# NOTES.

## *Preparation of* N-*Bromosuccinimide by an Electrolytic Process.* By M. LAMCHEN.

FEW methods for the preparation of *N*-bromosuccinimide have been reported, viz., treatment of succinimide with *N*-bromoacetamide (Seliwanow, *Ber.*, 1893, **26**, 425), or with bromine and sodium hydroxide (Lengfeld and Stieglitz, *Amer. Chem. J.*, 1893, **15**, 215), or quickly brominating an ice-cold alkaline solution of succinimide (Ziegler *et al.*, *Annalen*, 1942, **551**, 80); 75—81% yields are reported in the latter process. *N*-Bromoacetamide used in the first method is obtained (Hofmann, *Ber.*, 1882, **15**, 408) by treating acetamide with bromine and ice-cold sodium hydroxide. All these methods thus employ bromine and sodium hydroxide, the function of which is to produce the hypobromite ion required for the reaction. Half of the bromine used is converted into bromide and is useless for the process; also, at least one equivalent of sodium hydroxide is consumed. In the process described below, hypobromite ions are produced without the use of bromine and with the use of only a small quantity of sodium hydroxide: an ice-cold solution of succinimide and sodium bromide is electrolysed between platinum electrodes with just sufficient sodium hydroxide to keep the solution colourless. Of every two bromide ions discharged at the anode, one again enters the solution as a bromide ion after reaction with hydroxyl ions. Thus, for every bromide ion discharged one molecule of *N*-bromosuccinimide is formed, one hydroxyl ion is produced, and one molecule of hydrogen is liberated. *N*-Bromosuccinimide alone has a low solubility in cold water and separates as a solid on the anode. Every bromide ion is effectively utilised, and the hydroxyl ions required are produced in the process.

The *N*-bromosuccinimide produced varies in colour from straw-yellow to white depending on the conditions used. The crude unwashed product melted at 163°, but by washing it once with a small quantity of ice-cold water the melting point is raised to 178·5°. Yields are 66% for the crude and 54% for the washed product.

The crude product could not be dissolved in benzene but after being washed with water it dissolved quite readily. The same phenomenon was observed with a sample of commercial material. The product is evidently covered with a layer of a benzene-insoluble, water-soluble substance. Ziegler also reported (*Annalen*, 1942, **551**, 80) that benzene was not satisfactory as a solvent for recrystallisation and used water. He considered the covering layer to be succinimide, but from the wash-liquor the present author could recover only *N*-bromosuccinimide. It is believed that the benzene-insoluble substance in this experiment may be sodium succinate because on evaporation of the filtrate at room temperature (or in a vacuum-desiccator) sodium succinate crystallises (its formation is to be expected).

Variation of the current density from 0·03 to 0·3 amp. per square inch made no difference to the reactions taking place in the process and the same products were obtained in all cases as long as it was low enough to avoid heating of the solution. At higher current densities the product was formed faster and was yellower, but yields were better. If the solution is allowed to become hot the yield drops very rapidly. The use of a rocking anode facilitated the peeling off of the product and gave a slightly better yield and a paler product.

*Experimental.*—Water was saturated with succinimide and an equimolecular amount of sodium bromide was then dissolved in the solution. This solution was electrolysed between platinum electrodes, at a current density of 0·3 amp. per sq. in., in an ice-bath, and 10% sodium hydroxide solution was added drop by drop till the solution no longer became brown. The anode, if stationary, was shaken at intervals to allow the *N*-bromosuccinimide to drop off; a rocking anode was generally used. When 10 g. of succinimide were used with electrodes 1½ in. square, 3—4 hours sufficed for completion of the reaction. The bulk of the yield was formed during the first hour. 10 G. of crude product, m. p. 163°, were obtained. After filtration, 10 g. of succinimide and 10·3 g. of sodium bromide were dissolved in the filtrate, and the solution was again electrolysed, giving a further yield of 11·85 g. (66%) (m. p. 163°).—UNIVERSITY OF CAPE TOWN, SOUTH AFRICA. [*Received, August 15th*, 1949.]

### *Preparation of* N-*Acetyl*-N-*methylurea by an Electrolytic Process.* By M. LAMCHEN.

THE electrolytic method for the preparation of *N*-bromosuccinimide described by the author (preceding note) indicated that imido-hydrogen atoms could be substituted by bromine atoms during electrolysis of an aqueous solution of an imide, sodium bromide, and a small quantity of sodium hydroxide. When the electrolysis is carried out in an ice-cold solution the reaction proceeds only as far as the *N*-bromoimide which, if fairly insoluble in water, is precipitated. This was the case with *N*-bromosuccinimide; when, however, a saturated ice cold solution of acetamide, containing sodium bromide and sufficient sodium hydroxide to keep it colourless, was electrolysed for 10 hours, *N*-bromoacetamide, being soluble, did not crystallise from the solution.

