

LETTERS TO THE EDITOR

adrenal glands were removed as quickly as possible after death, weighed and ground up in a mortar with sand and acid. The mixture was filtered

TABLE I.
MEAN VALUES FOR NORADRENALINE AND ADRENALINE CONTENT OF SUPRARENAL GLANDS.

Animal	mg./g. fresh tissue		approximate percentage of adrenaline in the mixture
	adrenaline	noradrenaline	
Rabbit	0.485	traces	100
Rat	1.1	0.13	90
Cattle	2.0	0.6	77
Guinea-pig	0.26	0.08	77
Cat	0.8	0-0.65	55-100
Dog	0.8	0-0.85	49-100
Fowl	2.01	8.09	20

and the filtrate tested for adrenaline and noradrenaline on the following pharmacological preparations; the blood pressure and nictitating membrane of the spinal cat¹, the isolated rectum of the chick², and the isolated ileum of the rabbit. The mean value of extracts from 18 fowls was 8.09 mg. of noradrenaline per g. of fresh tissue of 2.01 mg. of adrenaline per g. (see Table I).

The significance of this finding is not yet clear. It is not that noradrenaline is more active on the blood pressure of the fowl than is adrenaline, for comparisons show that the latter amine is about twice as potent as the former (just as it is in the rabbit where the glands contain only adrenaline). Perhaps it may be that the adrenal medulla is not strongly stimulated very frequently and that the small adrenaline content is sufficient for its immediate needs. Also the methylating process in the fowl may be a slow one. It is certainly of interest that intravenous doses of dibenamine do not reverse the vasoconstrictor action of adrenaline in the fowl³. A similar resistance to adrenergic blockage by ergot was noted many years ago. Another interesting point is that in man the adrenal glands contain about 75 per cent. of adrenaline and 25 per cent. of noradrenaline, and yet in medullary tumours (pheochromocytoma) noradrenaline predominates, with adrenaline only about 10 per cent. of the mixture.

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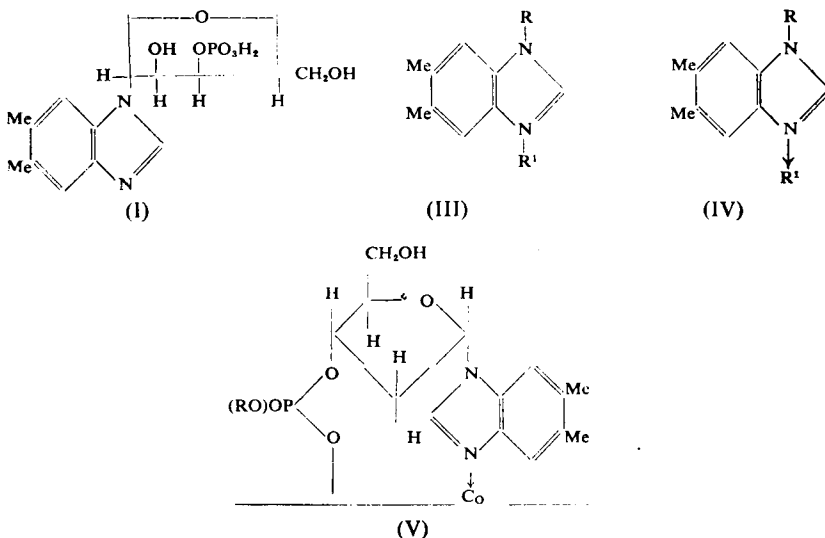
The Mode of Linkage of Component α in Vitamin B₁₂

SIR,—A comparison of the absorption spectra of component α (I)^{1,2,3,4}, and vitamin B₁₂ (II) reveals an anomaly. Thus whereas (I) shows a well-resolved fine structure band or "notch" at $\lambda=2850$ Å in dilute acid and $\lambda=2880$ Å

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in dilute alkali, (II) shows only an inflection in this region which is, moreover, unchanged in position over the pH range 2-12. Some factor or factors are therefore operative in the "component α combination" existing in (II) which affect the contribution made by the benziminazole chromophore of (I) to the spectrum of B_{12} . A consideration of the ways in which the chromophoric character of (I) can be affected sufficiently to abolish the resolution of this "notch" without interfering with the wavelength position of the main benziminazole band and its subsidiary features leads, by a process of elimination, to the conclusion that the nitrogen atom in position 3 (N^3) of (I) is involved in some form of combination within the B_{12} molecule. This combination, on theoretical grounds, would appear to be a linkage of covalent (III) or co-ordinate (IV) character.

Spectroscopic measurements of quaternary derivatives of benziminazole eliminate (III) from further consideration. Platinic chloride complexes of 1-substituted benziminazoles, however, which possess the structural feature (IV), show anomalous spectral characteristics in marked accord with those established for the benziminazole contribution in (II).



Studies of the action of cyanide on the spectrum of B_{12} lead to the conclusion that the reversible formation of a purple " B_{12} -cyanide" complex is dependent upon co-ordination of cyanide ion with cobalt. As this co-ordination leads to a partial abolition of the anomaly observed in the component α contribution to the B_{12} spectrum, i.e., to greater resolution of the inflection at $\lambda=2885 \text{ \AA}$, it is concluded that N^3 in (I) is probably linked directly to cobalt by a co-ordinate link as shown in (V). The cobalt-containing complex represented graphically in (V) as a straight line is visualised as a planar structure spatially akin to the porphyrins, the benziminazole ring lying perpendicularly to this plane.

A full account of this work is being submitted for publication in your Journal.

It is a pleasure to acknowledge the encouragement of the Directors of The British Drug Houses, Ltd., in this work.

LETTERS TO THE EDITOR

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Conversion of Vitamin B_{12b} into Vitamin B₁₂

SIR.—The spectra^{1,2} of vitamins B₁₂ and B_{12b}, resemble each other in general character, but differ considerably in the position and magnitude of particular features. A structural similarity is thus evident between the two compounds³ which is reflected in certain of their chemical reactions. On treatment with cyanide ion⁴ in aqueous solution, both compounds form purple cyanide complexes having the *same* absorption spectrum, which is markedly different from those of the two vitamins. On removing cyanide from the complex, vitamin B₁₂ reverts to its original state, as shown by its absorption spectrum, microbiological activity, chromatographic behaviour⁵, and general crystallographic appearance. On removing the cyanide from the B₁₂-cyanide product, however, the spectrum does not revert to that of B_{12b}, but is strikingly similar to that of B₁₂. The regenerated material, moreover, shows further properties similar to those of B₁₂, viz. microbiological activity against *Lactobacillus lactis* Dorner and behaviour on paper chromatography⁵. These observations lead to the conclusion that B_{12b} may be converted, through intermediate formation of a cyanide complex, into a substance which, as far as can be ascertained at present, is identical with vitamin B₁₂. As B₁₂ appears to form the major constituent of the B₁₂ group of factors in materials derived from the *in vitro* fermentation of micro-organisms, the above conversion assumes preparative importance.

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