ABSTRACTS OF PAPERS PUBLISHED IN OTHER JOURNALS

CHEMISTRY

ALKALOIDS

Alkaloids, Paper Chromatography of. J. E. Carless and H. B. Woodhead. (*Nature, Lond.*, 1951, **168**, 203.) Buffered filter paper was used for the separation of the strongly basic solanaceous alkaloids, and the feebly basic water-insoluble alkaloids of ergot. In the case of solanaceous alkaloids, separation of atropine and hyoscine occurs, and buffers of *p*H 5 to 9 were used, a weak solution of iodine in potassium iodide and water being used to detect the alkaloid on the paper. Graphical representations of separations obtained at various *p*H values of a mixture of apoatropine, methyl nitroatropine, atropine and hyoscine are given. Similar separations can be made of brucine and strychnine; morphine, narcotine, cocaine and the quinine alkaloids give spots of varying R_F, using butanol and buffered paper. By the use of buffered filter papers over the range *p*H 2·2 to 6, varying degrees of separation of the water-insoluble alkaloids of ergot have been carried out, the most satisfactory solvent being diethyl ether saturated with water. Quantitative estimations by elution of the alkaloid were not satisfactory, recoveries varying from 75 to 88 per cent. using 15 to 40 μg. of ergotoxine. No resolution of ergotoxine into ergocristine, ergocornine or ergokryptine was observed in the systems used. By the use of variations in *p*H and different solvents, very complex mixtures of alkaloids should be separable provided that partition coefficients and/or the *p*H's differ. R. E. S.

Brucine, a New Reduction Product of. S. P. Findlay. (*J. Amer. chem. Soc.*, 1951, **73**, 3008.) In the hope of obtaining brucidine, brucine was treated with lithium aluminium hydride. A new product, m.pt. 188° to 189° C., containing two hydrogen atoms fewer than brucidine was obtained and named dehydrobrucidine. Brucine apparently behaves peculiarly in this reaction, because strychnine, α-colubrine, β-colubrine and dihydrobrucine are reduced in the expected manner by lithium aluminium hydride. The identity of the ring structure of the colubrines with that of strychnine and brucine is established because, like strychnidine and brucidine, α- and β-colubridine are oxidised by chromic acid to diketonucidine. A. H. B.

Cinchona Alkaloids, Optical Isomers of. P. Baranger and R. Maréchal. (*C.R. Acad. Sci. Paris*, 1951, **233**, 550.) Quinine and quinidine can be separated into optical isomers by chromatography, cinchonine and cinchonidine cannot. The alkaloids were purified in the normal way by hot recrystallisation of the sulphates or bases, and these are called A in the table below. Aqueous solutions were made by adding a concentrated alcoholic solution to a large volume of water, double-distilled in glass. The concentration was about 0·04 per cent. The *p*H was adjusted to 11 with ammonia, and the chromatographic material used was resublimed and powdered paradichlorbenzene. The adsorbed base was washed out by N hydrochloric acid, whence it was reprecipitated by ammonia; this is called B. The non-adsorbed base was extracted with trichlorethylene, the base taken up by N hydrochloric acid and reprecipitated by ammonia; this is called C. B and C were obtained in equal proportions from quinine and quinidine, and had the following properties:

	M.p.	α 15° C. D	Solubility in water at 20° C.
Quinine A	172° C.	−284·3	0·061
Quinine B	166	−310	0·050
Quinine C	205	−258	0·035
Quinidine A ..	171	+334	0·056
Quinidine B ..	169	+310	0·042
Quinidine C ..	166	+354	0·022

Under the same conditions cinchonine and cinchonidine give 15 parts of B to 7 parts of C, but the rotation and m.pts. are the same as those of A. H. D.

Scopadonnine, a New Scopolamine Alkaloid. W. Kussner and H. W. Voightlander. (*Arch. Pharm. Berl.*, 1951, **284**, 197.) The new alkaloid is obtained by dimerisation of aposcopolamine by heating for several hours. It is thus comparable with the product (belladonnine) which has previously been obtained by dimerisation of apoatropine. The product has lost the unsaturated character of aposcopolamine, and is difficult to saponify. G. M.

ANALYTICAL

Acetylsalicylic Acid, Phenacetin, and Caffeine, and Combinations with Codeine or Thenylpyramine, Infra-red Analysis of. T. V. Parke, A. M. Ribley, E. E. Kennedy and W. W. Hilty. (*Anal. Chem.*, 1951, **23**, 953.) A method is described for the simultaneous determination, by infra-red spectrophotometry, of acetylsalicylic acid, phenacetin and caffeine in pharmaceutical products, even in the presence of codeine phosphate or thenylpyramine hydrochloride, and without separation. The method applies infra-red absorption in the 5 to 7 μ region to a solution made directly in chloroform, and relative freedom from mutual interference permits direct calculation of results. Diluents present in the tablets and powders analysed were shown to exhibit no interference in the 5 to 7 μ region. Codeine is determined by infra-red absorption at 10·62 μ following extraction into carbon disulphide. Thenylpyramine is determined by ultra-violet absorption. In mixtures of acetylsalicylic acid, phenacetin, caffeine and thenylpyramine hydrochloride, the average deviation of analyses of weighed samples was less than 2 per cent. for all components. About 1 hour per sample was required for the complete analysis of the above mixture, including all weighings, preparation of samples, and calculation of results. The method is suitable for routine control analysis of these mixtures. A. H. B.

