XXIX.—*Diortho-substituted Benzoic Acids. Part V.*
Formation of Salts from Diortho-substituted Benzoic
Acids and Organic Bases.

By JOHN JOSEPH SUDBOROUGH and WILLIAM ROBERTS.

IN a previous communication on this subject (Lloyd and Sudborough, *Trans.*, 1899, 75, 580), it has been shown that stereochemical influences only slightly affect the reactions between substituted benzoic acids and organic bases, these influences being completely masked by the effect of the comparative strengths of the acids and bases. Since the publication of this earlier paper, Emil Fischer (*Ber.*, 1900, 33, 345, 1967) has drawn attention to the fact that diortho-substituted tertiary bases are incapable of combining with an alkyl iodide to yield quaternary ammonium compounds. As the earlier experiments were not carried out with bases of this type, we have tried to prepare salts from diortho-substituted alkylated arylamines of the type of dimethyl-

mesidine and various substituted benzoic acids, including those with two ortho-substituents. We have also attempted to combine the same acids with diethyl- α - and β -naphthylamines.

s-Trinitrobenzoic acid forms salts with all the bases examined; 2:4:6-tribromo-3-aminobenzoic acid also forms salts with a number of the bases, but not many have been obtained in a crystalline form. It would thus appear that the introduction of ortho-substituents into the acid and basic molecules does not prevent the formation of salts, provided that the acid is very strong and the base not too weak.

In addition, we have attempted to settle a point raised in the earlier paper (*ibid.*, p. 583), namely, the behaviour of various organic bases towards a weak diortho-substituted acid of the type of *s*-trimethylbenzoic acid. The acid forms a well-defined, crystalline salt with a strong base such as benzylamine, and also dissolves readily in 33 per cent. aqueous trimethylamine solution, but all attempts to combine it with tertiary bases such as dimethylmesidine, dimethyl- ψ -cumidine, bromodimethyl-*m*-xylidine, and diethylaniline have given negative results; in each case, the unaltered acid crystallised out from the different solvents, even when two or three times the theoretical amount of base was employed. It is clear that the loss of the function of salt formation is not due to the presence of ortho-substituents in the basic molecules, because a simple base like diethylaniline is incapable of forming a salt with this acid. In order to determine whether it is due to ortho-substituents in the acid molecule, we have endeavoured to prepare salts from the same bases and mono-substituted benzoic acids containing substituent methyl, bromo-, and nitro-groups. The fact that no salts are formed from either *m*-toluic acid and dimethylaniline, or *p*-toluic acid and dimethylaniline or ψ -cumidine indicate that the presence of ortho-substituents in the acid molecule is not necessary in order to inhibit salt formation.

In addition to the normal salts formed by the union of one molecule of acid with one of the base, we have obtained a number of acid salts formed by the union of two molecules of acid with one of the base, as, for example, the acid salts derived from ψ -cumidine and *o*-toluic acid, dimethyl- ψ -cumidine and *m*-nitrobenzoic acid, ψ -cumidine and *m*-nitrobenzoic acid, dimethyl- ψ -cumidine and tribromoaminobenzoic acid, and dimethyl- ψ -cumidine and *o*-nitrobenzoic acid. These compounds are similar to the acid potassium and ammonium salts derived from substituted benzoic acids, which have been recently described by Farmer (*Trans.*, 1903, 83, 1440). According to this investigator, the probable constitution of these acid salts is represented by the formula
$$\begin{array}{c} \text{R}-\text{CO} \\ \text{R}\cdot\text{CO}\cdot\text{O} \end{array} > \text{O} < \begin{array}{c} \text{K} \\ \text{H} \end{array}$$
 and the molecule contains a quadrivalent oxygen atom. With such a formula, it is quite possible that inhibition

through stereochemical influences should occur. If ortho-substituents retard or prevent the formation of additive compounds involving the carbonyl residue of the substituted benzoic acid (compare Trans., 1899, 75, 581), it is quite possible that ortho-substituents would also prevent the conversion of the bivalent oxygen atom of the hydroxyl group into a quadrivalent oxygen. We might therefore expect that diortho-substituted benzoic acids would not give rise to acid salts. Although we have not particularly investigated this question, we have met with only one such salt derived from dimethyl- ψ -cumidine and tribromoaminobenzoic acid.

