248. *The Preparation of the Halogenophenylacetic Acids.*

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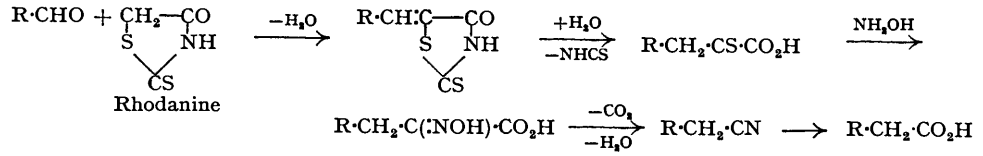
The chloro- and bromo-phenylacetic acids have been prepared by the rhodanine method and derivatives obtained. Other methods of preparation have also been examined. Attempts to separate the bromo-acids obtained by Bedson's method (*J.*, 1880, **37**, 94) by means of the acid chlorides, naphthalides, etc., were only partly successful. In the preparation of the β-naphthalides some ββ′-dinaphthylamine was obtained, but attempts to prepare this substance by Knoevenagel's second method (*J. pr. Chem.*, 1914, **89**, 23) yielded only *N*-aryl-β-naphthylamines.

SINCE no good method is available for the preparation of all the halogenophenylacetic acids it was decided to apply Gränacher's synthesis (*Helv. Chim. Acta*, 1922, **5**, 610; 1923, **6**, 458) the course of which is represented as follows:



By this means Julian and Sturgis (*J. Amer. Chem. Soc.*, 1935, **57**, 1126) and Plucker and Amstutz (*ibid.*, 1940, **62**, 1512) obtained excellent yields of other substituted acetic acids.

This method obviously depends on a satisfactory preparation of rhodanine and this at first presented much trouble. We followed the instructions of Julian and Sturgis (*loc. cit.*) by passing ammonia into carbon disulphide in a mixture of ethanol and ether, obtained rhodanine, and traced the frequent poor yield to the first stage of the reaction, *i.e.*, the preparation of ammonium dithiocarbamate. It has long been known that the above reactants may yield either ammonium trithiocarbonate or dithiocarbamate according to the conditions employed (Zeise, *Schweigger's J.*, 1824, **41**, 98; Debus, *Annalen*, 1850, **73**, 26; Mulder, *J. pr. Chem.*, 1868, **103**, 178; Freund and Bachrach, *Annalen*, 1895, **285**, 201). It was clear from the work of these authors that excess of ammonia favours formation of the trithiocarbonate, and excess of carbon disulphide that of the dithiocarbamate. The effect of temperature is not so clearly discernible. For example, Debus's statement (*loc. cit.*) that temperatures of 30—40° give mainly trithiocarbonate, and 10—15° dithiocarbamate, is seemingly not in agreement with Mulder's observation (*loc. cit.*) that at 30—40° he obtained only dithiocarbamate. The explanation is found in the ammonia concentration, which appears to be determinative, the more concentrated the ammonia solution the greater the tendency for trithiocarbonate formation. Ammonia, of course, is much more soluble in cold than in hot ethanol. Accordingly, when we passed ammonia through a "well-cooled alcoholic solution of carbon disulphide" (Julian and Sturgis, *loc. cit.*), *i.e.*, at about − 5°, the main product which separated was ammonium trithiocarbonate, but with the solution temperature maintained at 10—15° ammonium dithiocarbamate was obtained in fair yield. It is highly probable, however, that even under favourable conditions the dithiocarbamate is formed not only directly by interaction of carbon disulphide and ammonia, but also (with loss of yield) from the trithiocarbonate and ammonia according to the following reactions, each known to occur readily under appropriate conditions.

$$CS_2 + 2NH_3 \longrightarrow NH_2{\cdot}CS{\cdot}S{\cdot}NH_4$$
$$NH_2{\cdot}CS{\cdot}S{\cdot}NH_4 + 2NH_3 \longrightarrow CN{\cdot}S{\cdot}NH_4 + (NH_4)_2S$$
$$CS_2 + (NH_4)_2S \longrightarrow CS(S{\cdot}NH_4)_2$$
$$CS(S{\cdot}NH_4)_2 \xrightarrow{EtOH} NH_2{\cdot}CS{\cdot}S{\cdot}NH_4 + H_2S$$

