709. *Properties and Reactions of Free Alkyl Radicals in Solution. Part VI.* Reactions with* N-*Halogenoanilides.*

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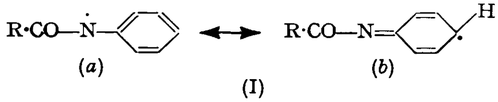
2-Methoxycarbonyl-2-propyl radicals abstract the *N*-halogen atom from an *N*-halogeno-anilide, giving the corresponding methyl α-halogeno*iso*butyrate together with products derived from the newly formed acylamino-radical, •NAr•COR. From *N*-chloroacetanilide there is obtained methyl α-*p*-acetamidophenyl*iso*butyrate. *N*-Chlorobenzanilide gives 4-benzamido-*N*-benzoyldiphenylamine, and a similar product results from *N* : 2′ : 4′-trichlorobenzanilide. *N* : 2′ : 4′ : 6′-Tetrachlorobenzanilide yields both benzoyl chloride and 3 : 5-dichloro-1 : 4-benzoquinone 1-(2 : 4 : 6-trichloro-anil). These results indicate that acylamino-radicals are mesomeric, and couple to give C–C or N–C, and not N–N, bonds.

The study of the reactions of free alkyl radicals with " positive " halogen compounds (Part III, *J.*, 1952, 2240) has now been extended to an investigation of the decomposition of dimethyl αα′-azo*iso*butyrate in the presence of a number of *N*-halogenoanilides. It has been found that 2-methoxycarbonyl-2-propyl radicals $MeO_2C{\cdot}CMe_2{\cdot}$ abstract the nitrogen-linked halogen atom, forming the corresponding methyl α-halogeno*iso*butyrate in 35—50% yield, together with products of different types derived from the newly-formed nitrogen radicals (I). Sufficient azo-ester to ensure complete reaction of the *N*-halogenoanilide was always used.

The nitrogenous reaction products were never the hydrazine derivatives which would have resulted from nitrogen–nitrogen union of the acylamino-radicals (I) of canonical form (*a*) but were invariably products containing stable carbon–nitrogen or carbon–carbon bonds indicative of reaction through forms such as (*b*). Thus *N*-chloroacetanilide yielded 6% of methyl α-*p*-acetamidophenyl*iso*butyrate (II) by reaction of a 2-methoxycarbonyl-2-propyl radical with a radical in form (I*b*), whereas *N*-chlorobenzanilide under similar conditions gave 26% of 4-benzamido-*N*-benzoyldiphenylamine (III) by interaction of two acylamino-radicals in forms (*a*) and (*b*) respectively. From the analogous reaction with *N*-bromo-acetanilide, however, only methyl α-bromo*iso*butyrate and *p*-bromoacetanilide could be isolated.



(I)

N : 2′ : 4′-Trichlorobenzanilide gave 54% of a product similar to (III), undoubtedly 2-benzamido-*N*-benzoyl-3 : 5 : 2′ : 4′-tetrachlorodiphenylamine (IV), whilst *N* : 2′ : 4′ : 6′-tetrachlorobenzanilide yielded 4% of 3 : 5-dichloro-1 : 4-benzoquinone 1-(2 : 4 : 6-tri-chloroanil) (V) and 35% of benzoyl chloride. These last products clearly result from the expected intermediate (VI); hydrolysis of the Ph•CO•N: group may well have occurred during the chromatographic separation of the reaction products. Intractable substances of higher molecular weight were also formed, and unfortunately these sometimes constituted the major part of the reaction product. As noted previously (Bickel and Waters, *Rec. Trav. chim.*, 1950, **69**, 312), poly(methyl methylacrylate) is to be expected as an end product in the decomposition of the azo-ester.

The structure of (II) has been established by hydrolysis to α-*p*-aminophenyl*iso*butyric acid which (i) gave only a *di*bromo-derivative and (ii) by hypophosphite deamination yielded α-phenyl*iso*butyric acid, identical with an authentic specimen. α-*o*-Aminophenyl-*iso*butyric acid would, by ring closure to 3 : 3-dimethyloxindole, have exhibited quite different properties. The dibenzoyl derivative (IV) lost only one benzoyl group on hydrolysis; the product gave a typical " diphenylamine-blue " colour reaction, and it can

