ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ANALYTICAL

Ascorbic Acid, Perinaphthindanetrione Hydrate Assay of. M. S. el Ridi, R. Moubasher and Z. Hassan. (*Science*, 1950, **112**, 751.) The reaction of perinaphthindanetrione hydrate with ascorbic acid to form the reddish colour of dihydroxy-perinaphthindone was found to be in good agreement with Beer's law and was used to determine ascorbic acid in solution. The amount of the reduction product produced was estimated from the intensity of absorption at 475 mμ, advantage being taken of the fact that the excess of the reagent, which should always be present, does not absorb at this region of the spectrum. In the actual determination 5 ml. of a solution of ascorbic acid in ethanol (11 mg./100 ml.) was added to 1 ml. of perinaphthindanetrione hydrate in ethanol (2 mg./ml.); the resulting mixture, kept in a stoppered vessel, gradually developed colour and reached maximum intensity after 10 minutes; the stability of the colour permitted measurement at any time from 10 minutes to 24 hours after mixing. For pure dihydroxy-perinaphthindone two bands were exhibited having $E_{1\text{ cm.}}^{1\text{ per cent.}}$ 345 mμ = 525, and $E_{1\text{ cm.}}^{1\text{ per cent.}}$ 475 mμ = 150. Among other biological substances, glucose, fructose, alanine, leucine, isoleucine, phenylalanine, lactic acid, acetoacetic acid, pyruvic acid, urea, uric acid, acetone and dehydroascorbic acid were examined and did not interfere under the conditions given for the reaction. R. E. S.

Calcium, Colorimetric Determination of, with Murexide. H. Ostertag and E. Rinck. (*C.R. Acad. Sci., Paris*, 1950, **231**, 1304.) An aqueous solution of murexide has a violet colour which is turned to a yellowish-red by calcium ions. The reaction is best carried out at *p*H 6, the absorption of the solution being determined between 500 and 550 mμ. The presence of magnesium first decreases the sensitivity, but after the ratio of magnesium to calcium reaches 40, further addition of magnesium produces no more reduction in colour. Thus it is possible to determine calcium in presence of any quantity of magnesium, if interference by the latter is prevented by the addition of a sufficient quantity of magnesium nitrate. Using a 10 cm. cell, quantities of calcium ranging from 0·1 to 1 mg. may be determined with an accuracy of 1 per cent. G. M.

Procaine penicillate, Assay of. M. I. Bessot. (*Ann. pharm. franc.*, 1950, **8**, 520.) A quantity of material, containing 20 to 50 mg. of base, is dissolved in 50 ml. of phosphate buffer (*p*H7), and precipitated with 4 ml. of 10 per cent. solution of silicotungstic acid, added in small portions. After standing for a few minutes, the precipitate is filtered off on a layer of asbestos, washed with water, dried and weighed; 4·046 g. of the precipitate is equivalent to 1 g. of procaine base. Alternatively, the mixture may be made up to 100 ml. and one aliquot used for the iodimetric determination of penicillic acid after filtration. G. M.

Thiosemicarbazide as a Reagent for the Identification of Aldehydes, Ketones, and Quinones. P. P. T. Sah and T. C. Daniels. (*Rec. Trav.*

Chim., Pays-Bas, 1950, **69,** 1545.) A series of 118 thiosemicarbazones of aldehydes, ketones and quinones were prepared and characterised, and those physical properties of value for the identification of the corresponding carbonyl compound were recorded. The thiosemicarbazones were in general highly active agents against the growth *in vitro* of *M. tuberculosis,* the degree of activity depending on (1) the presence of the thiosemicarbazide group in the molecule, (2) the position of the carbonyl group, (3) the nature of the chain (aliphatic, aromatic, alicyclic, or quinone), (4) the nature of the substituted group on the benzene ring, and (5) the orientation of the substituted group on the aromatic nucleus. A number of thiosemicarbazones derived from 4-methoxy-3-methyl-propiophenone, meta-hydroxybenzaldehyde, 2-hydroxy-1-naphthaldehyde, 2-acetyl-naphthalene, citral, and para-phenyl-acetophenone were found to cause complete inhibition of growth of *M. tuberculosis* H37 Rv from 14 to 21 days in a concentration of 0·002 mg./10 ml. R. E. S.

Sulphate, Volumetric Determination of. J. R. Munger, R. W. Nippler and R. S. Ingols. (*Anal. Chem.,* 1950, **22,** 1455.) The disodium salt of ethylenediaminetetraacetatic acid can be used for determining the concentration of barium ions using Eriochromeschwarz T, as the indicator. In order to determine sulphate in a solution, a known excess of barium chloride solution is added and the excess of barium ion is then determined. Since the barium is in excess, complete precipitation of barium sulphate is brought about even at very low sulphate concentrations and it is unnecessary to remove the precipitate of barium sulphate before titrating the excess barium ion; the value of the combined calcium and magnesium ion concentrations is required for calculating the sulphate ion concentration. Details of the methods used, particularly those for obtaining satisfactory end-points, are given. A number of waters with known sulphate ion concentrations were prepared and analysed using the technique described; the results were compared with the theoretical values and agreed to within approximately 1 per cent. at the higher concentrations used. In order to use the method in the presence of copper, manganese, cobalt, and nickel ions, the modifications given by Diehl, Goetz, and Hach (*J. Amer. Water Works Ass.,* 1950, **42,** 40) for total hardness must be used; for concentrations of copper up to 10 p.p.m. the method of Betz and Noll (*J. Amer. Water Works Ass.* 1950, **42,** 49) using a different buffer system is used; manganese up to 2 p.p.m. does not interfere with the accuracy of the test, although it does change the colour of the indicator when sufficient is used. R. E. S.

