Model Studies of Coenzyme B_{12} Dependent Diol Dehydratase. 1.[1] Synthetic, Physical Property, and Product Studies of Two Key, Cobalt-Bound, Putative Diol Dehydratase Intermediates

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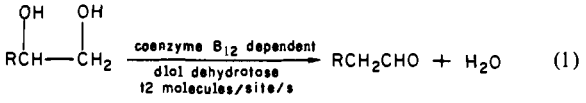
Abstract: Following a brief introduction to the controversial question of cobalt participation or nonparticipation in the adenosylcobalamin (coenzyme B_{12}) dependent diol dehydratase rearrangement reaction, $HOCH_2CH_2OH \rightarrow CH_3CHO + H_2O$, the two key, cobalt-bound, putative diol dehydratase intermediates, Co–$CH(OH)CH_2OH$ (**1**) and Co–CH_2CHO (**2**), are prepared and studied by using the coenzyme B_{12}, Schiff base, model system, $RCo[C_2(DO)(DOH)_{pn}]X$. The first synthesis, in 80% yield, and isolation of the often postulated, but unproven, intermediate **1** are reported in a carbonate-protected form, Co–$\overline{CHO(CO)OCH_2}$, compound **3**, $\overline{CH_2O(CO)OCH}$–$Co[C_2(DO)(DOH)_{pn}]Cl$ (**3**). Following the full characterization of **3** by 360-MHz ^1H NMR, IR, and X-ray crystallography, including its unexpectedly complex solution NMR behavior and axial 1,5,6-trimethylbenzimidazole binding constant, the MeO^--catalyzed deprotection in MeOH of **3** is described. The resultant rearrangement reaction and complete stoichiometry to 1 equiv of $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$, 0.5 equiv each of $CH_3OCO_2CH_3$ and $CH_3OCO_2^-$, and 95 ± 4% CH_3CHO are reported. The observed stoichiometry and mass and charge balance suggest that a $\cdot CH_2CHO$ intermediate is formed, and evidence is presented suggesting that the CH_3OH solvent is the H· source, $\cdot CH_2CHO + CH_3OH \rightarrow CH_3CHO + \cdot CH_2OH$. Following the examination of several unsuccessful routes, the intermediate expected from cobalt-participation pathways, Co–CH_2CHO, was prepared, $OHCCH_2Co[C_2(DO)(DOH)_{pn}]I$ (**7**), and found to be reasonably stable as previously observed for all the other known formylmethyl complexes, and, therefore, apparently not an intermediate in the MeO^--catalyzed deprotection and rearrangement reaction of **3**. The results of attempts to use seven protecting groups other than carbonate and the relative advantages and disadvantages of carbonate-protected **3** are then summarized and discussed. In the following paper,[1b] a kinetic and mechanistic study of the rearrangement reaction is presented.

Introduction

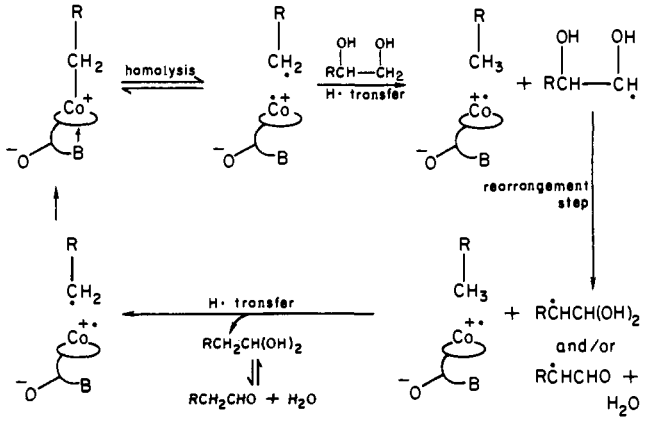
The precise molecular mechanism of the eleven enzymatic, adenosylcobalamin (coenzyme B_{12}, Figure 1) dependent rearrangement reactions has remained uncertain in spite of a considerable amount of previous investigation.[3,4] One of the better studied B_{12} dependent enzymes, diol dehydratase[5] (eq 1), became



(1)

the focus of our investigations[1,6,7] because it appeared possible to probe directly, at least using B_{12} models and eventually in the enzyme-free coenzyme, the long-standing question of whether or not cobalt participates in the so-called rearrangement step or steps of the reaction.

Scheme I



The generally accepted diol dehydratase mechanism (Scheme I) includes the well-known evidence for Co–C(5′) bond homolysis[8] and subsequent participation by the C(5′) radical as an obligatory H· transfer site.[8,9] Chemical model studies supporting the

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(2) (a) University of Oregon. (b) University of Colorado.

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(4) For recent reviews see: (a) Golding, B. T. "Inorganic Biochemistry"; The Chemical Society: London, 1979; Vol. I, p 75. (b) Krouwer, J. S.; Babior, B. M. *Mol. Cell. Biochem.* **1977**, *15*, 89. (c) Babior, B. M.; Krouwer, J. S. *CRC Crit. Rev. Biochem.* **1979**, *6*, 35. (d) Abeles, R. H.; Dolphin, D. *Acc. Chem. Res.* **1976**, *9*, 114. (e) Babior, B. M. *Ibid.* **1975**, *8*, 376. (f) Abeles, R. H., ref 3a, p 373.

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(6) (a) Finke, R. G.; Smith, B. L.; Droege, M. W.; Elliott, C. M.; Hershenhart, E. *J. Organomet. Chem.* **1980**, *202*, C25. (b) Elliott, C. M.; Hershenhart, E.; Finke, R. G.; Smith, B. L. *J. Am. Chem. Soc.* **1981**, *103*, 5558. (c) Finke, R. G.; Smith, B. L.; McKenna, W. A.; Christian, P. A. *Inorg. Chem.* **1981**, *20*, 687. (d) Finke, R. G.; Smith, B. L.; Mayer, B. J.; Molinero, A. A. *Ibid.* **1983**, *22*, 3677.

(7) Finke, R. G.; Schiraldi, D. A.; Mayer, B. J. *Coord. Chem. Rev.*, in press.

(8) (a) Valinsky, J. E.; Abeles, R. H.; Fee, J. A. *J. Am. Chem. Soc.* **1974**, *96*, 4709. (b) Cockle, S. A.; Hill, H. A. O.; Williams, R. J. P.; Davies, S. P.; Foster, M. A. *Ibid.* **1972**, *94*, 275. (c) Valinsky, J. E.; Abeles, R. H.; Mildvan, A. S. *J. Biol. Chem.* **1974**, *249*, 2751. (d) Finlay, T. H.; Valinsky, J.; Mildvan, A. S.; Abeles, R. H. *Ibid.* **1973**, *248*, 1285. (e) Eagar, R. G., Jr.; Bachovchin, W. W.; Richards, J. H. *Biochemistry* **1975**, *14*, 5523.

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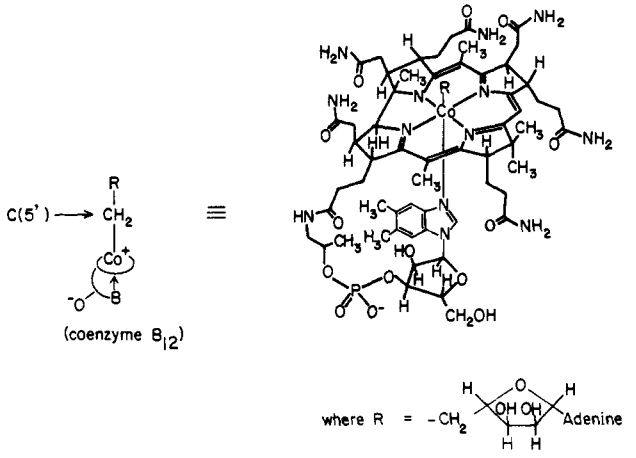
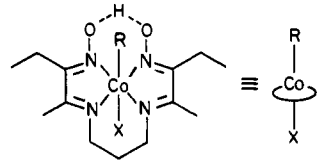


Figure 1. The structure of adenosylcobalamin (Coenzyme B_{12}) and the abbreviation for the coenzyme that is used throughout the text.

homolysis[6d,10,11] and H· transfer steps[12] have appeared, but the question of the subsequent steps and of cobalt participation or nonparticipation has remained unanswered. In particular, neither studies of the enzymes[13] nor recent theoretical,[14] pulse radiolysis,[15] Co(III) π-complex,[16] or other model studies[12] have been able to provide a consistent or convincing picture of the rearrangement step. It is important to note that the starting point for many of the previous studies is the *assumption* that the $B_{12(r)}$, Co(II), and RCH(OH)ĊHOH radicals of Scheme I combine to form Co–

Chart I



$RCo[C_2(DO)(DOH)_{pn}]X$

R; X

3,  ; Cl

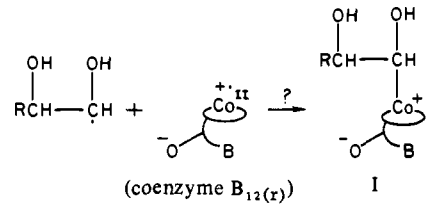
4,  ; H_2O; PF_6^-

5,  ; Bz-Me; PF_6^-

6,  ; CH_3CN; BPh_4^-

7, CH_2CHO; I

CH(OH)CHROH (**1**, eq 2), a postulated, key intermediate in the overall rearrangement shown in eq 1 and Scheme I.