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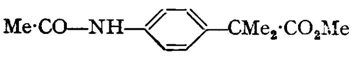
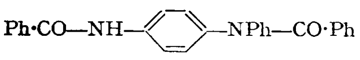
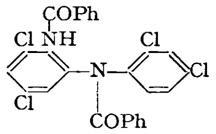
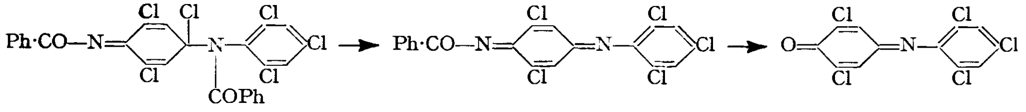
* Part V, *J.*, 1952, 4666.

therefore be concluded that the hydrolysis had removed the benzoyl group attached to the secondary nitrogen of the diphenylamine system. The structure of (III) has been fully established by direct comparison with a synthetic product obtained from *N*-benzoyl-4-nitrodiphenylamine (Lellmann, *Ber.*, 1882, **15**, 826) by reduction and further benzoylation. The amides (III) and (IV) give similar infra-red spectra, from which the presence of N–H links and two differently arranged C=O links (in –NH·CO– and =N·CO–) was evident. The anil (V), m. p. 142·5°, was prepared synthetically by condensation of 2 : 6-dichloro-1 : 4-benzoquinone with *s*-trichloroaniline. The isomeric 2 : 6-dichloro-1 : 4-benzoquinone 1-(2 : 4 : 6-trichloroanil), which could also result by this condensation, but is not formed, presumably owing to the steric effect of the flanking chlorine atoms in the quinone, is described by Bradfield, Cooper, and Orton (*J.*, 1927, 2854) as " bronzy-red needles, m. p. 163°."


(II)


(III)


(IV)


(VI) + Ph·COCl (V)

EXPERIMENTAL

Interaction of N-*Chloroacetanilide and Dimethyl αα′-Azo*isobutyrate.—A solution of the *N*-chloroanilide (purity 100%; 17·0 g., 0·1 mole) and the azo-ester (34·5 g., 0·15 mole) in dry benzene (" AnalaR "; 50 ml.) was gradually heated during 0·5 hr. in such a way as to produce a regular evolution of nitrogen, and finally refluxed for 1·5 hr. The crystalline precipitate obtained on storage of the product overnight at 0° was combined with the small quantities of solid obtained by successive treatments of the mother-liquor with light petroleum (b. p. 80—100°). The whole when recrystallised twice from benzene containing a little light petroleum gave *methyl α-*p*-acetamidophenyl*isobutyrate (II) (1·4 g., 6%), glistening plates, m. p. 164° (Found: C, 66·6; H, 7·0; N, 5·8. $C_{13}H_{17}O_3N$ requires C, 66·4; H, 7·2; N, 5·95%). Removal of the solvents from the combined residues gave an oil which afforded methyl α-chloro*iso*but rate (4·8 g., 35% calc. on the chloroamide), b. p. 38°/17 mm., characterised by conversion into α-chloro*iso*butyramide, m. p. 119—121° (Found: Cl, 29·2. Calc. for C_4H_8ONCl: Cl, 29·2%). After removal of dimethyl tetramethylsuccinate (5·7 g.) a distillate, b. p. 110—125°/0·25—0·2 mm., was obtained which on trituration with light petroleum gave acetanilide (0·45 g.), m. p. and mixed m. p. 114°; a viscous residue (12·7 g.) remained.

*Hydrolysis of Methyl α-*p*-Acetamidophenyl*isobutyrate.—(a) *Alkaline hydrolysis.* The acetamido-ester (0·9 g.) in alcohol (20 ml.) was treated with potassium hydroxide (1·5 g.) in water (7·5 ml.) and refluxed for 2 hr. Evaporation of the product to dryness under diminished pressure and acidification of the residue gave *α-*p*-acetamidophenyl*isobutyric *acid*, which after crystallisation from water and then from toluene formed colourless blades, m. p. 168—169° (Found: C, 65·6; H, 7·0; N, 6·2. $C_{12}H_{15}O_3N$ requires C, 65·1; H, 6·8; N, 6·3%).

(b) *Acid hydrolysis.* The acetamido-ester (1·35 g.) was refluxed for 3 hr. with hydrochloric acid (36%; 25 ml.). The solution was evaporated to dryness under reduced pressure and the residue was dissolved in aqueous ammonia and decolorised (charcoal). Acidification gave *α-*p*-aminophenyl*isobutyric *acid*, which on crystallisation from water and then from toluene gave buff needles (0·8 g.), m. p. 168—169° (decomp.) (Found: C, 67·4; H, 7·5; N, 7·6. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3; N, 7·8%). Treatment of the amino-acid with acetic anhydride at 100° for 5 min. gave the acetamido-acid, m. p. 168—169°, undepressed in admixture with the sample obtained as above. Benzoylation of the amino-acid under Schotten-Baumann conditions with a slight excess of benzoyl chloride, followed by acidification and refluxing of the solid reaction product with carbon tetrachloride to remove benzoic acid, gave *α-*p*-benzamido-*

*phenyl*iso*butyric acid*, which crystallised from aqueous alcohol in plates, m. p. 221·5—223° (Found: C, 71·9; H, 6·19; N, 5·14. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·04; N, 4·94%).

