107. *Molecular Rearrangements. Part IV.* The Thermal Rearrangement of* N-*Chloroacetanilide.*

By C. C. Beard, J. R. B. Boocock, and W. J. Hickinbottom.

Evidence is presented in support of the view that the rearrangement of *N*-chloroacetanilide in the fused state is an intermolecular chlorination.

It is known that *N*-chloroacetanilide changes above its melting point into a mixture of *o*- and *p*-chloroacetanilide; other *N*-chloroacylarylamides behave similarly.[1-5] There are already sufficient observations to exclude belief that this migration is a true intramolecular rearrangement, if the term is used in the strict sense of implying that the chlorine remains within the confines of the molecule. Thus, Bradfield[5] found that at 100° *N*-chloroacetanilide gives, not only *o*- and *p*-chloroacetanilide, but also some acetanilide and 2,4-dichloroacetanilide as well as unidentified material and acid fumes. Chattaway and Orton[3] observed the formation of benzoyl chloride from *N*-chlorobenzanilide at 120—130°; some 4′-chlorobenzanilide was also formed. Benzoyl chloride was also formed when *N*,2,4-trichlorobenzanilide was heated: a tar was also produced from which 2′,4′-dichlorobenzanilide was isolated. From *N*,2,4-trichloro-formanilide and -acetanilide, chlorine is liberated on heating and from the residue 2,4-dichloro-formanilide or -acetanilide can be isolated.

The work described in the present paper was undertaken to obtain further evidence which might provide a suitable working hypothesis for the course of the thermal rearrangement.

Bender's observation[1] that *N*-chloroacetanilide could chlorinate *p*-nitroaniline and acetoacetic ester provides a significant clue: that *N*-chloroacetanilide can act as a chlorinating agent. Some evidence to support this has been obtained in earlier work with alkylbenzenes, but no valid conclusions could be drawn from these observations until there was clear and unambiguous evidence of the absence of hydroperoxides in the alkylbenzenes and that none develops in the course of the reaction.

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* Part III, *J.*, 1959, 1873.

[1] Bender, *Ber.*, 1886, **19**, 2272.
[2] Slosson, *Ber.*, 1895, **28**, 3265.
[3] Chattaway and Orton, *J.*, 1899, **75**, 1046.
[4] Porter and Wilbur, *J. Amer. Chem. Soc.*, 1927, **49**, 2145.
[5] Bradfield, *J.*, 1928, 351.

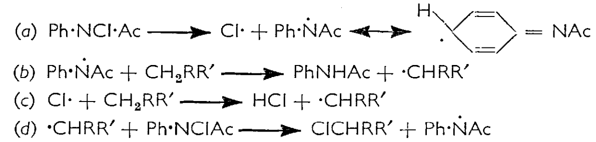
When precautions are taken to exclude the presence or development of hydroperoxides it is found that *N*,2,4,6-tetrachloracetanilide chlorinates boiling toluene to give benzyl chloride: *p*-xylene is similarly chlorinated in the side chain.

When *N*,2,4,6-tetrachloroacetanilide is replaced by *N*-chloroacetanilide, chlorination of toluene also occurs, to give benzyl chloride, but this reaction is accompanied by thermal rearrangement to 4-chloroacetanilide. When, *N*-chloroacetanilide is heated with *o*- or *p*-nitroaniline, instead of toluene, in a suitable solvent, this rearrangement is suppressed and chlorination of the nitroaniline is the only recognisable reaction. Acetoacetic ester and acetylacetone are similarly chlorinated.

It is now evident that, if the thermal rearrangement of *N*-chloroacetanilide is carried out in a suitable solvent, the chlorine can be transferred to the solvent with the formation of acetanilide. The extent to which this transfer occurs depends on the solvent. In readily substituted solvents such as acetylacetone, acetoacetic ester, or nitroaniline, the transfer is complete, and there is no formation of *p*-chloroacetanilide. But in other solvents, where the chlorination is slower, as in toluene or acetophenone, the chlorination of the solvent and formation of *p*-chloroacetanilide occur simultaneously.

