Synthesis of Corrins. Part I. Nickel and Cobalt 1,19-Dimethylcorrin and 1,19-Dimethyl-4,5-dihydrocorrin Perchlorates

By **A. W. Johnson** * and **W. R. Overend**, School of Molecular Sciences, University of Sussex, Falmer, Brighton BN1 9QJ

Condensation of dipyrromethane with 2-formyl-5-methylpyrrole yields, 1,19-dimethyl-1,19-dideoxybiladiene-*ac* dihydrobromide, which can be cyclised in the presence of nickel or cobalt ions to give the corresponding metal 1,19-dimethyltetradehydrocorrin salts. Hydrogenation of these salts under a wide variety of experimental conditions gives a mixture of the metal 1,19-dimethyl-corrin and -4,5-dihydrocorrin salts, which have been separated and isolated as the perchlorates. The corrin has also been isolated as the neutral dicyanocobalt(III) complex.

THE demonstration [1] that the biosynthesis of vitamin B_{12} depends on porphobilinogen (I) led us to investigate the synthesis of the corrin ring system (II), which as a cobalt(III) complex represents the chromophore of vitamin B_{12}, based on pyrrolic intermediates. We have reported [2] that the hydrogenation of nickel(II) 8,12-diethyl-1,3,7,13,17,19-hexamethyltetradehydrocorrin chloride (III; R = H, X = Cl) or nickel(II) 1,7,8,12,-13,19-hexamethyltetradehydrocorrin perchlorate at 160° under 100 atm of hydrogen in the presence of freshly prepared Raney nickel (grade W2) [3] gave the corresponding nickel(II) corrin perchlorates, but these were obtained only as amorphous solids. The failure to obtain crystalline corrins in this way was ascribed to the number of isomers theoretically present, consequent on the several new asymmetric centres created during the hydrogenation. When the chloride (III; R = Me, X = Cl) was hydrogenated at 100° under 100 atm of hydrogen, a product was obtained and isolated as the crystalline perchlorate. This was originally formulated [4] as a nickel(II) monodehydrocorrin salt (IV), *i.e.* containing seven conjugated double bonds, although this structure is now known to be incorrect and the product will be reformulated as an isomer of the nickel(II) corrin salt in a forthcoming paper. The difference in the courses of the two hydrogenations was ascribed to steric hindrance between the alkyl groups at C-1, C-2, C-18, and C-19.

It seemed therefore that in order to obtain crystalline corrin derivatives by this general approach, it would be preferable to avoid asymmetric β-carbon atoms in the product, as indeed was the case in the initial synthesis of the corrin (V) by Eschenmoser and his co-workers.[5] In the present paper we describe the application of the pyrrole-based synthesis to the preparation of crystalline nickel(II), cobalt(II), and cobalt(III) derivatives of 1,19-dimethylcorrin (VI). Our synthesis required the initial preparation of 1,19-dimethylbiladiene-*ac* dihydrobromide (VII), which has been cyclised to metal salts of 1,19-dimethyltetradehydrocorrin (VIII), and these in turn have been hydrogenated to the compounds (VI). Thus the complete corrin synthesis comprises three main stages.

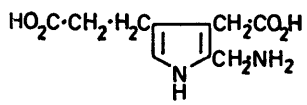
Several possibilities existed for the preparation of 1,19-dimethylbiladiene-*ac* dihydrobromide (VII). In the first instance, the condensation of 2-formyl-5-methylpyrrole with 2,2′-dipyrromethane [6] under a variety of conditions produced only dipyrromethene salts, identified by the characteristic absorption maximum at 476 nm; it was shown that these products did not arise from either of the starting materials alone. However, 2,2′-dipyrromethane is unstable in acidic solutions; for example, an n.m.r. spectrum of 2,2′-dipyrromethane in deuteriochloroform–trifluoroacetic acid showed total destruction of the compound in 2 min. 2,2′-Dipyrromethane was prepared conveniently by borohydride

[1] R. C. Bray and D. Shemin, *J. Biol. Chem.*, 1963, **238**, 1501.
[2] I. D. Dicker, R. Grigg, A. W. Johnson, H. Pinnock, K. Richardson, and P. van den Broek, *J. Chem. Soc.* (*C*), 1971, 536.
[3] R. Mozingo, *Org. Synth.*, 1955, Coll. Vol. 3, p. 181.
[4] D. Dolphin, R. L. N. Harris, J. L. Huppatz, A. W. Johnson, and I. T. Kay, *J. Chem. Soc.* (*C*), 1966, 30.
[5] E. Bertele, H. Boos, J. D. Dunitz, F. Elsinger, A. Eschenmoser, I. Felner, H. P. Gribi, H. Gschwend, E. J. Meyer, M. Pesaro, and R. Scheffold, *Angew. Chem. Internat. Edn.*, 1964, **3**, 490.
[6] R. Chong, P. S. Clezy, A. J. Liepa, and A. W. Nichol, *Austral. J. Chem.*, 1969, **22**, 229.

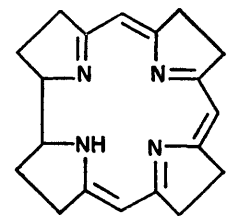
reduction of dipyrrolyl ketone, itself obtained by the action of phosgene on pyrrolylmagnesium bromide. Pyrocoll (IX) [7] was identified as a by-product from this last reaction.

At this stage we considered the use of brominated pyrrolic intermediates which were more stable and which were expected to lose the bromine substituents by hydrogenolysis in the final step. Thus diethyl 3,3′,4,4′-tetrabromodipyrromethanedicarboxylate (X; R = CO_2Et) was hydrolysed to the corresponding acid (X; R = CO_2H), but this did not yield the corresponding biladiene-*ac* salt by condensation with 2-formyl-5-methylpyrrole. This was ascribed to the resistance of the acid (X; R = CO_2H) to decarboxylation, as has been observed with brominated pyrrolecarboxylic acids.[8] Attempts were also made to obtain the diformyl derivative (X; R = CHO) through the thioester (X; R = CO·SEt). The pyrrolic thioester (XI; R = H) was converted into the 3,4-dibromo-derivative (XI; R = Br) with bromine in pyridine, but desulphurisation of (XI; R = Br) with Raney nickel gave only a low yield of the required formylpyrrole (XII). However, compound (XII) was obtained in high yield by bromination of a solution of 2-formyl-5-methylpyrrole in pyridine, but we were unable to establish experimental conditions to monohalogenate the 5-methyl group of either (XII) or the corresponding condensation product (XIII) of (XII) with malonodinitrile. For these reasons the use of brominated pyrrolic intermediates was abandoned.

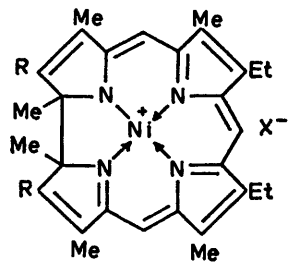
Clezy *et al.*[6] have also described a preparation of 5,5′-diformyl-2,2′-dipyrromethane (XIV), by formylation of 2,2′-dipyrromethane with benzoyl chloride and *NN*-dimethylformamide. Our initial attempts to condense compound (XIV) (modified preparation) with 2 mol. equiv. of 2-methylpyrrole in methanolic hydrogen bromide gave only dipyrromethene salts formed by decomposition of the required biladiene (VII). However, when the condensation was carried out in chloroform solution at room temperature, a maximum yield of the biladiene salt was obtained after 5 min; longer reaction periods caused decomposition to dipyrromethenes, which was also promoted by the presence of polar solvents. This observation led us to examine the condensation of 2,2′-dipyrromethane with an excess (4 mol. equiv.) of 2-formyl-5-methylpyrrole in chloroform solution; the reaction then proceeded in a similar manner and gave 1,19-dimethylbiladiene-*ac* dihydrobromide (VII). This method obviated the necessity for preparing 5,5′-diformyl-2,2′-dipyrromethane, and was the method of choice for preparing the 1,19-dimethylbiladiene-*ac* dihydrobromide (VII), although because of its instability we were unable to isolate the salt in the pure form or as a metal complex; attempts at purification by recrystallisation or chromatography led to further decomposition to the dipyrromethene. Accordingly compound (VII) was cyclised without further purification.