Although the conversion of benzaldehydes into phenylacetonitriles involves four stages, the overall yields are reasonably good, *viz.*, 57, 47, and 62% for the *o*-, *m*-, and *p*-chloro-, and 49, 44, and 38% for the corresponding bromophenylacetonitriles, respectively. Unfortunately, further losses, sometimes considerable, occur in the hydrolysis to the acids. The preparation of the halogenophenylacetic acids by the Gränacher method, therefore, leaves much to be desired. This is in agreement with Hahn and Schulz's findings on the preparation of methoxyphenylacetic acids (*Ber.*, 1939, **72**, 1302); they did not give any experimental details, but evidently encounted difficulties in the last two stages of the synthesis. Similarly, Barltrop (*J.*, 1946, 958) prepared 2 : 3-dimethoxyphenylacetonitrile in 24% yield from the benzaldehyde, the greatest losses occurring in the last two stages.

Efforts were made to separate the mixture of *o*- and *p*-bromophenylacetic acids obtained by Bedson's method (*loc. cit.*) by fractional distillation of the acid chlorides and ethyl esters. This being unsuccessful, chromatographic separation of the anilides, *p*-toluidides, and β-naphthalides was attempted in the hope that the process would be facilitated by the fluorescence of these compounds. Although they fluoresced in benzene they did not on the column, the only fluorescent bands being due to impurity. Chromatographic separation was therefore "blind" and only partly successful.

In the preparation of the naphthalides by heating the acids with β-naphthylamine, ββ-dinaphthylamine was also obtained. This substance is not obtained (unless in negligible quantities) when β-naphthylamine is heated alone, but with catalytic amounts of iodine excellent

yields result (Knoevenagel, *loc. cit.*). In our experiments the catalyst is presumably the halogenophenylacetic acid.

Knoevenagel (*loc. cit.*) also found that β-naphthylamine when heated with aromatic amines and a trace of iodine gives ββ′-dinaphthylamine. We have found this to be true for the halogenoanilines, but, with aniline and the toluidines, *N*-phenyl- or *N*-tolyl-β-naphthylamines are invariably obtained. We have not been able to explain this discrepancy between Knoevenagel's results and ours.

In our chromatographic work we noted that β-naphthylamine and its derivatives are more strongly adsorbed than the corresponding α-derivatives. This is in agreement with other observations. β-Benzoylnaphthalene is more strongly adsorbed than the α-compound (Campbell and Easton, unpublished results), and naphthalene dyes with amino- or hydroxy-groups in the β-position are more strongly adsorbed from aqueous solutions on alumina than the α-isomers (Ruggli and Jensen, *Helv. Chim. Acta*, 1935, **18**, 624; 1936, **19**, 64). How far this rule holds remains to be determined, as adsorption is affected by the nature of the solvent, position of other substituents, etc. (cf. Ruggli and Jensen, *loc. cit.*, 1936).

Experimental.

Unless otherwise stated, the preparation, purification, and properties of substances are those given in the literature, and the chromatographic separations were carried out on alumina (Brockmann) with benzene as solvent and developer. The purity of all products was checked by the sharpness of their m. p.s on a Kofler or a Fuchs micro-m. p. apparatus (*Mikrochem.*, 1934, **15**, 242; *Mikrochim. Acta*, 1937, **2**, 317). The analyses were done by Drs. Weiler and Strauss, Oxford.

Preparation of Rhodanine.—Ammonia from a cylinder was passed fairly rapidly into a stirred mixture of carbon disulphide (250 g.), alcohol (200 c.c.), and ether (200 c.c.), the temperature being kept at 5—15° (but not lower) by ice–water. After 4 hours 170 g. of ammonium dithiocarbamate had separated and was added to a solution of sodium chloroacetate, prepared according to Julian and Sturgis (*loc. cit.*), equivalent to 146 g. of chloroacetic acid. A further 65 g. of ammonium dithiocarbamate were obtained by passing ammonia into the filtrate for 2 hours. This was added to another portion of chloroacetate solution equivalent to 56 g. of the acid. The solutions were combined and after an hour were run into 302 c.c. of 10N-hydrochloric acid heated to 80—90° and kept at this temperature during the addition. The solution was kept overnight, and the rhodanine separated, washed with water, and dried in air; yield, 125 g. (44% calc. on ammonium dithiocarbamate); m. p. 165—170°.

