NOTES.

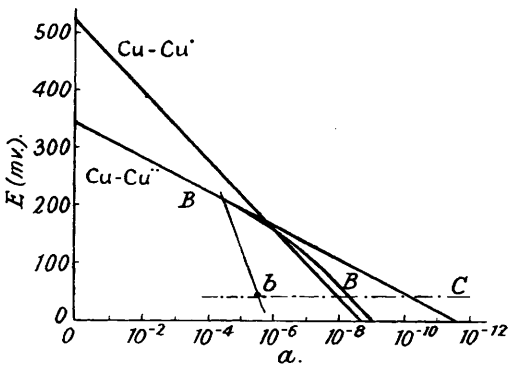
The Behaviour of the Copper Electrode in Dilute Copper Sulphate Solutions. By A. A. MOUSA.

THE behaviour of the copper electrode in dilute copper sulphate solutions has recently been reported by Tourky and El Wakkad (*J.*, 1948, 749). The potential–activity curves obtained by the authors showed a break which was assumed to signify a pure Cu–Cu$^{\cdot}$ electrode reaction in solutions of cupric-ion activity, $a_{Cu^{\cdot\cdot}}$, lower than $\sim 10^{-4}$. Such an assumption, however, is not justifiable since it would involve a complete breakdown of the equilibrium $Cu^{\cdot\cdot} + Cu \rightleftharpoons 2Cu^{\cdot}$ which should necessarily be maintained whenever metallic copper is in contact with any of its ions in solution. The method to be used to interpret the results and which leads to the above assumption is discussed below, and an explanation for the break observed is put forward.

In the first place, the different values assigned to the equilibrium constant K of the reaction $Cu^{\cdot\cdot} + Cu \rightleftharpoons 2Cu^{\cdot}$ were discussed in detail and 10^{-6} was selected as the most snitable value for calculations. Since, however, a true thermodynamic equilibrium should necessarily satisfy the identity of the different potentials Cu–Cu$^{\cdot\cdot}$, Cu–Cu$^{\cdot}$, and Cu$^{\cdot\cdot}$–Cu$^{\cdot}$ in one and the same solution, the use of any particular value for K other than that which is determined by an equation such as

$$E_{0(Cu-Cu^{\cdot\cdot})} + 0{\cdot}030 \log a_{Cu^{\cdot\cdot}} = E_{0(Cu-Cu^{\cdot})} + 0{\cdot}060 \log a_{Cu^{\cdot}}$$

is not permissible and leads to unnecessary complications. With the values chosen for $E_{0(Cu-Cu^{\cdot\cdot})}$ and $E_{0(Cu-Cu^{\cdot})}$, *viz.* 0·3457 and 0·5220 v., respectively, K amounts to $10^{-5\cdot877}$. Setting K as 10^{-6} instead of $10^{-5\cdot877}$ accounts, although in part only, for the non-identity of the calculated potentials, at least in solutions of high cupric-ion activity where, by subtracting $0{\cdot}5a_{Cu^{\cdot}}$ supposed to be in equilibrium, the original cupric-ion activity remained practically unchanged.



In the second place, the Cu–Cu$^{\cdot\cdot}$ potential in different cupric-ion activities ($a_{Cu^{\cdot\cdot}}$) was calculated as $0{\cdot}5\,(E_{Cu-Cu^{\cdot}} + E_{Cu^{\cdot\cdot}-Cu^{\cdot}})$, a procedure which is valid only if the system is in true thermodynamic equilibrium. That this was not the case with the calculated activities would have readily been revealed if solutions of $a_{Cu^{\cdot\cdot}}$ infinitesimally lower than 10^{-6} had been considered, in which case the Cu$^{\cdot\cdot}$–Cu$^{\cdot}$ potential would have been found to acquire, at a limit, an infinite negative potential.

The reason for such an abnormality, as referred to above, lies undoubtedly in setting $a_{Cu^{\cdot}}(e)$ as equal to $\sqrt{[a_{Cu^{\cdot\cdot}}(o) \times K]}$ instead of $\sqrt{[a_{Cu^{\cdot\cdot}}(e) \times K]}$ where $a_{Cu^{\cdot\cdot}}(o)$ is the original cupric-ion activity, and $a_{Cu^{\cdot\cdot}}(e)$ and $a_{Cu^{\cdot}}(e)$ are respectively the cupric- and cuprous-ion activities at equilibrium. With the equilibrium state represented as such $Cu^{\cdot\cdot} + Cu \rightleftharpoons 2Cu^{\cdot}$, the equation $a_{Cu^{\cdot\cdot}}(o) = a_{Cu^{\cdot\cdot}}(e) + 0{\cdot}5\sqrt{[a_{Cu^{\cdot\cdot}}(e) \times K]}$ should then hold and can be solved for $a_{Cu^{\cdot\cdot}}(e)$ with any known value for $a_{Cu^{\cdot\cdot}}(o)$ as illustrated by the data in the following table.