An *N*-bromo-amide would lose hydrogen bromide in warm sodium hydroxide solution, to form the *iso*cyanate (cf. the Hofmann degradation of amides), which would react with suitable compounds. If thus the electrolysed solution of acetamide, sodium bromide, and sodium hydroxide is allowed to become hot, or if the electrolysis is carried out without cooling, the *N*-bromoacetamide, if formed, should lose hydrogen bromide to give methyl *iso*cyanate. In practice white crystals soon appeared and more separated after cooling. These were identified (mixed m. p.) as *N*-acetyl-*N*-methylurea, formed by reaction of the methyl *iso*cyanate with unchanged acetamide.

From a fresh solution 67% yields, calculated on the acetamide, were obtained, but if the filtrate of a previous experiment was used 70—80% yields were obtained. The product is almost pure and is quite white.

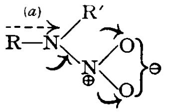
Previous methods are those of Young and Clark (*J.*, 1898, **73**, 364; methylamine is treated with acetylurethane) and of Odendal (*Annalen*, 1918, **416**, 228; acetamide is heated with bromine and sodium hydroxide until the solution becomes acid and yellow). Odendal records yields of up to 75%, but the pH is critical and if the solution is slightly too alkaline the yield drops to zero and the process proceeds in a different way. For every molecule of acetamide he used one molecule of sodium hydroxide and more than one molecule of bromine. The electrolytic process described above eliminates the use of bromine and requires only small quantities of sodium hydroxide as the bulk of the required hydroxyl ions are obtained from the electrolysis of the solution; also all the bromide ions should be available for the process and the subsequent splitting off of hydrogen bromide should again regenerate the bromide ions.

Variations of current densities between 0·03 and 0·3 amp. per sq. in. made no difference to the product except that it was formed much faster and yields were better at the higher current densities.

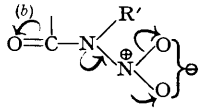
*Experimental.*—A saturated solution containing acetamide (30 g.) and sodium bromide (15 g.) is electrolysed between platinum electrodes at 0·3 amp. per sq. in. with just sufficient sodium hydroxide (10%) added to prevent the solution becoming brown. Further small quantities of sodium hydroxide may be needed later. Crystals form in the solution after ½—1 hour, depending on the current density. After about 10 hours the solution was cooled and filtered, and the product (20·2 g.) was washed with ice-cold water. After recrystallisation from benzene it had m. p. 180—181° (Found: C, 41·6; H, 6·8. Calc. for $C_4H_8O_2N_2$: C, 41·4; H, 6·9%).—UNIVERSITY OF CAPE TOWN, S. AFRICA. [*Received, August 15th*, 1949.]

### *The Hydrolysis of* NN′-*Dinitro-oxamide*-NN′-*bis*-(2-*ethyl Nitrate*). By J. VAUGHAN.

THE preparation and properties of this dinitrate (III) have been investigated by Wright *et al.* (*e.g.*, Stuart and Wright, *Canadian J. Res.*, 1948, **26**, *B*, 401). The hydrolysis of this compound is of interest because on theoretical grounds it appears that aqueous hydrolysis should proceed quite readily. When the group $-NR'\cdot NO_2$ is linked to an alkyl group R, as in (I), the new R–N linkage should be relatively



(I.)



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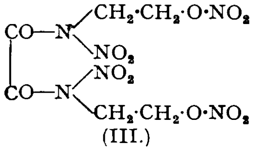
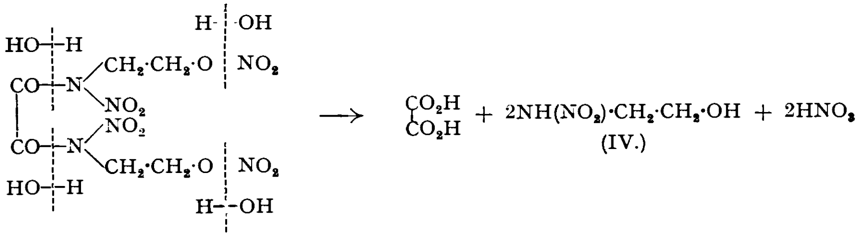


(III.)