In many experiments when the temperature was kept below 0° ammonium trithiocarbonate was the main product.

Ammonium trithiocarbonate and dithiocarbamate are distinguished in several ways. The former with a solution of sodium chloroacetate followed by acidification in the cold gives carboxymethyl trithiocarbonate, $CS(S{\cdot}CH_2{\cdot}CO_2H)_2$, bright yellow crystals, m. p. 172°, and the latter, thiocarbamylthioglycollic acid, $NH_2{\cdot}CS{\cdot}S{\cdot}CH_2{\cdot}CO_2H$, pale yellow crystals, m. p. 137°. The trithio-compound rapidly turns orange then red and finally decomposes on exposure to air, though these changes occur less readily if the substance is purified by washing with alcohol; but the dithio-compound is stable under these conditions. Decisive colour tests are also available. A few mg. of the substance in two drops of sodium hydroxide are treated with two drops of a freshly prepared sodium nitroprusside solution. The trithiocarbonate gives a red colour and the dithiocarbamate a blue deepening to violet: dithiocarbamate with some trithiocarbonate gives a purple shade. Finally, the trithiocarbonate with solutions of stannous chloride and lead acetate gives dark red and bright red precipitates respectively; dithiocarbamate gives buff and yellow precipitates.

Preparation of Benzylidenerhodanines.—Molecular quantities of aldehyde and rhodanine were dissolved in glacial acetic acid (5 c.c. per g. of aldehyde) and refluxed in an oil-bath with fused sodium acetate (twice the weight of rhodanine) for half an hour. The product was washed with a little glacial acetic acid, well with water, and dried at 70°; yield, 80—97%. These rhodanines were recrystallised from glacial acetic acid. *o*-Chlorobenzylidenerhodanine, pale yellow needles, m. p. 192°; yield, 97% (Found: Cl, 12·8. Calc. for $C_{10}H_6ONClS_2$: Cl, 13·9%). Andreasch (*Monatsh.*, 1928, **49**, 132) obtained the substance as brown-red needles, m. p. 169°, which were obviously impure. m-*Chlorobenzylidenerhodanine*, pale yellow elongated prisms, m. p. 233°; yield, 93% (Found: Cl, 14·1%). p-*Chlorobenzylidenerhodanine*, yellow needles, m. p. 231—232°; yield, 93% (Found: Cl, 14·0%). o-*Bromobenzylidenerhodanine*, orange needles, m. p. 183·5°; yield, 80% (Found: Br, 22·6. $C_{10}H_6ONBrS_2$ requires Br, 26·7%); repeated analyses were also unsatisfactory, but the impure substance gave pure products in the later stages of the synthesis. m-*Bromobenzylidenerhodanine*, yellow needles, m. p. 238°; yield, 90% (Found: Br, 26·1%). p-*Bromobenzylidenerhodanine*, yellow elongated prisms, m. p. 237—238°; yield, 84% (Found: Br, 27·9%).

Preparation of β-Phenylthiopyruvic Acids.—The procedure of Julian and Sturgis (*loc. cit.*) proved unsatisfactory and the following modification was used. The benzylidenerhodanine was cleaved with 8% sodium hydroxide (8 c.c. per g. of benzylidene compound) by heating in a water-bath at 50—55°. The mixture was well stirred until a clear or nearly clear solution was obtained. The solution was filtered if necessary, cooled in an ice–salt mixture, and acidified *rapidly* with 3N-hydrochloric acid with stirring. The stirring and cooling were continued for 10 minutes, and the acid thus obtained washed with water and dried in a vacuum over calcium chloride. Crystallisation of the acids was difficult (cf. Grănacher, *loc. cit.*), but a good yield of pure acid was obtained by dissolving the crude substance in the minimum quantity of cold alcohol, filtering, and adding 1—2 times the volume of cold water with stirring and shaking. After 2 hours the acid was dried in a vacuum over calcium chloride. Further purification was effected by crystallisation from methanol, light petroleum, etc., but the crude acids were used for