$a_{Cu^{\cdot\cdot}}(o)$.	$a_{Cu^{\cdot\cdot}}(e)$.	$a_{Cu^{\cdot}}(e)$.	E.	$a_{Cu^{\cdot\cdot}}(o)$.	$a_{Cu^{\cdot\cdot}}(e)$.	$a_{Cu^{\cdot}}(e)$.	E.
$10^{-0\cdot9902}$	$10^{-1\cdot0000}$	$10^{-3\cdot4385}$	+0·3157	$10^{-5\cdot8024}$	$10^{-6\cdot0000}$	$10^{-5\cdot9385}$	0·1657
$10^{-1\cdot9975}$	10^{-2}	$10^{-3\cdot9385}$	0·2857	$10^{-6\cdot5495}$	10^{-7}	$10^{-6\cdot4385}$	0·1357
$10^{-2\cdot9922}$	10^{-3}	$10^{-4\cdot4385}$	0·2557	$10^{-7\cdot1700}$	10^{-8}	$10^{-6\cdot9385}$	0·1057
$10^{-3\cdot9756}$	10^{-4}	$10^{-4\cdot9385}$	0·2257	$10^{-7\cdot7167}$	10^{-9}	$10^{-7\cdot4385}$	0·0757
$10^{-4\cdot9273}$	10^{-5}	$10^{-5\cdot4384}$	0·1957	$10^{-8\cdot7368}$	10^{-10}	$10^{-7\cdot9385}$	0·0457

N.B.—In obtaining these results the equation was solved by fixing values for $a_{Cu^{\cdot\cdot}}(e)$; the corresponding values for $a_{Cu^{\cdot\cdot}}(o)$ were then calculated. K was set as $10^{-5\cdot877}$.

The above derived activities stand, no doubt, for true thermodynamic equilibria through which the identity of the different potentials is satisfied. Hence, the copper electrode potential, E (column 4), can be readily deduced from any of the following equations:

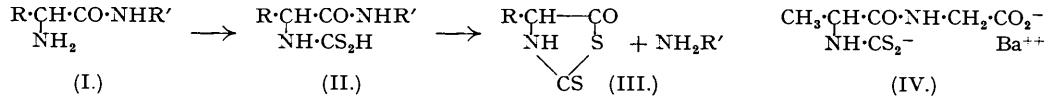
$$E = E_{0(Cu-Cu^{\cdot\cdot})} + 0{\cdot}030 \log a_{Cu^{\cdot\cdot}}(e)$$
$$= E_{0(Cu-Cu^{\cdot})} + 0{\cdot}060 \log a_{Cu^{\cdot}}(e)$$
$$\text{or} = E_{0(Cu^{\cdot\cdot}-Cu^{\cdot})} + 0{\cdot}060 \log a_{Cu^{\cdot\cdot}}(e)/a_{Cu^{\cdot}}(e)$$

Now, by plotting E against $a_{Cu^{\cdot\cdot}}(o)$ the theoretical curve B–B, shown in the figure, is obtained, manifesting a break which possesses its own slope and does not coincide with that for the pure Cu–Cu$^{\cdot}$ system. It should be emphasised, however, that the trend of the curve depends in the first place on the non-appearance of a solid phase that would participate in an ion-determining system, which is hardly the case with aqueous solutions. According to Tourky and El Wakkad's findings (*J.*, 1948, 740), the precipitation pH value of CuOH at a protected copper surface is ~6·8, a value which necessarily approximates to that of the most dilute solution used ($a_{Cu^{\cdot\cdot}} \sim 10^{-5\cdot5}$). As denoted by the theoretical curve B–B, the $a_{Cu^{\cdot}}(e)$ at this dilution is $\sim 10^{-5\cdot8}$. The product $a_{Cu^{\cdot}} \times a_{OH^{\prime}}$ thus exceeds the solubility product S of CuOH which will then be precipitated with consequent lowering of $a_{Cu^{\cdot}}$ to $S/a_{OH^{\prime}}$ or $\sim 10^{-8}$ (with 10^{-15} as the most probable value for S). The cuprous-ion activity is thus fixed through the separation of CuOH and will be kept at the above value as long as the pH remains constant. Any excess of cupric ion over that necessary to maintain

the equilibrium state (horizontal line *C*) will be reduced at the metal surface to cuprous, a process which will lead only to the further development of the solid phase separated. The potential, on the E–$a_{Cu^{\cdot\cdot}}(o)$ plot, will then be denoted by the point *b*. The trend of the break manifested thereby is not at all comparable with that for the pure Cu–Cu$^{\cdot}$ system; hence its extrapolation to meet the potential axis is insignificant. The author is pleased to know that Prof. Tourky agrees to the above amendment which explains adequately the conclusions in the original paper.—FACULTY OF SCIENCE, FOUAD I UNIVERSITY, ABBASSIA, CAIRO, EGYPT. [*Received, June 16th*, 1949.]