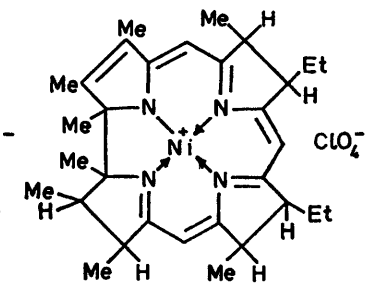
(I)



(II)



(III)



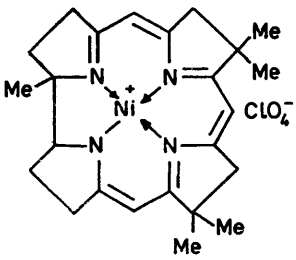
(IV)

When a methanolic solution of 1,19-dimethylbiladiene-*ac* dihydrobromide (VII) was added to a solution of nickel(II) acetate and sodium acetate in methanol and the mixture aerated for 3 h at room temperature, cyclisation occurred to give a salt of nickel(II) 1,19-dimethyltetradehydrocorrin (VIII; M = Ni). This was purified by chromatography and converted into the perchlorate, which was crystallised. The yield of the cyclised product was variable (2—22%) owing to competitive decomposition of the biladiene. When the reaction was carried out at reflux temperature, as is usual for the cyclisation of the deca-alkylbiladiene-*ac*

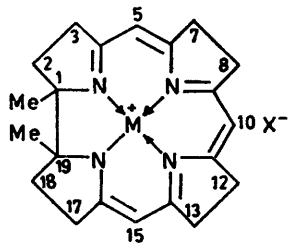
[7] J. D. Mold, R. E. Means, and A. G. Kallianos, *Tobacco Sci.*, 1960, **4**, 130 (*Chem. Abs.*, 1960, **54**, 25597.)

[8] H. J. Anderson and S.-F. Lee, *Canad. J. Chem.*, 1965, **43**, 409.

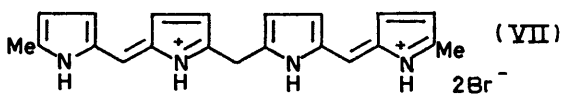
salts,[4] no cyclised material was obtained. The efficiency of the cyclisation was markedly improved by use of *NN*-dimethylformamide as solvent, in which both the biladiene salt and nickel acetate are very soluble.



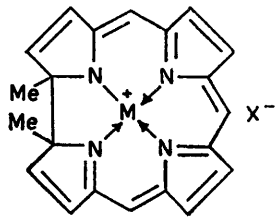
(V)



(VI)

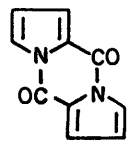


(VII)

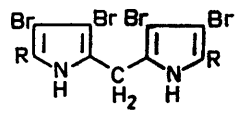


(VIII)

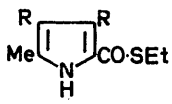
Reaction was then essentially complete in 15 min without the addition of a base; presumably traces of dimethylamine were liberated from the solvent but in



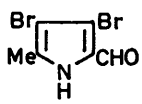
(IX)



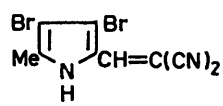
(X)



(XI)



(XII)

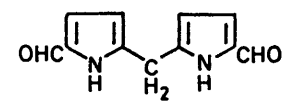


(XIII)

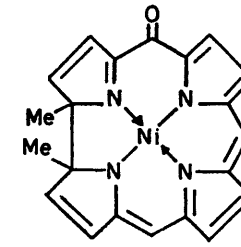
cases where the cyclisation appeared to be slow, addition of a little methanol sufficed to accelerate it. Bases such as ammonia, piperidine, or even sodium acetate caused decomposition of the product under these conditions. The use of cobalt(II) acetate in dimethyl sulphoxide proved to be the best method for the preparation of cobalt(II) 1,19-dimethyltetradehydrocorrin perchlorate (VIII; M = Co; X = ClO_4) (26% after purification).

The n.m.r. spectrum of nickel(II) 1,19-dimethyltetradehydrocorrin perchlorate was relatively simple and comprised a complex of signals between τ 1·68 and 2·4 corresponding to the three *meso*-protons and eight β-protons. The six angular methyl protons gave a sharp singlet at τ 9·23, which corresponded closely to the analogous signals in the spectra of the β-alkyl-substituted nickel tetradehydrocorrin salts.[4] The visible spectra of compounds (VIII; M = Ni or Co) showed that the eight β-alkyl groups cause a hypsochromic shift of *ca.* 10 nm; in addition they bring about a marked increase in volatility and in solubility in organic solvents. The diminished volatility of the salts (VIII) resulted in more extreme experimental conditions being required for mass spectral measurements. The mass spectra of the nickel(II) and cobalt(II) 1,19-dimethyltetradehydrocorrin perchlorates (VIII) showed base peaks at *m/e* 380 and 381 respectively, *i.e.* $(M^+ - 2)$ like the corresponding octa-β-alkyl perchlorates, although with these compounds a weaker peak corresponding to M^+ was sometimes observed. With the more volatile octa-β-alkyltetradehydrocorrin nitrates, a base peak corresponding to M^+ was observed.

Marked differences in chemical reactivity between the nickel(II) and cobalt(II) complexes (VIII; M = Ni or Co) were also observed. The nickel complex was relatively stable to acids, *e.g.* no decomposition was observed when the n.m.r. spectrum of a solution in trifluoroacetic acid was measured. On the other hand, the nickel complex was very sensitive to bases, and under mild conditions reacted to give a blue neutral product which decomposed on attempted isolation. Stronger bases resulted in rapid decomposition of the nickel complex, probably through the neutral 5-oxo-derivative (XV), which was observed as a transient green solution which formed a purple salt with acid. The electronic spectra of these products were similar to those of the corresponding octa-β-alkyl derivatives.[9] The cobalt(II) complex (VIII; M = Co) was cleaved rapidly at room temperature by 0·05N-hydrochloric acid to give a solution with a spectrum which resembled that of a biladiene-*ac* salt; 2N-sodium hydroxide caused rapid decomposition with no isolable products.



(XIV)



(XV)

Hydrogenation of nickel(II) 1,19-dimethyltetradehydrocorrin perchlorate (VII; M = Ni, X = ClO_4) at 160° and 100 atm of hydrogen for 2 h in presence of

[9] A. Hamilton and A. W. Johnson, *J. Chem. Soc.* (*C*), 1971, 3879.

Raney nickel as employed for the nickel hexa-β-alkyl-substituted tetradehydrocorrin chloride (III; R = H, X = Cl) gave a bright yellow solution. The product was precipitated as the perchlorate and purified by chromatography on alumina; a yellow crystalline product was obtained, which was mainly the corresponding nickel corrin (VI; M = Ni, X = ClO_4), but contained a small quantity of a by-product. It was soon found, however, that the foregoing hydrogenation conditions were unnecessarily severe, and that reaction at room temperature and pressure gave the nickel corrin after only 1 h, although the impurity was still present. In fact the nickel tetradehydrocorrin can act as its own hydrogenation catalyst; when a solution of the perchlorate under 80—100 atm of hydrogen was heated at 160° for 4 h in the absence of added catalyst small amounts of the corresponding corrin (up to 12·5%) could be isolated and none of the by-product was detected. The use of the homogeneous catalyst, tris(triphenylphosphine)rhodium-(I) chloride [10] under 100 atm of hydrogen and 160° for 2 h gave a low yield (<10%) of the corrin and once again apparently none of the by-product. Milder homogeneous hydrogenations gave low yields of partially hydrogenated products which were not identified completely, although one product had a visible spectrum characteristic of a nickel AD-bisdehydrocorrin salt.[2]

The best method for the separation of the nickel corrin and the by-product was treatment of the mixed perchlorates with hydrochloric acid in methanol saturated with sodium chloride. The resulting mixed salts were chromatographed on silica with 9 : 1 chloroform–acetone, which separated the more polar by-product from the nickel corrin chloride (VI; M = Ni, X = Cl), and both products were then reconverted to the crystalline perchlorates.

The nickel(II) 1,19-dimethylcorrin perchlorate (VI; M = Ni, X = ClO_4) is thus the first crystalline corrin to be synthesised from pyrrolic intermediates. The electronic spectrum (Figure 1) is similar to those of other synthetic corrins; a hypsochromic shift of <5 nm is observed when the spectrum is compared with that of the 3,7,8,12,13,17-hexa-β-alkyl derivative and a small bathochromic shift of *ca.* 2 nm. in comparison with the spectrum of (V).[5] The n.m.r. spectrum of compound (VI; M = Ni, X = ClO_4) contained a singlet at τ 3·68 (C-10 H) and another at τ 4·0 (C-5 and C-15 H), and the absence of signals at lower field indicated complete hydrogenation of the ββ-double bonds. A six-proton singlet (slight splitting sometimes observed) at τ 8·53 corresponded to the C-1 and C-19 angular methyl groups, and this represents a 0·7 p.p.m. downfield shift as a consequence of hydrogenation. A comparison of these signals with those of other synthetic corrins is seen in Table 1, where the shielding of the C-10 proton caused by β-alkyl groups is apparent. Twelve of the β-methylene protons of structure (VI; M = Ni) were observed as a broad-based singlet at τ 6·73, and an ill-defined multiplet (4H) centred at τ 7·67 is associated with the protons at C-2 and C-18.

