Transformations of Some Nickel Tetrahydrocorrin Tertiary Esters

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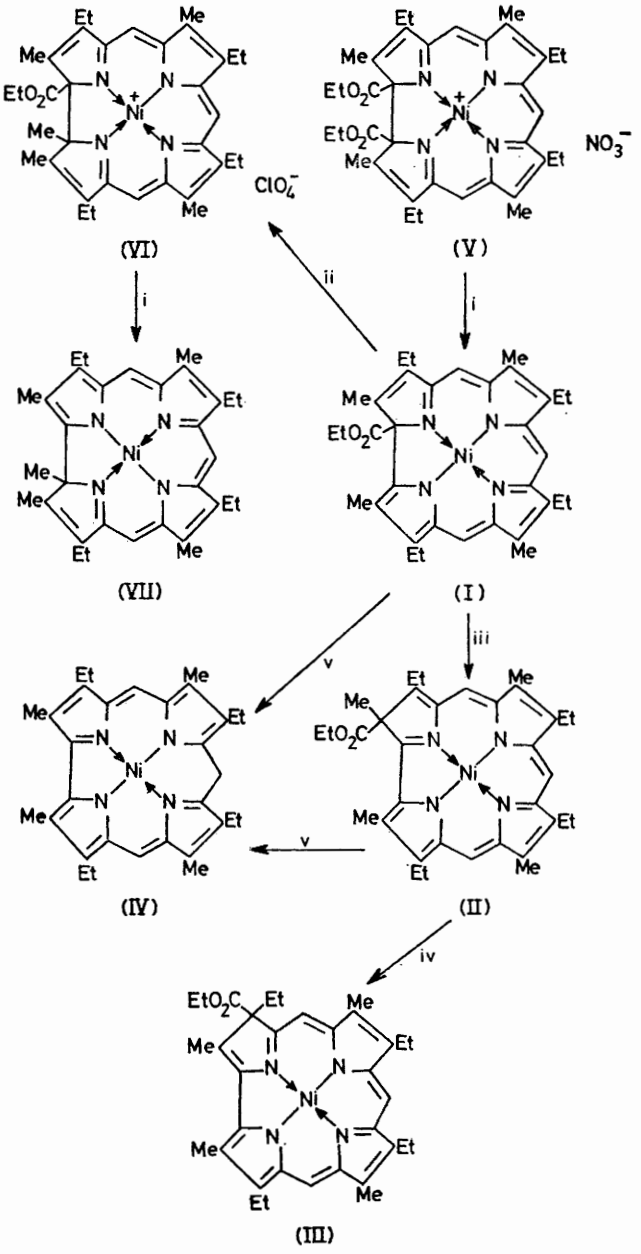
Summary $LiAlH_4$ reduction of tertiary ester groups at C–1, C–2, or C–3 in a nickel tetradehydrocorrin results in rapid elimination of the substituent; methylation of the 1-monoester occurs at C–19 and subsequent removal of the ester gives the nickel 1-methyltetradehydrocorrin; rearrangement of the ester group at C–1 to C–2 in neutral nickel tetrahydrocorrins is rapid even at room temperature, and when the product is heated a further rearrangement of the ester to C–3 takes place.

IT is now established[1] that although uroporphyrinogen III lies on the biosynthetic pathway to vitamin B_{12}, the C–20

meso-carbon does not become the C–1 methyl substituent of the B_{12} chromophore but is expelled[2] (possibly as formaldehyde, implicating an angular hydroxymethyl or equivalent substituent) and that the C–1 methyl group has its origin in methionine. Such reactions, *i.e.* methylation at C–1 of a corrin and expulsion of angular hydroxymethyl groups, have not been encountered in the total or partial B_{12} syntheses reported so far. However, in the nickel tetradehydrocorrin series we have observed that a tertiary ester grouping at C–1, C–2, or C–3 (I, II, III) is rapidly expelled (*ca.* 2 min.) during $LiAlH_4$ reduction as evidenced by the colour change from green to red. All three esters gave the same nickel corrole (IV, λ_{max} 359, 401 sh, 416 sh, and 654 nm), formed in the reduction as the red anion (λ_{max} 382 sh, 401, 428 sh, 523, 558, and 590 nm). The precise nature of the reductive elimination of the angular ester groups has still to be determined. The three esters were prepared in a sequence starting from the nickel 1-ethoxycarbonyltetradehydrocorrin (I), itself produced by expulsion of one ester group from the nickel 1,19-diethoxycarbonyltetradehydrocorrin nitrate (V) by the action of methanolic sodium hydroxide at room temperature.[3] It has since been found that reduction of (V) with sodium and ethanol at room temperature is a method for the ready conversion of (V) into (I) and (VI) into (VII), particularly in the former case, as the unstable neutral product is precipitated from the reaction mixture. The structure of (I) is now supported by spectral data [λ_{max} 352, 416, 654, 745 sh, and 809 nm; δ_H 1·2 (t, Me of peripheral Et and ester), 2·32, 2·35, 2·47, and 2·52 (s, peripheral Me), 2·80 (q, CH_2 of peripheral Et), 4·05 (q, CH_2 of ester), and 6·00, 6·73, and 7·10 (s, *meso*-H); ν_{max} 1724 cm^{-1}].

We have reported previously[3] that (I) is unstable and that when it is heated under reflux for 1 h in chlorobenzene, the ester group migrates from C–1 to C–3 to give (III) but we have now shown that when a solid sample of (I) is kept for 2 days at ambient temperature with exclusion of light or in dichloromethane solution for 12 h, the intermediate product (II) containing a C–2 angular ester group is formed (46%), m.p. 153—156 °C (decomp.). The ester (II), the first example of its kind, rearranged to (III) when heated for 1 h in chlorobenzene at 130 °C and it is interesting that the esters (III) were originally[4] assigned the structure (II). The n.m.r. spectra of (II) and (III) confirm the structural assignments, as in (II) the band (δ, 1·82) associated with the C-2 methyl substituent is shifted upfield compared with those [δ, 2·44 (1) and 2·56 (2)] associated with the methyl groups at C-18, C-7, and C-13, respectively. In the spectrum of (III), the C-3 ethyl group signal (δ, 0·25 for $CH_2{\cdot}CH_3$) is similarly displaced upfield[3] (8-, 12-, and 17-$CH_2{\cdot}CH_3$ at δ 2·94). The double ester migration (I→II→III) provides experimental support for the mechanism previously suggested.[3]

We have also observed the first synthetic sequence leading to a 1-methyltetradehydrocorrin where the methyl group is introduced by direct methylation. Such a reaction sequence is also unknown in the corrin series. Methylation (for the corresponding allylation, see ref. 3) of the nickel 1-ethoxycarbonyltetradehydrocorrin (I) with a large excess of methyl iodide in dry dichloromethane for 24 h at room temperature, chromatography, and crystallisation in the presence of nickel perchlorate, gave the nickel 1-ethoxycarbonyl-19-methyltetradehydrocorrin salt (VI) in 12% yield, m.p. 235—240 °C (decomp.). Reduction with sodium and ethanol gave the nickel 1-methyltetradehydrocorrin (VII).



SCHEME. i, Na–EtOH. ii, MeI, $NaClO_4$. iii, 2 days in solid state at room temp. or 12 h in CH_2Cl_2. iv, 1 h in PhCl at 130 °C. v, $LiAlH_4$ then H^+.

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