the next stage in the synthesis. β-*o*-Chlorophenyl acid, prisms (methanol), m. p. 134—135°; yield, 72% (Found: S, 15·3. Calc. for $C_9H_7O_2ClS$: S, 14·9%); further crystallisation from light petroleum (b. p. 100—120°) gave needles, m. p. 142—143°. Andreasch (*loc. cit.*) gives m. p. 119—120°. m-*Chlorophenyl acid*, straw-coloured needles (light petroleum, b. p. 100—120°), m. p. 134°; yield, 84% (Found: S, 14·7%). *p*-Chlorophenyl acid, m. p. 164—167°; yield, 84% (Found: S, 15·1%); recrystallisation from ethanol gave yellow prisms, m. p. 169—171°, which resolidified, and melted finally at 202—204°. Gendelman (*Monatsh.*, 1922, **43**, 537) obtained it as pale yellow needles (alcohol), m. p. 157°. An oil was also obtained which on trituration with aqueous alcohol gave a product only slightly soluble in *iso*propyl alcohol. It separated from a large volume of boiling ethanol in yellow prisms, m. p. 221—222°, and is probably *bis*-(m-*chlorocinnamic acid*) α-*disulphide*, $[C_6H_4Cl\cdot CH{:}C(CO_2H)\cdot S-]_2$ (Found: C, 50·9; H, 3·0; Cl, 17·3; S, 15·1. $C_{18}H_{12}O_4Cl_2S_2$ requires C, 50·6; H, 2·8; Cl, 16·6; S, 15·1%). *o-Bromophenyl acid*, m. p. 134—139°, yield, 70%; separated from light petroleum (b. p. 100—120°) in lemon-yellow elongated prisms, m. p. 142—143° (Found: S, 11·3. $C_9H_7O_2BrS$ requires S, 12·4%). m-*Bromophenyl acid*, pale yellow needles (light petroleum, b. p. 100—120°), m. p. 133—134°, yield, 81% (Found: S, 12·7%). p-*Bromophenyl acid*, m. p. 165—180°, yield, 75% (Found: S, 11·45%); efforts to purify this substance further were unsuccessful.

Preparation of α-Oximino-β-phenylpropionic Acids.—The most satisfactory results were obtained by refluxing the thioketo-acids with an alcoholic solution containing 3 mols. of hydroxylamine. The calculated quantity of hydroxylamine hydrochloride was dissolved in the minimum amount of warm water and added to 2·5N-alcoholic sodium hydroxide, sufficient to liberate the base. Alcohol was then added to bring the volume of solution to 10 c.c. per g. of thioketo-acid. The sodium chloride was removed, the thioketo-acid added, and the solution refluxed until no more hydrogen sulphide was evolved (about ½ hour). The alcohol was removed by vacuum distillation from a water-bath, the residue taken up in dilute sodium hydroxide, the solution filtered, and the filtrate acidified with concentrated hydrochloric acid. The oximino-acid was well washed with water, and dried in a vacuum over potassium hydroxide. The crude acid was used for the next stage of the synthesis, but a sample was crystallised for analysis. No attempt was made to isolate the *cis*- and *trans*-oximino-acids.

α-*Oximino-β-halogenophenylpropionic acids*: o-*Chlorophenyl*-, yield, 83%, m. p. 146—148°, raised by crystallisation from aqueous ethanol to 156° (Found: N, 6·78. $C_9H_8O_3NCl$ requires N, 6·56%). m-*Chlorophenyl*-, m. p. 145—148°, yield, 100%; colourless needles (benzene), m. p. 149° (decomp.) (Found: N, 6·74%). p-*Chlorophenyl*-, most samples had m. p. 170° (decomp.), but one had m. p. 182°; yield, 100% (Found: N, 6·17%). o-*Bromophenyl*-, m. p. 150°, yield, 100%; colourless needles (benzene), m. p. 150° (decomp.) (Found: N, 5·34. $C_9H_8O_3NBr$ requires N, 5·43%). m-*Bromophenyl*-, m. p. 151°, yield, 93%; colourless crystals (benzene), m. p. 151° (Found: N, 5·47%). p-*Bromophenyl*-, m. p. 168—169°, yield, 85%; elongated prisms (toluene), m. p. 173° (Found: N, 5·28%).