stable because the electrophilic tendency of the amino-nitrogen atom can be partly met by the electron-donating effect (*a*) of the alkyl group. When the group $-NR'\cdot NO_2$ is linked to a carbonyl group, as in (II), the electrophilic tendency of the amino-nitrogen atom and the electromeric effect (*b*), caused by the strong displacement towards the carbonyl oxygen, combine to make the carbonyl carbon susceptible to nucleophilic attack. The carbonyl–N linkage in (II) should thus be relatively unstable to hydrolysis. This argument is supported by the fact that ethylenedinitroamine, a compound of type (I), is very much more stable to hydrolysis than nitrourea, a compound of type (II). Ethylenedinitroamine may be prepared by the action of boiling water on dinitroethyleneurea (Franchimont and Klobbie, *Rec. Trav. chim.*, 1888, **7**, 17), but nitrourea is readily decomposed by hot water and the decomposition is accelerated by the presence of bases (Sidgwick's " Organic Chemistry of Nitrogen," 1937, p. 280). Compound (III), like nitrourea, should be fairly readily attacked by warm water, but the possibility of the alkyl nitrate groupings also undergoing hydrolysis is to be borne in mind.

Preliminary experiments on the hydrolysis of (III), which is insoluble in water, have been carried out at 49° with a stationary amide–water interface. The results can be summarised as follows : (i) the acidity developed is, approximately, accounted for by the oxalic and nitric acids formed; (ii) within the limits of experimental error the *molar* ratio of nitric to oxalic acid formed is 2 : 1.

On the basis of these preliminary results, therefore, the hydrolysis of the substituted oxamide can be represented thus



$$\begin{matrix}CO_2H\\CO_2H\end{matrix} + 2NH(NO_2)\cdot CH_2\cdot CH_2\cdot OH + 2HNO_3$$

(IV.)

Monoethanolnitroamine (nitro-2-hydroxyethylamine) (IV) contains an acidic hydrogen atom; it might be expected, therefore, that this would be estimated in the total acidity. However, in the presence of acids, this compound is readily decomposed into ethylene glycol and nitrous oxide (Franchimont, *Rec. Trav. chim.*, 1902, **21**, 50). It was established during the present work that nitrous oxide was formed during the hydrolysis in amount corresponding to at least two-thirds of the theoretical.

*Experimental.*—Hydrolysis was followed by determination of the loss in weight of the amide and estimation of hydrolysis products. The substituted oxamide was recrystallised from acetone, dried *in vacuo* over phosphoric oxide, and passed through a 100-mesh B.S. sieve. Portions (0·5 g.) were each placed in contact with distilled water (40 ml.) in 100-ml. conical Pyrex flasks fitted with standard ground-glass stoppers. 0·01 G. of lauryl alcohol was also added in each case in order to get thorough wetting of the crystals, and the flasks were then placed in a thermostat at 49°. Although the lauryl alcohol would probably increase the rate of hydrolysis, it was considered unlikely that the course of hydrolysis would be affected. In this way an approximately constant initial area of interface between amide and water could be assumed.

Flasks were removed at intervals, and the solid residue filtered off. This was dried and weighed, and the m. p. of each precipitate indicated that pure (III) had been recovered. The filtrates in each case gave positive tests for the presence of oxalic and nitric acids. The complete filtrate then underwent the following sequence of determinations : (i) of total acidity by titration, (ii) of oxalic acid as calcium oxalate by permanganate, (iii) of nitric acid by " nitron." In no case could more than a trace of nitrous acid be detected in the filtrate, using the Griess–Ilosvay reagent. The results are summarised in the table.

| Time (days) at 49°. | Wt. of compound taken (g.). | % not hydrolysed. | Total acidity (ml., N/10). | Nitric acid (ml., N/10). | Oxalic acid (ml., N/10). |
|---|---|---|---|---|---|
| 4 | 0·4995 | not determined | 17·4 | 9·1 | 9·4 |
| 8 | 0·5002 | 51·9 | 29·3 | 16·8 | 15·1 |
| 12 | 0·5000 | 26·9 | 40·7 | 19·6 | 19·5 |
| 17 | 0·5087 | 20·4 | 46·8 | 22·6 | 24·9 |
| 25 | 0·5021 | 14·3 | 48·6 | 24·4 | 25·1 |

The author thanks the Chief Scientist of the Ministry of Supply for permission to publish this work, which was carried out in the Armament Research Department of the Ministry in 1945.—CANTERBURY UNIVERSITY COLLEGE, CHRISTCHURCH, NEW ZEALAND. [*Received, September 29th,* 1949.]