(2)

There is no convincing evidence for **1**. In fact, all attempts to detect this intermediate with the enzyme have failed,[13] and the available ESR experiments argue against **1**, the data being fully consistent with a Co(II)· and substrate R· influencing each other at distances >10 Å.[13c,d] The only *suggestive* evidence for **1** was that its formation was apparently needed to explain the early diol dehydratase ^{18}O labeling and stereochemical studies.[17a,b] More recent ^{18}O labeling and stereochemical studies[17c] have greatly changed this picture, however, with some mechanism (such as a protein-bound radical mechanism)[7,17c] other than the stereospecific formation and stereospecific further reaction of **1** now being required. In fact, **1** is not even necessary to explain the early stereochemical results, and the interested reader is referred elsewhere[7] for a discussion of this point. Furthermore, the formation of **1** from $B_{12(r)}$, $Co(II)^+$· and RCH(OH)ĊHOH should be hindered by a redox side reaction to give $B_{12(s)}$, Co(I) + RCH(OH)CHO + H^+, known to occur at $k = 4 \pm 2 \times 10^9$ M^{-1} s^{-1} for the related α-hydroxy radical, $(CH_3)_2$ĊOH, with $B_{12(r)}$.[18] Disproportionation (H· atom transfer) to yield Co–H and HOC-

(10) Although photochemical Co–C bond homolysis in models is very well-known, *quantitative* studies of the thermal homolysis of this bond have only recently appeared. (a) Halpern, J. *Acc. Chem. Res.* **1982**, *15*, 238. (See also: ref 3b, Chapter 14.) (b) Halpern, J.; Ng, F. T. T.; Rempel, G. L. *J. Am. Chem. Soc.* **1979**, *101*, 7124. (c) Schrauzer, G. N.; Grate, J. H. *Ibid.* **1981**, *103*, 541. (d) Ng, F. T. T.; Rempel, G. L.; Halpern, J. *Ibid.* **1982**, *104*, 621. (e) Tsou, T. T.; Loots, M.; Halpern, J. *Ibid.* **1982**, *104*, 623. (f) Gjerde, H. B.; Espenson, J. H. *Organometallics* **1982**, *1*, 435. (g) Reference 6d.

(11) For structural model studies related to the homolysis step see: (a) Marzilli, L. G. *Prog. Inorg. Chem.*, in press. (b) Randaccio, L.; Bresciani-Pahor, N.; Toscano, P. J.; Marzilli, L. G. *J. Am. Chem. Soc.* **1981**, *103*, 6347. (c) *Ibid.* **1980**, *102*, 7372. (d) Marzilli, L. G.; Toscano, P. J.; Randaccio, L.; Bresciani-Pahor, N.; Calligaris, M. *J. Am. Chem. Soc.* **1979**, *101*, 6754. (e) Marzilli, L. G.; Toscano, P. J.; Ramsden, J. H.; Randaccio, L.; Bresciani-Pahor, N. In "Catalytic Aspects of Metal Phosphine Chemistry"; Alyea, E. C., Meek, D. W., Eds.; American Chemical Society: Washington, DC, 1982; Adv. Chem. Ser. No. 196. (f) Chemaly, S. M.; Pratt, J. M. *J. Chem. Soc., Dalton Trans.* **1980**, 2259 (part 17); 2267 (part 18); 2274 (part 19).

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(13) (a) Woodward, R. B., in ref 3a, p 73. (b) Reference 4b, p 105. (c) Boas, J. F.; Hicks, P. R.; Pilbrow, J. R.; Smith, T. D. *J. Chem. Soc., Faraday Trans. 2* **1978**, *74*, 417. (d) In ribonucleotide reductase, similar ESR signals are observed, including both kinetically competent[13f,g] and noncompetent ones. See also this discussion, ref 3a (p 502) and ref 4b (p 65). (e) Coffman, R. E.; Ishikawa, Y.; Blakley, R. L.; Beinert, H.; Orme-Johnson, W. H. *Biochim. Biophys. Acta* **1976**, *444*, 307. (f) Blakley, R. L.; Orme-Johnson, W. H.; Bozdeck, J. M. *Biochemistry* **1979**, *18*, 2335. (g) Hamilton, J. A.; Tamao, Y.; Blakley, R. L.; Coffman, R. E. *Ibid.* **1972**, *11*, 4696. (h) Buettner, G. R.; Coffman, R. E. *Biochim. Biophys. Acta* **1977**, *480*, 495.

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(15) (a) Mulac, W. A.; Meyerstein, D. *J. Am. Chem. Soc.* **1982**, *104*, 4124. We thank Professor Meyerstein for providing us with a copy of this work prior to publication. (b) Elroi, H.; Meyerstein, D. *Ibid.* **1978**, *100*, 5540. (c) Blackburn, R.; Kyaw, M.; Phillips, G. O. *J. Chem. Soc., Faraday Trans. 1* **1975**, *71*, 2277.

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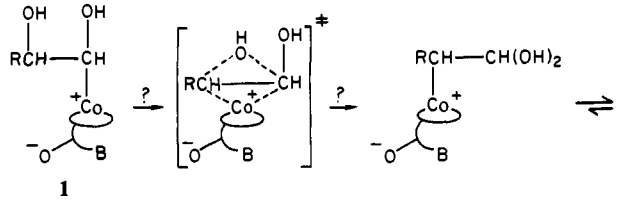
H═CHOH (⇌ $HOCH_2CHO$) also has some precedent[10,15a] and, therefore, could be a rearrangement-inhibiting side reaction.

If, however, one ignores for the moment the evidence against the formation of **1** and assumes, as is often done, that it does form, the literature[12,14-16] strongly suggests that it is generally accepted that rearrangement of **1** proceeds via a Co(III) π-complex (eq 3). One immediate problem with this mechanism is that the



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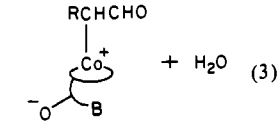
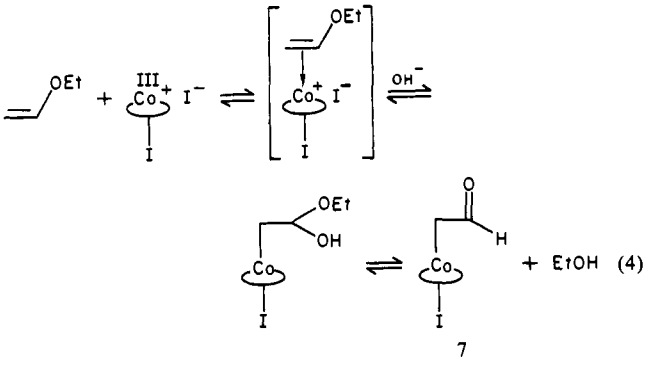


2 (3)

$Co–CH_2CHO$ formylmethyl product[19] (**2**) has been prepared and is too stable[20] to be a catalytic intermediate, in the absence of significant enzyme effects.

The acceptance of the π-complex mechanism is surprising, since a Co-assisted, OH migration (i.e., a Co, OH 1,2-interchange, eq 3) has never been experimentally demonstrated. The existence of Co(III) π-complexes must be considered as firmly established, on the basis of numerous synthetic[16] and labeling and stereochemical studies,[21] as well as Brown's recent direct NMR observation[22] of a π-complex. We have even used Co(III) π-complex chemistry (eq 4) to prepare the formylmethyl complex (**7**, Chart



7 (4)

I) in the B_{12} model system employed in the present work. However, existing Co(III) π-complex studies only suggest, somewhat indirectly, the Co(III) π-complex mechanism shown in eq 3, since these studies generally consist of β-OH (or OR) addition or loss, the reversible second step of eq 4, but not OH migration. They also do not demonstrate the kinetic dominance of the β-OH cleavage over simple homolytic cleavage[10] of the Co–C (α-OH) bond in **1**, since the models used prior to the present study contained only *β-OH but not both β-OH and α-OH groups*. Since recent work has shown that Co–C bonds in B_{12} models are generally weak[10] and that metal–C (α-OH) bonds are even weaker,[23] due to the significant influence of the α-OH group on the stability of the radical, $RCH(OH)\dot{C}HOH$, one can argue that the absence of both α- and β-OH groups in previous studies is a significant omission. Thus, neither the kinetic competence of the established Co(III) π-complex mechanism nor an OH-migration–π-complex mechanism have been experimentally established.

An important approach to the key intermediate **1** and its reactions is Meyerstein's most recent pulse radiolysis study[15a] that generates $HOCH_2\dot{C}HOH$ in the presence of Co(II), $B_{12(r)}$. Although reaching essentially the opposite conclusion relative to Blackburn's earlier, apparently incorrect work[15c] concluding **1** did not form, Meyerstein's study appears to provide evidence for the formation of metastable **1** at pH 7, but *no* rearrangement to $Co–CH_2CHO$ (**2**) or CH_3CHO. Instead, only an apparent side reaction to Co(I) and $HOCH_2CHO$ was observed, although just UV–visible characterization of the cobalt products was reported, the pulse radiolysis technique providing too little organic products for traditional methods of characterization.