Deamination of α-p-*Aminophenyl*iso*butyric Acid*.—To a paste of the amino-acid (0·36 g.) in hydrochloric acid (36%; 4 ml.) and water (4·5 ml.) at 0° was added sodium nitrite (0·15 g.) in water (5 ml.), and the resulting diazo-solution was treated with sodium hypophosphite (3·2 g.) in water (6 ml.). After the addition was complete, nitrogen began to be evolved. The product (0·3 g.), which had crystallised after storage of the mixture overnight at 0°, was washed with water and than had m. p. 74—77°. Crystallisation from water (charcoal) and finally from light petroleum (b. p. 40—60°) gave α-phenyl*iso*butyric acid, m. p. 76·5—78°, undepressed in admixture with an authentic specimen (Brander, *Rec. Trav. chim.*, 1918, **37**, 67) (Found: C, 73·1; H, 7·4. Calc. for $C_{10}H_{12}O_2$: C, 73·1; H, 7·4%).

α-(4-*Amino*-3 : 5-*dibromophenyl*)iso*butyric Acid*.—The amino-acid (0·36 g.) in glacial acetic acid (7 ml.) was gradually treated with a 10% solution of bromine in glacial acetic acid (7 ml.) at room temperature; after 20 min. an excess of bromine was still present. The product was poured into water; the resulting solid crystallised from aqueous alcohol in feathery prisms, m. p. 166·5—168° (Found: Br, 47·1. $C_{10}H_{11}O_2NBr_2$ requires Br, 47·4%).

Interaction of N-*Bromoacetanilide and Dimethyl* αα′-*Azo*iso*butyrate*.—The decomposition of the azo-ester (10·0 g.) with *N*-bromoacetanilide (purity, 93%; 5·35 g.) in benzene (20 ml.) was carried out as described for the *N*-chloroanilide, and gave rise to methyl α-bromo*iso*butyrate (2·0 g., 48% calc. on the bromoanilide), b. p. 40—47°/11—16 mm., characterised by conversion into α-bromo*iso*butyramide, m. p. 144°, which did not depress the m. p. of an authentic specimen (cf. Part III, *loc. cit.*). The only product which could be isolated from the tarry involatile residue was *p*-bromoacetanilide, m. p. and mixed m. p. 166—168°.

Interaction of N-*Chlorobenzanilide and Dimethyl* αα′-*Azo*iso*butyrate*.—A solution of the *N*-chloroanilide (purity 97%; 23·2 g., 0·1 mole) and the azo-ester (34·5 g., 0·15 mole) in dry benzene (50 ml.) was gently heated in such a way that the evolution of nitrogen was steady and controlled. After 2·75 hr. only a trace of the chloroanilide remained. Distillation of the resulting orange-yellow solution through a short column gave (i) benzene containing methyl *iso*butyrate (1·4 g.), identified by the method of Bickel and Waters (*loc. cit.*) by preparation of *S*-benzylthiuronium *iso*butyrate, m. p. and mixed m. p. 142—144°, and of *iso*butyranilide, m. p. 104°. The residual oil was repeatedly shaken with light petroleum (b. p. 40—60°), and the combined extracts were fractionated, yielding (ii) methyl α-chloro*iso*butyrate (6·2 g., 45%), b. p. 30—40°/11 mm. (amide, m. p. and mixed m. p. 119—119·5°), (iii) dimethyl tetramethylsuccinate (6·6 g.), b. p. 92—98°/11 mm., m. p. 31—32°, characterised by conversion into di-*S*-benzylthiuronium tetramethylsuccinate, m. p. and mixed m. p. 144—146°, and also into di-*p*-nitrobenzyl tetramethylsuccinate, m. p. and mixed m. p. 146—148°, and (iv) (2·9 g.), b. p. 150—160°/11 mm., consisting largely of trimethyl 2 : 3 : 5-trimethylhexane-2 : 3 : 5-tricarboxylate.