Aspirin, Phenacetin, and Caffeine in Mixtures, Spectrophotometric Determination of. M. Jones and R. L. Thatcher. (*Anal. Chem.*, 1951, **23**, 957.) A simple, reliable control procedure for the assay of aspirin, phenacetin and caffeine in pharmaceutical products, based on the ultra-violet absorption of the three substances, is presented. Caffeine and phenacetin are determined together in chloroform solution after the removal of aspirin with sodium bicarbonate. The aspirin-sodium bicarbonate solution is acidified, and the aspirin extracted and determined spectrophotometrically in chloroform. The entire procedure can be completed in about 2 hours, and the precision is ± 2 per cent. for aspirin and phenacetin and ± 5 per cent. for caffeine. A. H. B.

Camphor in Spirit of Camphor, Determination of. A. Özger. (*Pharm. Acta Helvet.*, 1951, **26**, 177.) The method of the British Pharmacopœia for the determination of camphor gives results which are too low, owing to decomposition of the dinitrophenylhydrazone by heat on the evaporation of the alcohol.

In the U.S.P. method this heating is avoided and the results are more accurate. In the volumetric determination with hydroxylamine hydrochloride, choice of indicators is important, and the author recommends methyl orange for the first neutralisation, with phenol red or thymolphthalein for the titration. G. M.

Castor Oils, Determination of Acetyl Values of. J. P. Riley. (*Analyst*, 1951, **76**, 40.) In the present work a comparison has been made between the British Standards Institution (B.S.I. No. 684, 1950) and the Association of Official Agricultural Chemists methods for the determination of acetyl values, both of which depend on the determination of the saponification values of the oil and the acetylated oil. It has been found that both methods give very similar results, but it is suggested that where results of high accuracy are required the saponification values both of the oil and its acetyl compound should be the mean of at least 5 determinations. The accuracy of the B.S.I. method has been tested by using pure specimens of methyl ricinoleate and methyl 12-hydroxystearate; and it is concluded that with care results having an accuracy of ± 1 per cent. can be obtained. The acetyl value method, when applied to castor oils, does not give a true estimate of the amount of ricinoleo-glycerides present, since small amounts (about 0·6 per cent.) of 9 : 10-dihydroxystearo-glycerides are also estimated. The dihydroxystearic acid may be determined with sufficient accuracy by crystallisation of the mixed fatty acids of the oil, after removal of unsaponifiable matter, from ethyl acetate at 0° C.; the precipitated dihydroxystearic acid, which has a low solubility is weighed after filtration and washing, and to this weight is added a correction for its slight solubility in the ethyl acetate used as solvent and for washing. From the acetyl value and the percentage of dihydroxystearic acid, the percentage of ricinoleic acid in the oil can be calculated. The other principal constituent of castor oils is linoleic acid, to the extent of about 4 to 6 per cent., which may be determined by spectrophotometric examination of the mixed acids (after removal of unsaponifiable matter), after alkali isomerisation at 180° C. for 60 minutes under the conditions of Hilditch *et al.* (*Analyst*, 1945, **70**, 67). Oleic and saturated acids, which occur in small amounts in the oil, are determined by iodine value and by difference respectively. Examples are given of results obtained in the complete analysis of castor oils. R. E. S.

Karl Fischer Reagent, Review of the Use of. A. G. Jones. (*Analyst*, 1951, **76**, 5.) The theory of the use of the Karl Fischer Reagent is discussed and the various methods are reviewed. The visual end-point method by direct and back titration can be used if approximate results only are required in non-coloured solutions; the electrometric end-point can also be used with both forms of titration. The "dead-stop" electrometric end-point with either a direct or a back titration was most commonly used and gave accurate results. Examples of types of apparatus and electrometric titration circuits are given. A number of uses are briefly reviewed including the determination of the degree of hydration of salts and the method of following the course of various organic reactions in which water is liberated or consumed. R. E. S.

Methoxy and Ethoxy Groups in Admixture, Micro-detection of. C. J. de Wolff, A. L. O. M. Smithuis and A. F. C. Sterk. (*Pharm. Weekbl.*, 1951, **86**, 429.) About 0·1 mg. of material is heated with 10 ml. of 50 per cent. sulphuric acid to 200° C. in a sealed apparatus as described previously (*Pharm. Weekbl.*, 1951, **86**, 273). The top is cut off and the reaction mixture is distilled after the addition of 20 ml. of 50 per cent. potassium hydroxide. The distillate is redistilled with 4N sulphuric acid to remove bases, and oxidised with a red

hot copper wire. If a methoxy group was present, a violet red colour is given on the addition of Schiff's reagent, turning blue on the addition of an equal volume of 70 per cent. sulphuric acid. For the detection of the ethoxy group, the first distillate is heated in a sealed tube with solid potassium dichromate and a little concentrated sulphuric acid to 150° C., and then distilled. Acetic acid may be detected in the distillate by the lanthanum nitrate reaction. For the detection of methyl and ethyl esters, the original hydrolysis is carried out with 20 ml. of 4N sodium hydroxide at 150° C. G. M.