Finally, it should be mentioned, and we note it has been stressed by Golding,[4a,14b,12a] that nine studies[24] of $HOCH_2\dot{C}HOH$ (a) show that such α-hydroxy radicals are up to 10^5 more acidic, $pK_a \sim 10–12$,[24] than the parent alcohol (cf. the significant effect of the α-OH on the radical stability mentioned earlier), (b) provide ample precedent for a free radical fragmentation reaction without cobalt participation, $HOCH_2\dot{C}HOH \rightarrow \cdot CH_2CHO + H_2O$, that occurs with base or acid catalysis at[24i] $3 \times 10^6\ s^{-1}$ and[24e] $8 \times 10^5\ s^{-1}$, respectively, $HOCH_2\dot{C}HOH + OH^- \rightleftharpoons H_2O + HOCH_2\dot{C}HO^- \rightarrow \cdot CH_2CHO + OH^-$, $HOCH_2\dot{C}HOH + H^+ \rightleftharpoons H_2O^+–CH_2\dot{C}HOH \rightarrow H_3O^+ + \cdot CH_2CHO$, and (c) show that α-hydroxy radicals and especially their conjugate bases are strong reductants, $R_2\dot{C}OH$, $E_{1/2}$ ca. −1.3 V vs. SCE.[25]

It is hoped that this relatively brief presentation of a much more voluminous, sometimes conflicting and confusing literature will help place in perspective the question of cobalt participation or nonparticipation. In our opinion, the interest and emphasis on this question and **1** are justified due to the possible finding, in the

(19) For references to formylmethyl transition-metal complexes in B_{12}, cobaloximes, $CpFe(CO)(PPh_3)(CH_2CHO)$, and $HIrCl(PMe_3)_3(CH_2CHO)$ see a–g: (a) Reference 16. (b) Silverman, R. B.; Dolphin, D. *J. Am. Chem. Soc.* **1976**, *98*, 4633. (c) Vickery, T. M.; Wright, E. E.; Kok, R. A. *Inorg. Nucl. Chem. Lett.* **1979**, *15*, 317. (d) Curzon, E. H.; Golding, B. T.; Wong, A. K. *J. Chem. Soc., Chem. Commun.* **1982**, 63. (e) Bodnar, T.; Coman, G.; La Croce, S.; Lambert, C.; Menard, K.; Cutler, A. *J. Am. Chem. Soc.* **1981**, *103*, 2471. (f) Milstein, D.; Calabrese, J. C. *Ibid.* **1982**, *104*, 3773. (g) Milstein, D. *Ibid.* **1982**, *104*, 5227.

(20) (a) σ–π hyperconjugation (vertical stabilization) appears to be responsible for the so-called β-effect[19f,20b] and $\nu_{CO} \sim 1635–1665\ cm^{-1}$ in these complexes. (b) Brown, K. L.; Zahonyi-Budo, E. *J. Am. Chem. Soc.* **1982**, *104*, 4117.

(21) (a) Reference 19d. (b) Brown, K. L.; Ingraham, L. L. *J. Am. Chem. Soc.* **1974**, *96*, 7681. (c) Golding, B. T.; Holland, H. L.; Horn, U.; Sakrikar, S. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 959. (d) There are at least 25 papers in the literature on such π-complexes; additional references can be found in the lead references provided.[16,21] (e) A Pt–π-vinyl alcohol complex has been studied by crystallography: Hillis, J.; Francis, J.; Ori, M.; Tsutsui, M. *J. Am. Chem. Soc.* **1974**, *96*, 4800. Cotton, F. A.; Francis, J. N.; Frenz, B. A.; Tsutsui, M. *Ibid.* **1973**, *95*, 2483. (f) Ag^+-olefin complexes are also well known: Fueno, T.; Kajimoto, O.; Furukawa, J. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 782.

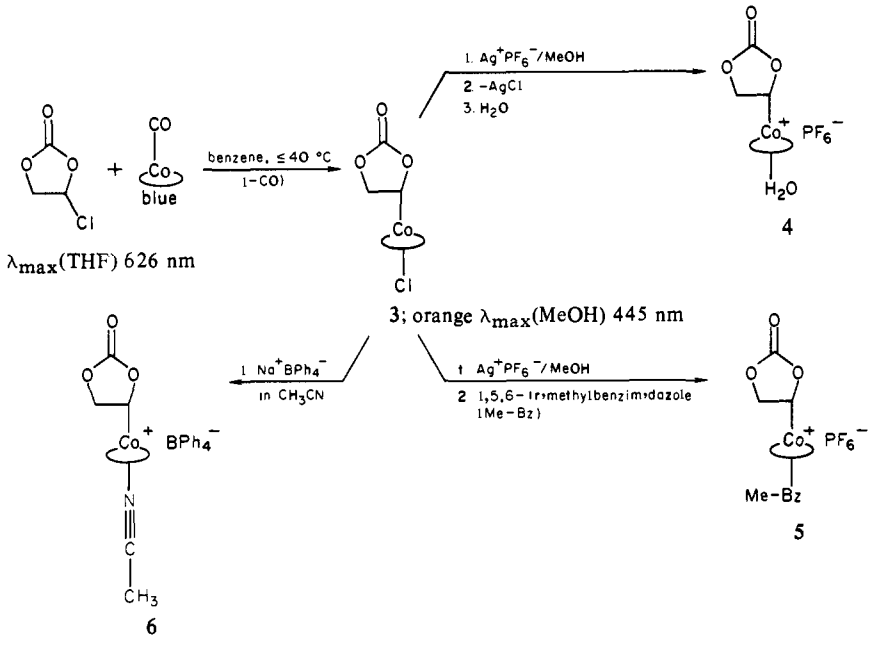
(22) Brown, K. L.; Ramamurthy, S. *Organometallics* **1982**, *1*, 413.

(23) (a) Although several stable α-hydroxy/metal complexes are now known,[23c-h] $(OC)_5MnCH(OH)Ph$ is unstable even at −50 °C and yields $HMn(CO)_5$ and PhCHO,[23b] a result that may be relevant since $\cdot Mn(CO)_5$ is isoelectronic and isostructural with d^7, 5-coordinate, square-pyramidal, base-on Co(II). Recent work[23g] is consistent with Gladysz's work, and the studies presented herein suggesting that α-hydroxy alkyl complexes of the first transition-metal series will be rare due to weak M–C bonds. (b) Gladysz, J. A.; Selover, J. C.; Strouse, C. E. *J. Am. Chem. Soc.* **1978**, *100*, 6766. (c) Vaughn, G. D.; Gladysz, J. A. *Ibid.* **1981**, *103*, 5608. (d) Casey, C. P.; Jones, W. D. *Ibid.* **1980**, *102*, 6154 and reference 1 therein. (e) Espenson, J. H.; Bakač, A. *Ibid.* **1980**, *102*, 2488; **1981**, *103*, 2721; **1981**, *103*, 2728. (f) Brown, K. L.; Clark, G. R.; Headford, C. E. L.; Marsden, K.; Roper, W. R. *Ibid.* **1979**, *101*, 503. (g) Wayland, B. B.; Woods, B. A.; Minda, V. M. *J. Chem. Soc., Chem. Commun.* **1982**, 634. (h) Kirker, G. W.; Bakac, A.; Espenson, J. *J. Am. Chem. Soc.* **1982**, *104*, 1249.

(24) (a) Pikaev, A. K.; Kartasheva, L. I. *Int. J. Radiat. Phys. Chem.* **1975**, *7*, 395. (b) Buley, A. L.; Norman, R. O. C.; Pritchett, R. J. *J. Chem. Soc. B* **1966**, 849. (c) Livingston, R.; Zeldes, H. *J. Am. Chem. Soc.* **1966**, *88*, 4333. (d) Gilbert, B. C.; Larkin, J. P.; Norman, R. O. C. *J. Chem. Soc., Perkin Trans. 2* **1972**, 794. (e) Bansal, K. M.; Grätzel, M.; Henglein, A.; Janata, E. *J. Phys. Chem.* **1973**, *77*, 16. (f) Venter, P. J.; van der Linde, H. J.; Basson, R. A. *J. Chem. Soc., Chem. Commun.* **1972**, 187. (g) Burchill, C. E.; Perron, K. M. *Can. J. Chem.* **1971**, *49*, 2382. (h) Steenken, S.; Schulte-Frohlinde, D. *Tetrahedron Lett.* **1973**, 653. (i) Steenken, S. *J. Phys. Chem.* **1979**, *83*, 595. See also ref 24e.

(25) The value −1.3 V (SCE) is for $(CH_3)_2\dot{C}OH$,[25a] and differs slightly from the value quoted in a review of this area.[25b] The experimental value for $HOCH_2\dot{C}HOH$, ca. −1.0 V (SCE), is a peak potential, E_p, containing kinetic effects and referring to the couple $R\cdot/ROH$ and not $R\cdot/R^+$ as previously noted.[15a] It is, however, similar to $R\cdot/R^+$ $E_{1/2}$ values measured by others.[25c] (a) Lilie, V. J.; Beck, G.; Henglein, A. *Ber. Bunsenges. Phys. Chem.* **1971**, *75*, 458. (b) Endicott, J. F. In "Concepts in Inorganic Photochemistry"; Adamson, A. W., Fleischauer, P. D., Eds.; Wiley-Interscience: New York, 1975; pp 88–92. (c) Jaun, B.; Schwartz, J.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 5741.

Scheme II



case of cobalt participation, of a novel role for cobalt or, in the case of nonparticipation, the *significant, resultant simplification* of the controversial area of mechanistic B_{12} chemistry with, in the case of diol dehydratase at least, the Co–C bond of the cofactor simply serving as Nature's C(5′) radical source following homolysis with the *protein* and not the cofactor serving to bind, control, and direct the (protein) "bound radicals".

In a preliminary communication[1a] in 1980, we described our "protected intermediate" approach to the synthesis of **1**, where it was prepared in a carbonate-protected form **3** (Chart I) due to the anticipated instability of the α-hydroxyalkyl–cobalt bond in **1**. The approach was to preform the Co–C bond, thereby removing the assumption of Co–C bond formation and "inviting" cobalt participation. The model employed was our modification[6] of Costa's B_{12} model, which we have shown[6a,b] is the closest electrochemical mimic from among simple Schiff base, B_{12} model systems. Herein we provide (a) the full details of the preparation, characterization, and physical properties of **3–6**, the carbonate-protected forms of **1**, (b) product studies demonstrating the catalytic MeO^- in MeOH deprotection of **3** and resultant products, including 95 ± 4% CH_3CHO, and (c) the synthesis, after numerous unsuccessful routes, of the Co–CH_2CHO formylmethyl complex, **7**, its characterization, and conditions of stability and instability.