The residue from the light petroleum extraction crystallised from alcohol as colourless prisms (7·1 g.), m. p. 195—200°. This product (2·0 g.) was dissolved in benzene and submitted to chromatographic separation on alumina; elution with benzene afforded a *compound* (0·11 g.), m. p. 176—178° (Found: C, 72·7; H, 4·5; N, 6·6; Cl, 8·3. $C_{26}H_{19}O_2N_2Cl$ requires C, 73·1; H, 4·45; N, 6·6; Cl, 8·3%), and further elution with benzene–chloroform (330 ml., 1 : 1) gave 4-benzamido-*N*-benzoyldiphenylamine (III) (1·46 g., 26% calc. on the chloroanilide), m. p. 202·5—203° (Found, on material dried at 100° *in vacuo*: C, 79·2; H, 5·2; N, 7·2. Calc. for $C_{26}H_{20}O_2N_2$: C, 79·6; H, 5·1; N, 7·1%). The infra-red spectrum, which was identical throughout the range 3·0—15·0 μ with that of the synthetic specimen described below, exhibited the following features: 3·02 μ (N–H); 6·02 and 6·12 μ (amide I bands); 6·25, 6·30, 6·71 μ (aromatic system); 6·55, 6·64 μ (amide II bands). A solution of the material in concentrated sulphuric acid was warmed gently and then cooled; addition of a trace of sodium nitrite then produced an intense "diphenylamine-blue" colour. No colour was produced unless the solution had been previously heated (conversion of :N·COPh into :NH). Hydrolysis of the dibenzoyl compound with 20% alcoholic sulphuric acid for 6 hr. gave a solution from which ethyl benzoate could be distilled in steam; this was characterised by hydrolysis to benzoic acid, m. p. and mixed m. p. 121°; attempts to isolate pure crystalline material from the dark residue were unsuccessful.

Distillation of the ultimate residues from the crystallisation of (III) yielded benzanilide (0·2 g.), b. p. <180°/0·5 mm., which when crystallised from light petroleum had m. p. and mixed m. p. 156—158°. The involatile residue (12 g.) consisted largely of poly(methyl methylacrylate).

Preparation of 4-*Benzamido*-N-*benzoyldiphenylamine* [cf. Bayer & Co., D.R.-P. 296,964 (*Chem. Zentr.*, 1917, **21** (I), 717)].—Granulated tin (40 g.) was added in portions to a mechanically stirred solution of *N*-benzoyl-4-nitrodiphenylamine (Lellmann, *loc. cit.*) (4 g.) in glacial acetic acid (160 ml.) and hydrochloric acid (36%; 45 ml.) at 90°. When the reaction had subsided, a further quantity (25 ml.) of hydrochloric acid was added and the mixture was heated at 100° for 1 hr. The solution was filtered and made alkaline, and the sold product was isolated and crystallised from aqueous alcohol, giving 4-amino-*N*-benzoyldiphenylamine (66%), m. p. 183·5—184° (Found: C, 78·9; H, 5·7; N, 9·6. Calc. for $C_{19}H_{16}ON_2$: C, 79·2; H, 5·6; N, 9·7%). Bayer & Co. record m. p. 178°. The amino-amide was benzoylated in acetone solution under Schotten–Baumann conditions, yielding 4-benzamido-*N*-benzoyldiphenylamine, m. p. 202—203·5° (Found: C, 79·9; H, 5·2; N, 7·2%). The mixed m. p. with the sample obtained as above was 203°. Biehringer and Busch (*Ber.*, 1902, **35**, 1971) record m. p. 203° for this product, which they obtained by dibenzoylation of 4-aminodiphenylamine.

Interaction of N *: 2′ : 4′-Trichlorobenzanilide and Dimethyl αα′-Azo*iso*butyrate.*—A solution of the *N*-chloroanilide (purity 97%; 18·1 g.) and the azo-ester (15·0 g.) in dry benzene (40 ml.) was gradually heated during 25 min. and finally refluxed for 2 hr.; no chloroanilide remained (negative starch–KI test). On cooling of the pale red solution to 0° and scratching, 2-*benzamido*-N-*benzoyl*-3 : 5 : 2′ : 4′-*tetrachlorodiphenylamine* (IV) (5·55 g.) crystallised; a further quantity (2·85 g.) was obtained by treatment of the mother-liquor with light petroleum. Crystallisation from xylene and then from *iso*amyl alcohol gave colourless prisms (54%), m. p. 220° (Found: C, 59·3, 59·4; H, 3·4, 3·2; N, 5·3; Cl, 26·5. $C_{26}H_{16}O_2N_2Cl_4$ requires C, 58·9; H, 3·0; N, 5·3; Cl, 26·7%). The infra-red spectrum exhibited the following diagnostic features: 3·10 μ (N–H); 5·96 and 6·04 μ (amide I); 6·24, 6·33, 6·40, 6·70 μ (aromatic system); 6·58—6·62 μ (amide II). Distillation of the light petroleum extract gave methyl α-chloro*iso*butyrate (3·2 g., 40%), b. p. 40—43°/18—21 mm. (amide, m. p. and mixed m. p. 119—121°), and dimethyl tetramethylsuccinate (2·4 g.), b. p. 102—112°/15 mm. Chromatography of the ultimate residues gave 2′ : 4′- dichlorobenzanilide (1·1 g.), m. p. and mixed m. p. 117—118°.