Morphine in Poppy Capsules, Estimation of. M. Valente. (*Boll. chim. farm.*, 1951, **90**, 223.) The following method based on that of Wuest and Frey is recommended. After freeing the capsules from seeds and drying at 100° C. they are ground in a mortar. 100 g. of coarse powder is placed in a percolator and covered with 300 ml. of ethanol (70 per cent.) containing 5 per cent. of hydrochloric acid and left for 2 days. Then the ethanol is drained off and replaced with 300 ml. of hot water. After 2 days this is drained off, and, after recovery of the ethanol, the two percolates are evaporated on a water-bath. To the residue 2 g. of calcium hydroxide and 20 ml. of water are added, shaken for a long time and filtered, sodium carbonate is then added to the filtrate, and it is shaken and filtered again. The morphine is extracted from the filtrate with 60 ml. of a mixture of equal parts of butanol and benzene, and 20 ml. of dilute sulphuric acid is added to the butanol-benzene solution. After 24 hours the aqueous liquid, in which the morphine is found, is treated with sodium carbonate in slight excess in the presence of ethyl ether, into which the morphine passes. The ethereal solution is evaporated to dryness in a tared dish and weighed. Poppy heads from Brindisi and Taranto yielded 0·0776 and 0·0921 per cent. respectively and a sample from Bari 0·1012 per cent. H. D.

Sugars, Colorimetric Determination of. M. Dubois, K. Gilles, J. K. Hamilton, P. A. Rebers and F. Smith. (*Nature, Lond.*, 1951, **168**. 168.) A simple, rapid method for the colorimetric determination of ketoses and aldoses and their methyl derivatives on a sub-micro scale is reported. The orange-yellow colour, produced by adding sulphuric acid (5 ml.) to the sugar solution (2 ml.) containing phenol, is permanent; its optical density (measured at 490 mμ for hexoses and hexuronic acid and their derivatives and at 475 mμ for pentoses and their derivatives) when referred to a standard curve gives the concentration of the sugar. This method, which is applicable to all carbohydrates with either a free or potential reducing group, is particularly useful for determining sugars which have been separated by partition chromatography using phenol-water as the solvent. The sugars can be extracted from the strips of paper cut from the chromatogram by simply immersing in water at room temperature, and thus there is no danger of decomposing the sugars.

A. H. B.

GLYCOSIDES, FERMENTS AND CARBOHYDRATES

Esterases, Spectrophotometric Determinations of. B. H. J. Hofstee. (*Science*, 1951, **114**, 128.) Salicylic acid strongly absorbs ultraviolet light of wavelength 290 mμ to 300 mμ, whereas acetylsalicylic acid and other fatty acid esters of salicylic acid do not. This fact allows a spectrophotometric determination of esterases in general to be made, because hydrolysis of as little as 0·01 μM of salicylic esters can be detected. The reference cell contained buffer, substrate and water to a final volume of 3 ml. The control cell contained

buffer substrate, water, and enzyme to a final volume of 3 ml. The other cells contained, in addition to the elements of the control cell, substances the influence of which upon the enzyme reaction were to be observed. Thus the influence of spontaneous hydrolysis on the observed increase of absorption was cancelled. Spontaneous hydrolysis was considerable in many cases. The esterolytic activity of normal blood serum with acetylsalicylic acid as substrate was investigated. The observed activities are apparently due entirely to choline esterase (*s*-type) because there is practically complete inhibition by eserine concentrations less than 10^{-5}M, and parathione and tri-*o*-cresylphosphate cause inactivation and Ca^{++}, Mn^{++}, and Mg^{++} cause activation. It was found that steapsin liberates only traces of salicylic acid from acetylsalicylic acid, but causes a significant rate of hydrolysis of longer chain fatty acid esters of salicylic acid. In the case of the hydrolysis of butyrylsalicylic acid, steapsin is not inactivated by eserine and this enzyme seems to act in the absence of Ca^{++}. Evidence is submitted which suggests that the observed hydrolysis of the salicylic acid esters is effected by the same enzyme that hydrolyses glycerides such as monobutyrin and tributyrin. A. H. B.

***Strophanthus Intermedius* Pax, Glycosides of Seeds of.** M. R. Salmon, E. Smith and W. G. Bywater. (*J. Amer. chem. Soc.*, 1951, **73**, 3824.) The seeds of *Strophanthus intermedius* were extracted according to the general method of Katz (*Helv. Chim. Acta*, 1948, **31**, 993), and the resulting aqueous solution of the total glycosides was then extracted successively with ether and chloroform. From the ether extract were obtained a crystalline material which agreed in properties with Reichstein's substance 761, and an approximately equal amount of oily glycosides which did not yield crystalline material after chromatography. The chloroform extract yielded a crystalline material from which were obtained, after chromatography, Reichstein's Substance 761 and substance 762. The total yield of ether- and chloroform-soluble components from *Strophanthus intermedius* seeds was 4·5 per cent. of which 2·2 per cent. was crystalline glycosides. Substance 761 gave sarverogenin upon hydrolysis with dilute acid.

A. H. B.

INORGANIC CHEMISTRY

Mercuric Chloride, Volatility when Evaporating Aqueous Solutions. I. Bellucci and A. Casini. (*Ann. Chim.*, 1951, **41**, 374.) Mercuric chloride is very volatile in dilute aqueous solutions, for instance a solution containing 1 mg. in 100 ml. exposed to air at ordinary temperatures will lose 24 per cent. in 48 hours. When evaporated on a water-bath to half its volume 38·7 per cent. is lost. Sodium chloride will reduce, and hydrochloric acid, chlorine or albumen will prevent, this loss, but the use of the latter substances is not always convenient. The authors found that the addition of an excess of potassium iodide will prevent it and this can be conveniently combined with Rupp's method of estimation. To 10 ml. of 0·1N mercuric chloride (0·1358 g. of the salt) add 1·5 g. of potassium iodide in 15 ml. of water, 5 ml. of 10 per cent. sodium hydroxide solution and, with agitation, 2 ml. of formaldehyde solution diluted with 10 ml. of water, shake thoroughly for 2 minutes, acidify with acetic acid and add 20 ml. of 0·1N iodine, shaking again to dissolve the precipitated mercury and titrate with 0·1N thiosulphate. This also works satisfactorily with 0·01N solutions, using the same amounts of the other reagents, and no loss occurred if the solution of mercury was evaporated to dryness on the water-bath after adding the potassium iodide. H. D.