In the accompanying paper,[1b] a kinetic and mechanistic study of the CH_3CHO forming methanolysis of **3** is reported, evidence which we believe argues effectively against the participation of cobalt. In a third manuscript,[7] the relevance or nonrelevance of these model studies and of the known α-hydroxy radical chemistry to diol dehydratase is presented, considerations which lead to a single, simplified and unified mechanism of action that has been, at least in part, previously suggested and that we prefer to call the "bound-radical mechanism".[7]

Results and Discussion

Synthesis and Characterization of 3–6. A reasonably large-scale, efficient, and clean synthesis of **3** and its derivatives was required. We have used approximately 750 g of the $ICo[C_2(DO)(DOH)_{pn}]I$ model system in all of our mechanistic studies[6] over the last 5 years.[2] This provides a good justification for the initial use of the model system, since the equivalent cost of cyanocobalamin is considerable at current prices. Although somewhat unusual, but quite reasonable on the basis of our oxidative-addition studies[6c] to OC–Co–$[C_2(DO)(DOH)_{pn}]$, it seemed likely that the oxidative addition of chloroethylene carbonate to the blue cobalt(I) carbonyl complex would provide a clean route to **3**. Oxidative addition in benzene of chloroethylene carbonate to the Co^ICO complex does in fact provide **3** in 80% yield in 0.5 g (to 1.0 g) quantities as shown in Scheme II, with small amounts of Co(II), $Co[C_2(DO)(DOH)_{pn}]Cl$ (or Co(III), $Co[C_2(DO)(DOH)_{pn}]Cl_2$ in O_2) as the major side products. The analogous reaction with $Rh^I[C_2(DO)(DOH)_{pn}]$ is of interest due to the greater stability of Rh–C(α-OH) bonds[23g] and is currently under study.[11] Desired derivatives of **3**, **4–6**, were prepared by the unexceptional chemistry shown in Scheme II.[6c]

Determining the exact structure of **3** proved to be more of a problem. The repeatedly good elemental analysis and characteristic IR band expected for a cyclic carbonate, ν_{CO}(**3**, KBr) = 1778 cm^{-1}, were very suggestive from the start as was the observation of two diastereotopic ligand CH_3 singlets, δ 2.4 in the 100-MHz ^1H NMR (Figure 2A). However, much of the rest of the 100-MHz NMR (Figure 2A) was nearly uninterpretable, and to make matters worse, when **3** was placed in CH_3OH, the solvent that proved optimum for further studies, the ^1H NMR broadened (Figure 2B) as if decomposition were occurring to a paramagnetic product such as Co(II).

A breakthrough was provided by a higher field, 360-MHz ^1H NMR (Figure 3). The now well-known spectral simplification is still striking (Figure 2A vs. 3A), and with the aid of five decoupling experiments, the spectrum was fully assigned to the structure and labeling scheme given in the inset on Figure 3. A tabulation of the numerical data for Figure 3A and the five decoupling experiments are provided in the Experimental Section and as supplementary material. The important diagnostic feature in the ^1H NMR is the numerous sets of diastereotopic and thus chemical shift nonequivalent hydrogens due to, and proving the presence of, the chiral carbon attached directly to cobalt. The difference in chemical shift observed between, for example, the diastereotopic CH_3 groups d and k, Figure 3 inset, is $\Delta\delta = 0.06$, similar to that observed for analogous R–Co cobaloxime complexes,[26] $\Delta\delta$ (CH_3 groups) = 0.01–0.07, depending upon the alkyl.

The reason for the unexplained, more complicated ^1H NMR in CD_3OD was also uncovered with the aid of 360-MHz and other experiments. The possibility of paramagnetic Co(II) broadening in **3** in the CD_3OD spectrum (Figure 2B) was ruled out by showing that the CH_3 group of added toluene remained sharp and the fact that O_2, added to the solution to oxidize any Co(II), did not affect the spectrum. The 360-MHz NMR (Figure 3B) spectrum showed

(26) (a) Naumberg, M.; Duong, K. N. V.; Gaudemer, F.; Gaudemer, A. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1970**, *270*, 1301. (b) Gaudemer, A.; Gaudemer, F.; Diep, L. *Bull. Soc. Chim. Fr.* **1972**, 884.

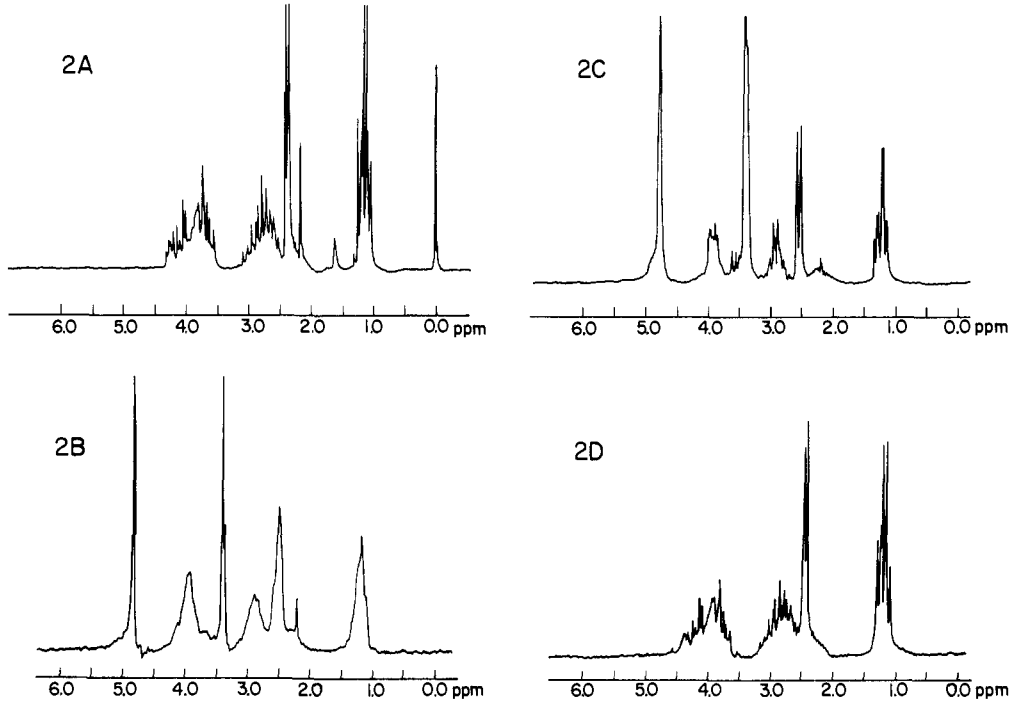


Figure 2. 100-MHz ^1H NMR spectra of **3** in $CDCl_3$ (A), in CD_3OD (B), in CD_3OD after treatment with $Ag^+PF_6^-$ (C), and after removal of the CD_3OD under vacuum from the sample used for spectrum B, followed by redissolving the solid in $CDCl_3$ (D).

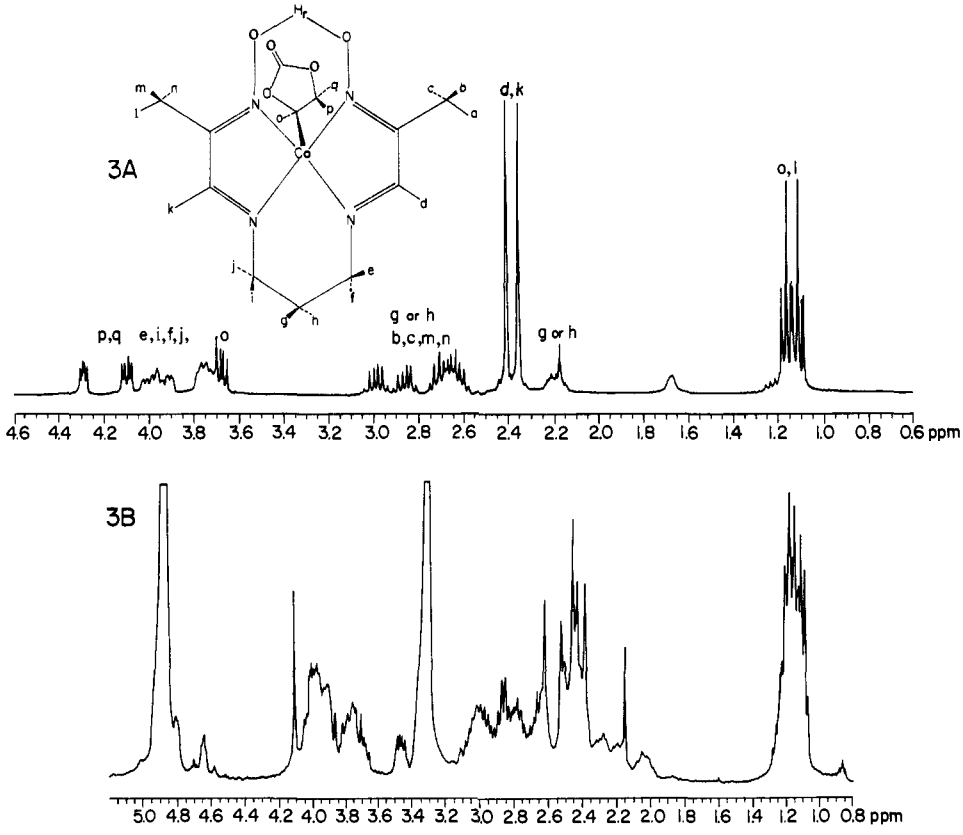


Figure 3. 360-MHz ^1H NMR spectra of **3** in $CDCl_3$ (A) and in CD_3OD (B). The assignments given in (A) refer to the labeling scheme given on the structure shown in the inset.

that the 100-MHz NMR spectrum in Figure 2B really contains considerable fine structure, and suggested that the observed 100-MHz spectrum was probably a composite of several, possibly three, forms of **3** in solution. Since conductivity measurements demonstrated that the axial Cl^- in **3** is ionized in CH_3OH (see Experimental Section), it seemed likely that the several forms of **3** differed in their average positions, on the NMR time scale, of the Cl^-, i.e., that ion pairing[27] was responsible for the complex NMR spectrum observed in CD_3OD. This explanation is fortified by the 100-MHz NMR experiments shown in Figure 2C,D. An