Halogenophenylacetonitriles.—The crude oximino-acid was added to acetic anhydride (4 c.c. per g. of acid), and the mixture warmed gently under reflux. The flame was removed as soon as a vigorous reaction occurred, and after this had ceased the mixture was refluxed for 10 minutes. The acetic anhydride was removed by distillation under reduced pressure from a water-bath, and the residue extracted with ether, which was then washed with sodium carbonate solution and finally with water. The solution was dried ($CaCl_2$), the ether removed by distillation, and the residue distilled in a vacuum. *o*-Chlorophenylacetonitrile, b. p. 123—125°/11 mm., yield, 64% (Found: N, 9·75. Calc. for C_8H_6NCl: N, 9·25%). *m*-Chlorophenyl-, b. p. 134—136°/10 mm., yield, 55% (Found: N, 9·80%). *p*-Chlorophenyl-, b. p. 137—139°/12 mm., colourless needles (light petroleum, b. p. 40—60°), m. p. 31—32° (lit., 29—30°), yield, 80% (Found: N, 9·5%). *o*-Bromophenyl-, b. p. 140—141°/13 mm., yield, 88% (Found: N, 7·88. Calc. for C_8H_6NBr: N, 7·14%). *m*-Bromophenyl-, b. p. 145—147°/10 mm., yield, 70%; needles (light petroleum, b. p. 40—60°), m. p. 27—28° (Found: N, 7·52%). *p*-Bromophenyl-, b. p. 152—156°/10—12 mm., yield, 72%; lamellæ (light petroleum, b. p. 40—60°), m. p. 48° (lit., 47°) (Found: N, 7·07%).

Halogenophenylacetic Acids.—The nitriles were hydrolysed by boiling with 60% sulphuric acid or preferably 20% alcoholic potassium hydroxide. *o*-Chlorophenylacetic acid, m. p. 93—95° (lit., 96°) (Found: Cl, 19·6. Calc. for $C_8H_7O_2Cl$: Cl, 20·84%) [p-*nitrobenzyl* ester, prisms (ethanol), m. p. 70—71° (Found: N, 4·51. $C_{15}H_{12}O_4NCl$ requires N, 4·57%)]. *m*-Chlorophenylacetic acid, plates (aqueous ethanol), m. p. 77° (lit., 76°) (Found: Cl, 21·1%) [p-*nitrobenzyl* ester, colourless crystals (ethanol), m. p. 74—75° (Found: N, 4·87%); p-*toluidide*, crystals (dilute acetic acid), m. p. 138° (Found: N, 5·62. $C_{15}H_{14}ONCl$ requires N, 5·4%)]. *p*-Chlorophenylacetic acid, needles (light petroleum, b. p. 80—100°), m. p. 104—106° (lit., 105°) (Found: Cl, 21·7%) [p-*nitrobenzyl* ester, elongated prisms (ethanol), m. p. 117° (Found: N, 4·77%)]. *o*-Bromophenylacetic acid, m. p. 104—105° (lit., 105—106°; 109°), needles (light petroleum, b. p. 80—100°), identical with a specimen prepared from *o*-bromobenzoyl chloride by the Arndt–Eistert method (Fieser and Kilmer, *J. Amer. Chem. Soc.*, 1940, **62**, 1356) [p-*nitrobenzyl* ester, plates (methanol), m. p. 74—75° (Found: N, 4·4. $C_{15}H_{12}O_4NBr$ requires N, 4·0%); p-*toluidide*, elongated prisms (glacial acetic acid), m. p. 183—184° (Found: N, 4·8. $C_{15}H_{14}ONBr$ requires N, 4·61%); ethyl ester, elongated prisms (light petroleum, b. p. 40—60°), m. p. 38—39° (lit., 35—36°) (Found: Br, 33·1. Calc. for $C_{10}H_{11}O_2Br$: Br, 32·9%); *anilide*, elongated prisms (ethanol), m. p. 153—154° (Found: Br, 27·6. $C_{14}H_{12}ONBr$ requires Br, 27·6%)]. *m*-Bromophenylacetic acid, needles (water), m. p. 102—103° (lit., 100°) (Found: Br, 37·0. Calc. for $C_8H_7O_2Br$: Br, 37·2%) [p-*nitrobenzyl* ester, crystals (methanol), m. p. 75—76° (Found: N, 4·3%); p-*toluidide*, crystals (dilute acetic acid), m. p. 135° (Found: N, 4·7%)]. *p*-Bromophenylacetic acid, m. p. 113—115° (lit., 114°), identical with a specimen prepared by the method of Czaplicki, Kostanecki, and Lampe (*Ber.*, 1909, **42**, 828) (see below) [p-*nitrobenzyl* ester, elongated prisms (ethanol), m. p. 128—129° (Found: N, 4·25%); p-*toluidide*, prisms (benzene), m. p. 203° (Found: N, 4·66%); *anilide*, m. p. 174—176° (Found: N, 4·75%. $C_{14}H_{12}ONBr$ requires N, 4·82%)].

