On the role of alkylcobalamins in the vitamin B_{12}-catalyzed reductive dehalogenation of perchloroethylene and trichloroethylene†

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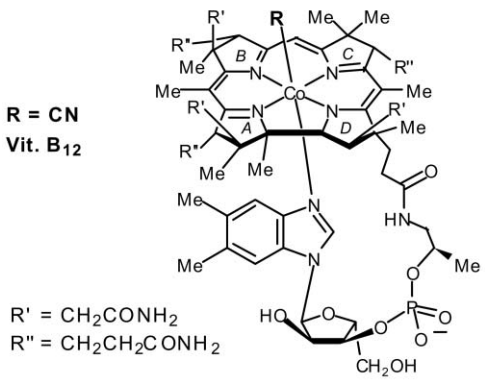
Theoretical studies are presented on the structures and reactivity of chlorinated ethylcobalamins, potential intermediates in the vitamin B_{12}-catalyzed reductive dehalogenation of the environmental pollutants perchloroethylene and trichloroethylene; the results suggest an alternative mechanism of catalysis.

Perchloroethylene (PCE) and trichloroethylene (TCE) are priority pollutants found in many terrestrial and groundwater environments.[1] Several anaerobic organisms use corrinoid-dependent enzymes to reductively dechlorinate these toxic compounds in a process that is coupled to energy metabolism.[2] Catalytic vitamin B_{12} has also been used for dechlorination of PCE and TCE in the presence of a sacrificial reductant.[3] The mechanism of this process has attracted much attention due to its potential importance for new remediation strategies as well as for the involvement of unusual organocobalamins.[4]

In the abiotic process, PCE is converted to TCE and then dichloroethylene (DCE, predominantly the *cis*-isomer) and eventually acetylene, ethylene and ethane. Early results prompted the suggestion that the first step proceeds by dissociative electron transfer (ET) from Co(I) to PCE yielding Co(II) and a trichlorovinyl radical.[5] The expected diffusion-controlled coupling of these radicals prompted futile attempts to synthesize and study trichlorovinyl (and dichlorovinyl) cobalamins. Subsequent studies with isolated chlorovinylcobalamin indicated that these type of compounds are reactive under the dechlorination conditions and we suggested that a trichlorinated organocobalamin, if formed in the reaction with PCE, would not be detectable.[4d–f] Two recent reports[6] offer compelling additional evidence against a simple outer sphere ET mechanism, indirectly supporting the intermediacy of organocobalamins.

Discussion of these complexes has focused predominantly on chlorovinylcobalamins since species with corresponding masses have been detected by mass spectrometry.[4a] Here we present the results of theoretical calculations on the chlorinated *alkyl*cobalamins that would result from nucleophilic attack of the Co(I) form of B_{12} on PCE and TCE (see Fig. 1). Inspection of the calculated



structures, Co–C bond strengths, and redox chemistry suggest an alternative, more likely pathway for reductive dehalogenation of PCE and TCE that proceeds *via* these complexes.

The structures of models[7] of the three alkylcobalamins expected from nucleophilic attack of cob(I)alamin on PCE and TCE were optimized in the gas phase using density functional theory (DFT) with the B3LYP functional[8] and a 6-31G(d) basis set[9] for the main elements (C, N, H, Cl) and TZV basis set[10] for Co.[4e,11] Relevant structural features are included in Table 1 alongside the calculated Co–C bond dissociation enthalpies, vertical electron affinities, and standard reduction potentials of both the *base-on* and *base-off* complexes.[12] Also included are the corresponding data for models of the product of nucleophilic addition of cob(I)alamin to *cis*-DCE and the well-studied methylcobalamin for comparison.[4e]

The tetrachloroethylcobalamin model **A** arising from reaction with PCE has the longest and weakest Co–C bond, shortest Co–N bond and largest Co–C–C bond angle. Proceeding down Table 1, evidence for a *trans* effect is clear, with elongation of the Co–N bond with decreasing Co–C bond length. This contrasts with the inverse *trans* effect seen experimentally and computationally in

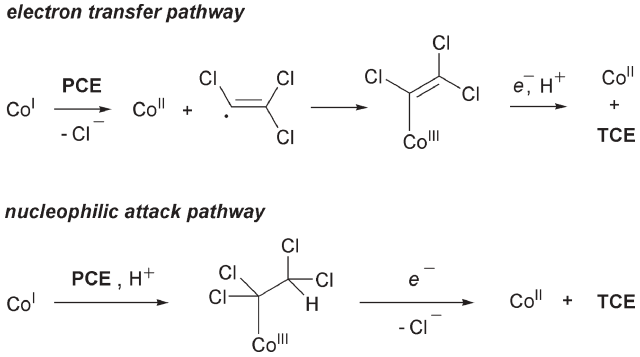


Fig. 1 Mechanistic possibilities for the vitamin B_{12}-catalyzed conversion of PCE to TCE. Ligands on the Co are omitted for clarity.