The lack of β-alkyl substituents in the nickel corrin salt was associated with a low volatility, so that relatively extreme conditions were necessary in order to obtain the mass-spectrum, which showed the base peak at *m/e* 387 ($M^+ - 4$). It is known [2] that nickel corrin salts lacking β-*gem*-alkyl substituents can undergo dehydrogenation in rings B and C. The main fragmentation ions were caused by successive loss of the two angular methyl groups.

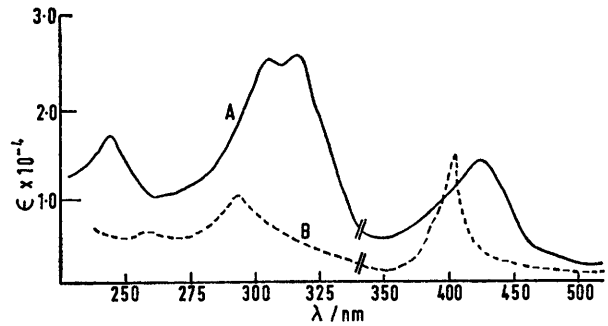


FIGURE 1 Electronic spectra of (A) nickel 1,19-dimethylcorrin perchlorate and (B) nickel 1,19-dimethyl-4,5-dihydrocorrin perchlorate

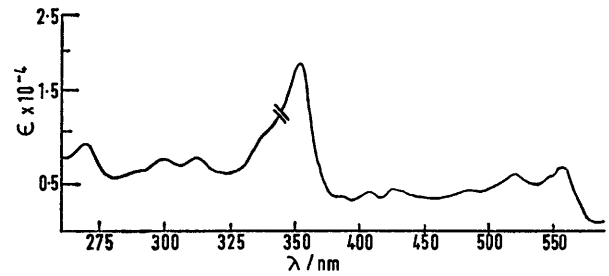


FIGURE 2 Electronic spectrum of dicyanocobalt(III) 1,19-dimethylcorrin

The by-product from the nickel 1,19-dimethylcorrin perchlorate preparation was also isolated as its perchlorate, which formed pale orange-yellow crystals. The mass spectrum was identical with that of the nickel corrin salt, which suggested that the by-product was an isomer and was again susceptible to dehydrogenation, presumably in rings B and C. However, the visible spectrum of the by-product showed a marked hypsochromic shift (*ca.* 28 nm) compared with that of the corrin (Figure 1), which led us to consider structures in which one of the terminal double bonds was unconjugated. Nevertheless, all attempts, *e.g.* treatment with acid, photolysis, mild thermolysis, to isomerise the by-product to the corrin failed, and the salt was recovered unchanged. The accepted dihydrocorrin structure (XVI) for the by-product was deduced on the basis of the 100 MHz n.m.r. spectrum. The only signal below τ 6 was a singlet (2H) at τ 4·4, which was resolved in the spectrum of a solution in mixed deuteriodichloromethane and hexadeuteriobenzene, and two overlapping singlets (each 1H) at τ 4·56 were observed. Thus no signal which could be

[10] J. A. Osborn, F. H. Jardine, J. F. Young, and G. Wilkinson, *J. Chem. Soc.* (*A*), 1966, 1711.

associated with a vinylic proton was present and thus isomeric nickel corrin structures such as (XVII) or (XVIII) were eliminated. The angular methyl groups of (XVI) corresponded to two singlets in the n.m.r. spectrum at τ 8·54 and 8·82, confirming the asymmetric nature of the salt. The twelve β-protons at positions 3,7,8,12,13, and 17 were associated with a broad-based singlet at τ 7·07 and the remaining seven protons at positions 2,4,5, and 18 with an ill-defined multiplet between τ 7·4 and 8·4.

Further support for a dihydrocorrin structure for the ring system of the hydrogenation by-product was obtained by the hydrogenation of the nickel 1,19-dimethylcorrin perchlorate at 200° under 120 atm of hydrogen for 4 h with an excess of W2 Raney nickel catalyst; a 57% conversion into the nickel 1,19-dimethyl-4,5-dihydrocorrin perchlorate (XVI) was achieved. Hydrogenation of the nickel corrin salt under the conditions under which it was formed together with the by-product, *viz.* 25 atm of hydrogen at room temperature overnight, caused no change, so that in the hydrogenation of the nickel tetradehydrocorrin perchlorate, addition to the C-5 *meso*-position must occur before the corrin itself is obtained. Under a wide range of reaction conditions a fairly constant ratio of corrin to dihydrocorrin derivatives was observed (see Experimental section).

The nickel 1,19-dimethylcorrin and 1,19-dimethyldihydrocorrin perchlorates were both stable to strong acids; for example they withstood several hours heating under reflux with trifluoroacetic acid. In contrast, a marked difference in reactivity towards bases was observed. Thus the nickel dihydrocorrin complex (XVI) was unchanged after being heated under reflux in methanolic sodium hydroxide, whereas the nickel corrin perchlorate (VI; M = Ni, X = ClO_4) was decomposed rapidly at room temperature even by mild bases, *e.g.* methanolic sodium acetate, when a transient blue colouration was observed. No nickel BC-bisdehydrocorrin salt was observed however, in contrast to the behaviour of nickel octa-β-alkylcorrin salts, which were readily dehydrogenated in the presence of alkali.[2] No isolable products were obtained from attempted dehydrogenations of nickel 1,19-dimethylcorrin perchlorate with sulphur, palladium–charcoal, chloranil, or 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ).

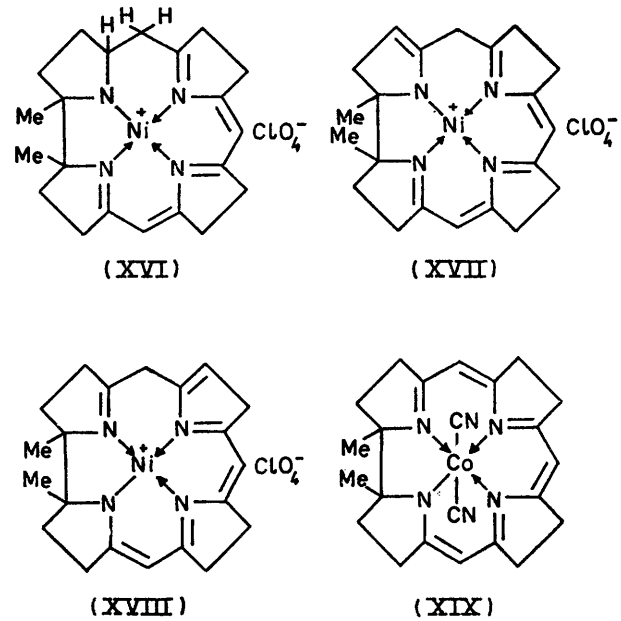
In the cobalt series, hydrogenation of the analogue of (III; R = Me, X = ClO_4) over W2 Raney nickel at 100° and with 100 atm of hydrogen gave an amorphous product, isolated as the dicyanocobalt(III) derivative and ascribed in AD-bisdehydrocorrin structure.[4] Substitution of either the C-2 and C-18, or the C-19 methyl substituents in the cobalt analogue of (III; R = Me) by hydrogen permitted the formation of the corresponding cobalt corrins after hydrogenation at 175° and with 100 atm pressure but again the products were amorphous.[12,13]

TABLE 1

N.m.r. signals (τ values) of nickel(II) and dicyanocobalt(III) corrin complexes

	C-5 and C-15 H		C-10 H		C-1 and C-19 Me	
Corrin	Ni^{II}	$(CN)_2Co^{III}$	Ni^{II}	$(CN)_2Co^{II}$	Ni^{III}	$(CN)_2Co^{III}$
1,19-Dimethyl	4·00	4·43	3·68	4·43	8·53	8·58
8,12-Diethyl-1,3,7,13,17,19-hexamethyl [2]	4·04	4·26	3·93	4·12		8·5—8·64
1,7,8,12,13,19-Hexamethyl [2]	3·94		3·8		8·63	
1,8,8,13,13-Pentamethyl [5]	3·9, 3·97		3·75		8·5	
1,2,2,7,7,12,12-Heptamethyl [11]		4·56, 4·6		4·44		8·69—8·76

Hydrogenation of cobalt(II) 1,19-dimethyltetradehydrocorrin perchlorate (VI; M = Co, X = ClO_4) at 175° and 100 atm of hydrogen resulted in complete decomposition, indicating a substantial difference in the thermal stability between the nickel and cobalt corrins. However hydrogenation at room temperature and 25 atm of hydrogen overnight gave a product which, after treatment with aqueous potassium cyanide solution followed by chromatography (t.l.c. on alumina in chloroform saturated with potassium cyanide), revealed the presence of two easily separated products as a strong pink band and a weaker orange band. The pink product was obtained as dark red crystals (71·5%; from dichloromethane–hexane), the visible spectrum of which (Figure 2) was almost identical with that quoted for *rac*-dicyanocobalt(III) 1,2,2,7,7,12,12-heptamethylcorrin by Eschenmoser.[11] The electronic spectra of the dicyanocobalt(III) corrins contain ten well-defined absorptions with



[11] I. Felner, A. Fischli, A. Wick, M. Pesaro, D. Bormann, E. L. Winnacker, and A. Eschenmoser, *Angew. Chem. Internat. Edn.*, 1967, **6**, 864.