The Removal of Terminal Groups from Peptides. By A. L. LEVY.

COOK, HEILBRON, AND LEVY (*J.*, 1948, 201) described the first example of an unusual reaction of α-amino-amides, namely the cyclisation of *N*-dithiocarboxyglycine amide (II; R = R′ = H) with cold mineral acid to give 2-thiothiazolid-5-one (III; R = H) in high yield, with resulting fission of the peptide linkage. An analogous series of transformations has since been carried out with the amides of DL-phenylalanine and DL-phenylglycine (Billimoria and Cook, *J.*, 1949, 2323), DL-alanine (Cook and Levy, in the press), and L-tyrosine, L-leucine, DL-methionine, DL-norleucine, L-glutamine, DL-α-amino*iso*butyric acid and DL-aminomalonic acid (Davis and Levy, to be published). A particularly interesting example of this reaction arises when NH_2R' represents an amino-acid or peptide, in which case it should provide a method for the removal, and identification, of the terminal group in the peptide or polypeptide (I). This possibility has now been realised in the following four examples.



(I.) (II.) (III.) (IV.)

DL-Alanylglycine in 2 equivalents of 0·34N-barium hydroxide was shaken with carbon disulphide for 19 hours at room temperature, whereafter evaporation afforded the colourless *barium* salt (IV). This was acidified with N-hydrochloric acid to pH 3—4 to give 2-thio-4-methylthiazolid-5-one (III; R = Me) in 75% yield. Similarly, when DL-alanylglycylglycine was shaken with carbon disulphide and 0·34N-barium hydroxide, acidification of the resulting solution gave (III; R = Me). Glycylglycine was condensed with carbon disulphide as in the two previous examples, whereafter acidification precipitated 2-thio-5-thiazolidone (III; R = H) in 51% yield. DL-Phenylalanylglycine in 2 equivalents of N-potassium hydroxide was combined with carbon disulphide at room temperature, whereafter addition of hydrochloric acid caused the separation of 2-thio-4-benzylthiazolid-5-one (III; R = CH_2Ph).

Finally, it is interesting to note that Léonis (*Compt. rend. Lab. Carlsberg, Sér. Chim.*, 1948, **26**, 315) has utilised the reaction of amino-acids and peptides with carbon disulphide in a quantitative manner to determine the number, and to a limited extent the type, of terminal amino-groups present. In combination with the above results, this should provide a useful method for elucidating the amino-acid sequence in peptides, and this possibility is being investigated.

A preliminary account of another method for the determination of amino-acid sequences, which involves removal of the terminal residue under anhydrous acid conditions as a 3-phenyl-2-thiohydantoin, has been described by Edman (1st. International Congress of Biochemistry, Cambridge, 1949; *Arch. Biochem.*, 1949, **22**, 573).

Experimental.—DL-Alanylglycine (Cook and Levy, in the press) (0·584 g.) in 0·339N-barium hydroxide (23·6 c.c., 2 equivs.) was shaken with carbon disulphide (1 c.c.) for 19 hours in a nitrogen atmosphere, and the resulting orange solution (pH 9) decolorised with a stream of carbon dioxide, which also removed a little free barium hydroxide as barium carbonate. Evaporation in a vacuum yielded *barium* (*N-dithiocarboxyalanyl)glycine* (IV), which recrystallised from aqueous ethanol as a colourless, microcrystalline powder, m. p. above 280°, and was dried at 100°/0·1 mm. (Found: C, 19·4; H, 3·7; N, 7·6. $C_6H_8O_3N_2S_2Ba$ requires C, 20·1; H, 2·2; N, 7·8%). The barium salt (1·45 g.) in water (8 c.c.) was acidified with N-hydrochloric acid (8 c.c.) (pH then 3), whereupon 2-thio-4-methylthiazolid-5-one (III; R = Me) crystallised in needles, m. p. 125—126° (0·45 g., 75%). When acidification was effected with acetic acid, (III; R = Me) separated more slowly, and in poorer yield.

DL-Alanylglycylglycine (Fischer, *Ber.*, 1903, **36**, 2982) (0·61 g.) in 0·339N-barium hydroxide (18 c.c., 2 equivs.) was shaken with carbon disulphide (1 c.c.) for 18 hours in a nitrogen atmosphere, and the yellow-orange solution acidified with 2N-hydrochloric acid (3·2 c.c.). Extraction with ethyl acetate, after drying and evaporation, yielded 2-thio-4-methylthiazolid-5-one, m. p. 122—125°.