ORGANIC CHEMISTRY

Antihistamines, Geometrical Isomers of. D. W. Adamson, P. A. Barrett, J. W. Billinghurst, A. F. Green and T. S. G. Jones. (*Nature, Lond.*, 1951, **168**, 204.) Further study of 1-*p*-chlorophenyl-1-α-pyridyl-3-pyrrolidinoprop-1-ene (405C49) has revealed the presence of an isomeric base (496C50) in the product of dehydration. The isomers were separated by fractional crystallisation of their oxalates (405C49 base, m.pt. 61° to 62° C.; oxalate, m.pt. 184° C. (decomp.); 496C50 base, oil; oxalate, m.pt. 156° to 157° C. (decomp.)). The bases were apparently geometrical isomers each giving a high yield of the same ketone (*p*-chlorophenyl α-pyridyl ketone, m.pt. 63° C.) on oxidation with chromic acid, and the same propylamine ($n_D^{19°C}$, 1·570; oxalate, m.pt. 147° C.), when catalytically hydrogenated. The ultra-violet absorption spectra are given and have been interpreted as indicating that in 405C49, as in α-pyridyl-ethylene, the α-pyridyl and ethylenic groups are approximately co-planar, on the generally accepted assumption that this configuration is required for maximal electronic interaction of the two groups to which the characteristic light absorption is related. By the same reasoning, the *p*-chlorophenyl group of 496C50, rather than the α-pyridyl group, is in the same plane as the ethylenic group. Outstanding differences in chemical behaviour of the isomers were observed. The dehydration of many related α-pyridyl carbinols has been re-investigated. In each case the results were similar to the example quoted above: two isomers were formed, one being chemically stable and exhibiting the α-pyridylethylene type of spectrum, the other being relatively unstable and having a spectrum similar to the corresponding substituted phenylethylene. Separation of the isomers was usually effected by fractional crystallisation of the oxalates or by chromatography, the progress of the separation being followed by measurements of the ultra-violet absorption spectra. The pharmacological properties of the isomers differed in an interesting manner, high and specific antihistamine activity being shown only by the isomers having the α-pyridylethylene type of structure, the other isomers of each pair invariably being considerably less active in this respect. In contrast, other pharmacological activities were approximately of the same low order in both isomers. R. E. S.

Nitrogen Mustards. E. Wilson and M. Tishler. (*J. Amer. chem. Soc.*, 1951, **73**, 3635.) The methods of preparation and other chemical data relating to many compounds belonging to the general class of nitrogen mustards, which were synthesised for testing as chemotherapeutic agents against neoplastic diseases, are reported. The compounds and structural variants of the effective nitrogen mustard N-methyl-β : β′-dichlorodiethylamine, and have the general formula $R - N(CH_2CH(X)Y)_2$. The variations consisted of: (1) a change in the nature of the R-group; (2) the introduction of an additional β : β′-dichlorodiethylamino group; (3) substitution of the β-chloro-*n*-propyl group (X = Cl, Y = CH_3) for the usual β-chloroethyl group (X = Cl, Y = H); (4) introduction of an additional β : β′-dichlorodipropylamino group into the molecule; (5). substitution of bromine for chlorine; (6) substitution of fluorine for chlorine. Some of the compounds combined some of the above variations. A. H. B.

BIOCHEMISTRY

GENERAL BIOCHEMISTRY

Adrenaline and Noradrenaline; Effects of Stimulation of Rat Adrenals. A. S. Outschoorn. (*Nature*, 1951, **167**, 722.) Three drugs, insulin 1 unit, morphine hydrochloride 2 mg., and tetrahydro-β-naphthylamine carbonate 7·5

mg. per 100 g. of rat, known to cause a release of adrenal medullary hormone were administered subcutaneously to groups of 2 to 4 rats. The rats were killed at varying times after injection simultaneously with equal numbers of uninjected controls. Extracts were made of the adrenals and the amounts of adrenaline and noradrenaline in each individual's glands estimated. The mean concentrations of the amines, in terms of bodyweight per rat in the injected groups, were calculated as percentages of the mean concentrations in the control groups killed in each experiment simultaneously with the injected. The results obtained show that with prolonged activity of the glands utilisation of adrenaline increasingly outpaces synthesis; all three drugs caused a depletion. The amounts of noradrenaline, however, did not follow the trend of the methylated amine; neither morphine nor tetrahydronaphthylamine produced any lowering of the content of noradrenaline below the range of the controls, and insulin produced no more than a transient and statistically nonsignificant depletion. These results suggest that under certain conditions of adrenal medullary activity there is either no output of noradrenaline, or an output with which synthesis can keep pace. There does in fact seem to be a tendency for the earliest response of the glands to be an increased production of noradrenaline even while the demand for adrenaline can still be met; although this increase was too small to be significant it occurred following all three of the agents used. S. L. W.