[12] A. W. Johnson, *Chem. in Brit.*, 1967, **3**, 253.

[13] R. Grigg, A. W. Johnson, and P. van den Broek, *Chem. Comm.*, 1967, 502.

several inflections and therefore provide a useful means of identification of this ring system. Our red hydrogenation product was thus formulated as dicyanocobalt(III) 1,19-dimethylcorrin (XIX). The n.m.r. spectrum contained a singlet (3H) at τ 4·43 associated with the *meso*-protons and another (6H) at τ 8·58 due to the C-1 and C-19 angular methyl groups. The β-methylene protons, with the exception of those at C-2 and C-18 are observed as a broad-based singlet at τ 6·98 (12H) and the remaining four protons at C-2 and C-18 correspond to an ill-defined multiplet between τ 7·4 and 8·37. In the mass spectrum of (XIX), the base peak at *m/e* 388 corresponded to (*M* − 4 − 2CN) but a small peak at *m/e* 390 (13%) was also present. The main fragment ion at *m/e* 358 corresponded to the loss of the two angular methyl groups. Ready dehydrogenation of metal corrin complexes in the mass spectrometer therefore seems to be a general phenomenon.

The by-product obtained from the hydrogenation was isolated as orange prisms in variable yield (up to 11%). The electronic spectrum shows a hypsochromic shift of 100 nm from that of the main product, consistent with the red-to-orange colour change, and it seems probable that the by-product is the dicyanocobalt(III) complex of 4,5-dihydrocorrin, as in the nickel series [*cf.* (XVI)]. The product was more volatile than the corresponding corrin and in the mass spectrum the base peak occurred at *m/e* 392 (*M* − 2 − 2CN), but peaks were also observed at *m/e* 394 (11%, *M* − 2CN), 390 (93%), and 388 (7%), thus providing a further example of dehydrogenation of these compounds in the mass spectrometer. The main fragment ion at *m/e* 360 (*M* − 4 − 2CN − 2Me, 37%) again corresponded to the loss of the angular methyl groups.

When the hydrogenation product of cobalt(II) 1,19-dimethyltetradehydrocorrin perchlorate was worked up without cyanide treatment, the corresponding cobalt(II) corrin could be isolated as its perchlorate (VI; M = Co, X = ClO_4). This compound was very susceptible to oxidation, but it could be obtained as lustrous dark brown crystals (22%). The electronic spectrum was similar to that of the corresponding nickel complex (VI), and the mass spectrum showed the base peak at *m/e* 388 (*M* − 4) with a small peak at *m/e* 390 (24%) and the expected fragment peaks due to loss of the methyl groups. The (*M* − 2) peaks observed with the cobalt but not the nickel complexes are a measure of increased volatility. The cobalt(II) complex of 4,5-dihydrocorrin was not observed and presumably was lost during crystallisation. Treatment of the cobalt(II) 1,19-dimethylcorrin perchlorate with potassium cyanide gave the dicyanocobalt(III) complex in quantitative yield.

Deuteriation of the β-unsubstituted corrins has been examined. When nickel 1,19-dimethylcorrin perchlorate (VI; M = Ni, X = ClO_4) was dissolved in deuteriotrifluoroacetic acid, exchange of all three *meso*-protons occurred in <1 min, *i.e.* in less time than it took to transfer the sample to the n.m.r. spectrometer. The rate of exchange of the β-protons was much less; two β-protons were exchanged after 24 h and two more after 175 h. Further reaction was very slow and only *ca.* 0·5 proton was exchanged after another 140 h. It has not been possible to define the precise positions of β-deuteriation other than to say that the C-2 and C-18 protons were not involved (n.m.r.). Deuterium exchange of the *meso*-protons of the nickel 1,2,3,7,8,12,13,17,18-nonaalkyltetradehydrocorrin salts is also rapid, the C-5 and C-15 protons exchanging after 10 min and the C-10 proton after 15 min.[14] Deuteriation of compound (VI; M = Ni, X = ClO_4) under basic conditions with [$^2H_5$]-pyridine–deuterium oxide (1 : 1) produced no observable change after 7 days at 30°, and after 5 h at 100° substantial decomposition of the corrin occurred although the n.m.r. and mass spectra showed that approximately two β-protons and none of the *meso*-protons had undergone exchange. Deuteriation of the dicyanocobalt(III) corrin (XIX) with trifluoroacetic [^{2}H]acid could not be determined because of the sensitivity of the complex to strong acid. Some decomposition of the cobalt complex was also apparent in [^{2}H]chloroform–[$^2H_4$]acetic acid (1 : 1) but a slow exchange, *i.e.* a significant reduction of the n.m.r. signal after 24 h, of the *meso*-protons was observed. The mass spectrum of a sample isolated from this experiment after 24 h at room temperature indicated the presence of [$^2H_0$]- (8%), [$^2H_1$]- (20%), [$^2H_2$]- (25%), [$^2H_3$]- (21%), [$^2H_4$]- (4%), [$^2H_5$]- (8%), and [$^2H_6$]-material (4%). In a study of the deuteriation of the nickel(II) and dicyanocobalt(III) complexes of 1,8,8,13,13-pentamethylcorrin, Eschenmoser *et al.*[15] observed rapid exchange of the *meso*-protons under acidic conditions when no β-exchange was observed, and selective deuteriation at C-12 under basic conditions. It is clear that considerable enhanced stability of the corrins is brought about by the presence of β-alkyl substituents.

Deuteriation of the nickel dihydrocorrin perchlorate (XVI) in trifluoroacetic [^{2}H]acid showed that the *meso*-protons at C-10 and C-15 exchanged very rapidly, as in the case of the nickel corrin salt. The n.m.r. result was confirmed by the mass spectrum, which showed the main deuteriated ion at *m/e* 389 (*M* − 4), *i.e.* an increase of two mass units over the undeuteriated species. Exchange of the β-protons again was slow: approximately one proton had exchanged after 160 h (*m/e* 390) with indications from the mass spectrum of smaller amounts of more highly deuteriated species. The precise position of β-deuteriation was not determined.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. U.v. and visible spectra were determined with a Unicam SP 800 or SP 8000 spectrometer for solutions in chloroform (spectroscopy grade) unless otherwise stated. I.r. spectra were determined with a Unicam 200 instrument for Nujol mulls. N.m.r. spectra were measured for solutions in

[14] D. A. Clarke, R. Grigg, R. L. N. Harris, A. W. Johnson, I. T. Kay, and K. W. Shelton, *J. Chem. Soc.* (*C*), 1967, 1648.

[15] D. Bormann, A. Fischli, R. Keese, and A. Eschenmoser, *Angew. Chem. Internat. Edn.*, 1967, **6**, 868.

deuteriochloroform (unless otherwise stated) with Varian T60 and HA100 instruments, with tetramethylsilane as internal standard. Mass spectra were measured on an A.E.I. MS9 instrument with heptacosafluorotributylamine as internal standard. Light petroleum refers to the fraction b.p. 60—80° and alumina for chromatography was Spence type H.

Diethyl 3,3′,4,4′-Tetrabromo-2,2′-dipyrromethane-5,5′-dicarboxylate (with H. Pinnock).—(i) *Ethyl 3,4-dibromo-5-methylpyrrole-2-carboxylate.* Ethyl 5-methylpyrrole-2-carboxylate [16] (4 g) was stirred in 98% formic acid (500 ml), and a solution of bromine (12·5 g) in 98% formic acid (150 ml) was added during 30 min. After a further 30 min stirring, the pale pink material which had separated was removed, washed with 98% formic acid, and dried *in vacuo* (KOH) to give off-white needles (4·98 g) of the *product*, m.p. 175—177° (Found: C, 30·95; H, 2·9; N, 4·25. $C_8H_9Br_2NO_2$ requires C, 30·9; H, 2·9; N, 4·5%), $\lambda_{max.}$ 258 and 281 nm (ε 7760 and 13,840); $\nu_{max.}$ 733 (C–Br), 1281 (C–O), 1676 (C=O), and 3272 (NH) cm^{-1}; τ 5·55 (q, $CH_2{\cdot}CH_3$), 7·65 (s, CH_3), and 8·58 (t, $CH_2{\cdot}CH_3$).