The salts were usually analysed by determining the amount of acid present according to the method previously described (*loc. cit.*, 584). We have found that the majority of the salts can also be analysed by titrating their alcoholic solutions with standard baryta when phenolphthalein is used as indicator. The presence of the organic base does not interfere with the titration, and good results are obtained. For example, 20 c.c. of *N*/20 oxalic acid required 15.4 c.c. of baryta solution, and 20 c.c. of *N*/20 oxalic acid mixed with 6 drops of dimethyl- ψ -cumidine also required 15.4 c.c. of the same alkali solution.

EXPERIMENTAL.

A. Preparation of Bases.

Dimethyl- ψ -cumidine, $C_6H_2Me_3 \cdot NMe_2$ [$Me_3 : NMe_2 = 2 : 4 : 5 : 1$], was obtained by a method somewhat similar to that employed by Noeltig in the preparation of dimethyl-*m*-xylydine (*Ber.*, 1891, 24, 563); 20 grams of ψ -cumidine melting at 68° , 70 grams of methyl iodide, 47 grams of sodium carbonate, and 500 grams of water were heated in a reflux apparatus until all the iodide had disappeared; caustic potash solution was added and the base extracted with ether. The ethereal solution, when dry, gave 17 grams of a colourless oil distilling at 219° , which was characterised by the formation of its *platinichloride*.

0.3808 gave 0.1008 Pt = 26.47.

$(C_6H_2Me_3 \cdot NMe_2)_2, H_2PtCl_6$ requires 26.47 per cent.

Dimethylmesidine [$Me_3 : NMe_2 = 2 : 4 : 6 : 1$], obtained in a similar manner from mesidine, was freed from secondary base by heating in a sealed tube with methyl iodide and dry magnesia at 100° (Fischer, *Ber.*, 1900, 33, 1968).

Bromo-*m*-xylydine [$Me_2 : NH_2 : Br = 2 : 4 : 1 : 6$], melting at $46-47^\circ$, was obtained by Fischer's method (*ibid.*, 1971) and transformed into the tertiary base by the method employed in the case of mesidine.

Diethyl α - and β -naphthylamines were prepared by Morgan's

process (Trans., 1900, 77, 823). Of the acids employed, the 2:4:6-tribromo-3-aminobenzoic acid was prepared by the method already described (Trans., 1899, 75, 589), the *s*-trinitrobenzoic acid was kindly presented by the Chemische-Fabrik Griesheim, and the *s*-trimethylbenzoic acid was prepared from mesitylglyoxylic acid (Meyer, *Annalen*, 1888, 246, 139). Van Scherperzeil (*Rec. trav. chim.*, 1900, 19, 380) recommends heating the glyoxylic acid with concentrated sulphuric acid until no more carbon monoxide is evolved, but we find that in order to obtain a good yield the temperature should be carefully regulated, the best yields being obtained when the temperature is kept about 40°; above 50°, carbon dioxide begins to be evolved, and the trimethylbenzoic acid itself is destroyed. In one experiment, we obtained 2.05 grams of trimethylbenzoic acid from 2.5 grams of the glyoxylic acid (m. p. 152°). The magenta coloration produced when glyoxylic acid is dissolved in concentrated sulphuric acid is extremely characteristic.

B. Salts from *s*-Trinitrobenzoic Acid.

Dimethyl-ψ-cumidine 2:4:6-Trinitrobenzoate.—The salt,

slowly separated in the form of snow-white, small needles on mixing alcoholic solutions of the acid and base; it crystallises from benzene in small needles, dissolves in hot water, alcohol, or chloroform, but is insoluble in carbon disulphide or light petroleum. Like the salts of trinitrobenzoic acid already described, it has no definite melting point; on heating, it melts and decomposes, yielding a dark red oil; the temperature at which this occurs varies considerably with the rate of heating. When heated fairly rapidly, it begins to turn dark at 115° and melts at 120°.