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† Electronic supplementary information (ESI) available: All structures calculated in this work available in Cartesian coordinates as well as electronic energies and relevant thermochemical corrections. See DOI: 10.1039/b513624e

most organocobalamins, including chlorovinylcobalamins,[4e,f] whereby the Co–N bond contracts with decreasing Co–C bond length.[13] Complexes **A** and **C**, in which two chlorine atoms are on the β-carbon, have larger Co–C–C bond angles presumably due to steric interactions with the corrin ring as observed with the vinylcobalamins.[4d–f] The trichloroethylcobalamin model **C** is more than 4 kcal mol^{-1} lower in energy than the isomeric complex **B**. This suggests that attack of cob(I)alamin at the least hindered carbon of TCE will be favoured to yield **C**. Another argument favouring the formation of **C** over **B** is provided by the products formed upon reduction (*vide infra*).

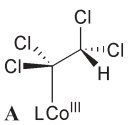
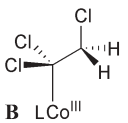
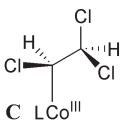
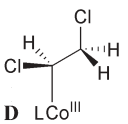
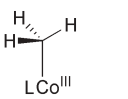
Reductive cleavage of organocobalamins typically proceeds *via* electron attachment to the corrin ring π_8* orbital. A ligand-to-metal charge transfer (LMCT) is then required to populate the σ_{Co-C}* orbital, which can lead to Co–C heterolysis.[14] Our previous work on vinylcobalamins[4e] showed that increasing chloride substitution leads to a lower-lying σ_{Co-C}*, and that in the *base-off* geometry[12] (in which the axial imidazole N atom is not coordinated to the Co atom thereby dropping the relative energy of the Co d_{z^2} orbital), the σ_{Co-C}* orbital is actually lower in energy than the π_8* orbital in the dichlorovinyl and trichlorovinyl cobalamin models, precluding the need for a LMCT and leading to much more positive reduction potentials. The ease of this reduction explained why we (and others) have not succeeded in preparing the dichlorovinyl and trichlorovinyl cobalamins.

Electron attachment to the chlorinated ethylcobalamin complexes in Table 1 reveals some interesting trends. The longer, weaker bonds of the chloroethylcobalamins relative to the chlorovinylcobalamins,[4e,f] leads to much more facile population of the σ_{Co-C}* orbital. Thus, electron attachment to the *base-on* form of the tetrachloroethylcobalamin model **A** is directly to σ_{Co-C}*, and results in an unbound structure from which the axial imidazole ligand dissociates upon relaxation. The same was observed for population of the σ_{Co-C}* orbital in the trichloroethylcobalamin model **B**, which is the LUMO + 1. As was found for the dichlorinated and trichlorinated vinylcobalamins, the *base-off* chloroethylcobalamin models **A**, **B**, **C** and **D** are all reduced with electron attachment to σ_{Co-C}* and lead to bound five-coordinate structures in the gas phase.

Solvent effects on the foregoing gas phase calculations were explored using the COSMO polarizable continuum model.[15] Geometry optimizations following electron attachment to the σ_{Co-C}* orbital of *base-on* **A** and **B** lead to elongation of the Co–C and anti C–Cl bonds with concommittant contraction of the C–C bond resulting in the elimination of chloride and formation of TCE and 1,1-DCE, respectively. Similarly, relaxation of the one-electron reduced *base-off* complexes of **A**, **B**, **C** and **D** lead directly to the elimination of chloride and formation of TCE, 1,1-DCE, *cis*-DCE and vinyl chloride (VC), respectively. Thus, while the one-electron reduced structures are bound in the gas phase, the large gains in energy associated with solvation of chloride ion and the Co(II) complex is expected to drive their decomposition in (aqueous) solution.

These findings provide new insights into the mechanism of B_{12}-catalyzed dechlorination of PCE and TCE. The *base-on* forms of chlorovinylcobalamins are favoured by more than three orders of magnitude at pH 7-9.[4e,f] Thus, whereas trichlorovinylcobalamin can only be reduced to TCE in its *base-off* form that is present in

Table 1 Relevant structural and thermodynamic features of models of potential chlorinated ethylcobalamins intermediates in the reductive dechlorination of PCE, TCE and *cis*-DCE. Data from calculations on the methylcobalamin model are included for comparison