Glycylglycine (Freudenberg, *Ber.*, 1932, **65**, 1191) (0·66 g.) in 0·339N-barium hydroxide (29·5 c.c., 2 equivs.) was shaken with carbon disulphide (1 c.c.) for 22 hours at room temperature, under nitrogen. The solution went through a maximum orange colour and then became yellower, and a little hydrogen sulphide was produced. A portion (10·5 c.c.) was acidified with concentrated hydrochloric acid (2·5 c.c.), whereupon 2-thiothiazolid-5-one (III; R = H) separated slowly; the solution and crystals were extracted with ethyl acetate to secure the full yield (0·12 g., 51%). The remainder of the dithiocarbamate solution (pH 8) was saturated with carbon dioxide (pH then 6·5), and evaporated to dryness in a vacuum to give yellow barium (*N*-dithiocarboxyglycyl)glycine, which could be precipitated cleanly from aqueous ethanol. It exhibited a bright red fluorescence in ultra-violet light.

DL-Phenylalanylglycine was conveniently synthesised by the procedure of Wessely and Sigmund (*Z. physiol. Chem.*, 1926, **157**, 91) from DL-anhydro-*N*-carboxyphenylalanine and glycine, the former reagent being prepared by an improved method (Levy, *Nature*, in the press). Thus, DL-phenylalanine (4 g.) was suspended in a solution (40% w/w) of carbonyl chloride in toluene (150 c.c.) and gently heated until refluxing. After boiling for a further 4 hours, the clear solution was cooled to 0°, and DL-anhydro-*N*-carboxyphenylalanine (2·7 g.), m. p. 125°, collected. A further 0·5 g. (total yield, 69%), m. p. 124°, was obtained by concentration of the filtrate. In another preparation, phenylalanine (1·0 g.) was heated

under reflux with carbonyl chloride in toluene (10% w/w; 25 c.c.) for 1·25 hours, whereafter the carboxy-anhydride (0·75 g.) crystallised, on cooling, in large blades, m. p. 128—129° to a clear liquid which evolved carbon dioxide vigorously at ~155°. A further 0·06 g. (total yield, 70%), m. p. 127—128°, was obtained from the filtrate.

The peptide (0·3 g.) in 1·1N-potassium hydroxide (2·7 c.c., 2·2 equivs.) was shaken with carbon disulphide (0·5 c.c.) for 3 hours in nitrogen, and the resulting solution extracted with ether, cooled to 0°, and acidified with concentrated hydrochloric acid (10 drops). 2-Thio-4-benzylthiazolid-5-one separated as a gum which slowly solidified, and recrystallised from ethanol in needles, m. p. 159°.

The author is grateful to Sir Ian Heilbron, D.S.O., F.R.S., and Dr. A. H. Cook for their helpful interest in this work, and to the Department of Scientific and Industrial Research for a Senior Research Award.—Imperial College of Science and Technology, S. Kensington, London, S.W.7. [*Received, August 24th*, 1949.]

The Action of Copper on Some Aryldiazonium Sulphates, and the Isolation of Copper Salts.

By Herbert H. Hodgson and John Habeshaw.

In view of the recent paper by Cowdrey and Davies (*J.*, 1949, S 48) in which the formation of copper complexes in the Sandmeyer reaction has been reported, some work done by us on a modified Gattermann reaction during 1935—1937 is of interest. It was found that, when copper reacted with aryldiazonium sulphates, deamination occurred to an extent which varied according to the amine employed, and also that the amount of phenol (or naphthol) which could be directly isolated by steam-distillation was generally less than expected. The steam-distillation residues contained copper compounds which were sparingly soluble in boiling water and were decomposed by alkali to give the phenol or naphthol. It would appear, therefore, that the low yield of phenol or naphthol could be accounted for in part by these copper salts. The salts are usually white, or yellow in the case of the nitro-compounds, do not melt but sinter and decompose when heated, and are attacked slowly by cold mineral acids, which become green, while the solid discolours and in some cases becomes black. Unfortunately, only analyses for the copper content of these materials are available but, as can be seen from the table, these correspond to the structure Ar·O·Cu. These and other reaction products are recorded in the table below.

Experimental.—Preparation of the reduced copper. A solution of crystallised copper sulphate (50 g.) in hot water (500 c.c.) was stirred with zinc dust (15 g.), added gradually, and the precipitated copper filtered off and washed.

