

The Orton Rearrangement. Part I. Preparation and Properties of N-Bromo- and N-Chloro-2 : 6-dimethylacetanilide.

By M. J. S. DEWAR and J. M. W. SCOTT.

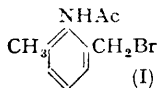
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N-Bromo- and *N*-chloro-2 : 6-dimethylacetanilide have been prepared, and their reactions studied with a view to kinetic experiments later. Both substances substantially conform to the usual behaviour of *N*-halogenoacylanilides.

IN connection with the Orton rearrangement of *N*-halogenoacylanilides, Dewar ("The Electronic Theory of Organic Chemistry," Oxford Univ. Press, 1949) suggested that it would be of interest to prepare *N*-bromo-2 : 6-dimethylacetanilide and study its properties, especially the rate of rearrangement. With a view to kinetic studies, the two compounds named in the title have been prepared, and their respective reactions investigated.

The *N*-bromo-compound has been rearranged in boiling water, in acetic acid, and with trichloroacetic acid in chlorobenzene (aprotic conditions). In all cases a substantial yield of the expected 4-bromo-compound was obtained but in acetic acid some 3-bromo-compound may also have been formed.

The *N*-bromo-compound was treated with sulphuric acid in acetic anhydride in the dark, in daylight, and in ultraviolet light. In each case the *N*-bromo-amide disappeared but the only product isolated was the unsubstituted amide. One case was, however, exceptional; after the *N*-bromo-compound had been left in acetic anhydride and sulphuric acid for some time a different product was obtained, the analysis of which indicated that the *N*-bromo-2 : 6-dimethylacetanilide had isomerised; as its m. p. differed from those of 3- and 4-bromo-2 : 6-dimethylacetanilide and *N*-bromoacetyl-2 : 6-dimethylaniline, the only possible structure for the compound appears to be (I), formed by internal bromination of one of the substituent methyl groups. This reaction could not be repeated, perhaps indicating that it involved some free-radical process.



The bromine in the compound (? I) was singularly unreactive, not being removed by alcoholic silver nitrate or by hot sodium hydroxide. This inertness might be expected, since S_N2 reactions would be sterically inhibited, and since S_N1 reactions would be sterically hindered in the sense that the methylene group of the intermediate carbonium ion would be initially perpendicular to the ring.

In the preparation of *N*-bromoacetyl-2 : 6-dimethylaniline it was not found possible to acylate 2 : 6-dimethylaniline in pyridine with bromoacetyl bromide. The reaction of propionyl chloride with the amine was investigated to ascertain whether steric factors were affecting the reaction. In this case, however, a good yield of 2 : 6-dimethylpropionanilide was obtained.

*cyclo*Hexene was readily brominated in the α -position with *N*-bromo-2 : 6-dimethylacetanilide in the presence of benzoyl peroxide as a catalyst. Steric factors should facilitate this particular reaction, since the loss of the bromine atom would yield a less hindered radical.

The *N*-chloro-compound, on treatment with the same rearranging reagents as the *N*-bromo-compound, gave what were assumed to be mixtures of isomers, *i.e.*, 3- and 4-chloro-2 : 6-dimethylacetanilide, together with a small loss of halogen to the solvent. It was not possible to separate these mixtures by chromatography or fractional crystallisation. Boiling water, however, seems to give only the 4-chloro-compound. The reason for this is not easy to see, although it has been previously reported that the orientation in the chlorination of anilides is somewhat dependent on the solvent used.

EXPERIMENTAL

2 : 6-Dimethylacetanilide was prepared from the corresponding amine and acetic anhydride. It was crystallised once from aqueous alcohol and had m. p. 178° (lit., 177°).

N-Bromo-2 : 6-dimethylacetanilide.—A mixture of 2 : 6-dimethylacetanilide (20 g.) and

potassium hydrogen carbonate (20 g.) was thoroughly powdered and added to distilled water (*ca.* 3000 ml.) with vigorous stirring. The suspension formed was cooled to 0° and treated (30 min.) with cold hypobromous acid (2 mol.) with constant stirring. Stirring was continued for a further 15 min. and the pale yellow solid which had formed was collected, washed with cold distilled water, and dried *in vacuo*. It crystallised from chloroform–light petroleum (b. p. 40–60°) in yellow prisms, m. p. 122–123° (18 g., 60%) (Found: active Br, 32.8. C₁₀H₁₂ONBr requires Br, 33.0%).