Cortisone, Detection in Body Fluids. C. L. Cope. (*Brit. med. J.*, 1951, **1**, 271.) A 24- or 48-hour collection of urine is acidified to about *p*H 1 with sulphuric acid, allowed to stand at room temperature overnight, and extracted by shaking in separating funnels with 4 successive quantities of chloroform, each equal to 15 per cent. of the total urine. The chloroform emulsions are then centrifuged and the clear chloroform phase evaporated to a volume of about 30 ml. The concentrated chloroform extract is transferred quantitatively to a small separating funnel and washed 3 times with 0·1N sodium hydroxide (6 ml.) and 3 times with water (6 ml.), each washing being extracted with chloroform, which is added to the extract. The washed chloroform solution is then evaporated to dryness. The most suitable solvent for injection is propylene glycol, 0·2 ml. of which is added to the dried extract. After dissolving by gently warming the tube to 45° C. normal saline solution 0·8 ml. is added and the tube shaken to give a homogeneous mixture. Blood is drawn from the tail vein of adrenalectomised mice to the 0·5 mark on a white-cell pipette, diluted to the top mark with Randolph's diluting fluid and eosinophil cells counted in duplicate in the Ruchs-Rosenthal chamber. The diluting fluid consists of 0·1 per cent. of phloxine and 0·1 per cent. of methylene blue, each dissolved separately in 50 per cent. propylene glycol; the solutions are mixed in the proportions of 2 of phloxine to 1 of methylene blue immediately before use. The equivalent of 12 hours' urine extract in 20 per cent. propylene glycol is injected subcutaneously and the animals returned to their cages. Further eosinophil counts are made at 4 and at 6 hours after injection. The significant response is the maximum drop in eosinophil cells expressed as a percentage of the initial value; this drop may be greatest at either 4 or 6 hours. The method is shown to be useful and practical for detecting cortisone-like activity in urine extracts; its applicability to blood is uncertain. S. L. W.

Vitamin B_{12}, Formation of a Competitive Antagonist of, by Oxidation. J. M. Beiler, J. N. Moss and G. J. Martin. (*Science*, 1951, **114**, 122.) Treatment of vitamin B_{12} in strong acid solution with hydrogen peroxide caused decolorisation, and this solution then exhibited a competitive antagonism to

vitamin B_{12}. The activity of this solution was assayed directly on *Lactobacillus leichmanii* 4797, and an inhibitory effect on the growth of this organism, counteracted by vitamin B_{12}, was exhibited. Only at the highest level of inhibitor tested was there incomplete counteraction. The solution was also tested on *Staph. aureus*, *S. typhosa*, and *Ps. aeruginosa*, three organisms which do not require preformed vitamin B_{12} as a growth factor, and no inhibitory effect was observed. It appears that the substance produced by the above treatment of vitamin B_{12} has a specific antagonistic effect to vitamin B_{12}, since it is counteracted by the vitamin and has no inhibitory effect where the vitamin is not an essential factor. A. H. B.

BIOCHEMICAL ANALYSIS

Amino-acids, A New Paper Chromatography Solvent for. F. Bryant and B. T. Overell. (*Nature, Lond.*, 1951, **168**, 167.) Mesityl oxide, which has previously been mentioned as a possible solvent for the paper partition chromatography of organic acids (Lugg and Overell, *Aust. J. Sci. Res.*, 1948, A.**1**, 98), has now been used as a solvent for the separation of amino-acids. Before use, the mesityl oxide is re-distilled and fractionated to prevent condensation in the presence of formic acid. The fractionated solvent alone does not give any movement of amino-acids; but the acid spots move when formic acid is added to the solvent system. The method of obtaining the most desirable mobile phase is to shake one volume of mesityl oxide with 1 volume of formic acid (85 per cent.) and 2 volumes of water. The paper is allowed to become equilibrated thoroughly in the vapours of the stationary phase before introducing the mobile phase. Small volumes of the mobile phase are made just prior to use and discarded after two days. A table of R_F values is recorded. A. H. B.

Methionine, Colorimetric Determination of. M. N. Rudra and L. M. Chouhbury. (*Analyst*, 1951, **76**, 432.) A method for the determination of methionine, involving modifications of previously reported methods, is described. 1 g. of air-dried powdered material was hydrolysed with 5 ml. of 20 per cent. hydrochloric acid for 24 hours. The basic amino acids were precipitated with 100 per cent. phosphotungstic acid, the filtrate was made up to a known volume (usually 8 to 10 ml.) and filtered through a dry filter. 4 ml. of the filtrate was taken, 2 ml. of 5N sodium hydroxide and 1 ml. of 1 per cent. sodium nitroprusside solution were added, the solution was warmed for 8 minutes in a water-bath at 40° C. and cooled in an ice-bath for 5 minutes, and then 2 ml. of concentrated hydrochloric acid was added to develop the red colour. A "Lumetron" photo-electric colorimeter with filter No. 530 was used for preparing the standard calibration curve for colour comparisons. A. H. B.

Nicotinamide, Fluorimetric Determination by Use of Synthetic Ion Exchange Resins. M. Kato and H. Shimizu. (*Science*, 1951, **114**, 12.) The fluorimetric determination of nicotinamide by treatment with cyanogen bromide solution under specific conditions, after the removal of other fluorescent substances according to the method of Chaudhuri and Kodiček (*Biochem. J.*, 1949, **44**, 343), failed in the case of the attempted determination of the nicotinamide content of silkworm because of the fluorescences caused by kynurenine, 3-hydroxykynurenine and other unknown substances. These contaminating fluorescences were completely eliminated by the use of KH–4B–Na (a synthetic cation exchange resin) and Amberlite IRA–400–OH (a synthetic anion exchange resin) and the estimation of nicotinamide was then performed without difficulty. The apparatus used and the details of the method are described. A. H. B.

