Ether extraction gave a 56 per cent yield of 4-cyano-1-phenylpyrazole, m.p. 94–95° (Lit.[2] 95°). Found: C, 70·8; H, 4·4; N, 24·8. Calc. for $C_{10}H_7N_3$: C, 71·1; H, 4·1; N, 24·8 per cent. A quantitative yield of 1-phenylpyrazole-4-carboxylic acid, m.p. 221–222°, was obtained on hydrochloric acid hydrolysis of the 4-cyanopyrazole.

The overall yield of 1-phenylpyrazole-4-carboxylic acid by this synthesis is greater than 50 per cent and the route should provide easy access to other 1-substituted pyrazole-4-carboxylic acids.

There is but one reference in the literature to a similar substitution by this method of a pyrazole-4-diazonium group by halogen and the yields were poor[6]. We have found that, utilizing cupric salts as catalysts at elevated temperatures, halogen can be introduced in good yield, for example, 1-phenylpyrazole-4-diazonium bromide gives 4-bromo-1-phenylpyrazole in 86 per cent yield.

D. G. O'Donovan
A. P. Carroll
J. Reilly

Chemistry Department,
University College,
Cork.
Nov. 28.

[1] Finar, I. L., and Godfrey, K. E., *J. Chem. Soc.*, 2293 (1954).
[2] Finar, I. L., and Lord, G. H., *J. Chem. Soc.*, 3314 (1957).
[3] Knorr, L., *Ber.*, **28**, 714 (1895).
[4] Hill, H. B., and Torrey, J., *Amer. Chem. J.*, **22**, 89 (1899).
[5] Balcom, D., and Furst, A., *J. Amer. Chem. Soc.*, **75**, 4334 (1953).
[6] Morgan, G. T., and Ackerman, I., *J. Chem. Soc.*, **123**, 1308 (1923).

BIOCHEMISTRY

3 : 3′-Diamidinocarbanilide: a New Drug Active against Babesial Infections

Quinuronium sulphate[1] is the commonly employed treatment for British bovine redwater and a single injection of 1 mgm. of this drug per kgm. of body-weight is effective in a high proportion of cases. But quinuronium sulphate has the disadvantage that even in therapeutic doses it produces toxic effects associated with parasympathetic stimulation. The diamidines, phenamidine and pentamidine, as their di-isethionates, and Berenil are well tolerated and are also used for the treatment of bovine babesiasis, but they are less active than quinuronium sulphate.

During the search for a new drug which would be at least as effective as quinuronium sulphate but without its toxic effects, a large number of compounds has been screened for activity against *Babesia rodhaini* in mice, and the most promising of these were tested against *Babesia divergens* in splenectomized calves. One of the best of these was M and B 5062*A* — 3 : 3′-diamidinocarbanilide di-isethionate, which was active against *B. divergens* in calves and produced none of the toxic effects associated with quinuronium sulphate. This activity of the 3 : 3′-diamidine was unexpected because of the inactivity of the corresponding 4 : 4′-diamidine. 3 : 3′-Diamidinocarbanilide di-isethionate[2] was prepared, among other methods, by the usual Pinner reaction on the corresponding dinitrile. It is a white, crystalline, anhydrous solid, m.p. 209° C. (decomposing at 256° C.) (found: N, 15·1; S, 11·6 per cent. $C_{15}H_{16}ON_6,2C_2H_6O_4S$ requires: N, 15·3; S, 11·7 per cent), and is approximately 100 per cent w/v soluble in water.

The acute toxicity (*LD*50) of M. and B. 5062*A* in mice was found to be 120 mgm./kgm. subcutaneously compared with 8 mgm./kgm. for quinuronium sulphate, while a comparison of the two compounds in non-infected, splenectomized calves after subcutaneous injection at a site behind the shoulder showed that the maximum tolerated dose of M. and B. 5062*A* was greater than 40 mgm./kgm., and that of quinuronium sulphate less than 4 mgm./kgm. There were no obvious symptoms of toxicity in the calves that received this dose of M. and B. 5062*A*. During the therapeutic activity tests two calves developed mild ataxia which lasted for about 3 hr. after treatment with a dose of 40 mgm./kgm.; otherwise no symptoms of systemic toxicity were observed.

In the therapeutic activity tests, seventeen calves infected, after splenectomy, with *B. divergens* were treated subcutaneously with M. and B. 5062*A* at doses between 3 and 40 mgm./kgm. body-weight. With all doses the intensity of the parasitæmia was reduced within 24 hr. and complete clearance was obtained within three days. In all the calves treated with 5 mgm./kgm. or higher doses, the hæmoglobinuria was cleared in 24 hr.

Further details, including a report on field investigations, will be published in due course.

We thank Mr. T. G. Mitchell for much technical assistance in the experiments with *B. rodhaini* and *B. divergens*.

J. N. Ashley
S. S. Berg
J. M. S. Lucas

May and Baker, Ltd.,
Research Laboratories,
Dagenham, Essex.
Veterinary Research Division,
Ongar, Essex.

[1] Kikuth, W., *Zbl. Bakt.*, **135**, 135 (1935).
[2] May and Baker, Ltd., and Berg, S. S., Appl. No. 40428/58.

Metabolism of 1-^{14}C Lignoceric Acid in the Rat

Lignoceric acid, the straight-chain, saturated C_{24} fatty acid, occurs in sphingolipids in amide linkage with the amino-alcohol sphingosine[1,2]. It has not been found in the ester linkages of neutral fat or glycerophosphatides, and very little information is available on its metabolism. In the work reported here, lignoceric acid labelled with ^{14}C carboxyl was administered to rats and its metabolic fate studied.

Lignoceric acid was isolated from peanut oil and converted to 1-^{14}C lignoceric acid, via 1-^{14}C tricosyl cyanide (modification of Anker's method for synthesis of myristic acid[3]). Contrary to the fatty acids of 18 carbon atoms or less, lignoceric acid did not form a soluble complex with serum albumin. Paper electrophoresis of a mixture of 1-^{14}C lignoceric acid and serum albumin (0·5–1 equivalent of the acid per equivalent of albumin) showed that the radioactive fatty acid did not migrate with the albumin but remained at the point of origin. 1-^{14}C lignoceric acid was therefore injected as a neutralized aqueous suspension into the tail vein of rats; the various organs were isolated and extracted with a 2:1 chloroform methanol mixture. Respiratory carbon dioxide labelled with carbon-14 was collected in some experiments, and, in others, the livers were removed, dried and extracted successively with acetone, petroleum ether and ethanol. The acetone and petroleum