ESSENTIAL OILS

Cinnamon Bark Oil, Seychelles. H. T. Islip and W. S. A. Matthews. (*Colon. Plant Anim. Prod.,* 1950, **1,** 119.) As the result of work conducted at the Imperial Institute and published in 1946, when it was found that this bark would not yield an oil of B.P. characters, the Director of Agriculture, Seychelles, sent further samples. A. From trees five years old. B., eighteen months old. C., nine months old. The volatile oil content was much below the minimum of 1·0 per cent. specified in the B.P. There were no major differences in composition of the oils from bark of different ages. The eugenol content of the oils was considerably lower than that of Ceylon oil. It is suggested that bark from authentic material of Ceylon origin grown in

the Seychelles should provide useful information. The characters of the oils were as follows.

Sample	Yield per cent.	Wt. per mil	$\alpha_D^{20°C}$	$n_D^{20°C}$	Cinnamic aldehyde per cent.	Solubility in alcohol 70 per cent. 15·5°C.	Phenols per cent.
A	0·365	0·9987	−2·12°	1·5759	68·1	Insoluble	4·0
B	0·335	0·9916	−2·72°	1·5685	63·0	in	3·4
C	0·295	0·9955	−2·56°	1·5712	64·9	10 vol.	4·4
B.P. 1948	Not less than 1·0	0·994 to 1·034	0° to −2°	1·565 to 1·582	50—65	Soluble in 3 volumes with not more than slight opaiescence	—

G. R. A. S.

Geranium Oil, Tanganyika. E. Brown, H. T. Islip, F. Major and W. S. A. Matthews. (*Colon. Plant Anim. Prod.*, 1950, **1**, 109.) Two samples, nos. 1 and 2, were distilled from leaves and stalks of *Pelargonium capitatum* and a third from a different species (not stated). All the samples were superior in odour to any Tanganyika oils previously examined at the Imperial Institute and were comparable with French colonial oils. Sample 1 had a high ester value, equivalent to 35·5 per cent. of geranyl tiglate. The characters were as follows.

	Sample 1	Sample 2	Sample 3
$d_{15·5°C.}^{15·5°C.}$	0·8944	0·8939	0·9079
$\alpha_D^{20°C.}$	−8°	−8·26°	−13·1°
$n_D^{20°C.}$	1·4631	1·4660	1·4740
Acid value	7·4	5·7	6·0
Ester value	84·3	77·5	69·6
equivalent to geranyl tiglate, per cent. ...	35·5	32·6	29·3
Ester value after acetylation	—	220·6	223·5
equivalent to geraniol, per cent.	—	72·7	73·8
Solubility in 70 per cent. alcohol at 15·5°C. ...	In 3·3 vol.	Not sol. in 10 vol.	Not sol. in 10 vol.
Solubility in 80 per cent. alcohol at 15·5°C. ...	—	Sol. in 0·7 vol. sl. opalescence in more	—

G. R. A. S.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Adrenochrome and its Derivatives. J. Harley-Mason. (*J. chem. Soc.*, 1950, 1276). The preparation of solutions of adrenochrome is discussed and the use of buffered solutions of sodium persulphate for the oxidation of adrenaline to adrenochrome is described. Hydrogenation of adrenochrome over palladium-charcoal gave rise to 5:6-dihydroxy-1-methylindole (I) and a second product $C_9H_{11}O_4N$ which on intensive drying lost a molecule of water to give 3:5:6-tri-hydroxy-1-methylindole(II). Similar

results were obtained with sodium dithionate as the reducing agent. It is suggested that these products are formed *via* the disproportionation of a common intermediate, a semi-quinone ion formed by the addition of one atom of hydrogen to adrenochrome. The mechanism of this reaction is discussed and the observation that reduction gives rise to stable optically active solutions (Green and Richter, *Biochem. J.* 1937, **31**, 596) has been confirmed in support of the proposed disproportionation mechanism. II is also obtained by the action of alkali on adrenochrome, is powerfully fluorescent and readily undergoes air oxidation in aqueous solution with loss of fluorescence to give 5 : 6 : 5 : 6′-tetrahydroxy-1 : 11-dimethylindigo. It is suggested that II is probably identical with the green fluorescent substance observed in the determination of adrenaline by the method of Gaddum and Schild (*J. Physiol.* 1934, **80**, 9p.). Formation of "adrenaline black" by oxidation of adrenaline takes place via adrenochrome, though the transformation from adrenochrome does not require further oxygen. Analysis of adrenaline black corresponds to a molecular formula $C_9H_9O_4N$, probably $C_9H_7O_3NH_2O$ or $C_9H_5O_2N_2$2HO. The structure of adrenaline black is discussed. From the reduction of 2-bromoadrenochrome only 2-bromo-5:6-dihydroxy-1-methylindole was isolated. J. B. S.