(27) (a) Szwarc, M., Ed. "Ions and Ion Pairs in Organic Reactions"; Wiley-Interscience: New York, 1972; Vol. I, pp 289, 311. (b) Goering, H. L.; Silversmith, E. F. *J. Am. Chem. Soc.* **1955**, *77*, 6249. This work shows that in *cis*- or *trans*-5-methyl-2-cyclohexyl *p*-nitrobenzoates, ion-pair formation does not lead to cis,trans isomerization.

aliquot of the same solution used for the spectrum in Figure 2B was treated with $AgPF_6$, the AgCl removed, and the spectrum of the resultant solution obtained (Figure 2C). This spectrum demonstrates that removal of the Cl^- yields a single solution species as its PF_6^- salt, i.e., that the presence of an anion like Cl^- is required to generate the complex NMR spectrum observed in CD_3OD. Figure 2D shows the NMR spectrum of an aliquot of the original CH_3OH solution used for spectrum 2B in which the CH_3OH was removed under vacuum and the sample was redissolved in $CDCl_3$. The NMR spectrum obtained (Figure 2D) is identical with that of freshly prepared **3** in $CDCl_3$ (Figure 2A) except for some presently unexplained change in the multiplet at δ 2.19. This NMR experiment demonstrates that no major irreversible changes in **3**, such as its decomposition, occur over about an hour in CD_3OD at 25 °C and is consistent with the ion-pairing explanation, since the Cl^- in **3** is not ionized in $CDCl_3$ by conductivity. The exact nature of the ion pairs, such as whether tight and/or solvent-separated forms are present, cannot be deduced from the present data. The fact that CH_3OH solutions of **3** conduct requires that dissociated ions be present in solution, a result verified by the addition of $Bu_4N^+Cl^-$, which causes a considerable sharpening of the CH_3OH ^1H NMR spectrum of **3** due to the Cl^- common ion effect. The NMR results require that the several forms interconvert slowly on the NMR time scale, a result seemingly inconsistent with the postulated interconversion of simple tight and solvent-separated ion pairs. A more likely but unproven possibility, based on the ion-pairing literature,[27] is that the NMR distinct species differ by having a Cl^- above and below the plane of the equatorial tetradentate macrocycle in tight and/or solvent-separated ion pair form.

The ν_{CO} IR data for **3** is also somewhat interesting and deserves a brief examination. It is characteristic of a carbonate as noted earlier, ν_{CO}(KBr) = 1778 cm^{-1}, but especially reminiscent of ethylene carbonate, $\overline{OCH_2CH_2OC{=}O}$ where two bands are observed in the carbonyl region.[28] These two bands arise from the interaction (Fermi resonance) of a ν_{CO} in the region of 1810–1870 cm^{-1} and the overtone $2\nu_7$ = 2 (890) = 1780 cm^{-1}. The result is that two bands are observed, $\nu(CHCl_3)$ = 1812, 1785 cm^{-1}, whose exact positions and relative intensities are quite solvent dependent. For **3**, one to two bands depending upon the solvent are observed in the carbonyl region, ν(pyridine) = 1974 cm^{-1}, $\nu(CH_3CN)$ = 1794 cm^{-1}, $\nu(CH_3OH)$ = 1805, 1780 cm^{-1}. Clearly, these IR data demonstrate the presence of a cyclic carbonate carbonyl in **3**.

The single-crystal, X-ray diffraction structural analysis of **3** was of interest, especially the Co–C bond length in such a compound with an oxygen atom α to the Co–C bond. Repeated attempts with different crystals failed to produce a high-precision X-ray structure of **3**. The best results, significantly better than the earlier R_f = 13.6% structure,[1] were obtained as the BPh_4^- salt (compound **6**, Chart I). A large crystal was found to belong to the monoclinic crystal system, space group $P2_1/n$, with a unit cell of dimensions a = 12.133 (3) Å, b = 24.027 (5) Å, c = 13.876 (3) Å, β = 92.91 (3)°, and Z = 4. The crystals diffracted weakly, often a sign of disorder, and of 4153 independent reflections, only 1326 were observed to have intensities greater than $3\sigma(I)$. Some additional data, the source of the disorder problem, and an ORTEP plot are provided as supplementary material, the final discrepancy indices being R_f = 0.086 and R_{wf} = 0.091. The data served primarily to confirm the structure deduced from the spectroscopic data, with average Co–N (ring) lengths being 1.880 (9) Å, Co–N (axial CH_3CN) = 1.979 (10) Å, and Co–C (ethylene carbonate) = 2.034 (27) Å, values consistent with other, related structures.[29]

Some additional physical properties, including its light and thermal stability, its solubility, and axial 1,5,6-trimethylbenzimidazole binding constant, were determined, properties necessary to understand how to optimally conduct the methanolysis (carbonate protecting group removal) experiments. The most important measurement was the axial 1,5,6-trimethylbenzimidazole binding in methanol to **4**, K_{assoc} = 90 ± 20 M^{-1}. As will be seen in the accompanying mechanistic paper, added axial 1,5,6-trimethylbenzimidazole has an important, inhibiting effect upon the CH_3CHO-forming, methanolysis reaction.

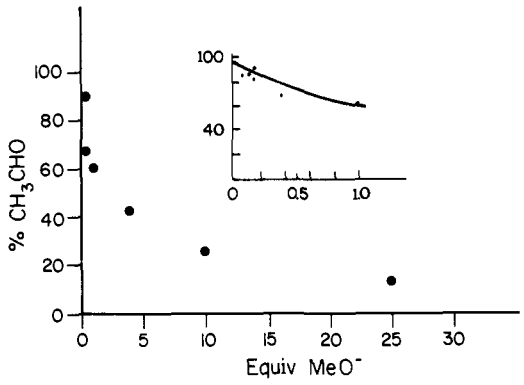
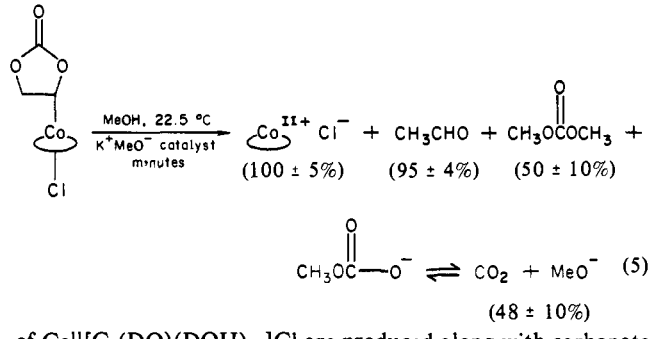


Figure 4. Acetaldehyde yield vs. equivalent of added CH_3O^-. The inset shows the data at ≤1 equiv of CH_3O^-.

Methanolysis Stoichiometry. The most significant feature of **3** is its catalytic deprotection by K^+MeO^- in MeOH, methanol being chosen after a survey of solvent systems, and the resultant stoichiometry eq 5), where 95 ± 4% of CH_3CHO and 100 ± 5% of $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$ are produced along with carbonate deprotection products, $MeOCO_2Me$ and $MeOCO_2^-$. Early control experiments revealed that KOH/MeOH, $[MeO^-]/[HO^-]$ = 4000/1 under the reaction conditions,[30] gave an identical stoichiometry to anhydrous K^+OMe^- prepared from potassium and dry MeOH, and that the PF_6^- salt, **4**, free from possible Cl^- ion-pairing effects, gave identical results (eq 5) in comparison to Cl^- containing **3**. Subsequent experiments were therefore performed with the more easily prepared **3** + KOH/MeOH. We also note that the stoichiometry (eq 5) has been repeatedly obeyed over a minimum of 25 experiments by several of us over the course of this study.



The reaction (eq 5) is easily followed by the orange to burgundy-red color change over a few minutes, characteristic of $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$ formation. This Co(II) product was characterized and quantified by its visible and ESR spectra in comparison to authentic samples prepared by $^1/_2[Cr(acac)_2]_2$ atom abstraction reduction of $Co^{III}[C_2(DO)(DOH)_{pn}]Cl_2$ (→Cl—Cr(acac)$_2$ + $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$) or, more easily, a Co(I) and Co(III) ⇌ 2Co(II) disproportionation reaction (OC—$Co[C_2(DO)(DOH)_{pn}]$ + $Co[C_2(DO)(DOH)_{pn}]Cl_2$ → CO + 2$Co^{II}[C_2(DO)(DOH)_{pn}]Cl$).

Acetaldehyde was identified by GC and GC/MS and was isolated as its 2,4-DNP derivative, unequivocally confirming its presence. At 1 equiv of MeO^-, 61 ± 6% of CH_3CHO is observed by GLC as previously reported,[1] but when the % CH_3CHO vs. MeO^- is studied (Figure 4), the % CH_3CHO rises to 95 ± 4%

(28) Angell, C. L. *Trans. Faraday Soc.* **1956**, *52*, 1178.
(29) Glusker, J. In "X-Ray Crystallography of B_{12} and Cobaloximes, Vitamin B_{12}", Dolphin, D., Ed.; Wiley: New York, 1981; Chapter 3.

(30) (a) One equivalent of 0.9 M KOH·XH_2O (85% KOH, 15% H_2O) in dry CH_3OH (pK_a = 15.5)[30b] added to a 1.1 × 10^{-2} M solution of **3** in CH_3OH yields 0.50 M H_2O (pK_a = 15.7) and a $[CH_3O^-]/[HO^-]$ = 4 × 10^3. (b) Streitwieser, A., Jr.; Heathcock, C. H. "Introduction to Organic Chemistry", 2nd ed.; MacMillan: New York, 1981; p 238.