(ii) *Ethyl 5-acetoxymethyl-3,4-dibromopyrrole-2-carboxylate.* The foregoing ester (1·86 g) in glacial acetic acid (50 ml) was treated with lead tetra-acetate (2·68 g); the solution was heated in an oil-bath at 100° for 24 h, cooled, and poured into water (500 ml). The precipitated solid was separated, washed with water, and crystallised from aqueous acetone to give *needles* (1·72 g), m.p. 121—124° (Found: C, 32·25; H, 3·0; Br, 43·15; N, 3·85. $C_{10}H_{11}Br_2NO_4$ requires C, 32·55; H, 3·0; Br, 43·3; N, 3·8%); $\lambda_{max.}$ 257 and 270 nm (ε 10,770 and 12,820); $\nu_{max.}$ 733 (C–Br), 1235 (C–O), 1288 (C–O), 1669 (CO_2Et), 1744 (OAc), and 3255 (NH) cm^{-1}; τ 4·91 (s, $CH_2{\cdot}OAc$), 5·65 (q, $CH_2{\cdot}CH_3$), 7·91 (s, $O{\cdot}CO{\cdot}CH_3$), and 8·64 (t, $CH_2{\cdot}CH_3$).

(iii) *Ethyl 3,4-dibromo-5-chloromethylpyrrole-2-carboxylate.* Ethyl 3,4-dibromo-5-methylpyrrole-2-carboxylate (6·22 g) dissolved in glacial acetic acid (60 ml) was stirred at 60° while redistilled sulphuryl chloride (2·97 g) in glacial acetic acid (5 ml) was added as quickly as possible with the temperature kept constant. The solution was then stirred at 70° for 30 min and cooled to room temperature. The crystals which separated were filtered off, washed with light petroleum, and dried *in vacuo* (KOH) to give off-white *needles* (5 g, 72%), m.p. 171—173° (Found: C, 27·75; H, 2·5; Cl, 10·15; N, 3·95. $C_8H_8Br_2ClNO$ requires C, 27·85; H, 2·35; Cl, 10·25; N, 4·05%); $\lambda_{max.}$ 217 and 274 nm (ε 11,540 and 13,830); $\nu_{max.}$ 735 (C–Br), 747 (C–Cl), 1293 (C–O), 1670 (C=O), and 3254 (NH) cm^{-1}; τ 5·39 (s, CH_2Cl), 5·56 (q, $CH_2{\cdot}CH_3$), and 8·58 (t, $CH_2{\cdot}CH_3$).

(iv) *Diethyl 3,3′,4,4′-tetrabromo-2,2′-dipyrromethane-5,5′-dicarboxylate.* The foregoing chloromethylpyrrolic ester (5 g) dissolved in glacial acetic acid (20 ml) was heated to boiling in an oil-bath. Water (20 ml) was added in 5 ml portions and the solution was heated under reflux for 1·5 h and then cooled to room temperature. The brown precipitate was separated, washed with water, and then dissolved in 95% aqueous ethanol (100 ml; charcoal) to give a green solution. After cooling to 0°, the product crystallised as *microneedles* (1·68 g, 38%), m.p. 201—203° (Found: C, 30·1; H, 2·3; N, 4·55. $C_{15}H_{14}Br_4N_2O_4$ requires C, 29·75; H, 2·35; N, 4·6%); $\lambda_{max.}$ 263 and 283 nm (ε 17,860 and 24,580); $\nu_{max.}$ 712 (C–Br), 1259 (C–O), 1670 (C=O), and 3231 (NH) cm^{-1}; τ 5·60 (q $CH_2{\cdot}CH_3$), 5·87 (s, bridging CH_2), and 8·58 (t, $CH_2{\cdot}CH_3$).

Ethyl 3,4-Dibromo-5-methylpyrrole-2-thiocarboxylate (with H. Pinnock).—Ethyl 5-methylpyrrole-2-thiocarboxylate [17] (2·12 g) was dissolved in methylene chloride (100 ml) and pyridine (10 ml). A solution of bromine (4 g) in methylene chloride (30 ml) was added dropwise with stirring during 1 h. After stirring at room temperature for 3 days, the solvent was removed under reduced pressure at room temperature and the remaining pale brown slurry was treated with water (500 ml). The precipitated solid was separated, washed well with water, and dried *in vacuo* (P_2O_5) to give a buff powder (3·76 g) which crystallised from chloroform–light petroleum as off-white *needles* (2·9 g, 71%), m.p. 171—174° (Found: C, 29·55; H, 2·8; Br, 49·4; N, 4·35; S, 10·05. $C_8H_9Br_2NOS$ requires C, 29·4; H, 2·75; Br, 49·4; N, 4·3; S, 9·8%); $\lambda_{max.}$ 255 and 310 nm (ε 5620 and 20,520); $\nu_{max.}$ 718 (C–S), 744 (C–Br), 1246 (C–O), 1596 (C=O), and 3266 (NH) cm^{-1}; τ 6·91 (q, $CH_2{\cdot}CH_3$), 7·66 (s, C-2 Me), and 8·65 (t, $CH_2{\cdot}CH_3$).

5-Methylpyrrole-2-carbaldehyde (with H. Pinnock).—Redistilled phosphoryl chloride (83 g) was added dropwise with stirring to dry *NN*-dimethylformamide (262 ml) at 0°. The solution was added to 2-methylpyrrole (43·4 g, 1 mol. equiv.) in *NN*-dimethylformamide (262 ml) at 0° with stirring during 30 min. The solution was kept at room temperature overnight, then was treated with water (5 l), and aqueous sodium hydroxide (10%) was added (to pH >12). The solution was saturated with sodium chloride and extracted with ether; the extract was washed, dried, and evaporated to give a solid which crystallised from light petroleum to give bright orange needles (38·9 g, 66·4%). A sample was purified further by sublimation under reduced pressure to give colourless needles, m.p. 74—75° (lit.,[18] 70°); $\lambda_{max.}$ 233 and 300 nm; τ 0·75 (s, CHO), 3·17 (t, C-3 H), 4·02 (t, C-4 H), and 7·68 (s, CH_3).

5-Methylpyrrol-2-ylmethylenemalononitrile was obtained (74%) by condensation with malononitrile in alkaline solution and formed pale yellow needles (from ethanol), m.p. 150—152° (Found: C, 68·5; H, 4·8; N, 26·75. $C_9H_7N_3$ requires C, 68·9; H, 4·45; N, 26·75%); $\lambda_{max.}$ 290 and 390 nm (ε 2750 and 71,400); $\nu_{max.}$ 1615, 2210 (C≡N), and 3310 (NH) cm^{-1}; τ ($CF_3{\cdot}CO_2H$) 3·00 [s, $CH{:}C(CN)_2$], 3·32 (m, C-3 H), 4·15 (m, C-4 H), and 8·03 (s, CH_3). Hydrolysis of the dinitrile in methanol with 30% sodium hydroxide under reflux regenerated 5-methylpyrrole-2-carbaldehyde (95·5%).

3,4-Dibromo-5-methylpyrrole-2-carbaldehyde (with H. Pinnock).—5-Methylpyrrole-2-carbaldehyde (30 g) was dissolved in a mixture of methylene chloride (1·3 l) and pyridine (218 g), and a solution of bromine (88 g, 2 mol. equiv.) in methylene chloride (600 ml) was added dropwise with stirring during 1 h. After being stirred at room temperature for 3 days, the solution was evaporated under reduced pressure to a slurry. Water (5%) was added and the precipitated solid was separated, washed with water, and dried *in vacuo* (P_2O_5) to give a powder. This crystallised from 90% aqueous acetone (charcoal) to give pale grey *needles* (44 g, 60%), m.p. 180—182° (Found: C, 26·9; H, 2·1; Br, 60·15; N, 5·45. $C_6H_5Br_2NO$ requires C, 27·0; H, 1·9; Br, 59·85; N, 5·25%); $\lambda_{max.}$ (EtOH) 297 and 307 nm (ε 6580 and 16,360); $\nu_{max.}$ 694 (C–Br), 1650 (C=O), and 3216 (NH) cm^{-1}; τ 0·59 (s, CHO) and 7·63 (s, CH_3).