General reaction procedure. A solution of the amine (5 g.) in sulphuric acid (25 c.c.; *d* 1·84) and water (150 c.c.) was diazotised below 5° with the calculated amount of sodium nitrite in water, the excess of nitrous acid removed by urea, and the mixture treated gradually at room temperature with the copper paste (rather than *vice versa*) to avoid the copper surface becoming coated with reaction products; the mixture was kept overnight, and then steam-distilled to remove the deaminated product (phenol or naphthol) and any volatile diaryl such as diphenyl. The steam-distillate was made alkaline and extracted with ether to remove all but the phenols, and then acidified cold with sulphuric acid and again extracted with ether to remove the latter. The steam-distillation residue was repeatedly extracted with hot water and the extracts were filtered hot; on cooling there separated, after several hours, white or yellow copper compounds of the respective phenol or naphthol. The final residue was extracted with hot aqueous sodium hydroxide to decompose any remaining copper compounds, washed with water, dried, and boiled with benzene to remove non-volatile diaryls and azo-compounds. In the cases of the nitro-naphthylamines, the products listed as (1) in the table are those obtained by the addition of copper to the solutions obtained after their diazotisation by the glacial acetic–nitrosylsulphuric acid procedure (Hodgson and Walker, *J.*, 1933, 1620), whereas the products listed as (2) are those obtained after dilution of the acid mixture with ice (100 g.).

Reaction Products (in g.) from Individual Amines (5 g.).

(The amounts are the mean of three experiments.)

Diazonium sulphate.	Deaminated product.	Azo-compound.	Free phenol or naphthol.	Total diaryl or dinaphthyl.	Copper compound. Yield.	Cu, %.	Cu, calc. %.
Benzene	—	0·2	0·5	0·3	None	—	—
o-Chlorobenzene	0·25	1·2	0·1	—	0·25	32·6	33·0
,,	0·6	2·0	0·2	—	0·25	32·8	33·0
o-Nitrobenzene	0·2	—	0·5	2·5	0·25	32·3	31·3
,,	0·4	—	0·6	2·0	0·3	32·7	31·3
,,	0·3	—	0·6	2·5	0·3	32·5	31·3
p-Toluene	0·65	0·48	0·8	—	None	—	—
Naphthalene-1	0·1	—	0·4	—	None	—	—
Naphthalene-2	0·2	—	2·1	—	None	—	—
4-Chloronaphthalene-1	—	2·4	0·5	—	0·5	26·0	26·2
1-Chloronaphthalene-2	—	2·0	0·4	—	0·4	25·8	26·2
2-Nitronaphthalene-1	0·7 (1) 0·25 (2)	1·0 (1)	0·5	1·3 (2)	0·8	25·8	25·1
4-Nitronaphthalene-1	0·4 (1) 0·15 (2)	1·5 (1)	0·2	2·0 (2)	0·3	26·0	25·1
1-Nitronaphthalene-2	0·5 (1) 0·15 (2)	1·5 (1)	0·2	1·3 (2)	0·3	25·9	25·1

In each case, the copper compound was ignited with nitric acid and the copper weighed as oxide after ignition.

The authors thank Imperial Chemical Industries Ltd., Dyestuffs Division for gifts of chemicals.—
TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, September 22nd,* 1949.]

---

*The Reduction of Toluene-*p*-sulphonic Esters.* By G. W. KENNER and M. A. MURRAY.

THE reduction of toluene-*p*-sulphonic esters has recently been studied by Schmid and Karrer (*Helv. Chim. Acta*, 1949, **32**, 1371) using lithium aluminium hydride and by ourselves (*J.*, 1949, S 178) using Raney nickel and hydrogen; the results of these two investigations form an interesting contrast. Whereas the customary hydrogenation converts the aryl toluenesulphonates into aromatic hydrocarbons, and the alkyl esters into alcohols, lithium aluminium hydride, in general, yields phenols and de-oxygenated aliphatic compounds respectively. As we remarked in our paper, this latter mode of fission is in line with the well-known heterolytic decompositions of toluene-*p*-sulphonic esters by nucleophilic reagents, and Schmid and Karrer (*loc. cit.*) have also drawn attention to the analogy between the reactions of lithium aluminium hydride and those of the Grignard reagents. It is therefore suggested that these reductions may be represented as follows, lithium aluminium hydride being regarded as a source of potential hydride ions :

$$Ar\cdot O\cdot SO_2\cdot C_7H_7 \xrightarrow{H^\cdot} Ar\cdot H + HO\cdot SO_2\cdot C_7H_7$$
$$Ar\cdot O\cdot SO_2\cdot C_7H_7 \xrightarrow{H^-} Ar\cdot OH + HO\cdot SO\cdot C_7H_7 \text{ and reduction products}$$

$$Alk\cdot O\cdot SO_2\cdot C_7H_7 \xrightarrow{H^\cdot} Alk\cdot OH + \text{reduction products of } HO\cdot SO\cdot C_7H_7$$
$$Alk\cdot O\cdot SO_2\cdot C_7H_7 \xrightarrow{H^-} Alk\cdot H + HO\cdot SO_2\cdot C_7H_7$$