0.7179 gave 0.438 trinitrobenzoic acid = 61.0.

$\text{C}_{18}\text{H}_{20}\text{O}_8\text{N}_4$ requires 61.2 per cent.

Dimethylmesidine Trinitrobenzoate, $(\text{NO}_2)_3\text{C}_6\text{H}_2\cdot\text{CO}_2\cdot\text{NHMe}_2\cdot\text{C}_6\text{H}_2\text{Me}_3$.—The salt, obtained in the form of small needles when alcoholic solutions of the two components were mixed, begins to darken at 105°, and is completely decomposed at 116—117°; it dissolves in the ordinary solvents on heating, but is decomposed by some of these, more especially water or alcohol. When boiled for a short time with alcohol, it yields crystals melting at 122°; these proved to be *s*-trinitrobenzene, as with diethyl-β-naphthylamine they furnished purplish-black needles melting at 115—116°.

0.8867 gave 0.5392 trinitrobenzoic acid = 60.8.

$\text{C}_{18}\text{H}_{20}\text{O}_8\text{N}_4$ requires 61.2 per cent.

Bromo-m-xylidine Trinitrobenzoate, $(\text{NO}_2)_3 \cdot \text{C}_6\text{H}_2 \cdot \text{CO}_2 \cdot \text{NH}_3 \cdot \text{C}_6\text{H}_2\text{Me}_2\text{Br}$.—This salt, which was prepared by mixing alcoholic solutions of the acid and base, slowly separated in yellow, prismatic crystals which begin to change colour at 130° , are completely decomposed at 150° ; it is soluble in warm alcohol.

0.7154 gave 0.3986 trinitrobenzoic acid = 55.6.

$\text{C}_{15}\text{H}_{13}\text{O}_8\text{N}_4\text{Br}$ requires 56.2 per cent.

When the alcoholic solution was boiled for a short time, it acquired a red colour, and small, red needles melting at $104\text{--}105^\circ$ were obtained on cooling. This substance, which is the additive compound, $\text{C}_6\text{H}_2\text{Me}_2\text{Br} \cdot \text{NH}_2 \cdot \text{C}_6\text{H}_3(\text{NO}_2)_3$, was also obtained by mixing alcoholic solutions of bromo-*m*-xylidine and trinitrobenzene.

0.3824 gave 0.1955 trinitrobenzene = 51.1.

$\text{C}_{14}\text{H}_{13}\text{O}_6\text{N}_4\text{Br}$ requires 51.5 per cent.

It dissolves readily in ether, benzene, chloroform, and warm alcohol.

Bromodimethyl-m-xylidine Trinitrobenzoate,

$(\text{NO}_2)_3 \cdot \text{C}_6\text{H}_2 \cdot \text{CO}_2 \cdot \text{NHMe}_2 \cdot \text{C}_6\text{H}_2\text{Me}_2\text{Br}$.

—The salt, which was obtained from alcoholic solutions, begins to change colour at 105° , and is completely decomposed at 108° .

0.6506 gave 0.3435 trinitrobenzoic acid = 52.8.

$\text{C}_{17}\text{H}_{17}\text{O}_8\text{N}_4\text{Br}$ requires 53.0 per cent.

Diethyl- α -naphthylamine s-Trinitrobenzoate.—This salt separated in the form of flat, slightly yellow plates when warm alcoholic solutions of the acid and base were mixed. The mother liquor, when kept for several days, deposited bright red needles melting at 95° . These consist of diethyl- α -naphthylamine-trinitrobenzene (Trans., 1903, 83, 1338), and if the alcoholic solution of the salt is boiled, it is completely converted into this compound.

The salt decomposes at $117\text{--}118^\circ$ and dissolves in alcohol, benzene, or chloroform.

0.5420 gave 0.3024 trinitrobenzoic acid = 55.8.

$\text{C}_{21}\text{H}_{20}\text{O}_8\text{N}_4$ requires 56.3 per cent.

