Carboxyalkylcobalamins: Effects of Carboxyl Substituents on Base-on / Base-off Equilibria and Mechanochemical Co–C Bond Cleavage*

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A series of primary and secondary carboxyalkylcobalamins with $(CH_2)_nCOOH$ groups ($n = 1 – 3$), $CH_2–CH(CH_3)COOH$, CH(R)COOH (R = CH_3, C_2H_5, n-C_3H_7), $CH(CH_3)(CH_2)_nCOOH$ ($n = 1, 2$) and $CH(COOH)CH_2COOH$ attached to cobalt were synthesized or generated *in situ*, mostly by the reaction of vitamin B_{12s} or hydridocobalamin with the respective α- or ω-substituted halocarboxylic acids and reactions with olefinic carboxylic or dicarboxylic acids. Their rates of decomposition and the activation parameters $\Delta G^{o\neq}$, $\Delta H^{o\neq}$ and $\Delta S^{o\neq}$ of Co–C bond cleavage were determined spectrophotometrically in aqueous solutions at different pH values. Carboxyalkylcobalamins are generally more stable in solution than comparable unsubsitituted alkylcobalamins. In secondary 1-carboxyalkylcobalamins this is attributable primarily to the inductive effect and smaller size of the carboxyl group. The presence of the carboxyl group also strengthens the axial interactions of cobalt with the 5,6-dimethylbenzimidazole (DMBZ) ligand, as evidenced through measurements of the pK_a of DMBZ in these organocobalamins. Although also susceptible to spontaneous ('mechanochemical') decomposition, carboxyalkylcobalamins can exist with significantly longer half-lives in their base-on forms than corresponding alkylcobalamins. Short-lived, but detectable spectroscopically in solution, is succinylcobalamin, the secondary dicarboxyalkylcobalamin with a $CH(COOH)CH_2COOH$ group attached to cobalt, a compound of interest as a model of a postulated intermediate in the coenzyme B_{12}-dependent methylmalonyl-CoA-succinyl-CoA mutase reaction.

Key words: Carboxyalkylcobalamins, Organocobalamins, Co–C Bond Cleavage Reactions, Vitamin B_{12}