p-Bromobenzaldehyde (20 g.), a freshly prepared solution of sodium hydrogen sulphite (80 c.c.), and ethanol (5 c.c.) yielded, on shaking, the crystalline bisulphite derivative, which was washed with several portions of cold water, then made into a paste with water, and stirred for 2 hours with potassium cyanide

(10 g.) in water (20 c.c.). Extraction with ether followed by evaporation yielded p-*bromomandelonitrile*, m. p. 60—70° (12·5 g.). A sample crystallised twice from benzene–light petroleum (b. p. 60—80°) had m. p. 78—79° (Found : N, 6·4. C_8H_6ONBr requires N, 6·6%). The nitrile (11 g.) was refluxed for 1 hour with 46 c.c. of hydriodic acid (*d* 1·94), the mixture poured into sodium hydrogen sulphite solution, and the resulting oil extracted with ether, which afforded, with sodium hydroxide followed by acidification, *p*-bromophenylacetic acid, m. p. 110—111° (yield, 1·5 g.); recrystallisation from light petroleum (b. p. 80—100°) and then aqueous ethanol gave m. p. 111·5—114° (Found : Br, 37·2. Calc. for $C_8H_7O_2Br$: Br, 36·8%). The ethereal layer gave a substance of unknown constitution which was crystallised from benzene; m. p. 126—127° (Found : C, 45·8; H, 3·33; N, 4·24; Br, 36·0%).

Phenylacetonitriles from Mandelonitrile Benzoates.—The method of Kindler and Peschke (*Arch. Pharm.*, 1933, **271**, 435) and Kindler and Gehlhaar (*ibid.*, 1936, **274**, 377) was investigated, platinum-black prepared by the method of Willstätter and Waldschmidt-Leitz (*Ber.*, 1921, **54**, 123) and tetralin purified by repeated shaking with concentrated sulphuric acid being used. *o*-Chlorobenzaldehyde (20 g.) was converted into *o*-chloromandelonitrile, which was then added to benzoyl chloride (27 g.) in pyridine (100 c.c.), and the solution kept overnight. Addition of water gave an oil which was extracted with ether and the ethereal layer washed with dilute hydrochloric acid, sodium carbonate, and finally water, and then dried ($CaCl_2$). On evaporation o-*chloromandelonitrile benzoate* was obtained as an oil (Found : N, 5·18. $C_{15}H_{10}O_2NCl$ requires N, 5·15%) which solidified after several weeks. Refluxing with platinum-black and tetralin resulted in removal of halogen as hydrogen chloride and no *o*-chlorophenylacetonitrile could be isolated. The method, however, was successfully applied to *p*-methoxyphenylacetonitrile benzoate, best prepared as follows. Anisaldehyde (20 g.) was added to sodium cyanide (15 g.) in water (20 c.c.), and benzoyl chloride (22 g.) added with vigorous shaking or stirring during 15 minutes, the temperature being kept at 35—40°. In an hour the oil began to solidify, a few drops of benzoyl chloride and a little sodium hydroxide were added, and stirring was continued 10 minutes longer. The pasty mass was triturated with dilute sodium hydroxide, and then washed successively with dilute sodium hydroxide, water, saturated sodium bisulphite, and water. Trituration with a little ethanol and drying in a vacuum gave a solid, m. p. 64—65° (yields in two runs 74 and 92%), from which *p*-methoxyphenylacetonitrile, b. p. 153—154/14 mm. (39% yield), was obtained.

Other methods were tried without much success. Catalytic reduction (platinised charcoal activated by palladium) of mandelic acids and nitriles (Zelinsky, Packendorff, and Leder-Packendorff, *Ber.*, 1934, **67**, 300) proved capricious; the azlactone method and the Willgerodt reaction gave poor yields; and the Arndt–Eistert synthesis, though giving reasonably good yields, was limited by slow formation of the intermediate diazoketone and the difficulty in working with diazomethane.