3,4-Dibromo-5-methylpyrrol-2-ylmethylenemalononitrile

[16] H. Fischer, H. Beller, and A. Stern, *Ber.*, 1928, **61**, 1074.
[17] E. Bullock, T.-S. Chen, and C. E. Loader, *Canad. J. Chem.*, 1966, **44**, 1007.
[18] H. Fischer, H. Beyer, and E. Zaucher, *Annalen*, 1931, **486**, 55.

(57%) formed orange crystals (from ethanol), m.p. 214—216° (decomp.) (Found: C, 34·2; H, 1·6; N, 13·2. $C_9H_5Br_2N_3$ requires C, 34·3; H, 1·6; N, 13·35%); $\lambda_{max.}$ 387 nm (ε 35,400), $\lambda_{infl.}$ 303 nm (ε 3670), $\lambda_{max.}$ (MeOH–0·2% NaOH) 255, 280, and 421 nm (ε 13,420, 12,520, and 52,780), $\lambda_{infl.}$ 402 nm (ε 32,210); $\nu_{max.}$ 1590 and 2210 cm^{-1} (C≡N); τ ($CDCl_3$–CF_3·CO_2H) 2·33 [s, $CH{:}C(CN)_2$] and 7·43 (s, CH_3). Alkaline hydrolysis regenerated the original formyl compound (83%).

Dipyrrol-2-yl Ketone.—A solution of freshly distilled pyrrole (79·5 g) in dry ether was added dropwise to a solution of ethylmagnesium bromide [from ethyl bromide (144 g) and magnesium (30 g) in ether (600 ml)] with external cooling. The mixture was then heated under reflux on a water bath for 2 h, cooled to room temperature, and then added dropwise with stirring to a solution of phosgene in toluene (500 ml; 12% w/v) at 25°. The mixture was stirred for 2 h and then poured on ice, which was allowed to melt overnight. The resulting slurry was filtered, and the magnesium salts were washed with ether. The organic layer was separated and the aqueous layer extracted with ether (3 × 100 ml). The combined ethereal washes and extracts were concentrated and the resulting oil was added to the toluene layer, which was then made alkaline with dilute ammonia. Water (200 ml) was added and the toluene azeotrope was distilled (84°); steam distillation then removed unchanged pyrrole. The resulting gum was dissolved in chloroform and made into a thick slurry on silica gel (60—120 mesh), and the solvent was removed under reduced pressure. The resulting powder was packed on the top of a column (90 × 5 cm) of silica gel in light petroleum and eluted with light petroleum–ethyl acetate (gradient) to give two major fractions: (i) pale orange plates (2·77 g; 12·6%), m.p. 272—273° (sealed tube) [m.p. of pyrocoll[7] (IX), 272·5°] (from light petroleum–ethyl acetate) (Found: C, 65·0; H, 3·5; N, 15·2. Calc. for $C_{10}H_6N_2O_2$: C, 64·5; H, 3·25; N, 15·05%); $\lambda_{max.}$ ($CHCl_3$) 276, 306, and 319 nm (ε 19,500, 15,490, and 17,780); $\nu_{max.}$ 1700 cm^{-1} (C=O); τ ($CDCl_3$–CF_3·CO_2H) 2·27 (m, C-3 H and C-8 H), 2·53 (m, C-1 H and C-6 H), 3·45 (t, C-2 H and C-7 H); *m/e* 186 (M^+), 156 (M^+ − CO), 130, 103, 93 (M^+ − C_4H_3NCO, 100%), 65 (C_4H_3N); (ii) pale yellow needles of dipyrrol-2-yl ketone (20·2 g, 21·4%), m.p. 157—160° (lit.,[19] 160—161°) (from light petroleum–ethyl acetate) (Found: C, 67·7; H, 5·3; N, 17·75. $C_9H_8N_2O$ requires C, 67·5; H, 5·05; N, 17·5%); $\lambda_{max.}$ 255 and 334 nm (ε 8130 and 34,660), $\lambda_{infl.}$ 291 and 345 nm (ε 9330 and 28,000); $\nu_{max.}$ 1570, 1470, and 1385 cm^{-1} (no max. between 1600 and 1750 cm^{-1}); τ ($CDCl_3$–CF_3·CO_2H) 2·67 (m, H at C-3, C-3′, C-5, and C-5′) and 3·5 (m, C-4 H and C-4′ H).

2,2′-Dipyrromethane.—Prepared (95%) (following Clezy *et al.*[6]) by borohydride reduction of dipyrrol-2-yl ketone, the product formed crystals, m.p. 72—73° (lit.,[6] 73°) (from light petroleum); τ 3·47 (2 pyrrolic H), 3·9 (4 pyrrolic H), and 6·13 (s, CH_2). It had turned black after being stored for *ca.* 3 months, but when the black product was dissolved in acetone, the solvent removed, and the resulting brown oil extracted exhaustively with light petroleum, the crystalline dipyrromethane could be recovered (>95%).

5,5′-Diformyl-2,2′-dipyrromethane (cf. *ref.* 6).—Dipyrrol-2-ylmethane (1·5 g) was dissolved in dry *NN*-dimethylformamide (10 ml) and benzoyl chloride (6 ml) was added dropwise with stirring during 10 min at 0—5°. The solution was stirred below 5° for 2 h and then at room temperature for 2 h. Benzene (20 ml) was added and after 30 min the crystalline pale yellow imine salt was separated and washed well with benzene but not allowed to become dry. The salt was then dissolved in aqueous 10% sodium acetate (20 ml) and slowly warmed to 35—40°; the product precipitated as pale yellow needles which were collected after 30 min (1·68 g, 81%). A portion sublimed under reduced pressure gave colourless needles, m.p. 219—222° (lit.,[6] 229—231°) (Found: C, 64·9; H, 5·4; N, 13·4. Calc. for $C_{11}H_{10}N_2O_2$: C, 65·35; H, 4·95; N, 13·85%); $\lambda_{max.}$ 287 and 305 nm (ε 28,860 and 33,450); $\nu_{max.}$ 1625 cm^{-1} (C=O).

1,19-Dideoxy-1,19-dimethylbiladiene-ac *Dihydrobromide* (VII).—(i). 2,2′-Dipyrromethane (25 mg) and 2-methylpyrrole-5-carbaldehyde (75 mg) were dissolved in methanol (10 ml), and aqueous hydrobromic acid was added (48%; 0·14 ml). An immediate reaction took place which was monitored by observing the visible spectrum of the mixture in chloroform. The absorption at 498 nm (biladiene salt) reached a maximum after *ca.* 5 min and then decreased steadily with a corresponding increase in the absorption at 470 nm (dipyrromethene salts). After 2 h no biladiene remained. For the subsequent cyclisations the product obtained after a reaction time of 5 min was used. Absorption due to the biladiene salt was almost totally obscured by the absorption at 470 nm when the visible spectrum of the reaction mixture was examined with methanol as solvent. The use of chloroform as reaction solvent gave the biladiene salt but more impurities were present. Attempted purification of the biladiene salt caused rapid decomposition.

(ii) 5,5′-Diformyl-2,2′-dipyrromethane (25 mg) and 2-methylpyrrole (40 mg) were dissolved in methanol (10 ml) and aqueous 48% hydrobromic acid (0·14 ml) was added. The reaction was similar to (i) and the mixture was treated similarly.

1,19-Dimethyltetradehydrocorrin Nickel(II) *Perchlorate* (VIII; M = Ni, X = ClO_4).—A solution of 1,19-dideoxy-1,19-dimethylbiladiene-*ac* dihydrobromide in methanol (20 ml) was prepared from 2,2′-dipyrromethane (100 mg) and 5-methylpyrrole-2-carbaldehyde (300 mg). After 5 min at room temperature this solution was added during 2—3 min to a solution of nickel acetate (1 g) in dry *NN*-dimethylformamide (100 ml) through which air was being bubbled. A colour change from green through yellow-brown to purple indicated the formation of the tetradehydrocorrin. If the reaction did not proceed satisfactorily, additions of sodium acetate (5 mg portions) were made until the purple colouration appeared. Aeration of the mixture was continued for 30 min and then the solvent was removed at 30—40° under reduced pressure. The residue was dissolved in the minimum of hot methanol, the solution was filtered, and sodium perchlorate (0·5 g) in hot water (50 ml) was added with swirling. The solution was then cooled to 0° and filtered, and the residue was dissolved in the minimum volume of acetone. This solution was chromatographed on a silica column in acetone until the eluate was colourless. The column was then eluted with sodium perchlorate in methanol (1% w/v) and the main purple fraction was collected. This was concentrated and water added until the product separated; this was filtered off, washed with water, and recrystallised from methanol–benzene to give deep purple *prisms* (86·5 mg, 26·2%), m.p. ≮300° (Found: C, 51·9; H, 3·65; N, 11·4. $C_{21}H_{17}ClN_4NiO_4$ requires C, 51·95; H, 3·5; N, 11·55%); $\lambda_{max.}$ (Me_2SO) 270, 358, and 571 nm (ε 16,040, 13,280, and 9280), $\lambda_{infl.}$ 450 nm (ε 4620) (the elec-

[19] H. Rapoport and C. D. Willson, *J. Amer. Chem. Soc.*, 1962, **84**, 630.

tronic spectrum of a solution in chloroform was similar but showed a general hypsochromic shift of *ca.* 2 nm); τ (CF_3·CO_2H) 1·68—2·4 (m, 8 β-H and 3 *meso*-H) and 9·23 (s, C-1 and C-19 Me); *m/e* 408, 394, 380 ($M^+ - 2$, 100%), 366, 353, 326, 190, 183, and 177.

