## 261. *The Halogenation of Phenolic Ethers and Anilides. Part VII. A New Method of Determining the Proportions of* o- *and* p-*Isomerides in a Mixture.*

By Brynmor Jones.

MIXTURES of isomeric derivatives of benzene are frequently analysed by the examination of physical properties such as freezing points, solubility, or density. Such methods have been successfully employed in very many cases, yet in so far as they necessitate the isolation and purification of the mixture they are often tedious and occasionally uncertain. Existing methods depending on a difference of chemical properties, however, are less trustworthy. It is, nevertheless, apparent that any physical or chemical property which discriminates sharply between isomerides may be employed. A method is now reported, suitable for use in nuclear chlorination reactions, which depends on the difference in the velocities of substitution of *o*- and *p*-isomerides, and permits of the rapid estimation of the proportions without isolation of the mixtures to be analysed. This method has been applied in the first instance to the determination of the proportions formed in the chlorination of three anilides.

Since the present method depends on a difference of nuclear reactivity of isomerides, the larger this difference the greater the sensitivity and the more accurate the determination of the proportions. For acetanilide the respective velocities, *k*(20°), are *o*-Cl 0·127, *p*-Cl 0·365, 2 : 4-$Cl_2$ 0·0007, and it is clear from these values that the accuracy of the method is not appreciably affected by the gradual accumulation of the dichloroanilide. Since similar differences in reactivity are apparent in all the *o*- and *p*-isomerides examined (cf. table and J., 1934, 210), it follows that mixtures of these will have reactivities lying between these limits, the exact value depending on the composition of the mixture. Such a mixture of *o*- and *p*-isomerides, obtained by controlled chlorination of an unsubstituted anilide with

1 mol. of chlorine, is analysed by carefully determining its velocity of further chlorination and observing the coincidence of the velocity with that of an artificial mixture of known composition.

The following table contains the values now found and those determined by Orton and Bradfield (J., 1927, 986) by a sublimation method and by the analysis of f. p. curves.

*Chlorination in acetic acid at* 20°.

| | O. and B.* | | Present values.† | |
|---|---|---|---|---|
| | *ortho-*. | *para-*. | *ortho-*. | *para-*. |
| Acetanilide | 32·5 | 67·5 | 29 | 71 |
| Benzanilide | 30·4 | 69·6 | 29 | 71 |
| Benzenesulphonanilide | 35·0 | 65·0 | 28·5 | 71·5 |

* Acetic acid, m. p. 16°. † " 99% Acetic acid."

When comparing these values, it should be realised that errors arising from any tendency to over-chlorination and particularly to under-chlorination affect the observed proportions differently. In the m. p. method such factors will tend to increase the apparent percentage of the *o*-isomeride. In the present method, on the other hand, under-chlorination is the more serious since traces of the parent substance will cause a rapid initial disappearance of chlorine and so result in an erroneously high value for the more active *p*-isomeride. Freedom of the mixture of isomerides from traces of the parent substance is therefore essential.

The error to which any individual determination is subject is difficult to estimate with certainty, but, the mean of two concordant experiments being taken, it is probable that for acet- and benz-anilides the proportions are accurate to ± 1%. Benzenesulphonanilide and its chloro-derivatives are less reactive, and the error here is probably higher. To minimise the introduction of accidental errors as far as possible, it is advisable to determine all the velocities for any one particular substance at the same time under identical conditions.

Although somewhat limited in application, the present method has the advantage of great rapidity since, once the materials have been prepared, a complete estimation can be carried out within a few hours.

The following new velocity coefficients required for the above discussion have been determined.

*Velocity coefficients for the chlorination of substances of the type o-*NHAc·$C_6H_4$X *in* 99% *acetic acid at* 20°.

$[Cl_2] = 0{\cdot}02M$; $[HCl] = 0{\cdot}0475M$.

| | Concn. of anilide, mols./l. | 0·02 | 0·06 | 0·10 |
|---|---|---|---|---|
| | Mol. proptn. of anilide | 1 | 3 | 5 |
| Group X. | Group Ac. | | | |
| *o*-Cl | $C_2H_5$·CO | — | 0·219 | — |
| ,, | $CH_3$·CO | 0·127 | 0·125 | 0·132 |
| ,, | $C_6H_5$·CO | 0·089 | — | — |
| ,, | $C_7H_7$·$SO_2$ | — | 0·0726 | 0·0758 |
| ,, | $C_6H_5$·$SO_2$ | — | 0·0433 | 0·0434 |

2 : 4-Dichloroacetanilide : $k = 0{\cdot}00073$.

$[Cl_2] = 0{\cdot}02M$; $[HCl] = 0{\cdot}05M$; $[\text{anilide}] = 0{\cdot}20M$.

## EXPERIMENTAL.

The success of the present method depends very largely on the smoothness and quantitative accuracy with which the initial chlorination of the parent anilide to the mixture of isomerides can be carried out. For the present requirements the regulated method of chlorination introduced by Orton and King (J., 1911, 99, 1185; *Ann. Reports*, 1928, 25, 143) is very suitable, since the addition of a minute amount of hydrochloric acid to the acetic acid solution containing the calculated amount of a chloroamine and anilide produces a low concentration of chlorine which maintains itself throughout the process, and at the same time precludes the occurrence of a high local concentration which might lead to poly-substitution. To ensure freedom of the mixture of isomerides thus obtained from traces of the parent anilide, 0·5% excess chlorine is employed, errors resulting thereby being of secondary importance.