CH_3CHO. Control experiments using authentic CH_3CHO and the $MeO^-/MeOH$ reaction conditions demonstrated that the major part of the CH_3CHO losses at higher MeO^- concentrations are due to the well-known facile aldol chemistry of acetaldehyde.[31] In MeOH, NMR experiments demonstrated that CH_3CHO is present largely as its hemiacetal, $CH_3CH(OH)(OMe)$.

The remaining carbonate-deprotection products of eq 5 were identified and quantified by IR in comparison to authentic samples, $CH_3OCO_2CH_3$ (ν_{CO}(MeOH) = 1755 cm^{-1}) and $CH_3OCO_2^-K^+$ (ν_{CO}(MeOH) = 1655 cm^{-1}). The MeO^--consuming formation of $CH_3OCO_2^-$ decreases at <1 equiv of MeO^-, as it must if the reaction is catalytic in MeO^-, with $MeOCO_2^-$ being undetectable at ≤0.1 equiv of MeO^-. Under these latter conditions, the product is CO_2 and a facile $CH_3OCO_2^- \rightleftharpoons CO_2 + MeO^-$ equilibrium[32] is present, as demonstrated by the addition of ≥0.5 equiv of MeO^- to the reaction products and IR detection of the ca. 50% $CH_3OCO_2^-$, ν_{CO} = 1655 cm^{-1}, that is generated. The observation of both $CH_3OCO_2CH_3$ and $CH_3OCO_2^-$ is interesting and has proven to be a very useful feature of the carbonate protected intermediate, **3**. Simple ethylene carbonate yields only $CH_3OCO_2CH_3$ as expected, $\overline{OCH_2CH_2OC}{=}O + MeO^-$ (catalytic)/MeOH → $HOCH_2\dot{C}HOH + CH_3OCO_2CH_3$. These results are those expected for the formation of the well-known tetrahedral intermediate by MeO^- attack at the carbonyl carbon of **3**, followed by its near statistical opening each of the two possible ways and eventual formation of 50% each of $CH_3OCO_2^-$ and $CH_3OCO_2CH_3$. Additional evidence for initial MeO^- attack at the carbonyl carbon and the intermediates shown in Scheme III will be presented in the following mechanistic paper.[1b]

The H· Source Question. The stoichiometry (eq 5) is complete except for the H· source required for CH_3CHO formation. Restated, the stoichiometry (eq 5), mass, and charge balance strongly suggest, although they do not prove, the formation of $\cdot CH_2CHO$[33] prior to CH_3CHO formation. There are only two possible sources of the required H·, the ligand or the CH_3OH solvent. The visible and ESR characterization of the $Co(II)^+$ Cl^- product appeared to rule out the ligand as a H· source, in spite of precedent for this process,[34] and this was confirmed by I_2 (0.5 ± 0.05 equiv) or $BrCCl_3$ oxidation of the Co(II) product and visible, TLC, and 360-MHz NMR characterization and 100 ± 5% quantification of the resultant product as authentic, ligand intact, $Co[C_2(DO)(DOH)_{pn}]X_2$.

Demonstration that CH_3OH was the H· source proved elusive under these basic conditions, however. There are numerous literature citations[35] that the CH_3OH methyl group (vs. the OH group) is the preferential H· source with the resultant $\cdot CH_2OH$ expected to give combination, $HOCH_2CH_2OH$, and disproportionation products, $0.5CH_3OH + 0.5\ H_2CO$, although these products are almost never adequately characterized, if at all.[35] Thermodynamic and kinetic considerations furthermore confirm that the reaction $\cdot CH_2CHO + CH_3OH \rightarrow CH_3CHO + \cdot CH_2OH$ should occur, $\Delta H_{(est)}$[36a-f] = −3 to −5 kcal/mol, 75 $M^{-1}\ s^{-1} < k_{(est)}$ < $10^5\ M^{-1}\ s^{-1}$.[36g,h] For the more exothermic reaction, Ph· + $CH_3OH \rightarrow PhH + \cdot CH_2OH$, $\Delta H_{(est)}$[36a-f] = −12 kcal/mol and k_{obsd}[36h] = $10^5\ M^{-1}\ s^{-1}$. Under basic conditions, $\cdot CH_2OH$, pK_a = 10.7,[24] would be fully deprotonated by MeO^-, yielding $\cdot CH_2O^-$, and one might expect the resultant negative charge to inhibit dimerization to $HOCH_2CH_2OH$ (after protonation) relative to H_2CO formation.

Direct ^1H NMR experiments in CD_3OD demonstrated that no $HOCH_2CH_2OH$ was present under conditions where a control showed that ≥10% was detectable and also showed that no H_2CO or $H_2C(OH)(OMe)$ were present. The use of $^{13}CH_3OH$ and ^{13}C NMR or dimedon, 2,4-DNP, or chromotropic acid tests[37] to detect H_2CO similarly failed, the expected result since control experiments demonstrated that even added H_2CO was not detectable due to the well-known, rapid consumption of formaldehyde under basic conditions.[38] A labeling experiment using CD_3OH to produce DCH_2CHO was precluded by a control experiment that demonstrated, as expected, rapid H/D exchange with the solvent hydroxyl and the methyl hydrogens of CH_3CHO. Given these control experiments demonstrating that H_2CO detection or labeling experiments were essentially impossible under the reaction conditions, other solvents were examined with the hope of observing their radical-derived oxidation products (solvent/product): $((CH_3)_2CHOH/(CH_3)_2CO$; $HOCH_2CH_2OH/HOCH_2CHO$; CH_3CH_2OH/CH_3CHO; $PhCH_2OH/PhCHO$). One could reasonably expect ethanol or ethylene glycol to be the best solvents, where 0.5 equiv of CH_3CHO, catalytic CH_3CHO formation,[39] and stoichiometric (0.5 equiv) $HOCH_2CHO$ formation, respectively, are the anticipated products. In practice, slower rates of alcoholysis, competing aldol chemistry, and other problems hinder experiments in these solvents. The desired participation by solvent was finally obtained by using carefully purified, PhCHO-free (negative 2,4-DNP test) $PhCH_2OH$ as a solvent. The aldehyde, PhCHO, was isolated and characterized as its 2,4-DNP in ca. 40% (52 ± 15% by GC) yield, results that are difficult to explain by any process other than $R\cdot + PhCH_2OH \rightarrow RH + Ph\dot{C}HOH$ and then under basic conditions $Ph\dot{C}HOH \rightarrow 0.5PhCHO + 0.5PhCH_2OH$.

The Putative (Formylmethyl)cobalt Intermediate, 7. A π-complex mechanism (eq 3) should produce the $Co{-}CH_2CHO$, formylmethyl intermediate, **7**, as should all other Co-participation mechanisms that we are aware of. Given the stability of all known formylmethyl complexes,[19,20] the lack of observation of this product and the observation of Co(II) instead (eq 5) are significant results that strongly argue against cobalt participation. An independent preparation and characterization of $Co{-}CH_2CHO$, **7**, in the present model system and a verification of its stability were clearly required, however.

Following the investigation of five unsuccessful routes, involving (i) Co(I) + $ClCH_2CHO$, (ii) 2Co(II) + $ClCH_2CHO$, (iii) Co(III) + $CH_2{=}CHOSiMe_3 + F^-$, (iv) Co(III) + R_3SnCH_2CHO, and (v) Co(III) + $LiCH_2CHO$ (details are provided as supplementary materials), the formylmethyl complex **7** was successfully prepared in ≥90% yield in a slow reaction, 20% conversion in 6 days, by Dolphin's method by using $Co^{III}[C_2(DO)(DOH)_{pn}]I_2$, ethylvinyl ether and moist, basic ethanol (the previous eq 4, which is repeated below). The product, **7**, was unambiguously characterized by 360-MHz ^1H NMR (δ($CDCl_3$) 8.97 (t, 1 H, J = 5.2 Hz, $Co{-}CH_2CHO$), 1.56 (d, 2 H, J = 5.2 Hz, $Co{-}CH_2CHO$) and IR

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(32) Pocker, Y.; Davison, B. L.; Deits, T. L. *J. Am. Chem. Soc.* **1978**, *100*, 3564 and references therein.
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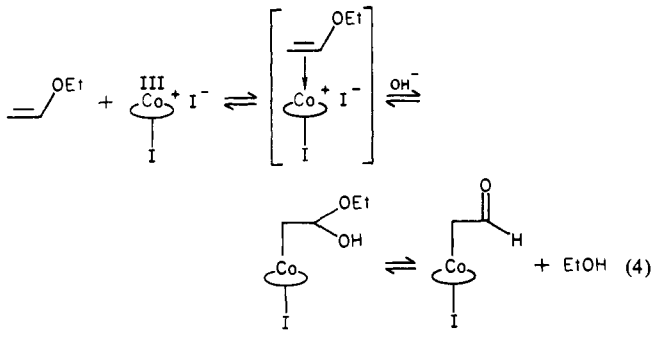

7

($\nu_{CO}(CHCl_3$ or $CH_3OH) = 1650\ cm^{-1}$) in comparison to literature formylmethyl complexes.[19] The diagnostically low, ν_{CO} = 1635–1665 cm^{-1}, carbonyl band is due to the so-called β-effect, in this case explained as σ–π hyperconjugation.[20] Significantly, **7** was relatively stable in $MeO^-/MeOH$ (no decomposition by IR or ^1H NMR for 1 h), or in $MeO^-/MeOH$ with added 1,5,6-trimethylbenzimidazole (ca. 10% loss by IR, a slight upfield shift in the ^1H NMR, δ 8.82 (t, J = 5 Hz, 1 H), 1.40 (d, J = 5 Hz, 2 H), and decrease by 20 cm^{-1} in the IR, $\nu_{CO}(CH_3OH) = 1630\ cm^{-1}$. Additional studies of **7** are provided in the Experimental Section. Although other mechanistic experiments with the Co–CH_2CHO complex, **7**, will be presented in the following paper,[1b] the present results with **7** would appear to rule out the π-complex mechanism (eq 3), any other cobalt-participation mechanism that should produce **7**, and the participation of **7** in Scheme III.