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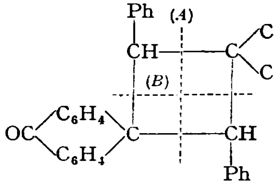
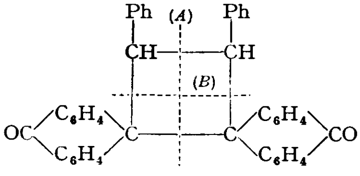
### *Reactions in Sunlight.* By FAWZY GHALI BADDAR.

MUSTAFA and ISLAM (*J.*, 1949, S 81) claimed that the dimer obtained by exposing 9-benzylideneanthrone in benzene solution to sunlight has the structure (II) because (i) it lacks colour, (ii) on being heated at 270° it regenerates the monomer, and (iii) it has the correct molecular weight. The product may equally, however, have the isomeric structure (I), which would give only 9-benzylideneanthrone on thermal decomposition, whether cleavage of the bonds occurs along (*A*) or along (*B*); if it has the isomeric structure (II), thermal decomposition would give rise to a mixture of the monomer, stilbene, and dianthraquinonyl. Stobbe and Bremer (*J. pr. Chem.*, 1929, **123**, 1) isolated two dimers of benzylideneacetophenone; that which gave stilbene on thermal decomposition was given a structure analogous to (II), whereas that which gave mainly the monomer was assigned a structure analogous to (I). The fact that the above authors failed to isolate any stilbene among the decomposition products supports structure (I) rather than (II).



(I.)



(II.)

Similarly, in the photo-reactions between retenequinone and 9-benzylidenexanthen or methyleneanthrone and between chrysenequinone and triphenylethylene (Mustafa, *J.*, 1949, S 83), the constituent molecules can theoretically unite in two ways to give two isomerides, which would give identical products on thermal decomposition.—FOUAD I UNIVERSITY, FACULTY OF SCIENCE, ABBASSIA, CAIRO, EGYPT. [*Received, October 5th,* 1949.]

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## 3-*Hydroxy*-4 : 5-*dimethoxybenzoic Acid Derivatives.* By J. R. ANSTEE and D. E. WHITE.

3-HYDROXY-4 : 5-DIMETHOXYBENZOIC ACID has been synthesised from gallic, 5-nitroveratric, and 5-bromoveratric acid. Späth and Röder's method starting from gallic acid (*Monatsh.*, 1922, **43**, 93) is most convenient for the preparation of the acid in quantity; the acid has been characterised by the acetyl derivative, which melts 10° higher than that prepared by Shriner and McCutchan (*J. Amer. Chem. Soc.*, 1929, **51**, 2193) from a low-melting sample of 3-hydroxy-4 : 5-dimethoxybenzoic acid.

Ethylation with ethyl sulphate and alkali gave 3 : 4-dimethoxy-5-ethoxybenzoic acid, m. p. 117—118°. Seshadri and Venkateswarlu (*Proc. Indian Acad. Sci.*, 1946, **23**, *A*, 296) describe this acid as melting as 164°, only 3° lower than their sample of trimethylgallic acid. This m. p. appears to be in error as the isomeric 3 : 5-dimethoxy-4-ethoxybenzoic acid (Bogert and Ehrlich, *J. Amer. Chem. Soc.*, 1919, **41**, 801) melts more than 40° lower than trimethylgallic acid.

*Methyl* and *ethyl* 3 : 4-*dimethoxy*-5-*ethoxybenzoate* were prepared with the appropriate alcohol and sulphuric acid.

*Experimental* (M. p.s are corr.).—3-*Hydroxy*-4 : 5-*dimethoxybenzoic acid.* Prepared by the method of Späth and Röder (*loc. cit.*), this acid formed colourless needles (from water), m. p. 195—196°, considerably depressed by admixture of syringic acid (m. p. 207°). When refluxed (1 g.) with acetic anhydride (5 ml.) and pyridine (1 drop) for 30 minutes, it gave an acetyl derivative (1 g.), isolated by pouring the mixture into water and forming long colourless prisms (from aqueous methyl alcohol), m. p. 148° (Found : C, 55·05, H, 5·2. Calc. for $C_{11}H_{12}O_6$: C, 55·0; H, 5·0%), considerably depressed by admixture with acetylsyringic acid (m. p. 184—186°).