From the fact that alkylbenzenes are chlorinated in the side chain and not the nucleus, it is assumed that the thermal chlorination by *N*-chloroacetanilides is a homolytic reaction.[6] On this basis, the initial phase can be taken as a homolytic dissociation (*a*). In the absence of a second substance the formation of *o*- and *p*-chloroacetanilide from *N*-chloroacetanilide proceeds by the scheme proposed in an earlier paper.[7]

When the thermal decomposition of *N*-chloroacetanilide is carried out in a solvent such as toluene or acetylacetone, chlorination of the solvent can be represented by:



In this scheme the chlorine atom from the thermal dissociation of the *N*-chloroacetanilide (*a*) may also take part in the reaction with the formation of hydrogen chloride (*c*). The amount formed, however, is not sufficient to alter the reaction from a free-radical chlorination to proton-catalysed chlorination, the characteristics of which are known already.

The possibility was also considered that these chlorinations may proceed by a bimolecular homolytic reaction between *N*-chloroacetanilide and the solvent without preliminary dissociation into free radicals. On such a scheme it is possible to represent the course of the reaction qualitatively. Yet the scheme outlined above is preferred since it can be used to account for the formation of molecular chlorine, acetyl chloride, and other by-products from the *N*-chloro-di- and -tri-chloroacylanilides when they are heated alone.

EXPERIMENTAL

N-Chloroacetanilide as a Chlorinating Agent.—(a) *Toluene.* To ensure that the toluene was free from peroxide and that none developed in the subsequent stages, toluene, freshly distilled from sodium, was refluxed for some hours with stannous chloride and distilled directly on to a known weight of *N*-chloro-compound. All these operations and the subsequent refluxing of the toluene solution of the *N*-chloro-compound were conducted in nitrogen and in absence of light.

When there was no longer a positive reaction for *N*-chloro-compound, the solution was chilled and any acetyl derivative which had separated was collected and washed with light petroleum. The solution was concentrated and light petroleum added. After filtration and

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[6] Cf. Robertson and Waters, *J.*, 1947, 492.

[7] Ayad, Beard, Garwood, and Hickinbottom, *J.*, 1957, 2981.

repetition of this treatment to remove as much as possible of the solid matter, the solution was distilled.

A preliminary study was made with *N*,2,4,6-tetrachloroacetanilide in boiling toluene. After 15 hours' refluxing, toluene (35 c.c.) and *N*,2,4,6-tetrachloroacetanilide (25 g.) gave 2,4,6-trichloroacetanilide, m. p. and mixed m. p. 205—206·5°, and benzyl chloride (7 g.; n_D^{20} 1·5333—1·5395), b. p. 68—69°/16 mm., n_D^{20} 1·5395 (Found: C, 66·2; H, 5·7; Cl, 27·3; labile Cl, 27·0. Calc. for C_7H_7Cl: C, 66·4; H, 5·6; Cl, 28·0%) [converted by the Sommelet reaction into benzaldehyde (semicarbazone, m. p. and mixed m. p. 209—210°) and benzoic acid, m. p. and mixed m. p. 120—121°].

Similar chlorinations were carried out with substantially the same results. *p*-Xylene with *N*,2,4,6-tetrachloroacetanilide gave 4-methylbenzyl chloride.

Toluene (155 c.c.) and *N*-chloroacetanilide (25 g.), refluxed together for 52 hr., gave a mixture of acetanilide and *p*-chloroacetanilide (Found: Cl, 18·25, 18·3, 18·5, for different preparations. Calc. for C_8H_8ONCl: Cl, 20·9%) which were both obtained pure by fractional crystallisation. Nearly pure benzyl chloride (~0·8 c.c.) was also isolated (*S*-benzylthiuronium picrate, m. p. and mixed m. p. 184—185°; also gave benzaldehyde).