Diethyl- β -naphthylamine s-Trinitrobenzoate.—This salt, which was also obtained from alcoholic solutions of the acid and base, begins to darken at 125° and is completely decomposed at 132° ; it dissolves in hot water, alcohol, benzene, and chloroform, and, like its isomeride, shows a tendency to lose carbon dioxide and to form diethyl- β -naphthylamine-trinitrobenzene melting at 116° (Trans., 1903, 83, 1340). This transformation is practically quantitative when an alcoholic solution of the salt is boiled for a short time.

0.4736 gave 0.2641 trinitrobenzoic acid = 55.7.

$C_{21}H_{20}O_8N_4$ requires 56.3 per cent.

The changes which these salts undergo when their alcoholic solutions are boiled, illustrate remarkably well the difference in stability between the additive compounds of *s*-trinitrobenzene with aniline derivatives and those produced with naphthylamine derivatives.

Dimethyl- ψ -cumidine and dimethylmesidine, when boiled in alcoholic solution, yield the free base and *s*-trinitrobenzene, whereas diethyl- α - or - β -naphthylamine trinitrobenzoate yields the corresponding coloured additive compound of the base with *s*-trinitrobenzene.

In order to determine whether dimethyl- ψ -cumidine forms a definite compound with *s*-trinitrobenzene, we have made a number of experiments with different solutions, but in all cases, even when excess of the base was employed, crystals of unaltered *s*-trinitrobenzene were deposited. A coloured compound, obtained by crystallising *s*-trinitrobenzene from the base and allowing the crystals to dry in a desiccator containing a little of the free base, separated in small, bright red needles with no definite melting point, as when warmed they readily give up the base, leaving a colourless residue. When exposed to the air, the substance readily leaves a colourless residue of *s*-trinitrobenzene.

0.5 gave 0.2831 trinitrobenzene (m. p. 122°) = 56.62.

$C_{17}H_{20}O_6N_4$ requires 56.6 per cent.

An additive compound of trinitrobenzene and ψ -cumidine, obtained by mixing together alcoholic solutions of the constituents, crystallises in long, slender, purple-brown needles melting at 115° , and is much more stable than the compound of aniline with trinitrobenzene.

0.3036 gave 41.3 c.c. moist nitrogen at 17° and 765 mm. $N = 15.9$.

$C_{15}H_{16}O_6N_4$ requires 16.09 per cent.

C. Salts from 2:4:6-Tribromo-3-aminobenzoic Acid.

Dimethylmesidine 2:4:6-Tribromo-3-aminobenzoate,

$NH_2 \cdot C_6HBr_3 \cdot CO_2 \cdot NHMe_2 \cdot C_6H_2Me_3$.

—The salt was obtained by dissolving the acid in ether, adding a slight excess of dimethylmesidine, and allowing the greater part of the ether to evaporate; it crystallised from water in small needles, softening at 147° and melting at 163 — 165° .

0.8002 gave 0.5677 tribromoaminobenzoic acid = 70.9.

$C_{18}H_{21}O_2N_2Br_3$ requires 69.6 per cent.

The salt readily dissolves in alcohol, and also to a less extent in ether, benzene, chloroform, or hot water, but is very sparingly soluble in light petroleum.

Dimethyl-ψ-cumidine Hydrogen Tribromoaminobenzoate,

—When the acid and base were mixed in molecular proportion, the mixture did not set to a solid mass, but remained pasty, and when the mixture was crystallised from benzene, in which it is only moderately soluble, nodular aggregates of small, colourless needles melting at 145·5—146° were obtained. When titrated in alcoholic solution with standard baryta, using phenolphthalein as indicator, 0·4062 required 17·85 c.c. of *N*/20 Ba(OH)₂.

The amount required for the normal and acid salts,

and $2(\text{NH}_2 \cdot \text{C}_6\text{HBr}_3 \cdot \text{CO}_2\text{H}), \text{C}_6\text{H}_2\text{Me}_3 \cdot \text{NMe}_2$, are 15·48 and 17·84 c.c. respectively.