Product (IV) (1·0 g.) was refluxed with potassium hydroxide (1·0 g.) in alcohol (40 ml.) for 1·5 hr. Potassium benzoate was slowly precipitated, and on acidification gave benzoic acid, m. p. and mixed m. p. 121°. The filtrate was evaporated and the residue washed with water and repeatedly crystallised from alcohol, giving 2-*benzamido*-3 : 5 : 2′ : 4′-*tetrachlorodiphenylamine* (0·75 g.), colourless plates, m. p. 227·5° (Found: C, 53·6; H, 3·0; N, 6·8; Cl, 33·2. $C_{19}H_{12}ON_2Cl_4$ requires C, 53·6; H, 2·8; N, 6·6; Cl, 33·3%). The addition of a trace of sodium nitrite to a solution of this compound in cold concentrated sulphuric acid gave an intense " diphenylamine-blue " colour.

Interaction of N *: 2′ : 4′ : 6′-Tetrachlorobenzanilide and Dimethyl αα′-Azo*iso*butyrate.*—A solution of the *N*-chloroanilide (purity 96%; 20·8 g.) and the azo-ester (15·0 g.) in dry benzene was refluxed for 2·5 hr. ($CaCl_2$ guard-tube), the initial decomposition of the azo-ester being carried out with caution. The solvent was removed and the residual dark red tar was treated with light petroleum (b. p. 40—60°; 150 ml.). The extract was decanted and fractionated, yielding (i) methyl α-chloro*iso*butyrate (3·25 g., 41% calc. on the chloroanilide), b. p. 46·5—51°/34—40 mm. (amide, m. p. and mixed m. p. 119—121°) and (ii) a fraction, b. p. 82—100°/10 mm., which contained benzoyl chloride, for, on treatment with aniline, benzanilide, m. p. and mixed m. p. 162°, was obtained. In another experiment, quantitative hydrolysis of fraction (ii) indicated that the yield of benzoyl chloride was 35% (calc. on the chloroanilide). After the distillation there remained an involatile residue (10·7 g.). The red tar remaining after the treatment of the reaction product with light petroleum was diluted with benzene–light petroleum (b. p. 80—100°) and filtered. Chromatography of the filtrate yielded 3 : 5-*dichloro*-1 : 4-*benzoquinone* 1-(2 : 4 : 6-*trichloroanil*) (V) (0·4 g., 4%) which crystallised from alcohol in long purplish-red needles, m. p. 143° (Found: C, 40·9; H, 1·3; N, 4·1; Cl, 49·5. $C_{12}H_4ONCl_5$ requires C, 40·5; H, 1·1; N, 3·9; Cl, 49·9%).

Reaction between s-*Trichloroaniline and* 2 : 6-*Dichloro*-1 : 4-*benzoquinone.*—(i) To a solution of the amine in warm alcohol was added a hot solution of an equivalent amount of the quinone in the same solvent. The pale red solution was filtered and concentrated, yielding the *addition compound*, m. p. 80·5°, which formed black needles with a green reflex (Found: Cl, 47·2. $C_6H_2O_2Cl_2,C_6H_4NCl_3$ requires Cl, 47·4%). Attempted recrystallisation led to partial decomposition. (ii) Equivalent amounts of the amine and the quinone were refluxed together in glacial acetic acid; a pale brown solution was obtained, but on addition of a few drops of concentrated sulphuric acid, a purplish-red colour developed. After the whole had been refluxed for 0·5 hr., it was poured on ice, neutralised, and extracted with benzene. The dried extract, diluted with an equal volume of light petroleum (b. p. 80—100°), was chromatographed on alumina. Unchanged quinone passed rapidly through; elution of the more strongly absorbed band gave a dark red gum, whence a small quantity of the required quinone anil was obtained by repeated crystallisation from alcohol; it had m. p. 142·5°, undepressed in admixture with the specimen obtained previously.

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