For the initial chlorination of the anilides to the mixtures of isomerides the following procedure was adopted. To one molecular proportion of the anilide dissolved in a small quantity of purified acetic acid in a 100 c.c. flask was added one molecular proportion (+ 0·5% excess) of chlorine in the form of a chloroamine. An amount of water, which, together with that present in the acetic acid and that to be added in the form of constant-boiling solution of hydrochloric acid, would make up 1 c.c., was added, and the solution made up nearly to the 100 c.c. mark with more acetic acid. When the solution had attained the temperature of the thermostat, 1/30th molecular proportion of hydrochloric acid was added, the contents of the flask thoroughly mixed by shaking, and the flask replaced in the thermostat. When all the chlorine had reacted, an amount of pure silver acetate equivalent to the hydrochloric acid (+ 5% excess) used was added. The precipitated silver chloride was filtered off quickly through a thoroughly dry apparatus or, better, allowed to settle, whereupon an aliquot portion of the solution was withdrawn and the velocity of further chlorination determined in the same manner as for the artificial mixtures.

The velocities of chlorination of mixtures of isomerides were determined by the method previously described (cf. earlier parts of this series), except that now all the titrations relating to one particular substance were withdrawn at identical times. Since the velocity of reaction is sensitive to small variations in the water content of the medium, care is necessary to ensure that this is the same in all measurements. A microburette graduated in 0·02 c.c. was employed, and each recorded value is the mean of two independent determinations.

The values of the proportions now recorded were obtained by extrapolation of the titres of the different mixtures at identical times, and not by a comparison of velocity coefficients. Since the mixtures consist of two isomerides of different reactivity, velocity coefficients obtained from the ordinary expression for a bimolecular reaction are not true constants. It is clear that such values should decrease gradually as the reaction progresses. That this decrease was not shown in the present cases is apparent from the values for "unknown I" (0·2195, 0·2174, 0·2187), and can be accounted for by loss of chlorine when successive portions are withdrawn and the air space above the solution increases in volume. In slow chlorinations of the type now considered this phenomenon has been frequently observed in the course of this work when equimolecular proportions of reactants are employed. Experiments by Gwyn Williams (Thesis, Bangor, 1927) on acetic acid solutions of chlorine have established the correctness of this view by showing that errors which arise owing to the volatility of the chlorine can be eliminated by keeping the air space to a minimum, and by maintaining the same concentration of chlorine in the indrawn air as in the air above the solution.

The results of the measurements are given in the following tables.

*Benzanilide, $T = 20°$.*

| | Titres (c.c.) ($t_0$ = 12·00 c.c. $N$/30-$Na_2S_2O_3$). | | | | Titres (c.c.) ($t_0$ = 12·00 c.c. $N$/30-$Na_2S_2O_3$). | | |
|---|---|---|---|---|---|---|---|
| Time, mins. | 120 | 204 | 273 | Time, mins. | 120 | 204 | 273 |
| "Unknown I"...... | 7·86 | 6·36 | 5·46 | 70% *p*- + 30% *o*- | 7·89 | 6·36 | 5·49 |
| 73% *p*- + 27% *o*- | 7·80 | 6·27 | 5·37 | 67% *p*- + 33% *o*- | 7·96 | 6·48 | 5·61 |

Proportions over three intervals of time: $p$ = 71, 70, 71. Mean 71%.

*Acetanilide.*

| Time, mins. | 120 | 235 | 305 | Time, mins. | 120 | 235 | 305 |
|---|---|---|---|---|---|---|---|
| "Unknown II" ... | 7·19 | 5·16 | 4·40 | 70% *p*- + 30% *o*- | 7·22 | 5·19 | — |
| 73% *p*- + 27% *o*- | 7·10 | 5·09 | 4·34 | 67% *p*- + 33% *o*- | 7·35 | 5·33 | 4·58 |

Proportions over three intervals of time: $p$ = 71, 71, 71. Mean 71%.

*Benzenesulphonanilide.*

| Time, mins. | 120 | 185 | 263 | Time, mins. | 120 | 185 | 263 |
|---|---|---|---|---|---|---|---|
| "Unknown III" ... | 8·74 | 7·72 | 6·78 | 73% *p*- + 27% *o*- | 8·75 | 7·65 | 6·65 |
| | | | | 70% *p*- + 30% *o*- | 8·81 | 7·76 | 6·78 |

Proportions over three intervals of time: $p$ = 73·5, 71, 70. Mean 71·5%.

*Materials.*—Throughout, carefully purified materials are necessary, freedom from impurities reactive towards chlorine being essential. All anilides were therefore crystallised at least thrice from ethyl alcohol or glacial acetic acid. The chloroamine, dichloramine-T, was purified by solution in hot glacial acetic acid and crystallisation induced by the addition of a few c.c. of an approximately *N*/5 aqueous solution of bleaching powder. All solutions of the chloroamine were carefully standardised before use. An acetic acid stable to chlorine was obtained by distillation from chromic oxide according to the method of Orton and Bradfield (J., 1927, 983).

The author thanks the Chemical Society for a grant.

THE UNIVERSITY, SHEFFIELD.

[*Received, June 4th,* 1936.]