CHEMOTHERAPY

2 : 4-Diaminopyrimidines; A New Series of Antimalarials. E. A. Falco, L. G. Goodwin, G. H. Hitchings, I. M. Rollo and P. B. Russell. (*Brit. J. Pharmacol.*, 1951, **6**, 185.) A series of derivatives of 2 : 4-diaminopyrimidine was prepared and tested for antimalarial activity. High activity was shown by many members against *P. gallinaceum* in chicks and *P. berghei* in mice, substances with a 5-phenyl substituent being the most active, 5-benzyl and 5-phenoxy derivatives being somewhat less active. Substitution of halogen or nitro groups in the *para* position of the benzene nucleus of the 5-substituent was found to enhance activity. Substitution of an alkyl group in the 6-position enhanced activity, and, in the 5-phenyl derivatives, a peak of activity was reached with the 6-ethyl compound. 2 : 4-Diamino-5-*p*-chlorophenyl-6-ethylpyrimidine was found to be 60 times as active as proguanil against *P. gallinaceum* and 200 times as active against *P. berghei*. Longer chain alkyl derivatives were less active. The drugs were also found to be active against the blood-forms of *P. cynomolgi* in monkeys but to have no pronounced action on the exoerythrocytic stages. It is hoped that these drugs will prove of value in the suppression and treatment of human malaria, and especially in the treatment of proguanil-resistant strains. S. L. W.

1 : 2 : 3 : 4-Tetrahydrocarbazolylcarboxylic Acid Esters with Local Anæsthetic Activity. H. W. Murphy. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 373.) The hydrochlorides of β-diethylaminoethyl, 3-(2-methylpiperidino) propyl, 3-di-*n*-butylaminopropyl, 3-morpholinopropyl, and 1-methyl-3-diethylaminopropyl esters of 1 : 2 : 3 : 4-tetrahydro-6-carbazolylcarboxylic acid were prepared, characterised and studied for local anæsthetic activity, toxicity and irritation. All are potent local anæsthetics when applied topically, but concentrated solutions are irritating. They have anæsthetic activity comparable to that of dibucaine but are more stable in solution and have lower toxicities. The 3-di-*n*-butylaminopropyl ester salt appeared to be the best local anæsthetic of the compounds prepared. They do not interfere with the action of sulpha drugs and they have a germicidal action. The local anæsthetic activity of the amino-ester hydrochlorides of the isomeric 8-carboxylic acid was lacking or of a very low order, but the compounds from either acid were capable of relaxing smooth muscle. The irritant effects, toxicity and limited solubility in the presence of salts, might limit the utility of even the highly active anæsthetic compounds prepared. A. H. B.

Thiocyanates, Antifungal Activity of a Series of. L. Landis, D. Kley and N. Ercoli. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 321.) The substances tested comprised 8 derivatives of 2-phenoxyethyl thiocyanate, 6 of 3-phenoxypropyl thiocyanate and 6 of 4-phenoxybutyl thiocyanate. They were examined for fungicidal, fungistatic and sporostatic activity against *Tricophyton mentagrophytes*, *T. purpureum*, *Epidermophyton floccosum*, *Cryptococcus neoformans*, *Microsporum felineum* and *Aspergillus fumigatus*, and simultaneously compared with undecylenic acid, propionic acid, 8-hydroxyquinoline, and similar substances. The fungistatic activity indicated that the most effective of all the substances tested was 3-(*p*-bromo)phenoxypropyl thiocyanate. The highest dilutions showing fungistasis were: 3-(*p*-bromo)phenoxypropyl thiocyanate, 1 in 90,000; undecylenic acid, 1 in 25,000; propionic acid, 1 in 10,000; and 8-hydroxyquinoline benzoate, 1 in 35,000. In the presence of 10 per cent. of rabbit

serum, the results were 3-(*p*-bromo)phenoxypropyl thiocyanate, 1 in 40,000; undecylenic acid, 1 in 5,000, propionic acid, 1 in 1,000; and 8-hydroxyquinoline benzoate, 1 in 9,000. G. R. K.

PHARMACY

NOTES AND FORMULÆ

Cortisone Acetate (Cortone Acetate). (*New and Nonofficial Remedies; J. Amer. med. Ass.*, 1951, **146**, 1422.) Cortisone acetate, $C_{23}H_{30}O_6$, is 11-dehydro-17-hydroxycorticosterone 21-acetate. It is a white, odourless powder, melting at 242° to 248° C. with decomposition, practically insoluble in water, slightly soluble in ether and alcohol, and freely soluble in chloroform. When dissolved in alcohol and treated with a saturated solution of 2 : 4-dinitrophenylhydrazine in 2N hydrochloric acid, it yields an orange-coloured precipitate which melts at 235° to 242° C. with decomposition, after recrystallisation from ethyl acetate. A 0·2 per cent. solution in acetone has $[\alpha]_D^{25°\,C}$, 177° to 185°; a 0·001 per cent. solution in alcohol exhibits an ultraviolet absorption maximum at about 2,380 Å ($E_{1\,cm}^{1\,per\,cent.}$, about 390). When dried over phosphorus pentoxide *in vacuo*, it loses not more than 3·0 per cent. of its weight; sulphated ash, not more than 0·1 per cent. It is assayed by determining the optical density of a 0·001 per cent. solution in alcohol at 2,380 Å and multiplying by 39 to obtain the concentration in mg./ml.; it contains 95·0 to 105·0 per cent. of cortisone acetate. G. R. K.