3 : 4-*Dimethoxy*-5-*ethoxybenzoic acid.* The above acid (18 g.) in 10% sodium hydroxide solution (80 ml.) was boiled under reflux during the addition, during 30 minutes, of ethyl sulphate (40 ml.) and 10% sodium hydroxide solution (132 ml.). Refluxing was continued for 1 hour, and ethyl sulphate (26 ml.) and 20% sodium hydroxide solution (40 ml.) added during the next 15 minutes. After refluxing for a further 30 minutes, ethanol (17 ml.) was removed by distillation, and the solution treated with charcoal, cooled, and acidified with hydrochloric acid. The acid (20 g.) formed colourless needles and plates from 10% alcohol (800 ml.) and after two crystallisations melted constantly at 117—118° (15 g.) (Found : C, 58·5; H, 6·35. Calc. for $C_{11}H_{14}O_5$ : C, 58·4; H, 6·2%).

*Methyl and ethyl esters.* A solution of 3 : 4-dimethoxy-5-ethoxybenzoic acid (5 g.) in the appropriate alcohol (50 ml.) was refluxed with sulphuric acid (0·2 ml.) for 8 hours and the ester isolated by distillation of the alcohol, dissolution of the residue in ether, and washing of the extract to remove acids. After drying ($Na_2SO_4$) and distillation of the ether the ester remained. The *methyl* ester crystallised as colourless needles, m. p. 51·5° (2·5 g.) (Found : C, 60·09; H, 6·76. $C_{12}H_{16}O_5$ requires C, 59·98; H, 6·71%), from 40% methyl alcohol. The *ethyl* ester was a colourless oil, b. p. 139—140°/3 mm., 105—106°/0·1 mm., $n_D^{16}$ 1·5268, $n_D^{23}$ 1·5160 (2·2 g.) (Found : C, 61·5; H, 7·4. $C_{13}H_{18}O_5$ requires C, 61·3; H, 7·1%).

The authors acknowledge financial support from the Commonwealth Research Grant to Australian Universities and microanalyses by Drs. Weiler and Strauss.—UNIVERSITY OF WESTERN AUSTRALIA. [*Received, October 24th,* 1949.]

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## *Certain Substituted Benzaldehydes and Substituted Benzaldehyde Dinitrophenylhydrazones.*

By J. B. BOWEN and E. M. WILKINSON.

DURING investigations on the adsorption of 2 : 4-dinitrophenylhydrazones on activated alumina, a series of substituted benzaldehyde 2 : 4-dinitrophenylhydrazones was prepared. Nine of these derivatives are new and it therefore seemed desirable to record the new data. The Stephen reduction of nitriles (*J.*, 1925, **127**, 1874) has been applied for the first time to the synthesis of four of the aldehydes used. These preparations are briefly recorded.

m-*Tolualdehyde.*—*m*-Tolunitrile (8·7 g.) was added to anhydrous stannous chloride (25 g.) dissolved in dry ether (50 c.c.) saturated with dry hydrogen chloride. After 2 days the crystals which had deposited were filtered off and steam-distilled. The aldehyde was ether-extracted from the distillate, dried, and distilled in an atmosphere of carbon dioxide. B. p. 198°/756 mm. Yield, 50%. Von Auwers (*Annalen*, 1915, **408**, 237) gives b. p. 195°/745 mm.

m-*Chlorobenzaldehyde.*—*m*-Chlorobenzonitrile (2·9 g.) and stannous chloride (10 g.) in dry ethereal hydrogen chloride (30 c.c.) gave similarly, after 24 hours, the aldehyde of b. p. 213—214° (53%). Erdmann and Schwechten (*ibid.*, 1890, **260**, 59) give b. p. 213—214°.

p-*Bromobenzaldehyde.*—*p*-Bromobenzonitrile (10 g.) and stannous chloride (21 g.) in dry ethereal hydrogen chloride (200 c.c.), when kept overnight, gave an aldehyde which, when similarly isolated and then recrystallised from dilute methanol, had m. p. 57° (62%). Adams and Vollweiler (*J. Amer. Chem. Soc.*, 1918, **40**, 1738) give m. p. 56—57°.

p-*Iodobenzaldehyde.*—*p*-Iodobenzonitrile (10 g.) in dry ether (50 c.c.) with saturated, dry, ethereal hydrogen chloride solution (150 c.c.) containing anhydrous stannous chloride (40 g.) gave similarly, after 24 hours, the aldehyde (56%), m. p. 77° (from aqueous ethanol). Willgerodt and Bogel (*Ber.*, 1905, **38**, 3451) give m. p. 78°.

In some cases more crystals of the aldimine stannichloride were deposited in the reaction flask on further storage, so that the yields could be improved a little if necessary.

The Sandmeyer procedure described by Clark and Read (*Org. Synth.*, Coll. Vol. I, p. 514) for the preparation of *o*- and *p*-tolunitrile was applied to obtain the necessary *m*-tolunitrile, *m*-chloro-, *p*-bromo-, and *p*-iodo-benzonitrile in 53, 59, 67, and 68% yield, respectively, from the appropriate amines.