Separation of Bromophenylacetic Acids.—The mixture of bromophenylacetic acids (17 g.) obtained by Bedson's method (*loc. cit.*) was esterified with ethanol and concentrated sulphuric acid, and the product fractionally distilled in a vacuum twice, the final fraction, b. p. 164—169°/55 mm. (12·5 g.), being collected. This proved to be a mixture, since hydrolysis gave an oil from which with difficulty a little *o*-bromophenylacetic acid, m. p. 109°, was obtained. When the mixture of esters was kept at room temperature it partly solidified, the crystals (3·5 g.), m. p. 27°, being ethyl *o*-bromphenylacetate (no depression with an authentic sample; and hydrolysis to *o*-bromophenylacetic acid, m. p. 108°).

The mixture of acids and thionyl chloride yielded a mixture of acid chlorides, b. p. 145—155°/47 mm., 130—146°/42 mm., which gave *o*-and *p*-bromophenylacet-*p*-toluidides (separated as below).

The mixture of acids was converted into the toluidides by heating with *p*-toluidine for ¾ hour. From the product, samples of *o*- and *p*-bromophenylaceto-*p*-toluidides were isolated by making use of the smaller solubility in boiling ethanol or benzene and the greater adsorbability on alumina of the latter compound. Quantitative separation, however, is very tedious.

The β-naphthalides were prepared from the mixture either of acid chlorides or of acids. The product of the first method was separated chromatographically with difficulty into the two isomers identical with samples prepared from the acid chlorides and β-naphthylamine. *o-Bromophenylaceto-β-naphthalide*, needles (benzene or methanol), m. p. 188—189° (Found : Br, 23·8. $C_{18}H_{14}ONBr$ requires Br, 23·5%), and p-*bromophenylaceto-β-naphthalide*, crystals (aqueous ethanol), m. p. 203—204° (Found : N, 3·9. $C_{18}H_{14}ONBr$ requires N, 4·11%), fluoresce in benzene but not on the chromatographic column, and the same holds for *phenylaceto-β-naphthalide*, colourless plates (ethanol), m. p. 162—163° (Found : N, 5·4. $C_{18}H_{15}ON$ requires N, 5·2%). In the second process the mixed acids (3 g.) were heated with β-naphthylamine (6 g.) in an oil-bath at 220° for ½ hour, the mixture poured into dilute hydrochloric acid, and the precipitate repeatedly extracted with warm dilute hydrochloric acid. 0·9 G. of the residue was dissolved in benzene (100 c.c.) and chromatographed on alumina (8″ × 1·3″) and developed with benzene–light petroleum (1 : 1 by vol.). From the filtrate 0·45 g. of colourless plates (light petroleum, b. p. 100—120°), m. p. 173—174°, was obtained and shown to be ββ′-dinaphthylamine by mixed m. p. with an authentic sample. It had the same brilliant livid blue fluorescence in the solid state and bright violet in benzene as a specimen prepared by heating β-naphthylamine with a trace of iodine (Knoevenagel, *loc. cit.*). In attempts to prepare this compound by heating β-naphthylamine and aniline with a trace of iodine (Knoevenagel, *loc. cit.*) the product, in spite of many variations of the conditions, was invariably *N*-phenyl-β-naphthylamine, m. p. 106—107° (lit., 108°); yield, 95%. *p*-Toluidine similarly gave *N*-*p*-tolyl-β-naphthylamine, m. p. 102—103° (lit., 102—103°), after chromatographic purification (yield, 95%), but *o*- or *m*-chloroaniline gave only ββ′-dinaphthylamine.

Chromatographic Separations.—α- and β-Naphthylamines (1 g. of each) were dissolved in benzene and passed through a column of alumina (1·7″ × 8″) and developed with benzene–light petroleum (4 : 1 by vol.). From the first 500 c.c. of filtrate α-naphthylamine (acetyl derivative, m. p. 155°) was obtained, and from the next 300 c.c. β-naphthylamine, m. p. 112° (mixed m. p.). Similarly, phenylaceto-β-naphthalide was more strongly adsorbed than the α-isomer (needles from benzene, m. p. 166—167°) (Found : 5·3. Calc. for $C_{18}H_{15}ON$: N, 5·2%).

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