1,19-*Dimethyltetradehydrocorrin Cobalt*(II) *Perchlorate* (VIII; M = Co, X = ClO_4).—A solution of 1,19-dideoxy-1,19-dimethylbiladiene-*ac* dihydrobromide in methanol (20 ml) was prepared from 2,2′-dipyrromethane (100 mg) and 5-methylpyrrole-2-carbaldehyde (300 mg). After 5 min at room temperature this solution was added during 2—3 min to a solution of cobalt(II) acetate tetrahydrate (1 g) in dimethyl sulphoxide (100 ml), through which air was being bubbled. A rapid colour change through yellow-brown to red occurred. On the occasions when the reaction appeared to stop at the former stage sodium acetate was added (2 mg portions) at 2 min intervals until the red colouration was observed. Aeration was continued for 20 min and the solvent was then removed under reduced pressure. The residue was dissolved in methanol; the solution was filtered and sodium perchlorate (200 mg) was added. Water was then added until the solution became cloudy, at which point it was extracted exhaustively with chloroform. The chloroform extracts were dried ($MgSO_4$), concentrated, and chromatographed on silica plates (0·5 mm) with 7 : 3 chloroform–acetone. The major red-purple band was removed and extracted with a solution of sodium perchlorate in methanol (1% w/v). Water was added and the solution was extracted with chloroform. The combined extracts were dried ($MgSO_4$) and evaporated until crystallisation occurred to give deep red *plates* (87 mg, 25·9%), m.p. ≮300° (Found: C, 52·2; H, 3·65; N, 11·65. $C_{21}H_{17}ClCoN_4O_4$ requires C, 51·9; H, 3·5; N, 11·55%); $\lambda_{max.}$ (Me_2CO) 356, 494, and 579 nm (ε 12,400, 10,040, and 7150) (in chloroform solution the spectrum was similar, with a general bathochromic shift of *ca.* 1 nm); *m/e* 395, 381 ($M^+ - 2$, 100%), 367, 354, 327, 190, 183, and 177.

1,19-*Dimethylcorrin Nickel*(II) *Perchlorate* (VI; M = Ni, X = ClO_4) *and* 1,19-*Dimethyl*-4,5-*dihydrocorrin Nickel*(II) *Perchlorate* (XVI).—1,19-Dimethyltetradehydrocorrin nickel perchlorate (100 mg) in methanol (25 ml) was hydrogenated at room temperature and 25 atm overnight in the presence of W2 Raney nickel (0·5 ml). The catalyst was removed and sodium perchlorate (100 mg) in water (100 ml) was added. The solution was extracted with chloroform; the extracts were dried ($MgSO_4$) and evaporated until crystallisation occurred. The crude product separated as bright yellow needles (80·5 mg, 79·0%), $\lambda_{max.}$ 242, 275, 302, 314, 400, and 428 nm, $\lambda_{infl.}$ 382 and 450 nm. This material was dissolved in methanol (80 ml) and 2N-hydrochloric acid was added until the solution became cloudy. Further methanol (20 ml) was added; the solution was then saturated with sodium chloride and stirred at room temperature for 2 days. After the addition of water (100 ml) the solution was extracted with dichloromethane and the combined extracts were dried ($MgSO_4$). The solution was then concentrated and applied in low concentration to silica t.l.c. plates (10 plates; 0·5 mm thick). The plates were eluted with 9 : 1 chloroform–acetone saturated with sodium chloride, dried in air, and eluted again. This procedure was repeated until the required separation was achieved (2—3 days). Three distinct bands were obtained: (i) a bright yellow band at the solvent front, (ii) a bright yellow polar band, and (iii) a slightly more polar pale orange band.

Band (i) proved to be a mixture of corrin and dihydrocorrin salts. The band was removed and extracted with methanolic sodium perchlorate (1% w/v). Water was added and the solution was extracted with dichloromethane (5 × 25 ml). The combined extracts were dried ($MgSO_4$) and evaporated to dryness. The visible absorption of the product was identical with that of the crude product isolated before, *i.e.* it was the unresolved mixture. It was re-treated with hydrochloric acid–sodium chloride and chromatographed again. At least three cycles were usually required for complete conversion of the perchlorate into the chloride salts.

Band (ii) proved to be the 1,19-dimethylcorrin salt, which was isolated as the perchlorate by the method already described. It formed bright yellow *needles* (45 mg, 44·1%), m.p. >300° (decomp.) (from dichloromethane–hexane) (Found: C, 50·9; H, 5·2; N, 10·95. $C_{21}H_{25}ClN_4NiO_4$ requires C, 51·2; H, 5·1; N, 11·4%); $\lambda_{max.}$ (CH_2Cl_2) 244, 266, 277, 304, 317, and 428 nm (ε 16,460, 9150, 10,610, 23,420, 24,880, and 13,540), $\lambda_{infl.}$ 390 and 450 nm (ε 7410 and 10,340); τ (CF_3·CO_2H) 3·68 (s, C-10 H), 4·0 (s, C-5 H and C-15 H), 6·73br (s, β-CH_2 at C-3, C-7, C-8, C-12, C-13, and C-17), 7·67 (m, β-CH_2 at C-2 and C-18), and 8·53 (s, Me at C-1 and C-19); *m/e* 404, 402, 387 ($M^+ - 4$, 100%), 371, 357, 329, 193·5, 186, and 178·5.

Band (iii) was the 1,19-dimethyldihydrocorrin salt, which was also isolated as the perchlorate by the method already described. It was obtained as pale orange-yellow *needles* (29 mg, 28·4%), m.p. >300° (decomp.) (from dichloromethane–hexane) (Found: C, 51·3; H, 5·4; N, 11·15. $C_{21}H_{27}ClN_4NiO_4$ requires C, 51·1; H, 5·45; N, 11·35%); $\lambda_{max.}$ (CH_2Cl_2) 259, 293, 340, and 400 nm (ε 6970, 9290, 2860, and 14,830), $\lambda_{infl.}$ 283 and 382 nm (ε 7150 and 8840); τ (100 MHz, CD_2Cl_2) 4·40 (s, C-10 H and C-15 H), 7·07br (s, β-CH_2 at C-3, C-7, C-8, C-12, C-13 and C-17), 7·40—8·40 (m, β-CH_2 at C-2 and C-18 and protons at C-4 and C-5), 8·54 (s, C-1 Me), and 8·82 (s, C-19 Me). Addition of 25% C_6D_6 to the n.m.r. sample solution led to the splitting of the singlet at τ 4·40 into two signals (1 : 1) at τ 4·56 (*J* 3 Hz); *m/e* 402, 387 ($M^+ - 6$, 100%), 372, 357 (successive loss of angular methyl groups), 329, 193·5, 186, and 178·5.

Further Hydrogenations of 1,19-*Dimethyltetradehydrocorrin Nickel*(II) *Perchlorate*.—A series of hydrogenations of the nickel tetradehydrocorrin salt (VIII; M = Ni) (10 mg) was carried out (each experiment in duplicate) with varying time, temperature, solvent, hydrogen pressure, catalyst, and catalyst–substrate ratio (Table 2). In each case the product from the autoclave was filtered, water (50 ml) was added, and the product was extracted into dichloromethane. After drying ($MgSO_4$), the visible spectrum of the solution was measured and the ratio of the corrin and dihydrocorrin salts was determined by use of the extinction coefficients previously calculated.

Hydrogenation of 1,19-*Dimethylcorrin Nickel Perchlorate* (VI; M = Ni, X = ClO_4).—(i) 1,19-Dimethylcorrin nickel perchlorate (20 mg) in methanol (10 ml) containing W2 Raney nickel (0·1 ml) was shaken at room temperature with hydrogen (50 atm) for 36 h. The mixture was then filtered; the filtrate was concentrated and aqueous sodium perchlorate was added until the product precipitated as bright yellow needles (12·5 mg, 92·5% recovery). The visible absorption spectrum showed no increased absorption at 402 nm due to the formation of dihydrocorrin.