*Preparation of the Dinitrophenylhydrazones.*—Except where otherwise stated, the general procedure for the preparation of these derivatives was to add a solution of the aldehyde in methanol to a slight excess of the reagent dissolved in sulphuric acid–methanol (1 : 10) or dilute hydrochloric acid. The derivatives so obtained were repeatedly recrystallised to constant m. p. using, in most cases, two different solvents in succession, and dried *in vacuo* at 100° for analysis. The *m*-amino-compound is an exception in this respect, in that we failed to recrystallise it in a satisfactory manner without decomposition. The solubilities in benzene at room temperature were determined by using a Spekker photoelectric absorptiometer to measure concentrations. The tungsten lamp in conjunction with the usual heat filters and " Ilford 601 " violet filters were suitable for all the solutions examined.

M. p.s were determined by using short-range Anschütz-type thermometers and are corrected except where otherwise specified.

m-*Aminobenzaldehyde* 2 : 4-*dinitrophenylhydrazone*. *m*-Aminobenzaldehyde was prepared *in situ* by Buck and Ide's method (*Org. Synth.*, Coll. Vol. II, p. 130), and its solution in aqueous hydrochloric acid added directly to a saturated solution of the reagent in the same medium. The brownish-red precipitate of the *dinitrophenylhydrazone* was washed with distilled water until free from chloride ions and dried in a vacuum desiccator. Solubility in benzene, 13 mg./100 ml. It decomposes from about 230° (Found : N, 23·0. $C_{13}H_{11}O_4N_5$ requires N, 23·3%).

p-*Aminobenzaldehyde* 2 : 4-*dinitrophenylhydrazone*. *p*-Aminobenzaldehyde, prepared *in situ* from *p*-nitrotoluene by Beard and Hodgson's method (*J.*, 1944, 4), was used immediately in dilute acid solution as described for *m*-aminobenzaldehyde. The precipitated *dinitrophenylhydrazone* was thoroughly washed until free from mineral acid and was obtained as a light-brown powder, m. p. 192·5—194·5° (slight decomp.), after recrystallisation from methanol (Found : N, 23·4. $C_{13}H_{11}O_4N_5$ requires N, 23·3%).

m-, bright yellowish-orange crystals (from aqueous pyridine and then from xylene) (solubility in benzene, 34 mg./100 ml.), m. p. 256—257° (Found : N, 15·2. $C_{13}H_9O_4N_4Br$ requires N, 15·3%), and p-*bromobenzaldehyde* 2 : 4-*dinitrophenylhydrazone*, bright orange crystals (from aqueous pyridine and then from xylene) (solubility in benzene, 25 mg./100 ml.), m. p. 256—257·5° (Found : N, 15·5%), were obtained by the general method.

p-*Carboxybenzaldehyde* 2 : 4-*dinitrophenylhydrazone* was prepared by adding the reagent in hot dilute hydrochloric acid to the aldehyde in the same solvent. The precipitated derivative was filtered hot and obtained as bright light-orange crystals from aqueous pyridine. It was further recrystallised from nitrobenzene. It was practically insoluble in benzene. M. p. 319·5—320·5° (uncorr.) (Found : N, 17·1. $C_{14}H_{10}O_6N_4$ requires N, 17·0%).

p-*Iodobenzaldehyde* 2 : 4-*dinitrophenylhydrazone* was obtained by the general method. The precipitated derivative was washed with boiling dilute hydrochloric acid and then with water. After recrystallisation from an aqueous pyridine–methanol and finally from xylene it yielded pale orange-brown crystals (solubility in benzene, 38 mg./100 ml.), m. p. 256·5—257·5° (Found : N, 13·7. $C_{13}H_9O_4N_4I$ requires N, 13·6%).

The standard method yielded 2 : 4-*dinitrophenylhydrazones* from *p*-carbomethoxybenzaldehyde, pale-orange, m. p. 263·5—265° (from aqueous pyridine) (Found : N, 16·4. $C_{15}H_{12}O_6N_4$ requires N, 16·2%) (solubility in benzene, 14 mg./100 ml.), *m*-methoxybenzaldehyde, brilliant red crystals (from pyridine and then from xylene) (solubility in benzene, 32·5 mg./100 ml.), m. p. 218·5—219·5° (Found : N, 17·7. $C_{14}H_{12}O_5N_4$ requires N, 17·7%), and *m*-tolualdehyde, bright orange-red crystals (from aqueous pyridine and then from xylene) (solubility in benzene, 152 mg./100 ml.), m. p. 211·5—212·5° (Found : N, 18·8. $C_{14}H_{12}O_4N_4$ requires N, 18·7%).