The already publicised reactions of lithium aluminium hydride, for example with carbonyl groups (see, *inter alia*, Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 1197, 2548) and epoxides (see, *inter alia*, Plattner, Heusser, and Kulkarni, *Helv. Chim. Acta*, 1948, **31**, 1885), as well as the characteristic inertness of unpolarised double bonds to this reagent are in accord with this interpretation. Further, at the suggestion of Professor V. Prelog, one of us allowed lithium aluminium hydride to react with strychnine methosulphate and found the major product to be strychnidine. That is, the amide linkage had been reduced and the methyl group, which is more susceptible to S_N2 reactions than the higher alkyl groups (cf. Hughes, *Trans. Faraday Soc.*, 1941, **37**, 607), had been displaced :

$$\gtrless N^+ - CH_3 \xrightarrow{H^-} \gtrless N + CH_4$$

The exceptional cases of 3-toluene-*p*-sulphonyl 1 : 2-5 : 6-di*iso*propylidene glucose and 1-toluene-*p*-sulphonyl 2 : 3-4 : 5-di*iso*propylidene fructose (Schmid and Karrer, *loc. cit.*) may well be examples of steric hindrance in such reactions.

Strychnidine.—Strychnine methosulphate (Clemo, Perkin, and Robinson, *J.*, 1927, 1589) (4·60 g.) was added during 15 minutes to lithium aluminium hydride (1·14 g.) in tetrahydrofuran (25 c.c.) with cooling. The mixture was shaken for ½ hour without cooling and then heated to boiling during 1½ hours before being poured into ice-water (70 c.c.). Chloroform (50 c.c.) was then added, the solid filtered off, and the filtrate extracted with chloroform after being made alkaline with ammonia. The solid was stirred with 3 portions of chloroform, and the combined extracts of the aqueous and the solid phase were dried and evaporated. Recrystallisation of the resulting solid (2 g.) from ethoxyethanol yielded strychnidine, m. p. 258° (in vac.; corr.) (undepressed by an authentic specimen), $[\alpha]_D^{19}$ −63° ± 3° (*c*, 1·5 in chloroform) (Found, in material sublimed at 150°/0·01 mm. : C, 78·5; H, 7·45. Calc. for $C_{21}H_{24}O_2N_2$: C, 78·7; H, 7·55%). UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE, and ROYAL HOLLOWAY COLLEGE, UNIVERSITY OF LONDON. [*Received, October 14th,* 1949].

The Preparation of 2-Ethoxyethyl Chloride and Bromide. By D. E. AMES and R. E. BOWMAN.

IN connection with another investigation we wished to prepare certain 2-alkoxyalkyl halides. There are many examples in the literature of such preparations, differing, however, very considerably with respect to the yields obtained. Bennett and his co-workers (*J.*, 1925, **127**, 1279; 1927, 270, 472), L. I. Smith *et al.* (*J. Org. Chem.*, 1939, **4**, 334), and Hurd and Fowler (*J. Amer. Chem. Soc.*, 1939, **61**, 249) used the appropriate thionyl halide in the presence of a base (Darzens, *Compt. rend.*, 1911, **152**, 1314). Use of phosphorus tribromide has been described by Palomaa and Kenetti (*Ber.*, 1931, **64***B*, 797), Harrison and Diehl (*Org. Synth.*, **23**, 32), Chalmers (*Canadian J. Res.*, 1932, **7**, 464), and Hurd and Fowler (*loc. cit.*) for the same purpose.

We employed the readily available 2-ethoxyethanol as model substance using Darzens's method with thionyl chloride and bromide under conditions described by Gerrard (*J.*, 1939, 100), and thereby obtained excellent, reproducible yields. Furthermore, we have confirmed the finding that the use of more than one molecular proportion of base reduces the yield although excess of thionyl halide is not deleterious.

The following method gave the best results : a mixture of the dry, purified base (1 mol.) and 2-ethoxyethanol (1 mol.) was cooled to −20° and the appropriate thionyl halide (1·1 mols.) added

with stirring at such a rate that the temperature did not rise above 0°. The reaction mixture was then allowed to warm to room temperature and thereafter heated at 100° (bath) for 2 hours. When cold, it was treated with dilute hydrochloric acid, and the product isolated with ether. The ethereal extracts were washed with dilute sodium hydroxide solution and dried (Na_2SO_4), and the solvent was removed by careful distillation through a Vigreux column. The product was then obtained by distillation of the residue. In this manner 2-ethoxyethyl chloride was obtained (yields in parentheses) by use of dimethylaniline (61%), pyridine (80%), or quinoline (84%). The bromide was obtained in 70% yield with pyridine as base.

