148°; $\nu_{max.}$ 820, 830, 980, 1008, 1070, 1308, 1370, 1390, 1490, 1540, 1600, 1645, 1670, 3080, and 3250 cm.$^{-1}$. Even after careful drying these had lost a considerable amount of bromine (Found: C, 28·6; H, 2·4. $C_8H_8Br_3NO$ requires C, 25·7; H, 2·1%). (iii) 2-Chloroacetanilide failed to yield an additive compound, and after the solution had stood for some hours 4-bromo-2-chloroacetanilide was isolated.

The authors are indebted to Mr. B. Semple, B.Sc., for the n.m.r. spectra.

HERIOT-WATT COLLEGE, EDINBURGH 1. [*Received, February 18th*, 1965.]

---

[5] R. H. C. Nevile and A. Winther, *Ber.*, 1881, **14**, 417.
[6] F. D. Chattaway and G. R. Clemo, *J.*, 1916, **109**, 91.
[7] W. H. Hurtley, *J.*, 1901, **79**, 1299.
[8] H. Franzen and E. Aaslund, *J. prakt. Chem.*, 1917, [2], **95**, 163.
[9] F. Bell, *J.*, 1932, 2734.
[10] Akt.-Ges. f. Anilinf., D.R.P. 157859.
[11] E. Noelting, O. N. Witt, and S. Ford, *Ber.*, 1885, **18**, 1667.