One of us (J. B. B.) gratefully acknowledges his indebtedness to the Chemical Society for a research grant and the other (E. M. W.) to the Department of Scientific and Industrial Research for a maintenance grant.—The Edward Davies Chemical Laboratories, University College of Wales, Aberystwyth. [*Received, October* 31*st*, 1949.]

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## *The Resolution of* p-*Chlorobenzhydrol.* By G. H. Green and J. Kenyon.

The main object in resolving *p*-chlorobenzhydrol into its optical isomerides was to compare the readiness with which alkyl–oxygen fission occurred during reactions of this compound and its derivatives with that of *o*-chlorobenzhydrol and its corresponding derivatives. The latter compounds were shown (Balfe *et al.*, *J.*, 1946, 797) to exhibit only negligible alkyl–oxygen fission due, doubtless, to the deactivating influence of the chlorine substituent. For this reason and also because it was found that *p*-chlorobenzhydryl hydrogen phthalate undergoes hydrolysis to the carbinol with extreme readiness further investigation of the reactions of *p*-chlorobenzhydrol and its derivatives was not proceeded with.

*Experimental.*—*p*-Chlorobenzhydrol was readily obtained in good yield by the reduction of *p*-chlorobenzophenone with either aluminium *iso*propoxide or, very conveniently, with zinc dust (an equal weight) and alcoholic sodium hydroxide (10 vols.; 10%). It separated from light petroleum in needles, m. p. 58·5—59·5°.

(±)-p-*Chlorobenzhydryl hydrogen phthalate.* A solution of phthalic anhydride (15 g.) in boiling anhydrous pyridine (10 g.) was rapidly cooled to about 50° and mixed with *p*-chlorobenzhydrol (20 g.), and the whole mass thoroughly stirred; it gradually stiffened and set solid within a few hours. It was then heated at 60° for 2 hours, cooled, and dissolved in acetone and the solution poured, with stirring, into water containing a slight excess of hydrochloric acid. The resulting solid was dissolved in ether, extracted therefrom with sodium carbonate (5%), and finally precipitated with cold dilute hydrochloric acid. (±)-p-*Chlorobenzhydryl hydrogen phthalate* separated from benzene in needles, m. p. 152° [Found (by titration in acetone–ethanolic solution with N/10-NaOH): *M*, 366·8. $C_{21}H_{15}O_4Cl$ requires *M*, 366·8].

(−)-p-*Chlorobenzhydryl hydrogen phthalate.* The only reasonably successful procedure for obtaining this compound appears to be to leave a solution of the brucine salt of the (±)-ester in ethyl acetate to evaporate at room temperature until a suitable amount of crystallisation has occurred.

A solution of the (±)-hydrogen phthalate (55 g.) and brucine (59·4 g.) in dry ethyl acetate (275 c.c.) was divided between eleven conical flasks (100 c.c.), each containing a "seed" of brucine salt, and left uncovered during 4 days. The various crystalline crops, m. p. 113° (decomp.), were separated by decantation of the mother liquors and each recrystallised twice more by the same procedure. Further recrystallisation was precluded owing to progressive decomposition of the salt, presumably by hydrolysis, into *p*-chlorobenzhydrol and brucine hydrogen phthalate. The recrystallised brucine salt was dissolved in acetone and decomposed with cold dilute hydrochloric acid, and the liberated acid ester purified by solution in sodium carbonate as described above (yield, 9 g.; m. p. 135°). It suffered no change either in m. p. or rotatory power by crystallisation from benzene.

(+)-p-*Chlorobenzhydryl hydrogen phthalate.* The combined mother liquors from the first crystallisation of the brucine salt on storage deposited two further small crops of salt which were removed by filtration. This final filtrate on decomposition yielded the (+)-acid ester (15 g.), m. p. 146°, $[\alpha]_{5461}$ +1·1° (*l*, 1·0; *c*, 26·7 in acetone solution).

(−)-p-*Chlorobenzhydrol.* The (−)-acid phthalic ester (5 g.) in hot methanol (50 c.c.) was mixed with sodium hydroxide solution (5 c.c.; 40%) and the whole heated on the steam-bath for 10 minutes. Water (200 c.c.) was added to the cooled solution to dissolve the precipitated sodium hydrogen phthalate, and the liberated carbinol was extracted with ether. It (3 g.) had m. p. 54—56°, unchanged by crystallisation from light petroleum.