(b) o-*Nitroaniline.* To *o*-nitroaniline (1·62 g.) in 1,1,2,2-tetrachloroethane (40 c.c.) at 100—120° *N*-chloroacetanilide (1·98 g.) was added portionwise. The resulting dark solution was extracted with boiling water (3 × 200 c.c.). The extract, on cooling, deposited orange needles of 4-chloro-2-nitroaniline, m. p. 115·5—116·5°. *p*-Chloroacetanilide could not be recognised in the product.

(c) p-*Nitroaniline.* To *p*-nitroaniline (1·62 g.) in boiling carbon tetrachloride (40 c.c.) was added *N*-chloroacetanilide (1·9 g.). After 5 min. a vigorous reaction took place and the solution became reddish-orange. After removal of the organic solvent by steam, the products were separated by fractional crystallisation from water into 2-chloro-4-nitroaniline, yellow needles, m. p. and mixed m. p. 106—107° (Found: C, 41·4; H, 3·2; N, 20·4; Cl, 16·1. Calc. for $C_6H_5O_2N_2Cl$: C, 41·7; H, 2·9; Cl, 16·2; N, 20·55%), and acetanilide, m. p. and mixed m. p. 113—114·5° (from benzene).

(d) *Ethyl acetoacetate.* Powdered *N*-chloroacetanilide (10·3 g.) was added in portions to freshly distilled acetoacetic ester (10 g.), with cooling after each addition. The reaction was completed by 30 minutes' shaking. Acetanilide separated and a further amount was obtained by diluting the liquid with light petroleum (b. p. $<40°$) [total yield, 6·44 g.; m. p. 113—114° (from water)]. Distillation of the light petroleum filtrate gave almost pure chloroacetoacetic ester, b. p. 80—88°/13 mm., n_D^{20} 1·4447—1·4464, whose identity was established by comparison with an authentic specimen (infrared spectroscopy) and by conversion into ethyl 2-amino-4-methylthiazole-5-carboxylate, m. p. and mixed m. p. 173—174°, by reaction with thiourea.

(e) *Acetylacetone.* *N*-Chloroacetanilide (8 g.) was added portionwise to freshly distilled acetylacetone (6 g.), as in (d). Treatment of the resulting pasty mass with light petroleum left acetanilide, m. p. 113—114·5° (from water). Distillation of the light petroleum extract gave nearly pure chloroacetylacetone, b. p. 40°/15 mm., n_D^{19} 1·4681 (infrared spectroscopy), converted by thiourea into 5-acetyl-2-amino-4-methylthiazole, m. p. 265—266° not depressed on admixture with a sample from chloroacetylacetone prepared in another way (Found: C, 46·5; H, 5·2; N, 18·1; S, 20·3. Calc. for $C_6H_8ON_2S$: C, 46·1; H, 5·2; N, 17·9; S, 20·3%).

(f) *Acetophenone.* Acetophenone (15 g.) was heated at 200° and *N*-chloroacetanilide (14 g.) added in portions. Trituration of the cooled melt with light petroleum gave 10 g. of a light brown solid from which *p*-chloroacetanilide, m. p. and mixed m. p. 175—176·5°, and acetanilide, m. p. and mixed m. p. 113—114°, were separated by fractional crystallisation from water. Distillation of the light petroleum extract gave acetophenone (11·45 g.) and a lachrymatory residue (4·45 g.) from which ω-chloroacetophenone was isolated by steam-distillation and crystallisation from light petroleum; this had m. p. and mixed m. p. 54—55° (Found: C, 62·4; H, 4·6; Cl, 22·9. Calc. for C_8H_7OCl: C, 62·1; H, 4·6; Cl, 22·9%). From it, 2-amino-4-phenylthiazole was prepared, having m. p. and mixed m. p. 147—148°.

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