(ii) A similar hydrogenation was conducted at 120 atm and 200° for 4 h and the product was treated as in (i). From the visible absorption spectrum the product was

estimated to consist of 42% corrin and 58% dihydrocorrin salts. The methanolic solution was diluted with 2N-hydrochloric acid (20 ml) and stirred with excess of sodium chloride for 3 days. Water was then added and the solution was extracted with dichloromethane (5 × 20 ml). The combined extracts were dried ($MgSO_4$) and chromatographed on a silica plate (0·5 mm) in 7 : 3 chloroform–acetone saturated with sodium chloride. When separation was achieved the lower pale yellow-orange band was extracted with a solution of sodium perchlorate in methanol (1% w/v); the extract was diluted with water and extracted with dichloromethane. The latter extracts were dried ($MgSO_4$) and evaporated to dryness and the product was crystallised from dichloromethane–hexane to give pale yellow-orange needles (10·2 mg, 51%) of 1,19-dimethyl-4,5-dihydrocorrin nickel perchlorate, identical (electronic and n.m.r. spectra) with an authentic specimen.

1,19-*Dimethylcorrin Cobalt*(II) *Perchlorate*.—1,19-Dimethyltetradehydrocorrin cobalt(II) perchlorate (VIII; M = Co, X = ClO_4) (50 mg) in methanol (25 ml) was hydrogenated at room temperature and 25 atm overnight in the presence of W2 Raney nickel (0·25 ml). The mixture was filtered and the filtrate reduced in volume (to *ca.* 10 ml) under reduced pressure. Aqueous sodium perchlorate (10% w/v) was added until precipitation occurred. The crude product was separated, washed with water, and dissolved in the minimum amount of dichloromethane. This solution was chromatographed on silica plates (0·5 mm) in 7 : 3 chloroform–acetone. The major orange-brown band was removed and extracted with sodium perchlorate in methanol (1% w/v); the extract was diluted with water and extracted with dichloromethane (5 × 25 ml). The latter extracts were dried ($MgSO_4$) and evaporated to dryness. The residue was recrystallised three times from dichloromethane–hexane at room temperature under nitrogen to give lustrous dark brown *crystals* (12 mg, 23·6%), m.p. >300° (decomp. from 110°) (Found: C, 51·4; H, 5·1; N, 11·4. $C_{12}H_{25}ClCoN_4O_4$ requires C, 51·05; H, 5·05; N, 11·35%); $\lambda_{max.}$ 254, 301, 390, and 449 nm (ε 12,830, 18,020, 4750, and 7780) $\lambda_{infl.}$ 354 and 423 nm (ε 5000 and 6220); *m/e* 404, 402, 390 ($M^+ - 2$, 24%) 388 ($M^+ - 4$, 100%), 372, 358, 345, 330, 179, 173, and 165.

Dicyanocobalt(III) 1,19-*Dimethylcorrin*.—(i) 1,19-Dimethyltetradehydrocorrin cobalt(II) perchlorate (50 mg) was hydrogenated as in the previous experiment; the mixture was filtered and the filtrate was poured into a solution of potassium cyanide (100 mg) in water (50 ml) and kept at room temperature for 1 h. The solution was extracted with dichloromethane (4 × 25 ml); the extract was washed with water (2 × 25 ml), dried ($MgSO_4$), and reduced in volume (to *ca.* 20 ml) under reduced pressure. It was then chromatographed on silica t.l.c. plates (0·5 mm) in 9 : 1 chloroform–acetone saturated with potassium cyanide. Two bands were observed, a strong pink band (i) and a slightly more polar orange band (ii).

The pink band was extracted with methanol and aqueous potassium cyanide solution was added (0·05%; 100 ml). The solution was extracted with dichloromethane (5 × 25 ml) and the extracts were dried ($MgSO_4$) and evaporated. The product, dicyanocobalt(III) 1,19-dimethylcorrin, crystallised from dichloromethane–hexane at room temperature under nitrogen to give dark red *prisms* (33 mg, 71·9%), which decomposed at 285—288° without melting (Found: C, 61·9; H, 5·8; N, 18·8. $C_{23}H_{25}CoN_6$ requires C, 62·15; H, 5·65; N, 18·9%); $\lambda_{max.}$ 269, 291, 299, 313, 356, 384, 406, 490, 524, and 563 nm (ε 7950, 4760, 5870, 5600, 19,070, 2540, 2820, 3790, 6100, and 6890), $\lambda_{infl.}$ 260, 264, 340, and 551 nm (ε 6010, 6520, 10,520, and 5500); τ 4·43 (s, C-5, C-10, and C-15 H), 6·98br (s, 12 × β-CH_2 excluding those at C-2 and C-18), 7·4—8·37 (m, β-CH_2 at C-2 and C-18), and 8·58 (s, C-1 and C-19 Me); *m/e* 402, 390, 388 ($M^+ - 2CN - 4$), 381, 367, 358 ($M^+ - 4 - 2CN - 2CH_3$), 331, 190, 185·5 (*m/2e*), 183·5 (*m/2e*), and 179.

The orange band was treated similarly and gave bright

TABLE 2

Anion	Catalyst	Temp. (°C)	Time of reaction	Pressure (atm)	Solvent	Ratio of Products: Corrin	Dihydrocorrin
ClO_4	W2 Raney Ni [a] (0·05 ml of ethanolic slurry containing 200 mg Ni per ml)	165	2 h	100	MeOH	71·4	28·6
ClO_4	W2 Raney Ni (0·05 ml)	50	1 h	100	MeOH	73·6	26·4
ClO_4	W2 Raney Ni (0·05 ml)	20	Overnight	25	MeOH	71·0	29·0
ClO_4	W2 Raney Ni (0·005 ml)	20	Overnight	25	MeOH	75·2	24·8
Cl	W2 Raney Ni (0·05 ml)	20	Overnight	25	MeOH	73·4 (*ca.* 7·5% yield)	26·6
ClO_4	W2 Raney Ni (0·05 ml)	20	1 h	1	MeOH	77·9	22·1
ClO_4	W2 Raney Ni (0·05 ml)	20	Overnight	25	9 : 1 MeOH–HOAc	73·7	26·3
ClO_4	30% Pd–C	20	Overnight	25	MeOH	52·0	48·0
ClO_4	30% Pd–C	20	10 min	1	MeOH	84·8	15·2
ClO_4	30% Pd–C	20	2 min	1	HOAc	91·2	8·8
ClO_4	Pt	20	Overnight	25	MeOH	81·1	18·9
ClO_4	$(PPh_3)_3RhCl$	20	Overnight	100	CH_2Cl_2	Product was AD-bisdehydrocorrin salt [b]	
ClO_4	$(PPh_3)_3RhCl$	160	2 h	100	CH_2Cl_2	100 (8% yield)	0
ClO_4		160	4 h	100	MeOH	100 Up to 12·5% yield)	0

[a] Ref. 3. [b] Ref. 2.

orange prisms (<1—5 mg, 1—11%), m.p. >300° (decomp.) of (probably) dicyanocobalt(III) 1,19-dimethyl-4,5-dihydrocorrin; $\lambda_{max.}$ 232, 310, 354, 439, and 464, $\lambda_{infl.}$ 256, 297, and 338 nm; *m/e* 406–404–402 (overlapping), 392–390–388 (overlapping; 392 100%), 376–374–372 (overlapping), 362–360–358 (overlapping), 196—195 (overlapping), 188·5–187·5–186·5 (*m*/2*e*; overlapping), and 181.

(ii) 1,19-Dimethylcorrin cobalt(II) perchlorate was dissolved in methanol (10 ml) and potassium cyanide (5 mg) in water (10 ml) was added. Chromatography showed the presence of only one bright pink band. The solution was extracted with dichloromethane (3 × 20 ml); the extracts were dried ($MgSO_4$) and concentrated and the product crystallised from dichloromethane–hexane at room temperature under nitrogen to give dark red prisms of dicyanocobalt(III) 1,19-dimethylcorrin (8·8 mg, 97·4%), identical (visible and n.m.r. spectra) with an authentic specimen.

We thank the Directors of Imperial Chemical Industries Limited, Dyestuffs Division, for permission for one of us (W. R. O.) to take part in this work. We also acknowledge gifts of intermediates from B.P. Chemicals (U.K.) Limited and from Imperial Chemical Industries, Pharmaceuticals Division.

[2/1024 *Received*, 8*th May*, 1972]