Penicillin; Phenyl Phenaceturate from Decomposition in Presence of Phenol. S. F. Kern, P. M. Terrill, M. M. Mann and R. G. Jones. (*Science*, 1950, **112**, 787.) Aqueous solutions of potassium penicillin G containing sodium citrate as buffer and phenol as preservative may be kept under refrigeration for relatively long periods without undergoing serious deterioration, but at temperatures of 25°C. or higher such solutions have been observed to deposit a colourless crystalline precipitate of phenyl phenaceturate. Identity with an authentic sample was established by chemical analysis, solubilities, melting-point, x-ray powder diagram and infrared absorption spectrum. The precipitate formed only in the presence of a buffer; in the absence of a buffer the solutions turned yellow on standing or warming. Potassium phosphate, as well as sodium citrate, was effective in promoting the formation of phenyl phenaceturate in solutions containing phenol and penicillin G. S. L. W.

Steroids, Paper Chromatography for Identification and Separation of. J. M. McMahon, R. B. Davis and G. Kalnitsky. (*Proc. Soc. exp. Biol., N.Y.*, 1950, **75**, 799.) Procedures using a filter paper chromatogram are described for the identification and separation on a micro-scale of the following steroids: cholesterol, ergosterol, 7-dehydrocholesterol, vitamin D_2 and vitamin D_3. For identification purposes, two methods can be used. In the first, the paper containing the spot is suspended 5 cm. above a bromine solution, either 0·25 per cent. in pyridine sulphate dibromide or 2 per cent. in chloroform or carbon tetrachloride, at 40°C., for 30 seconds. The paper is next sprayed with a saturated solution of potassium iodide in methanol and then with starch solution. The spot becomes dark blue, the surrounding area remaining colourless or becoming at most light blue. By this method 10μg. of cholesterol and even less of ergosterol can be detected. In the second method, which is more sensitive, the spot is sprayed with a 20 per cent. solution of antimony pentachloride in chloroform. Cholesterol gives a brown colour, darkening on standing; ergosterol and 7-dehydrocholesterol give a purplish-red colour changing to dark blue on standing; vitamins D_2 and D_3 develop a pink colour becoming brown on standing. With 5 microlitre spots, the amounts detectable are cholesterol 5 μg., ergo-

sterol 0·5 μg., 7-dehydrocholesterol 1 μg., vitamin D_2 2 μg., and vitamin D_3 3 μg. For separation, a wide variety of solvent mixtures was tried. Two were found to effect separation. A mixture of phenol 13·5 parts by volume, methanol 30 and water 56·5 (the proportion of phenol is highly critical) separated 7-dehydrocholesterol from cholesterol and ergosterol which were not affected. For the separation of 10 μg. quantities each of cholesterol, 7-dehydrocholesterol and vitamin D_3, the solvent used was a mixture of methanol 80, benzene 10, acid washed light petroleum (b.pt. 60° to 70°C.) 10. The circular filter paper containing the spot was placed over an evaporating dish containing the solvent, which in turn was placed in a similar dish containing ice water, the whole being covered by an inverted beaker. Antimony pentachloride in chloroform was used to identify the bands. In this procedure, the use of ice water is essential, since separation does not occur at 2°C., nor at room temperature. H. T. B.

Vaccine Lymph, Effects of Penicillin and Streptomycin on. V. N. Krishnamurthy. (*Brit. med. J.*, 1950, **2**, 1035.) Heavy bacterial contamination of vaccine lymph cannot be avoided in its preparation, especially in the tropics, and no method has yet been found consistently to give absolute sterility. The use of penicillin and streptomycin to reduce the contamination was therefore investigated. Earlier reports on the value of penicillin for this purpose have been favourable but the present author finds it disappointing and suggests that previous workers carried out sterility tests on lymph still containing penicillin. The addition of streptomycin to glycerinated lymph, the treated lymph being kept in cold storage for 1 week, resulted in a marked fall in the bacterial population. With a streptomycin concentration of 5000 μg./ml., the streptococcal colony was only 40 per ml. whereas untreated lymph gave a count of 240 million. Spores of *Bacillus subtilus* were inhibited but not killed. A combination of streptomycin 1000 μg./ml. and penicillin 1000 units per ml. gave even better results, the count being only 30 per ml. Vaccine pulp emulsified in water immediately after collection, treated with 5000 μg. of streptomycin per ml. and incubated at 37°C., contained only moulds after 24 hours, and even moulds were killed on increasing the concentration of streptomycin to 10,000 μg. per ml. The same result was obtained with 1000 μg. of streptomycin and 10,000 units of penicillin per ml. Application of both antibiotics to the vaccinated area of the calf twice daily for 5 days also gave good results. Neither of the antibiotics had any effect on the potency of the lymph during 6 months' contact and it is suggested that a combination of 500 μg. of streptomycin and 500 units of penicillin, which reduces the count to 200 organisms per ml., makes it possible to produce a purer lymph at a substantially lower cost. H. T. B.