Discussion and Conclusions

The goal of this first stage of the present work was (a) the high yield preparation and unambiguous characterization of a protected form of the postulated intermediate **1** (eq 2), (b) establishment of the conditions required for the deprotection of the protected intermediate, (c) establishment of the complete stoichiometry of any resultant "rearrangement"[41] reaction, and (d) the preparation, characterization, and stability/instability studies of the second, often postulated diol dehydratase intermediate, the formylmethyl complex, using the $Co[C_2(DO)(DOH)_{pn}]$ model system.

These goals were met by the 80% yield and full characterization of carbonate-protected intermediate, **3**, its MeO^--catalyzed deprotection in MeOH to yield near quantitative CH_3CHO, 1 equiv of $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$ and ca. 0.5 equiv each of $MeOCO_2Me$ and $MeOCO_2^-$, and the synthesis and study of the relatively stable formylmethyl complex, **7**. In principle, the ideal protecting group or collection of protecting groups would undergo deprotection at acidic, neutral, and basic pH. In the early phases of this work, seven other protecting groups (PG) that can be removed at different pH values were examined in an effort to prepare $\overline{OCH_2CH(Cl)O\text{–}PG}$ for oxidative addition to Co(I) analogous to our successful synthesis of **3**. In particular, the following protecting groups were examined: *tert*-butoxyboronate (PG = –B(OBu-*t*)), phenylboronate (PG = BPh), ortho ester (PG = $-C(CH_3)OCH_3$), bis(trimethylsilyl) (PG = $-SiMe_3$), diphenyl ketal (PG = $-CPh_2$), phosphate ester (PG = P(O)OPh), and thionocarbonate (PG = >C=S). Other than the thionocarbonate, which is still under investigation as part of the extension of these studies to cobalamins and cobinamides,[42] these protecting groups failed or proved far less satisfactory than the carbonate in **3**. (The investigation of the other protecting groups is documented in the supplementary material for the interested reader.) The major disadvantage of **3** is that its deprotection is limited to basic pH values. We note, however, that the optimum pH range for diol dehydratase is 6–10, not far from the pH range of 10–12 generally studied herein. Although the pH at the active site of diol dehydratase is unknown, we have argued elsewhere[7] for basic binding, $HOCH_2\dot{C}HOH$---base (protein), of the α-hydroxy radical. If correct, studies under basic conditions may prove most important.

Advantages of the carbonate-protected **3** include its easy, high-yield preparation, its ready deprotection with catalytic MeO^- in MeOH, its record 95% CH_3CHO formation, and the IR ($MeOCO_2Me$, $MeOCO_2^-$), GLC (CH_3CHO), and visible spectroscopy (Co(II)) handles provided by its subsequent, clean "rearrangement" reaction, eq 5. In the following mechanistic study, kinetic and nitroxide radical trapping experiments, the dramatic CH_3CHO-inhibiting effect of axial 1,5,6-trimethylbenzimidazole, and other mechanistic experiments are presented.[1b]

Experimental Section

(A) General. (i) Methods of Handling Air-Sensitive Compounds. All manipulations involving air-sensitive materials were handled by using standard Schlenk-tube techniques, an inert-atmosphere (N_2) Vacuum Atmospheres Inc. drybox, gas-tight syringes or stainless steel cannula for air-free transfers, and purified N_2, all as previously described.[6c]

(ii) Equipment. NMR spectra were obtained on a Varian XL-100 (100 MHz) and a Nicolet NT-360 FT NMR spectrometer (360 MHz). Early 360-MHz NMR spectra were obtained at the Stanford Magnetic Resonance Laboratory with the expert assistance of Dr. Lois Durham. IR spectra were recorded on a Beckman IR-10 and a Sargent-Welch 3-200 infrared spectrophotometer, using a matched pair of CaF_2 solution cells (International Crystals Inc.). UV–visible spectra were run on a Cary 15 spectrophotometer equipped with a Neslabs Inc. Exacal 100 and Endocal 350 temperature control unit, circulating 1:1 water/ethylene glycol through a jacketed cuvette holder, using either standard 1.0-cm quartz rectangular UV–visible cuvettes or a cylindrical 0.1-mm pathlength cell (Markson Scientific Inc.). ESR measurements were made on a Varian E-3 spectrometer. Gas chromatography was performed on a Hewlett-Packard Model 700 laboratory chromatograph, utilizing a flame ionization detector. Acetaldehyde was detected by GC by using a 21-ft 10% Carbowax 20M on 80–100 mesh Chromosorb W-HP column run isothermally at 70 °C. GC–mass spectra were recorded on a Hewlett-Packard 7620A GC interfaced to a Model 15930A mass spectrometer. Conductivity measurements were made with a Radiometer (Copenhagen) CDM 2e conductivity meter, a type CDC 114 cell (cell constant = 1.69 cm^{-1}), and a Yellow Springs Instruments Model 31 conductivity bridge and No. 3403 cell (cell constant = 1.00 cm^{-1}). Elemental analyses were obtained from the University of Oregon microanalytical laboratory.

(iii) Solvents. All solvents were distilled under nitrogen. Benzene (Baker) was distilled from CaH_2, methanol (Baker) from $Mg(OMe_2)$, ethanol (U.S.I.) from $Mg(OEt)_2$, pyridine (Fischer) from BaO, ethylene glycol (Aldrich) from Linde 4-Å molecular sieves, acetonitrile (Baker) from CaH_2, and isopropyl alcohol (Baker) from $MgSO_4$. Solvents were stored in 1-L brown bottles in the drybox, after being bubbled with N_2 in the box for at least 15 min. Deuterated NMR solvents, $CDCl_3$ (Aldrich), CD_3OD (KOR Isotope Chemicals), and CD_3CN (Aldrich), were used without further purification.

(iv) Other Chemicals. Commercially available chemicals that were used without purification include: ethylene carbonate, dimethyl carbonate, bromotrichloromethane, and vinylene carbonate (Aldrich), CO and CO_2 (Matheson), $AgPF_6$, $AgBF_4$, $NaBPh_4$, $(CH_3)_4NCl$, $(n\text{-}C_4H_9)_4NI$, and $[Ph_3P{=}N{=}PPh_3]^+Cl^-$ (Alfa), and ^{13}C-methanol (KOR Isotope Chemicals). Ethyl vinyl ether and triethylamine (Aldrich) were distilled immediately prior to use. 1,5,6-Trimethylbenzimidazole was prepared by the literature method.[43] The 2,4-dinitrophenylhydrazine (2,4-DNP),[44] dimedon,[45] and chromotropic acid[37] test reagents were prepared according to published methods. Chromium(II) acetoacetonate was a gift from Dr. Thomas Sorrell and was prepared by the published procedure.[46]

Neither repeated fractional distillations nor treatment with base and ether extraction followed by fractional distillation[47] proved effective in

(41) Strictly speaking, if the reaction $HOCH_2\dot{C}HOH \rightarrow \cdot CH_2CHO + H_2O$ is involved, this reaction is not a rearrangement reaction since $HOCH_2CHOH$ and $\cdot CH_2CHO$ are not isomers, i.e., do not have the same molecular formula.

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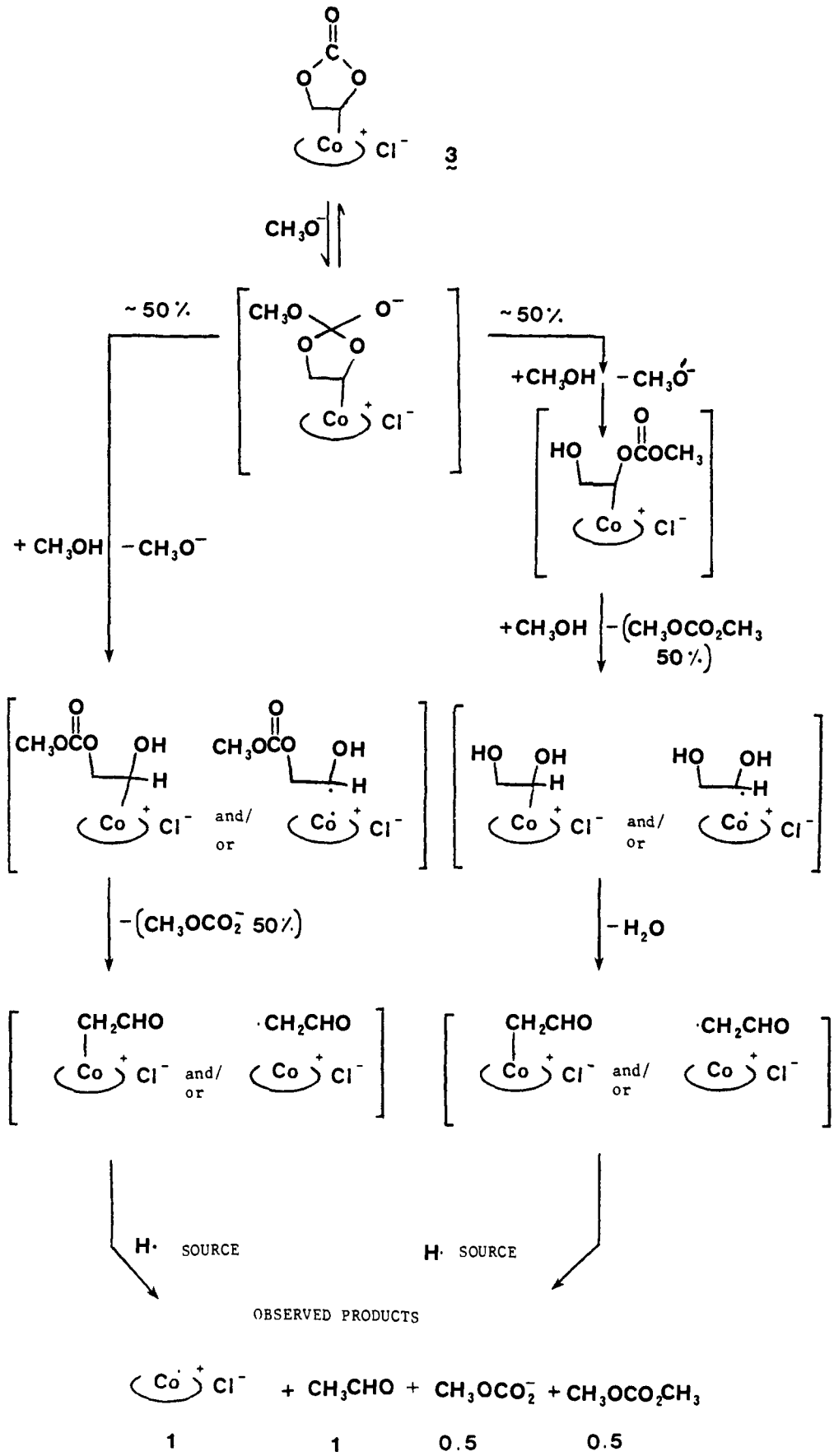
Scheme III