						Base-on		Base-off	
complex	r(Co–C)[a]	r(Co–N)[a]	∠(Co–C–C)[b]	∠(Co–C–Cl)[b]	Co–C BDE[c]	EA_{vert}[d]	E°[e]	EA_{vert}[d]	E°[e]
 **A**	2.130	2.187	119.3	106.4, 111.6	8.8	90.8 (σ_{Co-C}*)	n/b	111.3 (σ_{Co-C}*)	−0.50
 **B**	2.081	2.195	112.1	106.4, 111.6	16.2	87.0 (π_8*) 84.2 (σ_{Co-C}*)	−1.83 n/b	105.6 (σ_{Co-C}*)	−0.75
 **C**	2.021	2.197	119.1	115.6	23.6	86.9 (π_8*)	−1.78	98.8 (σ_{Co-C}*)	−0.94
 **D**	2.013	2.217	116.3	114.7	24.7	86.1 (π_8*)	−1.79	94.6 (σ_{Co-C}*)	−1.15
	1.960	2.241	n/a	n/a	36.5 expt: 37[f]	78.4 (π_8*)	−2.02	86.9 (π_8*)	−1.85

[a] In Å. [b] In °. [c] Bond dissociation enthalpy in kcal mol^{-1}.[8] [d] Vertical electron attachment energy in kcal mol^{-1}. The orbital to which the electron is attached is indicated in parentheses. [e] Standard reduction potential in Volts *versus* NHE; "n/a" - not applicable; "n/b" - gas-phase structure is not bound. [f] B. D. Martin, R. G. Finke *J. Am. Chem. Soc.* 1990, **112**, 2419.

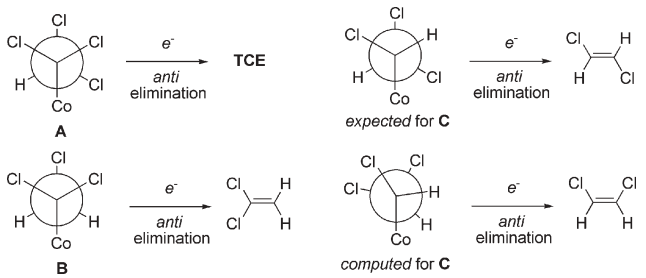


Fig. 2 Elimination of Cl^- from possible ethylcobalamin intermediates.

less than 0.06%, tetrachloroethylcobalamin is reduced directly to TCE from the *base-on* form that is present in >99% at equilibrium. Alternatively, TCE may be produced by homolysis of the weak Co–C bond in **A** followed by either (i) dissociative ET to the tetrachloroethyl radical, which leads directly to TCE and chloride, or (ii) abstraction of a vicinal chlorine atom by Co(II). Hence, we propose that most, if not all, TCE is produced from tetrachloroethylcobalamin instead of trichlorovinylcobalamin. Furthermore, complexes **B** and **D** cannot be major players in the dechlorination of TCE and *cis*-DCE because they generate 1,1-DCE and VC upon reduction, which are not significant observed products. On the other hand, complex **C** is a very likely contributor (*vide infra*) to the formation of *cis*-DCE from TCE.

The minimum energy conformation of the chlorinated ethyl moieties in **A**, **B** and **D** are typical staggered conformations, but the minimum energy conformation of **C** is noteworthy. As shown in Fig. 2, the trichloroethyl moiety of **C** is arranged such as to minimize interaction between the proximal chlorine atom and the corrin ring. This is important since the staggered conformation upon reductive *anti* elimination would provide *trans*-DCE, which is not a significant product in B_{12}-catalyzed dechlorination processes. On the other hand, one-electron attachment to the calculated lowest energy conformation of the *base-off* form of **C** leads to *cis*-DCE upon relaxation of the geometry of the one-electron reduced complex. *cis*-DCE is the observed dechlorination product of TCE. Since complex **C** has a computed redox potential for its *base-off* form (−0.94 V) that is less negative than the corresponding value for the various dichlorinated vinylcobalamins (−1.02 to 1.08 V),[4e] it would seem that complex **C** is as likely be the intermediate on the path to *cis*-DCE as a dichlorovinylcobalamin.[16]

In summary, reduction of **A** and **C**, the intermediates expected from nucleophilic attack of cob(I)alamin on PCE and TCE, respectively, leads to the spontaneous formation of the experimentally observed products TCE and *cis*-DCE. Reductive heterolysis of the Co–C bond of **A** is thermodynamically much favored over the reductive heterolysis of the Co–C bond in trichlorovinylcobalamin. Furthermore, the intermediacy of trichloroethylcobalamin **C** in the reduction of TCE to *cis*-DCE cannot be discounted. In contrast, since the intermediate generated upon nucleophilic addition to *cis*-DCE decomposes upon electron attachment to give VC, which is not a significant observed product, it is unlikely that this pathway is relevant in the dechlorination of *cis*-DCE. This supports results that suggest the intervention of chlorovinylcobalamins in this process.[4]

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16 Given the likelihood of greater steric interactions between the axial chloroethyl substituent and the substituents on the corrin ring, and the potential this has for lowering the energy of σ_{Co-C}* relative to π_8*, we performed a limited number of calculations on larger models wherein methyl groups were introduced at each position occupied by a methyl, acetamido or propionamido group in vitamin B_{12}. No significant change in structure or orbital ordering was determined.