BIOCHEMICAL ANALYSIS

Aneurine, Determination of. H. N. Ridyard. (*Analyst*, 1950, **75**, 634.) A detailed analysis has been made of the various factors affecting the recovery of known amounts of aneurine added to extracts. The fluorimetric method used was considered in four stages, namely, (1) extraction of the aneurine from the raw material either by steeping in acidified water, or by heating with dilute acid to boiling-point, adjusting to *p*H 4·5 and digesting with takadiastase or other source of phosphatase according as aneurine pyrophosphate (co-carboxylase) is absent or present, (2) oxidation of the aneurine to thiochrome with alkaline ferricyanide, a process said to be

only about 70 per cent. efficient, (3) extraction of the thiochrome by means of *iso*butanol, (4) fluorimetric examination of this extract. The factors studied in detail included the method of addition of the aneurine; the use of base exchange methods in purification; the errors involved in the oxidation stage; the *iso*butanol extraction stage; the effect of light absorption by substances other than thiochrome; and the effect of quenching. It was found that the addition of pure aneurine to extracts was a valuable method, but neither recovery of added aneurine nor consistency of results was an adequate measure of the agreement of a result with the amount of aneurine actually present in the sample. Factors affecting recovery of added aneurine were not linearly related to the total concentration of aneurine present in an extract, but deviations from linearity were small owing to the very low concentrations under consideration; nevertheless, in bran and probably other materials, part of each deviation appeared to be proportional to the square of the aneurine concentration. R. E. S.

Penicillin Mixtures, Paper Chromatographic Analysis of. P. B Baker, F. Dobson and A. J. P. Martin. (*Analyst*, 1950, **75**, 651.) A rapid method, requiring less than 8 hours for completion, has been developed for use as a routine procedure for estimating one or more species of penicillin in a mixture. The method is based on the fact that the relatively stable hydroxamic acid derivatives of the various penicillins show different partition coefficients between *iso*propyl ether-*iso*propanol and phthalate buffer at a given *p*H and can be separated by paper chromatographic procedures. Details of these procedures are given so that satisfactory results can be obtained with the volatile solvents used. A qualitative result was obtained by developing the chromatograms with dilute ferric chloride solution; a quantitative result could be attained by extracting the iron complexes of the various hydroxamic acids with butanol, measuring the light absorption of the resulting extract in a colorimeter, and reading the penicillin concentration from standard curves. The R_F values of hydroxamic acids from various penicillins were *n*-heptyl (K), 0·57; *n*-amyl (D), 0·27; pent-2-enyl (F), 0·20; benzyl (G), 0·13; *p*-hydroxybenzyl (X), 0·01. Results are given for the analysis of control mixtures containing several penicillins. R. E. S.

Proteins, Determination of, by Biuret Reaction. J. P. Dustin (*Bull. Soc. Chim. biol.*, 1950, **32**, 696.) The colour given by a protein in the biuret reaction depends on the concentration of copper. The optimum proportion of copper to protein is between 1 and 1·5, giving a violet colour, since in this range the intensity of colour is greatest, and it is less sensitive to variations in the ratio. The reagent used is prepared by dissolving 1·50 g. of crystalline copper sulphate and 6·0 g. of sodium potassium tartrate in about 500 ml. of water, adding 300 ml. of 10 per cent. sodium hydroxide (free from carbonate), cooling, and making up to 1 l. Although the absorption curves obtained from a number of proteins appeared to show maxima at different wave lengths, if a correction was applied for the absorption of the reagent itself, all the maxima were at 545 mμ. In some cases turbidity appears, especially when the concentration of alkali or protein is high or the reagent is old. It is therefore desirable in such cases to reduce the time allowed for development of the colour. A suitable concentration for the protein solution is 5 to 10 g./l. G. M.

Streptomycin and Dihydrostreptomycin, Volumetric Determination of. R. Delaby and F. Stephan. (*Ann. pharm. franc.* 1950, **8**, 513.) From

70 to 100 mg. of streptomycin, dissolved in 15 ml. of water, is treated with 15 ml. of Nessler's solution and 1 ml. of 10 per cent. solution of potassium iodide for 30 minutes at 20° to 25°C. After dilution with 20 ml. of water, the flask is placed in cold water and the contents are neutralised with hydrochloric acid, 1 ml. being then added in excess; 15 ml. of 0·1N iodine solution is added and, after solution is complete, the excess of iodine is titrated with 0·05 N sodium thiosulphate. 1 ml. of the thiosulphate is equivalent to 0·0187 g. of streptomycin calcium chloride. Dihydrostreptomycin does not interfere with this determination. For the determination of streptomycin and dihydrostreptomycin, 40 to 70 mg. in 10 ml. of water is treated with 50 ml. of 0·95 N potassium periodate solution. The oxidation is carried out at 45° to 50°C. for 1 hour. After cooling, 1 g. of sodium bicarbonate is added, followed by excess (30 to 35 ml.) of 0·1N potassium arsenite dissolved in 4 per cent. sodium bicarbonate solution, and 1 ml. of 10 per cent. solution of potassium iodide. After 20 minutes, the excess of arsenite is titrated back with 0·1N iodine. 1 ml. of the latter is equivalent to 0·004871 g. of dihydrostreptomycin as sulphate, or 0·00462 g. as hydrochloride, or 0·004983 g. of streptomycin as calcium chloride compound.