Rearrangements. (1) In boiling water. Pure *N*-bromo-2 : 6-dimethylacetanilide (1 g.) was added to boiling distilled water (*ca.* 50 ml.). The *N*-bromo-compound melted, forming globules which eventually solidified. The solid crystallised from absolute methanol in needles, m. p. 194–195°. Beilstein's "Handbuch" gives m. p. 193° for 4-bromo-2 : 6-dimethylacetanilide.

(2) In acetic acid. The pure *N*-bromo-acetanilide (10 g.) was dissolved in "AnalaR" glacial acetic acid (*ca.* 50 ml.), and the solution left in the dark until it no longer liberated iodine from acid potassium iodide solution (*ca.* 28 days). The acetic acid solution was then poured on ice, and the precipitate (9.5 g.) collected, washed, dried, and weighed (Found: Br, 32.7, 32.6. Calc. for C₁₀H₁₂ONBr: Br, 33.0%). It crystallised from absolute methanol in needles, m. p. 192–194° (7.1 g.). The mother-liquors yielded a solid which was not separated into pure components by chromatography or fractional crystallisation. If a solution of the *N*-bromo-compound in acetic acid was warmed, free bromine was liberated.

(3) Aprotic conditions. Pure *N*-bromo-2 : 6-dimethylacetanilide (5 g.) was dissolved in a 0.6*N*-solution of "AnalaR" trichloroacetic acid in pure chlorobenzene (*ca.* 25 ml.), and the solution left in the dark as in (2), *i.e.*, for *ca.* 28 days. The crystals that separated, when collected and washed with light petroleum (b. p. 40–60°), had m. p. 194°. Chloroform was added to the filtrate, and the acid removed by washing with potassium hydrogen carbonate solution. The non-aqueous layer was then dried, and the bulk of the solvent removed under reduced pressure. A further yield of solid, m. p. 193°, was obtained by addition of light petroleum (b. p. 40–60°). The total yield of solid was 4.2 g.

(4) In sulphuric acid and acetic anhydride. Three solutions of pure *N*-bromo-2 : 6-dimethylacetanilide (8 g.) in a mixture of concentrated sulphuric acid and acetic anhydride (30 ml.; 10% H₂SO₄ by vol.) were left respectively in the dark, in daylight, and in ultraviolet light, until they no longer liberated iodine from acid potassium iodide solution. In each case, the solution was then poured on ice, and the precipitated solid collected, washed, dried, and weighed; a portion of the solid was then crystallised from aqueous alcohol and tested qualitatively for bromine, with negative results. The yields, m. p.s, and mixed m. p.s with authentic 2 : 6-dimethylacetanilide were as below :

Conditions	Wt. (g.)	M. p.	Mixed m. p.	Conditions	Wt. (g.)	M. p.	Mixed m. p.
Dark	3.9	177°	177°	U.V. light ...	4.2	177–178°	177°
Daylight	4.1	177–178°	177				

Exceptional case. Pure *N*-bromo-2 : 6-dimethylacetanilide (1 g.) was dissolved in a solution of concentrated sulphuric acid in acetic anhydride (10 ml.; 10% H₂SO₄ by vol.), and the resulting solution left in daylight until it no longer liberated iodine from acid potassium iodide solution. The solution was then poured on ice, forming fine needles, m. p. 128–129° (from aqueous alcohol) (Beilstein gives the m. p.s of 3- and 4-bromo-2 : 6-dimethylacetanilide as 136° and 193°, respectively) (Found: C, 49.3; H, 4.9; N, 5.6; Br, 33.3. Calc. for C₁₀H₁₂ONBr: C, 49.6; H, 5.0; N, 5.8; Br, 33.0%).

N-Bromoacetyl-2 : 6-dimethylaniline.—Bromoacetyl bromide (8.3 g., 1 mol.) was added dropwise to 2 : 6-dimethylaniline (10 g., 2 mol.). The mixture became brown and then solidified. The product was boiled with "Norit" and methanol and then crystallised from methanol (6.3 g., 59%). Further crystallisation from methanol gave needles, m. p. 150–151° (Found: C, 49.3; H, 5.1; N, 6.1; Br, 33.3. C₁₀H₁₂ONBr requires C, 49.6; H, 5.0; N, 5.8; Br, 33.0%).