With dimethylaniline as base, an increase in the proportion of thionyl chloride (3 mols.) was without significant effect on the yield of product. Excess of base, *viz.*, 2-ethoxyethanol (1 mol.), dimethylaniline (2 mols.), and thionyl chloride (3 mols.), under the same conditions reduced the yield of chloride to 40%.

We are indebted to the Medical Research Council for a grant which has enabled one of us (D. E. A.) to take part in this work.—Birkbeck College, London, E.C.4. [*Received, October 21st*, 1949.]

Diterpenes. Part II. The Optical Rotation of Hosking's Kaurene. By Lindsay H. Briggs and W. I. Taylor.

Hosking (*Rec. Trav. chim.*, 1928, **47**, 578; 1930, **49**, 1036) described a diterpene, kaurene, m. p. 57—58°, from the essential oil of *Agathis australis* (" kauri "), and its hydrochloride, m. p. 110—111°, from which the hydrocarbon was regenerated by the action of alcoholic potassium hydroxide. It has been shown in Part I (*J.*, 1948, 1888) that the diterpene occurring in the oil has a lower m. p. (50°) and that it is isomerised to *iso*kaurene, m. p. 64°, on treatment of its hydrochloride with alkali. Both kaurene and *iso*kaurene form the same hydrochloride and dihydro-derivative, typical of compounds whose isomerism is caused by the change of the double bond from an exocyclic to an endocyclic position. The m. p.s of Hosking's products are intermediate between those of kaurene and *iso*kaurene and it would appear that in both cases he was dealing with an impure form of *iso*kaurene.

A larger discrepancy occurs, however, in the optical rotation of Hosking's and our product. Although Hosking's liquid diterpene fraction from which the kaurene was isolated was optically active, all the rotations observed on solid products derived therefrom had zero values. On the other hand, all our products had definite lævorotations (*loc. cit.*). With the number of asymmetric centres present in any tetracyclic structure possible for kaurene on an isoprene plan (possibly five) it is difficult to see how racemisation of all centres had occurred in Hosking's manipulation.

Through the courtesy of Professor L. Ruzicka, to whom we express our thanks, we have been able to re-examine an original sample of dihydrokaurene obtained by Hosking. No sample of kaurene remained but the dihydro-derivative on crystallisation from acetic acid had m. p. and mixed m. p. 86°, with $[\alpha]_D^{21}$ $-32° \pm 2°$ (*c*, 2·0 in chloroform) in agreement with that recorded by Briggs and Cawley in Part I (*loc. cit.*), *viz.*, $[\alpha]_D^{20}$ $-35·7°$ (*c*, 0·33 in chloroform), from which we conclude that the original kaurene was active also.

No adequate explanation can be advanced to explain these contrasting results.

One of us (W. I. T.) is indebted for a National Research Scholarship of New Zealand.—Auckland University College, Auckland, New Zealand; and Eidg. Technischen Hochschule, Zürich. [*Received, November 14th*, 1949.]

Dimorphism in Acenaphthene-3-aldehyde. By John H. Gorvin.

The aldehyde prepared from acenaphthene by the Gattermann synthesis was reported by Hinkel, Ayling, and Beynon (*J.*, 1936, 344) to melt at 87°; subsequently Fieser and Jones (*J. Amer. Chem. Soc.*, 1942, **64**, 1666) obtained by the *N*-methylformanilide—phosphorus oxychloride procedure a substance, m. p. 107·4—108°. Each of these products gave evidence of being acenaphthene-3-aldehyde.

In the present investigation no difficulty was encountered in the preparation of acenaphthene-3-aldehyde, m. p. 107—107·5° (corr.), by either method. It was therefore of interest to examine the product obtained by the earlier workers, and I am very grateful to Dr. L. E. Hinkel and Mr. E. E. Ayling, of University College, Swansea, for making available a specimen of their original crude aldehyde. The principal contaminant of this material proved to be a very small amount of tar which was difficult to remove completely by crystallisation from light petroleum (b. p. 60—80°); the crystals obtained had m. p. 87°. When however the warm petroleum solution was filtered through activated alumina held in a sintered-glass Büchner funnel the clear filtrate deposited crystals, m. p. 107—107·5°, of authentic acenaphthene-3-aldehyde. A similar product was obtained on hydrolysis of the anil, m. p. 97°, prepared by the Swansea workers (*loc. cit.*) from their aldehyde, m. p. 87°.