G. M.

CHEMOTHERAPY

Aliphatic Diamines. Structure and Amœbicidal Activity. D. M. Hall, S. Mahboob and E. E. Turner. (*J. chem. Soc.*, 1950, 1842.) A study has been made of long-chain diamines containing two primary amino groups and having the general formula $H_2N.CHR.(CH_2)_n.CHR.NH_2$. *In vitro* activities against *Entamœba histolytica* as high as 1 in 100,000 have been found within this series, the most active compounds are, 6:10-diaminopentadecane, 7:11-diaminoheptadecane, 7:12-diaminooctadecane and 7:11-diamino-5:13-heptadecane. Simple polymethylenediamines of low molecular weight (R = H, n = 1 or 2) are inactive. Introduction of alkyl groups (R) having 4, 5, 6 or 8 carbon atoms gives rise to active compounds when n = 3, but when n = 4 or 5 the distherapeutic effect of increasing molecular weight becomes apparent. In general, straight chain diamines are more active than the corresponding branched chain compounds. All the compounds in this series were obtained by the reaction sequence: $R\ CH(COOEt)_2 \rightarrow (COOEt)_2CR.(CH_2)_n.CR.(COOEt)_2 \rightarrow HOOC.CHR.(CH_2)_n\ CHR.COOH \rightarrow H_2N\ CHR.(CH_2)_n.CHR.NH_2$.

J. B. S.

α-Alkylglutaric Acids and their Derivatives as Antibacterial Agents. J. C. Roberts and B. Shaw. (*J. chem. Soc.*, 1950, 2842.) The method of Auwers and Titherley (*Liebig's Ann.*, 1896, **292**, 209) for the preparation of the lower α-alkylglutaric acids by simultaneous hydrolysis and decarboxylation of the appropriate triethylalkane-1:1:3-tricarboxylate with strong mineral acid was found to be inapplicable to the higher numbers of the series. The required alkane-1:1:3-tricarboxylate, prepared from an alkyl ester and β-iodopropionic ester was hydrolysed with alcoholic potassium hydroxide, the tricarboxylic acid isolated and decarboxylated at 180° to 195°C. Cyclic anhydrides could not be prepared by heating α-alkylglutaric acids, though loss of water occurred with the probable formation of linear anhydrides. Cyclic anhydrides were readily formed by reaction with acetic anhydride and treatment of these anhydrides is an organic solvent with primary amines gave rise to mixtures of *N*-substituted glutaramic acids, $COOH.CH_2CH_2CHR\ CONHR'$ and $COOH\ CHR.CH_2CH_2CONHR'$. Separa-

tion of these compounds was only effected with difficulty. None of the compounds tested showed notable tuberculostatic activity. J. B. S.

Amidone Derivatives as Analgesics. P. Ofner and E. Walton, A. F. Green and A. C. White. (*J. chem. Soc.*, 1950, 2158.) Compounds, in which the dimethylamino groups of amidone ($(CH_3)_2N.CHCH_3.CH_2.CPh_2.COC_2H_5$) and of isoamidone ($(CH_3)_2N.CH_2.CHCH_3.CPh_2.COC_2H_5$) have been replaced by piperidino and diethylamino groups, were prepared, along with a number of related ketones and ketimines. Unlike the original amidone series, the halides of the precursor nitriles of the piperidino and diethylamino analogues of isomidone were more readily isolated than the corresponding analogues of amidone nitrile. Ultra-violet absorption curves of amidone, isoamidone, and the piperidino analogues of these compounds, were recorded. The structure of these new ketones was determined by established methods. Dibasic compounds, ($(CH_3)_2N.CHCH_3.CH_2.CPh_2.CH_2.NH_2$) and ($(CH_3)_2N.CH_2.CHCH_3.CPh_2.CH_2.NH_2$), were prepared by the reduction of the corresponding nitriles, but neither they nor their acetyl derivatives showed appreciable analgesic activity. A number of compounds of type $C_5H_{10} > N.CH_2.CH_2.CH_2.CPh_2.R$ and $Et_2N.CH_2.CH_2.CPh_2R$ where R = CN, COMe, COEt, etc., were also prepared. Tests of analgesic activity showed:—(a) methyl branching in the basic side-chain, particularly in the β-position to the quaternary carbon atom, is an important factor in the development of analgesic activity; (b) small variations in the basic group have a relatively minor effect; (c) propionyl derivatives show maximal activity; (d) the ketimines are inactive. A. H. B.