(+)-p-*Chlorobenzhydrol.* The (+)-acid ester (7 g.) by similar treatment yielded (+)-*p*-chlorobenzhydrol (4 g.), m. p. 50—54°.

*Specific rotatory powers* (*l*, 1·0; temp. 20°).

| Solvent. | *c*, g./100 c.c. of solution. | $[\alpha]_{5893}$. | $[\alpha]_{5780}$. | $[\alpha]_{5461}$. | Solvent. | *c*, g./100 c.c. of solution. | $[\alpha]_{5893}$. | $[\alpha]_{5780}$. | $[\alpha]_{5461}$. |
|---|---|---|---|---|---|---|---|---|---|
| (−)-*p*-Chlorobenzhydryl hydrogen phthalate. | | | | | (+)-*p*-Chlorobenzhydrol. | | | | |
| Chloroform ... | 13·3 | −3·5° | −3·7° | −4·9° | Chloroform | 20·0 | +13·7 | +14·1 | +15·5 |
| Acetone ......... | 13·3 | 3·8 | 4·2 | 4·2 | | | | | |
| (−)-*p*-Chlorobenzhydrol. | | | | | | | | | |
| Acetone ......... | 13·3 | 18·7 | 20·4 | 21·7 | Chloroform | 6·7 | 32·1 | 34·1 | 38·0 |
| Ethanol (99%) | 6·7 | 18·9 | 20·3 | 22·2 | Benzene ... | 6·7 | 29·9 | 31·5 | 34·8 |
| Ethyl acetate | 6·7 | 23·4 | 24·3 | 27·6 | | | | | |

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## p-*Bishalogenoacetylbenzenes.* By W. C. J. Ross.

DURING the examination of possible cytotoxic substances containing two or more groupings capable of reacting with functional centres in biological systems (Everett and Ross, *J.*, 1949, 1972; Goldacre, Loveless, and Ross, *Nature*, 1949, **163**, 667) the preparation of *p*-bishalogenoacetylbenzenes was undertaken. These compounds had previously been prepared by Ruggli and Gassenmeier (*Helv. Chim. Acta*, 1939, **22**, 496) by direct halogenation of *p*-diacetylbenzene which was obtained by the sequence of reactions: *p*-xylene ⟶ terephthalic acid ⟶ terephthaloyl chloride ⟶ terephthalyldiacetoacetic ester ⟶ diacetylbenzene. The required compounds can be prepared more directly by the following route: terephthaloyl chloride ⟶ *p*-bisdiazoacetylbenzene ⟶ bishalogenoacetylbenzene.

p-*Bisdiazoacetylbenzene.* Terephthalic acid (3 g.), thionyl chloride (10 ml.), and pyridine (1 drop) were heated on a steam-bath for 3 hours. Dry benzene (30 ml.) was added, and the mixture was evaporated under reduced pressure. The chloride (2 g.), m. p. 82—84°, crystallised from light petroleum (b. p. 60—80°). Terephthaloyl chloride (1·5 g.) dissolved in dry ether (50 ml.) was gradually added to an ice-cooled ethereal (200 ml.) solution of diazomethane [from nitrosomethylurea (5 g.)]. Next day, the dense yellow precipitate (2 g.) was collected and recrystallised from benzene. It formed short needles, decomp. >370° when slowly heated but melting with decomp. when placed in a bath at 200°

(Found : C, 56·4; H, 3·2. $C_{10}H_6O_2N_4$ requires C, 56·1; H, 2·8%. The *diazo*-compound is difficult to analyse since it explodes on heating).

p-*Bishalogenoacetylbenzenes*. (*a*) The diazo-ketone (1 g.) was suspended in ether (50 ml.) and treated with concentrated hydrochloric acid (0·5 ml.). After the evolution of nitrogen had subsided the chloroacetyl compound separated. It formed needles, m. p. 186°, from methanol (Ruggli and Gassenmeier, *loc. cit.*, give m. p. 153°) (Found : C, 52·0; H, 3·6. Calc. for $C_{10}H_8O_2Cl_2$ : C, 52·0; H, 3·5%). (*b*) *p*-Bisbromoacetylbenzene, prepared similarly, formed prismatic needles, m. p. 176—177°, from methanol (Ruggli and Gassenmeier, *loc. cit.*, give m. p. 173°). (*c*) The bromo-ketone (500 mg.) and sodium iodide (500 mg.) in acetone (10 ml.) were warmed on a steam-bath for 10 minutes. The iodo-compound which separated on adding water gave needles, m. p. 135°, from aqueous methanol (Ruggli and Gassenmeier, *loc. cit.*, give m. p. 135°).

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