PHARMACOGNOSY

Peroxidase Content of Drugs, as Measure of Age. L. Hörhammer and R. Hänsel. (*Arch. Pharm. Berl.*, 1951, **284**, 110.) For determination of the peroxidase value of a drug, a portion (equivalent to about 1 g. of fresh drug) is rubbed down with 1 g. of sand and extracted for 3 hours with 50 ml. of water. The peroxidase determination is carried out by the method of Diemair and Häusser (*Z. analyt. Chem.*, 1941, **122**, 12) using 0·2 to 2 ml. of the extract and the leuco compound of 2 : 6-dichlorphenolindophenol with hydrogen peroxide. After 30 sec. the reaction is stopped by the addition of 50 ml. of acidified ether, and the colour is shaken out into the ether. Tests with a variety of drugs (including belladonna leaf and root, caraway fruit, male fern, colchicum seed, strophanthus seed, showed that in all cases old drugs had lost activity, which was often reduced to zero after several years storage. G. M.

Jalap Resins, Nomenclature of. P. Duquenois and G. E. Trease. (*Ann. pharm. franc.*, 1951, **9**, 114.) There is some confusion in the nomenclature of the resins of jalap. Names which have been given are: for the ether-soluble fraction, jalapine, scammonine and orizabine: and for the ether-insoluble fraction, jalappine, convolvuline. rhodeoretine and jalapurgine. In English practice scammonin is the soluble resin, convolvulin or jalapin the insoluble one; while on the Continent jalapine is the soluble resin and convolvuline the insoluble one. The confusion is due to W. Mayer, who changed jalapin into convolvulin and then called the resin of *Ipomoea orizabensis* (orizabin) jalapin. It is recommended that the name jalapine should not be used, but that the ether-soluble resin should be called scammonin and the insoluble resin convolvulin. This is justified by the fact that scammonin is in practice prepared from scammony. G. M.

Opium Poppy of Macedonia. B. Akačić, D. Marković and J. Petričič. (*Acta Pharm. Jug.*, 1951, **1**, 3.) The pure white variety of poppy (*Papaver somniferum* L. var. *album* D.C.) is seldom used in Macedonia for the production of opium; instead, a cross between this and a violet-grey form is used. The capsule is similar morphologically to those of other varieties but the latex vessels are always closely associated with the vascular strands. The alkaloids are practically all contained in the latex though traces occur in the epidermal cells. The upper part of the stem is also rich in alkaloid and contains 30 to 50 per cent. of the morphine content of the capsule. Where the soil composition was optimal the highest morphine content was found in the ripe unincised capsule; where not optimal the highest content was in the unripe capsule. Stabilisation by alcohol vapour immediately after collection had no apparent effect on the conservation of morphine during subsequent storage for 7 to 8 months; on the other hand samples which became mouldy lost much morphine. The morphine contents were determined by a method based on those of van Arkel (*Pharm. Weekbl.*, 1935, **72**, 366) and Wieland and Kappelmeyer (*Leibigs Ann.*, 1911, 382, 319). J. W. F.

PHARMACOLOGY AND THERAPEUTICS

Acenaphthene Derivatives, Fungistatic Properties of. J. E. McDavid and T. C. Daniels. (*J. Amer. pharm. Ass., Sci. Ed.*, 1951, **40**, 325.) Seven 5-substituted derivatives of acenaphthene (chloro, bromo, nitro, amino, sulpho (sodium salt), sulphonamido and carboxy) and two 5-substituted derivatives of acenaphthenequinone (chloro and bromo) were examined by the cup-plate method, using 7-day-old cultures of *Tricophyton mentagrophytes*. All the compounds displayed some fungistatic activity but in none was the effect more than moderate. G. R. K.

Adrenocortical Hormones, Assays on Small Laboratory Animals. M. Vogt. (*Analyst*, 1951, **76**, 478.) The three biological assays of cortical hormone on rodents of which enough is known to justify their use as routine or screening tests are discussed and practical details given. These assays are (1) the survival test in low environmental temperature, originated in 1938 by Selye and Schenker ("Cold test"); (2) the test using deposition of liver glycogen in fasting mice given glucose parenterally described by Venning, Kazmin and Bell in 1946; (3) the test using the fall in circulating eosinophils in the mouse described by Speirs and Meyer in 1949. A. H. B.

Adrenocorticotrophic Hormone Activity, Assessment of. M. Reiss, I. D. K. Halkerston, F. E. Badrick and J. M. M. Halkerston. (*Analyst*, 1951, **76**, 461.) The attempts to assess adrenocorticotrophic hormone activity biologically, such as those based on change of adrenal weight and those utilising histological changes within the adrenal cortex, are reviewed. The use of phosphorus–32 as an index of adrenal function is described. Indirect assay methods, based on changes due to adrenal hormones mobilised by the adrenocorticotrophic hormone, are also discussed. Results obtained using a number of the methods are reported. Because of the shortcomings of the biological assay it is pointed out that it would be a great advantage if the assay animal could be dispensed with and the influence of the hormone on adrenal cortex tissue *in vitro* investigated. A. H. B.

Adrenocorticotrophic Hormone, Adrenal Ascorbic Acid Depletion and Adrena, Repair Methods for the Bio-assay of. C. J. O. R. Morris. (*Analyst*, 1951-**76**, 470.) The technique of the adrenal repair method for the assay on the hypol physectomised rat is described and the methods that use histological evidence of repair as the criterion of activity are discussed. After a description and discussion of the adrenal ascorbic acid depletion method of assay, modifications are mentioned. A. H. B.

Adrenocorticotrophic Hormone, Ascorbic Acid Depletion Method for the Bio-Assay of, and the Use of Inhibition of Tissue Repair. B. E. Clayton and E. T. E. Prunty. (*Analyst*, 1951, **76**, 474.) The adrenal ascorbic acid depletion method for the assay of adrenocorticotrophic hormone is described, along with modifications and the results obtained. The hormone inhibits the formation of granulation tissue in response to trauma and this fact was used as the basis of its assay on mice. The details of the method are reported. A. H. B.