In preparations of the aldehyde carried out in these Laboratories the light-petroleum mother-liquor on one occasion deposited crystals, m. p. 85°, showing no melting-point depression on being mixed with the material of Hinkel, Ayling, and Beynon (*loc. cit.*). This substance similarly crystallised as the high-m. p. form after filtration of its light-petroleum solution through alumina.

As the amount of tarry material present in the crude aldehyde was quite inadequate to account for a melting-point lowering of 20° it was concluded that the impurity had stabilised a polymorphic modification of the aldehyde and had inhibited the change to the stable, high-m. p. form which would be expected to occur on fusion or long storage. Confirmation of this was obtained by undisturbed cooling of pure molten acenaphthene-3-aldehyde; often the melt crystallised rapidly to give the high m. p. form but sometimes it could be successfully supercooled with eventual solidification to a crystalline mass, m. p. *ca.* 89°, fusion of which was usually followed by crystallisation of the melt in the form, m. p. 107—107·5°.

The ease of conversion of the metastable into the stable form of the pure aldehyde is in striking contrast to the persistence of the low-melting form in its contaminated state. A rather similar case has previously been noted (Gorvin, *J.*, 1945, 734) in ethyl 3-sulphanilamidobenzoate; the form, m. p. 105°, recorded by an earlier group of workers persisted until the compound was carefully purified, whereupon conversion into a stable form, m. p. 153°, occurred immediately on fusion at the lower temperature. These examples of metastable states stabilised by impurities emphasise the importance of removal of all traces of contaminating tarry material from organic substances before recording physical constants; the increasing availability of activated adsorbents has in many cases greatly simplified this procedure.—WELLCOME LABORATORIES OF TROPICAL MEDICINE, LONDON, N.W.1. [*Received, November 18th*, 1949.]

Synthetic Ribonucleoside-2′ Phosphates: a Correction. By D. M. BROWN, L. J. HAYNES, and A. R. TODD.

IN a recent paper Michelson and Todd (*J.*, 1949, 2476) described the synthesis of a number of mononucleotides derived from the natural ribonucleosides, adenosine, guanosine, cytidine, and uridine. In the course of this work the benzylidene derivatives of adenosine and guanosine were phosphorylated and the protecting groups subsequently removed, yielding products which were assumed to be adenosine-2′ phosphate and guanosine-2′ phosphate. This assumption appeared to be warranted on the evidence that (i) the condensation product of guanosine with benzaldehyde was shown by Bredereck and Berger (*Ber.*, 1940, **73**, 1124) and by Gulland and Overend (*J.*, 1948, 1380) to be 3′ : 5′-benzylidene guanosine, and (ii) the behaviour of the products on acid hydrolysis was analogous to that of the substances described in the literature as uridine-2′ phosphate (Gulland and Smith, *J.*, 1947, 338) and cytidine-2′ phosphate (Gulland and Smith, *J.*, 1948, 1527), the two latter compounds having been prepared in strictly analogous fashion from benzylidene uridine and benzylidene cytidine.

Further investigation has shown, however, that the product we described as adenosine-2′ phosphate is in fact essentially adenosine-5′ phosphate; the latter compound can be isolated in high yield from the amorphous nucleotide described by Michelson and Todd (*loc. cit.*) and has been identified by periodate titration (absorption of 1 mole of oxidant/mole) and by comparison of chemical and physical properties including *X*-ray diffraction photographs. In the same way it has been found that the alleged cytidine-2′ phosphate of Gulland and Smith (*loc. cit.*), as prepared by us, is in fact cytidine-5′ phosphate. From the method of preparation and particularly from consideration of their acid hydrolysis curves, there can be little doubt but that the products described as uridine-2′ phosphate (Gulland and Smith, *loc. cit.*) and guanosine-2′ phosphate (Michelson and Todd, *loc. cit.*) also consist essentially of the corresponding 5′-phosphates.

The origin of 5′-phosphorylated nucleosides in these synthetic experiments is not yet clear but their production would seem to indicate either that a facile and unsuspected migration of acyl groups occurs at some intermediate stage or that the experimental evidence for the 3′ : 5′-structure of the benzylidene nucleosides (Gulland and Overend, *loc. cit.*) is not valid. If the former explanation should prove correct, the finding might well be of significance in the interpretation of nucleic acid structure based on hydrolytic studies. The whole question is at present being investigated in this laboratory, together with the problem of the synthesis of the true nucleoside-2′ phosphates and our results will be communicated in detail later. It seems, however, desirable at this stage to draw attention to the fact that the synthetic nucleotides described in the literature as nucleoside-2′ phosphates do not have the structure assigned to them, the more so as the recent findings of Carter and Cohn (*Fed. Proc.*, 1949, **8**, 190) have aroused interest in nucleoside-2′ phosphates as possible hydrolysis products of yeast ribonucleic acid.—UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, December 5th*, 1949.]