2 : 6-Dimethylpropionanilide.—Propionyl chloride (1.5 ml.) was added dropwise to a cooled solution of 2 : 6-dimethylaniline (1 g.) in dry pyridine (5 g.) with constant stirring. The resulting solution was poured into excess of dilute hydrochloric acid, and the precipitate collected, washed, dried, and weighed (1.3 g., 80%). A portion, crystallised from absolute methanol and then light petroleum (b. p. 80–100°), formed needles, m. p. 121° (Found: C, 74.6; H, 8.6; N, 7.7. C₁₁H₁₅ON requires C, 74.5; H, 8.5; N, 7.9%).

Bromination of cyclohexene.—Pure *N*-bromo-2 : 6-dimethylacetanilide (2 g.) was dissolved in purified cyclohexene (*ca.* 50 ml.), and a trace of benzoyl peroxide added. The solution was gently refluxed, the colour changing from yellow to red (*cf.* *N*-bromosuccinimide brominations)

with the separation of solid. When the solution no longer liberated iodine from acid potassium iodide solution, it was cooled, and the solid collected (m. p. 177°). The bulk of the unchanged *cyclohexene* was removed by distillation, light petroleum (b. p. 40—60°) added, and the solution chromatographed on alumina to remove the last traces of 2 : 6-dimethylacetanilide. The light petroleum was removed, leaving a small bulk of pleasant-smelling liquid (3-bromocyclohexene smells of geraniums), which was converted into 3-cyclohexenylthiuronium picrate by the usual method and this was crystallised from acetone and light petroleum (b. p. 40—60°) giving yellow blades, m. p. 160—161° (Found : C, 40.3; H, 3.9; N, 18.2; S, 8.1. $C_{13}H_{15}O_7N_3S$ requires C, 40.5; H, 3.9; N, 18.2; S, 8.3%).

N-Chloro-2 : 6-dimethylacetanilide.—Pure 2 : 6-dimethylacetanilide (10 g.) was thoroughly powdered with potassium hydrogen carbonate (10 g.), the mixture added to distilled water (2 l.), and the resulting suspension cooled (ca. 8°). A fresh solution of sodium hypochlorite (2 mol.), likewise cooled, was then added to the suspension with vigorous stirring. The solution eventually became turbid and after 1 hr. the *chloro-compound* formed was collected, washed, and dried. It crystallised from chloroform and light petroleum (b. p. 40—60°) on strong cooling in blades (6.3 g., 52%), m. p. 112—113° (Found : active Cl, 17.8. $C_{10}H_{13}ONCl$ requires Cl, 17.9%).

Rearrangements. (1) In boiling water. Pure *N*-chloro-2 : 6-dimethylacetanilide (1 g.) was added to boiling distilled water (ca. 50 ml.). The water became yellow and smelt of chlorine. When the reaction was complete the mixture was cooled, and the separated solid collected and crystallised several times from aqueous alcohol. It had m. p. 194°; Beilstein records m. p. 195° for 4-chloro-2 : 6-dimethylacetanilide.

(2) In acetic acid. Pure *N*-chloro-2 : 6-dimethylacetanilide (2 g.) was dissolved in "AnalaR" glacial acetic acid (10 ml.), and the solution warmed on a steam-bath until it no longer liberated iodine from acid potassium iodide solution (ca. 12 hr.). It was then poured on ice, and the precipitate collected, washed, and dried (Found : Cl, 17.5. Calc. for $C_{10}H_{13}ONCl$: Cl, 17.9%). The solid, crystallised several times from aqueous alcohol, still melted over a large range, 145—155°. A portion of the solid was chromatographed on alumina by using light petroleum (b. p. 60—80°) but no separation was achieved.

(3) Aprotic conditions. Pure *N*-chloro-2 : 6-dimethylacetanilide (2 g.) was dissolved in a 0.6*N*-solution of "AnalaR" trichloroacetic acid in chlorobenzene (ca. 10 ml.), and the solution left on a steam-bath in the dark until it no longer liberated iodine from acid potassium iodide solution (ca. 12 hr.). Chloroform was then added, and the acid removed by washing the non-aqueous layer with potassium hydrogen carbonate solution. The non-aqueous layer was dried, and the bulk of the solvent removed under reduced pressure. Light petroleum (b. p. 40—60°) was added to the residue, and the precipitated solid collected and dried (Found : Cl, 15.5. Calc. for $C_{10}H_{13}ONCl$: Cl, 17.9%). The solid was crystallised several times from aqueous alcohol but still melted over 144—155°. Chromatography, as before, gave no separation.

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QUEEN MARY COLLEGE, MILE END ROAD, LONDON, E.1.

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