Antihistamine Drugs; Method of Assessment of Activity in Man. A. A. C. Ross. (*Lancet*, 1951, **261**, 62.) After preliminary cleaning with ether, 4 areas of skin on the dorsal surface of the forearm (or the outer surface of the thigh) are exposed to ultra-violet radiation from a water-cooled mercury-vapour lamp by holding the quartz window of the lamp in contact with the skin for 15, 30, 45 and 60 sec. Small lead diaphragms are used, one for each length of exposure, so cut that the area exposed is constant (12·5 sq. cm.) for all exposures, but the outline of each differing to avoid confusion when recording results. Twenty-four hours after exposure the reactions are recorded as "−," negative "+" (faint erythema) or "++" (definite or intense erythema). Exposures are made first as controls and again a week or more later during treatment with antihistaminic drugs. The drugs are given in a dosage of 50 mg. by mouth at 10 p.m. on the day before irradiation, 50 mg. at 8 a.m., 3 p.m. and 10 p.m. on the day of irradiation and 50 mg. at 8 a.m. the next day. Irradiation is done in the early afternoon and the results assessed 24 hours later. A positive result is regarded as one where the erythema threshold is raised during the treatment with the antihistamine drug compared with the control. The paper records the comparative results of the test on 10 young adults using three antihistaminic drugs. S. L. W.

Dextran Sulphate as an Anticoagulant. K. Walton. (*Proc. Roy. Soc. Med.*, 1951, **44**, 563.) Dextran sulphate has a heparin-like anticoagulant action. When prepared from dextran of molecular weight 35,000 and over, it is unsuitable for therapeutic use, causing precipitation of fibrinogen, agglutination of platelets and deposition of granular material in reticulo-endothelial cells. In contrast, when prepared from dextran of molecular weight 20,000 and under, it has no effect on platelets and causes no deposits in reticulo-endothelial cells in experimental animals. One typical batch of this material, when assayed against International Standard Heparin, had an activity of 17 to 20 I.U./mg. It was found to be effective by parenteral injection only. When given intravenously to rabbits, a dose of 5 mg./kg. of body weight reduced the clotting time from 19 to 3 minutes in an hour and a half, and a dose of 10 mg./kg. body weight reduced it from 54 to 3 minutes in 3 hours. Doses up to 0·5 g./kg. body weight produced no toxic effects in the mouse, rat, rabbit, dog, or monkey. It seems probable that the anticoagulant action is due to the strong electro-negative charge upon the acidic groups, since it is opposed by strongly basic substances such as protamine. The presence of a co-factor in the serum or plasma is essential, and in its

presence the action is that of an antithrombin. If further chemical trials are satisfactory, dextran sulphate may serve as a cheap synthetic analogue of heparin.
G. R. K.

Laburnum Poisoning in Children. R. G. Mitchell. (*Lancet*, 1951, **261**, 57.) 10 recent cases of poisoning due to eating the pods or seeds of laburnum are reported. The ages of the children ranged from 3 to 10 years, with an average of 5½ years. There were no deaths. The symptoms usually commenced about 30 minutes after ingestion. The common features were nausea and vomiting, pallor and drowsiness, with dizziness and incoordination in the severest cases. There was no diarrhœa, and no record of headache or other pain, and none of the children had a temperature of over 98·8° F. The children usually looked pale, with tachycardia and dilated pupils. With gastric lavage, supplemented by stimulants such as nikethamide in the more severe cases, all the children completely recovered within 24 hours. The active principle of laburnum is an alkaloid, cytisine, which resembles nicotine in its actions. The dose of laburnum lethal to man has not been determined. 2 or 3 seeds may be sufficient to produce symptons, but a boy of 4 recovered after eating at least 18 seeds. The possibility of a fatal issue, however, renders immediate treatment imperative. Cytisine is rapidly excreted by the kidneys so an adequate fluid intake must be assured. S. L. W.

Morphine Derivatives, Pharmacological Properties of. R. Giudicelli, P. Chabrier and K. Kristensson. (*Therapie.*, 1951, **6**, 146.) The pharmacological properties of morphine alkaloids were compared with those of their hydrogenation products and with quaternary ammonium derivatives. The study of morpholylethylmorphine confirmed the view of Sumwalt, that ether-oxides of morphine all have a depressive action on the cough centre similar to that of codeine, and independent of the nature of the radical used. Among the various ether-oxides of morphine, morpholylethylmorphine is characterised by its low toxicity: which is 1/4 that of codeine, intravenously, and 2/15 subcutaneously. This compound also gives a dibromomethylate which has a curarising power 12 times that of the monobromomethylates of morphine and codeine and 1/35 that of curare, the toxicity being 1/50 that of curare. G. M.

Pituitary, Antidiuretic Hormone of the Posterior Lobe. C. Cavallero and M. Zanchi. (*J. Path. Bact.*, 1951, **63**, 249.) The antidiuretic activity of human posterior lobes was estimated by Burn's method. The glands were removed 10 to 25 hours after death from post-mortem material which included instances of disease in which disturbances of the water metabolism are known to occur. When expressed as antidiuretic potency per mg. of fresh neurohypophysial tissue, marked increases of hormone content were observed in cases of liver cirrhosis with ascites, arterial hypertension, cardiac œdema, diabetes mellitus, eclampsia and Addison's disease. A pronounced reduction of antidiuretic potency was found in single cases of diabetes insipidus and hæmochromatosis. S. L. W.