Analogues of DDT as Insecticides. E. J. Skerrett and D. Woodcock. (*J. chem. Soc.*, 1950, 2718.) A series of compounds isosteric with DDT has been prepared in which the chlorine atoms have been replaced by methyl groups and of general formula I [$RC_6H_4CH.CMe_3$) CHR'] I (R=R'=Cl) could not be obtained by the condensation of 1-*p*-chlorophenyl-2:2-dimethylpropan-1-ol with chlorobenzene in the presence of sulphuric acid or oleum. Reaction of *p*-chlorophenylmagnesium bromide with methyl trimethylacetate gave 1:1-di-*p*-chlorophenyl-2:2-dimethylpropan-1-ol which was reduced to the required compound. The pentamethyl analogue of DDT I (R=R'=Me) was obtained by a similar route. Reaction of *p*-chlorophenyl-1:1-dimethylethyl ketone with *p*-tolylmagnesium bromide and subsequent reduction of the resulting carbinol gave rise to the unsymmetrical isostere I (R=Cl, R'=CH_3). The attempted preparation of $CMeCl_2.CH(C_6H_4Cl)_2$ is reported; treatment of 1:1-di-*p*-chlorophenylacetone with PCl_5 over a wide range of reaction temperatures gave only $CRMe{=}C(C_6H_4Cl)_2$ as the main product. The corresponding monochloro analogue $CHMeCl.CH(C_6H_4Cl)_2$ was readily obtained by the condensation of ethyl di-*p*-chlorophenylacetate with methylmagnesium iodide and treatment of the resulting carbinol with PCl_5 at room temperature. The compound $CH(CHMe_2)(C_6H_4Cl)_2$ is also reported. None of the DDT analogues was active when tested as contact insecticides against *Calendra granaria*. J. B. S.

PHARMACY

DISPENSING

Morphine Injection, Stability of. M. P. Girard. (*Ann. pharm. franc.*, 1950, **8**, 571.) Deteriorated solutions of morphine contain oxydimorphine in addition to coloured oxidation products. Both of these can be eliminated

by passing the solution through a column of alumina, and eluting the column with alcohol (90 per cent.). Morphine is then determined in this solution, using the reaction of Guarino. Oxydimorphine may be detected in the original solution by the reaction of Leulier and Drevon (*Bull Soc. chim. biol.* 1932, **14,** 521.) The results of tests carried out on ampoules of morphine injection showed that, in spite of a *p*H from 2 to 2·3, deterioration was rapid, but could be prevented by the addition of sodium bisulphite equivalent to 0·05 per cent. of SO_2. Even after 15 years' storage such solutions showed no change in morphine content, when made with pure morphine. The only case in which the results were not altogether satisfactory was one in which a somewhat discoloured morphine had been used. G. M.

Testosterone Propionate, Sterilisation of Oily Solutions of. E. Diding, N. Å Diding and A. Elmqvist. (*Svensk farm. Tidskr.*, 1951, **55,** 1.) Solutions of testosterone propionate in oil were sterilised and tested biologically, and also assayed chemically by means of 2:4-dinitrophenylhydrazine. The melting points of recovered material were also determined. The results showed that there was no deterioration or inactivation of the testosterone propionate after heating for 12 hours at 140° to 150°C.

G. M.

NOTES AND FORMULÆ

***p*-Aminosalicylic Acid.** (*New and Nonofficial Remedies: J. Amer. med. Ass.*, 1950, **144,** 760.) *p*-Aminosalicylic acid is 4-amino-2-hydroxybenzoic acid, $C_7H_7O_3N$. It occurs as a white or nearly white bulky powder, which is odourless or has a slight acetous odour, m.pt. 135° to 140°C. with decomposition; soluble in water (1 in 500 at 25°C.) and in alcohol (1 in 21 at 25°C.). A saturated aqueous solution has *p*H 3·2 to 3·7. A 10 per cent. solution in water containing 10 per cent. of sodium bicarbonate is clear and not more than faintly yellow. When *p*-aminosalicylic acid is heated at 145°C., it loses carbon dioxide and yields *m*-aminophenol, which, after recrystallisation from toluene, melts at about 12°C. The diacetyl derivative, obtained by heating *p*-aminosalicylic acid with acetic anhydride and purified by re-crystallisation from benzene and alcohol, melts at about 191°C. A 0·0005 per cent. solution prepared as directed in the assay exhibits ultraviolet absorption maxima at about 2650 Å ($E\,^{1\ \text{per cent.}}_{1\ \text{cm.}}$, 856) and 2990 Å, and minima at 2440 and 2850 Å; the ratio of the optical densities at 2650 and 2990 Å is 1·50 to 1·56. *p*-Aminosalicylic acid contains not more than 30 p.p.m. of heavy metals, loses not more than 0·5 per cent. in weight when dried over phosphorus pentoxide for 5 hours and yields not more than 0·5 per cent. of sulphated ash. It is assayed by measuring the optical density at 2650 Å of a 0·0005 per cent. solution in phosphate buffer, and dividing by 85·6 to obtain mg./ml. It contains 96 to 102 per cent. of *p*-aminosalicylic acid. It is used either alone or in conjunction with the streptomycins in the treatment of tubercular infections. The recommended daily dose is 12(8 to 16)g., by mouth in 4 or more doses. G. R. K.