When decomposed with dilute hydrochloric acid and extracted with ether, 0·6024 gave 0·505 tribromoaminobenzoic acid = 83·8 per cent.

$\text{NH}_2 \cdot \text{C}_6\text{HBr}_3 \cdot \text{CO}_2\text{H}, \text{C}_6\text{H}_2\text{Me}_3 \cdot \text{NMe}_2$ and

require 69·6 and 82·1 per cent. respectively.

The same compound, obtained in the form of glistening, well-developed prisms by dissolving molecular quantities of the acid and base in alcohol, adding water, and allowing the solvent to evaporate slowly, melted at 146°.

0·3 required 13·24 c.c. of *N*/20 Ba(OH)₂ for neutralisation ; 2 mols. acid + 1 mol. base requires 13·17 c.c.

The melting point was not affected by crystallisation from benzene.

We have attempted to prepare the normal salt (1 mol. acid + 1 mol. base) by dissolving a mixture of the acid with twice its weight of base in hot benzene and allowing the solution to crystallise and also by dissolving the acid (1 mol.) in dry ether, and adding an ethereal solution of the base (4 mols.), but the same acid salt melting at 146° was obtained in both cases.

Attempts to obtain salts with diethyl-*α*- and -*β*-naphthylamines led to the formation of gummy, uncrystallisable masses.

D. Salts from 2:4:6-Trimethylbenzoic Acid.

Benzylamine 2:4:6-trimethylbenzoate is obtained by separately dissolving equivalent amounts of the acid and base in light petroleum and mixing the solutions; it crystallises from benzene in small, feathery, colourless needles melting at 165°.

0·3052 gave 0·1868 trimethylbenzoic acid = 61·2.

$\text{C}_{17}\text{H}_{21}\text{O}_2\text{N}$ requires 60·5 per cent.

Salts could not be obtained with this acid and any of the following

bases: dimethylmesidine, dimethyl- ψ -cumidine, bromodimethyl- m -xylidine, diethylaniline.

E. Salts of the Three Toluic Acids.

Benzylamine o-toluate, obtained from light petroleum solutions of the acid and base, crystallises from benzene in small prisms melting at 146°. It dissolves readily in water, and to a moderate extent in light petroleum.

0.4716 gave 0.2668 *o*-toluic acid = 56.5.

$C_6H_4Me \cdot CO_2 \cdot NH_3 \cdot CH_2Ph$ requires 55.9 per cent.

ψ -Cumidine hydrogen o-toluate, $2(C_6H_4Me \cdot CO_2H) \cdot C_6H_2Me_3 \cdot NH_2$, produced by mixing together ethereal or light petroleum solutions of the acid and base, crystallised from water in long, snow-white, silky needles, softening somewhat at 80° and melting at 82.5°. The same compound is obtained when an excess of the base is employed.

0.5 gave 0.3315 *o*-toluic acid (m. p. 105) = 66.3.

One mol. acid + 1 mol. base requires 50.18.

Two " " " " 66.8 per cent.

0.70 gram, when dissolved in sodium carbonate and extracted with ether, gave 0.236 gram of solid base = 33.7. The acid salt requires 33.2 per cent.

0.25 gram of the salt, when dissolved in ethyl alcohol, required 24.8 c.c. of *N*/20 baryta solution for complete neutralisation, using phenolphthalein as indicator. The acid salt requires 24.6 c.c.

Salts of *o*-toluic acid with dimethylaniline, dimethyl- ψ -cumidine and dimethylmesidine could not be obtained.

Definite salts could not be obtained either from *m*-toluic acid and ψ -cumidine or dimethylaniline, or from *p*-toluic acid and the same bases.

F. Salts from the Three Nitrobenzoic Acids.

ψ -Cumidine o-Nitrobenzoate.—This salt was obtained in the form of silky needles when ethereal or benzene solutions of the constituents were mixed; when crystallised from water, it formed long, silky, prismatic needles melting at 133—134°.

0.4137 gave 0.2260 *o*-nitrobenzoic acid = 54.6.

$C_{16}H_{18}O_4N_2$ requires 55.3 per cent.