Sodium Psylliate (Sylnasol). (*New and Nonofficial Remedies: J. Amer. med. Ass.*, 1950, **144,** 760.) Sodium psylliate is a mixture of the sodium salts of the liquid fatty acids obtained by saponification of the vegetable oil of the seeds of ispaghula (*Plantago ovata* Forskal). The fatty acids occur as a moderately viscous, amber to brown liquid with an oily odour, sp. gr., 0·925 to 0·930, iodine value, 130 to 180, acid value, 130 to 180. When 1 drop is treated with 1 ml. of chloroform and 1 drop of sulphuric acid,

a red to brown red colour develops. Sodium psylliate is prepared by dissolving the fatty acids in dilute sodium hydroxide. It is not separated and is usually administered as a 5 per cent. solution containing 2 per cent. of benzyl alcohol. Such solutions vary in colour from light amber to yellow, have a soap-like odour and are slippery to the touch. They foam readily on shaking, have *p*H 8·7 to 9·2, and are assayed by warming with hydrochloric acid in a water-bath, centrifuging and reading the volume of liberated fatty acids; the percentage of sodium psylliate is obtained from the formula: (reading × 1·25) − 0·2, where the factor 0·2 compensates for the benzyl alcohol. Sodium psylliate is used as a sclerosing agent. G. R. K.

PHARMACOGNOSY

Agar, Baltic. K. Förster. (*Pharm. Zentralh.*, 1950, **89**, 409.) Satisfactory agar can be made from algae growing in the Baltic Sea, but attempts to develop the production on a commercial scale have failed as the raw material does not grow with sufficient density to render its harvesting profitable. The author suggests the possibility of growing the algae in artificial basins, suitably manured. G. M.

Colchicum Seeds, Colchicine Content of, at Different Stages. J. Buchníček. (*Pharm. Acta Helvet.* 1950, **25**, 389.) The results of an examination of the seeds of *Colchicum autumnale* at different stages of ripening are summarised in the table.

Date	Character of		Seeds				
	Capsule	Seeds	Fruit	Dry Weight	Ash on Dry Weight	Colchicine on Dry Weight	Colchicine on Fresh Weight
			per cent.	per cent.	per cent.	per cent.	per cent.
May 19	Green	Small, soft	13·4	13·5	2·90	1·44	0·24
„ 26	—	Larger	18·0	15·4	2·80	1·33	0·25
June 2	—	Harder	23·0	18·8	2·61	1·28	0·27
„ 9	—	Large and hard	28·2	22·9	2·42	0·97	0·26
„ 16	—	—	33·8	28·9	2·23	0·90	0·29
„ 23	Dry, brown	Smaller, hard	42·5	33·1	2·36	0·81	0·31
„ 30	Slightly open	—	50·0	44·5	2·57	0·76	0·38
July 7	Open	Fully ripe	45·8	57·3	2·49	0·81	0·52

The colchicine was determined polarographically, after removal of ballast substances by precipitation with lead acetate. Although the colchicine content shows an apparent decrease, when calculated on the dry weight of the seeds, actually the total amount of colchicine increases steadily during the ripening. For maximum content, good ripening of the seeds is essential, and comparatively small differences in date of collection may make a large difference. G. M.

Stramonium Seeds, Fluorescence of. M. Kucera. (*Ann. pharm. franc.*, 1950, **8**, 564.) When dry, stramonium seeds show merely a whitish fluorescence in the neighbourhood of the hilum. When the seeds are immersed in water, with the seed coat removed, the albumen shows an intense fluorescence while zones of yellowish-green fluorescence appear at the surface of the water. Examination under glycerin shows that the fluorescence is

localised in the outer part of the albumen. In alkaline solution the colour of the fluorescence is golden yellow; and in acid bluish. Actually two fluorescent substances are present and may be separated by chromotography. One, giving a yellow colour, is destroyed by heating; the other, giving a blue fluorescence, is more stable. G. M.

PHARMACOLOGY AND THERAPEUTICS

Adrenochrome Derivative to Shorten Bleeding Time. H. Sobotka and N. Adelman. (*Proc. Soc. exp. Biol., N.Y.*, 1950, **75**, 789.) The trimethylammonium acethydrazone hydrochloride of L-adrenochrome (T.A.L.), one of a series of highly water-soluble derivatives, was used to observe whether chemical modification would impair the hæmostatic effect of the parent substance. The material was mixed with 4 per cent. of its weight of anhydrous disodium phosphate and stored in doses of 10 mg. in sterile ampoules. The contents were dissolved in sterile water immediately before use, giving a solution of *p*H 6·5. After preliminary tests had shown that the compound was safe to use, a group of 50 consecutively admitted children between the ages of 2 and 16, undergoing tonsillectomy and adenoidectomy, were studied. Two-thirds of the subjects received intramuscular injections of 10 mg. dissolved in 1 ml. of water immediately before operation, the remaining members of the group serving as controls. The bleeding times were measured by Ivy's method before injection and after recovery from anæsthesia. The injection shortened the bleeding time by an average of 38 per cent. in 32 subjects. 6 patients showed no response and in one the bleeding time was lengthened. Except for the 7 non-responsive cases who had an average pre-injection bleeding time of 141 seconds, as compared with 4 minutes in the responsive cases, the mean bleeding time in the remaining 25 cases was halved. It appears that only individuals with a short natural bleeding time fail to respond. H. T. B.