0.3 required 20.1 c.c. of *N*/20 baryta solution for neutralisation. The normal salt requires 19.9.

Dimethyl-ψ-cumidine hydrogen o-nitrobenzoate,

obtained by mixing equal weights of the acid and base in benzene solution and crystallising from this solvent, forms small, colourless crystals melting at 124·5.

0·50 required 40·5 c.c. *N*/20 baryta solution. The acid salt requires 40·2 c.c.

ψ-Cumidine m-nitrobenzoate was obtained in the form of long, colourless, feathery needles melting at 129·5—130°, when the acid was mixed with twice its weight of *ψ*-cumidine and crystallised from benzene.

0·3 required 20·05 c.c. *N*/20 alkali. The normal salt requires 19·9 c.c. 0·5 requires 33·4 c.c. The normal salt requires 33·16.

The acid salt, $2(\text{NO}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CO}_2\text{H}), \text{C}_6\text{H}_2\text{Me}_3 \cdot \text{NH}_2$, was obtained when a mixture of the acid (2 mols.) and base (1 mol.) was dissolved in benzene and allowed to cool; it crystallises from water in pale yellowish needles melting at 144°.*

0·40 required 34·3 c.c. of *N*/20 alkali. The acid salt requires 34·12 c.c.

A mixture of the two salts was obtained when equal weights of the acid and base were crystallised together from benzene or water.

The normal salt, when boiled with water, is partially transformed into the acid salt.

Dimethyl-ψ-cumidine hydrogen m-nitrobenzoate, obtained when molecular quantities of the acid and base are mixed in ethereal solutions, crystallises from benzene in small, colourless prisms melting at 119·5°, dissolves readily in alcohol, ether, or chloroform, but is only sparingly soluble in carbon disulphide or light petroleum, and crystallises from hot water in colourless, flat plates.

0·3566 gave 0·2362 *m*-nitrobenzoic acid = 66·2. The acid salt requires 67·2 per cent.

0·255 required 20·77 c.c. of *N*/20 alkali. The acid salt requires 20·52 c.c.

ψ-Cumidine p-nitrobenzoate, obtained by mixing ethereal solutions of the acid and base, separates from water in small, feathery crystals melting at 160°.

* The salt mentioned previously (Trans., 1899, 75, 595) as melting at 140—141° must have been the acid salt, but the specimen actually analysed must have been the normal salt melting at 129·5—130°.

0.3246 gave 0.1872 *p*-nitrobenzoic acid = 57.6.

$\text{NO}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CO}_2 \cdot \text{NH}_3 \cdot \text{C}_6\text{H}_2\text{Me}_3$ requires 55.3 per cent.

No definite salts could be obtained from dimethylaniline and the three nitrobenzoic acids.

G. Salts from the Three Bromobenzoic Acids.

ψ-Cumidine o-bromobenzoate, $\text{C}_6\text{H}_4\text{Br} \cdot \text{CO}_2 \cdot \text{NH}_3 \cdot \text{C}_6\text{H}_2\text{Me}_3$, slowly separates in the form of fine needles from an ethereal solution of the acid and base; it dissolves readily in benzene, alcohol, or hot water, and crystallises from either light petroleum or hot water in colourless needles melting at 106—106.5°.

0.555 gave 0.3286 *o*-bromobenzoic acid = 59.2. The normal salt requires 59.8 per cent.

0.50 required 29.87 c.c. of *N*/20 alkali. The normal salt requires 29.76 c.c.

ψ-Cumidine m-bromobenzoate crystallises from benzene in long, felted needles, melts at 98.5°, and is readily soluble in chloroform, alcohol, warm ether, or benzene.

0.50 required 29.7 c.c. of *N*/20 alkali. The normal salt requires 29.76 c.c.

No definite salts could be obtained from dimethylaniline and the three bromobenzoic acids, and an ethereal solution of *ψ*-cumidine and the *p*-bromo-acid slowly deposited crystals of the free acid melting at 251°.

CHEMICAL LABORATORIES,
UNIVERSITY COLLEGE OF WALES,
ABERYSTWYTH.