Chloramphenicol in Typhoid Fever. G. P. Wiedman and S. S. Paley. (*Amer. J. med. Sci.*, 1950, **220**, 389.) Two adult patients suffering from acute typhoid fever were treated with chloramphenicol, the treatment being started on the 11th and 14th day respectively of the disease. In each case there was a rapid and dramatic response, the fever subsiding by lysis in from 3 to 4 days. The initial dosage given to each patient was 2·5 g. followed by 0.25 g. every 2 hours until fever disappeared. The interval between doses was then decreased to 3 to 4 hours, and maintained for a total duration of 2 weeks. Stool culture for *Escherichia typhosa* remained positive for 6 days after commencement of chloramphenicol treatment in one case; in the other case, blood and stool cultures were negative at the time treatment began. No toxic reactions were noted in either case and both patients made an uneventful recovery. H. T. B.

Digitalis purpurea.* A Comparison with. *D. Lanata A Elmqvist, J. Karnell and H. Rydin. (*Acta Pharmacol Toxicol.*, 1950, **6**, 319.) Experimental and clinical comparisons were undertaken with powdered leaves. When administered parenterally in animals the effect of lanata drugs was shown to be from 2 to 4 times that of purpurea drugs, but administered orally to humans and mice one sample of lanata drug was equivalent to the same amount of purpurea drug while another was stronger. The authors conclude that whereas with purpurea preparations biological assays on animals

may serve as a basis for therapeutic dosage, the clinical activity of lanata leaves cannot with certainty be estimated by such assays using another lanata preparation as standard, even if the standard preparation has been tested both clinically and experimentally. Since every lanata preparation must therefore be tested not only biologically but clinically there would appear to be no valid reason why lanata preparations should be employed therapeutically for oral administration especially as they have no therapeutic superiority over purpurea preparations. S. L. W.

Procaine with Hyaluronidase as Local Anæsthetic. J. N. Thorpe. (*Lancet*, 1951, **260**, 210.) While local infiltration anæsthesia is the method of choice in reducing Colles's fracture and similar injuries, it suffers from the disadvantage that satisfactory anæsthesia is not attained until the anæsthetic agent has diffused into the tissues surrounding the fracture, which may take a quarter of an hour or more. This difficulty can be overcome by adding hyaluronidase to the injection to promote diffusion. For Colles's fracture the anæsthetic suggested is 20 ml. of 1 per cent. procaine hydrochloride solution to which is added 1000 " Benger units " of hyaluronidase. Two injections are made, the bulk of the solution being injected into the fracture hæmatoma and 2 to 3 ml. being infiltrated around the ulnar styloid process. Diffusion of the solution is rapid and the fracture can be manipulated as soon as the needle is removed. The fracture area remains pain-free for more than an hour. H. T. B.

Streptomycin; Enhancement of Action. R. J. W. Rees and J. M. Robson. (*Science*, 1950, **112**, 790.) Controlled experiments were conducted on rabbits and mice with tuberculous corneal lesions to compare the effect of (1) streptomycin and potassium iodide, (2) streptomycin alone, (3) potassium iodide alone. The enhancement of the action of streptomycin by potassium iodide, though not marked, was most definite in established caseous tuberculosis and became more evident only after prolonged treatment. The effect in very early lesions was much less definite. An experiment on mice using a combination of potassium iodide and *p*-aminosalicylic acid (2 per cent. in the diet) showed no enhancement of the effect of *p*-aminosalicylic acid. Further controlled experiments were conducted on mice infected intracorneally to compare the effect of (1) streptomycin *p*-aminosalicylate compound, (2) streptomycin alone, (3) *p*-aminosalicylic acid alone. All three produced a beneficial effect; streptomycin *p*-aminosalicylate was the least effective. S. L. W.

Vitamin B_1, Effect of, on Activity of Procaine. M. A. Quevauviller and J. Panouse-Perrin. (*Ann. pharm. franc.*, 1950, **8**, 533.) Vitamin B_1 increases the action of procaine not only on direct application to the nerves, but also when applied to the nerve endings, the action at first increasing with the amount of aneurine, then decreasing. The effect is not a potentiation but rather an exaltation of the action by a substance which is itself not anæsthetic. When injected parenterally with procaine, vitamin B_1 increases the broncho-dilatory action, as is shown by the delay in the appearance of histamin bronchospasm in the guinea-pig. G. M.