our hands at quantitatively removing benzaldehyde impurities from commercial benzyl alcohol. Treatment with the 2,4-DNP reagent was much more effective. To 10 mL of benzyl alcohol (Fischer) was added 5 mL of the 2,4-DNP reagent. The solution was filtered, and the filtrate gave a negative 2,4-DNP test. The organic fraction of the filtrate was mixed with 30 mL of diethyl ether, washed with 2 × 30 mL of water,

and dried ($MgSO_4$), and the ether was removed by rotary evaporation. Fractional distillation at 69–71 °C (2 torr) yielded 4 mL of colorless $PhCH_2OH$, which gave a negative 2,4-DNP test and was then stored under nitrogen.

(v) Preparation of 4-Chloro-2-dioxolanone (Chloroethylene Carbonate). (1) The preparation of 4-chloro-2-dioxolanone was accomplished by the photochemical chlorination of ethylene carbonate, *in* CCl_4, after the literature method failed in our hands.[48]

A solution of 161 g (1.83 mol) of ethylene carbonate in 250 mL of CCl_4 was irradiated with a 350-W sunlamp. Chlorine was passed into the reaction flask at a rate sufficient to maintain a pale yellow color in solution. After 130 min, excess Cl_2 was removed by bubbling the solution with N_2 for 15 min. Carbon tetrachloride was removed by a flask-to-flask distillation. Vacuum distillation gave 148 g (66%) of colorless chloroethylene carbonate: bp 130–139 °C (39 torr); IR ν_{CO} (neat film) 1825 cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si as an external reference) δ 4.8 (2 H), 6.6 (ABX pattern, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si as an external reference) δ 152.9, 86.2, 74.4; n^{25} 1.4513 (lit.[48] n^{25}_D 1.4530). The 4-chloro-2-dioxolanone was protected from light and was stored at −10 °C under nitrogen in sealed ampules. At room temperature, the liquid slowly yellows, but is easily repurified by redistillation.

(B) Syntheses. The cobalt complexes $Co[C_2(DO)(DOH)_{pn}]Cl_2$, $Co[C_2(DO)(DOH)_{pn}]I_2$, and $(CO)Co[C_2(DO)(DOH)_{pn}]$ were all prepared and characterized as previously detailed.[6c]

(i) Synthesis of 3, Chloro(2-oxo-1,3-dioxolan-4-yl)(2,10-diethyl-3,9-dimethyl-1,4,8,11-tetraazaundeca-1,3,8,10-tetraene-1,1-diol)cobalt(III), $\overbrace{CH_2O(C{=}O)O}CHCo[C_2(DO)(DOH)_{pn}]Cl$. This synthesis was accomplished by using the general oxidative-addition chemistry to $(CO)Co[C_2(DO)(DOH)_{pn}]$ we previously reported.[6c]

In the drybox, protecting the reaction vessel from light, 25 mL of benzene, 530 mg (1.28 mmol) of $(CO)Co[C_2(DO)(DOH)_{pn}]$, and 1.0 mL (13 mmol) of 4-chloro-2-dioxolanone were combined to give a deep blue solution. The reaction mixture was stirred at ≤40 °C for 6 h to give a red-orange solution. The flask was removed from the drybox and filtered to give 330 mg (48%) of an orange solid, which was collected and washed with 5 mL of benzene. The filtrate was evaporated to dryness to give an orange-brown solid, which was chromatographed on two 1000-μm SiO_2 plates with acetone. Three bands resulted on the TLC plates, green $Co[C_2(DO)(DOH)_{pn}]Cl_2$ (R_f 0.85), the orange chloroethylene carbonate adduct (R_f 0.60) and brown decomposition product(s) (R_f 0). The orange band was collected with acetone, evaporated to dryness, and combined with the previous orange solid to give a total of 550 mg of product (crude yield = 80%). Recrystallization from ethanol/acetone at −10 °C gave 412 mg (60%) of analytically pure orange solid after vacuum drying at room temperature (Anal. ($C_{16}H_{26}N_4O_5CoCl$) C, H, N); visible λ_{max} (MeOH) 450 nm; IR (KBr) ν_{CO} 1778 cm^{-1}, (MeOH) ν_{CO} 1805, 1780 cm^{-1}; ^1H NMR ($CDCl_3$, Me_4Si as an external reference) δ 1.12 (dd, J = 7, 5 Hz, 3 H), 1.17 (dd, J = 7.5 Hz, 3 H), 2.19 (m, 1 H), 2.36 (s, 3 H), 2.67 (m, 3 H), 2.86 (ABC_3 type, 1 H), 2.99 (ABC_3 type, 1 H), 3.67 (dd, J = 10, 7 Hz, 1 H), 3.74 (m, 2 H), 3.96 (m, 2 H), 4.19 (dd, J = 10, 7 Hz, 1 H), 4.28 (dd, J = 7, 5 Hz, 1 H), and 18.75 (s, 1 H, O–H–O). The ^1H NMR assignments were supported by five decoupling experiments, the results of which are provided as supplementary material.

(ii) Synthesis of 4, the (Aquo) Hexafluorophosphate Complex. A 100-mg (0.22-mmol) sample of the chloroethylene carbonate oxidative-addition product **3**, prepared as in (i) above, was added to 55 mg (0.22 mmol) $AgPF_6$ in MeOH. After removal of the AgCl, crystallization was accomplished at −22 °C. With H_2O addition to the methanol, crystals formed overnight (without the H_2O, no crystals formed over 1 week). The 73 mg (57%) of dark orange analytically pure crystals were collected, washed with 5:1 H_2O–MeOH, and dried at 25 °C under vacuum. (Anal. ($C_{16}H_{26}N_4O_5CoPF_6{\cdot}H_2O$) C, H, N.) (In related $R[Co](OH_2)]^+PF_6^-$ complexes,[6c] the H_2O was confirmed by a Karl Fischer titration.) The ^1H NMR spectrum appeared very similar to that shown in Figure 2A, but with ($-CH_2CH_3$) at δ 1.10 (t, 3 H) and 1.11 (t, 3 H), and ($-CH_3$) at 2.47 (s, 3 H) and 2.56 (s, 3 H) (vs. Me_4Si) in d_6-acetone.

(iii) Preparation and Attempted Isolation of 5, the 1,5,6-Trimethylbenzimidazole Hexafluorophosphate Complex. Complex **5** was cleanly generated in situ by treating a solution of 100 mg (0.22 mmol) of the chloroethylene carbonate oxidative addition product **3** in 10 mL of methanol with 39 mg (0.24 mmol) of 1,5,6-trimethylbenzimidazole and then 56 mg (0.22 mmol) of $AgPF_6$. Complex **5** was characterized by its spectral properties: visible λ_{max} (MeOH) 405 nm; ^1H NMR ($(CD_3)_2CO$, Me_4Si as an external reference) δ 1.03 (br t, 6 H), 2.29 (s, 3 H), 2.30 (s, 3 H), 2.50 (s, 3 H), 2.59 (s, 3 H), 2.60 (m, 2 H), 2.78 (br q, 4 H), 2.80 (m, 2 H), 3.81 (s, 3 H), 4.08 (m, 4 H), 4.75 (m, 1 H), 7.08 (s, 1 H), 7.35 (s, 1 H), 7.64 (s, 1 H).

Attempts to isolate **5** in nonprotic solvents gave at least some of the correct material (IR, NMR), but an analytically pure sample was never obtained. It is likely that trace amounts of H_2O are present that, with the benzimidazole base, give OH^-, which attacks the carbonate moiety in **5**.

(iv) Synthesis of 6, the (Acetonitrile) Tetraphenylborate Complex for X-ray Crystallography. The cobalt(III) carbonate complex **3** was converted into the tetraphenylborate salt as follows. To a solution of 130 mg (0.29 mmol) of **3** in 25 mL of methanol was added dropwise a solution of 150 mg (0.44 mmol) of $NaB(Ph)_4$ in 5 mL of water. Methanol (10 mL) was added, and the solution was filtered to remove NaCl. The volume of the filtrate was reduced by rotary evaporation until a bright orange powder precipitated. This powder was collected by filtration and crystallized from hot aqueous methanol. Subsequent crystallization from acetonitrile by methylene chloride vapor diffusion gave crystals that were adequate for X-ray analysis.

A summary of the X-ray crystallographic data, results, and GC ORTEP plot are provided as supplementary material.

(v) Successful Synthesis of the Formylmethyl Complex 7, $OHCCH_2Co[C_2(DO)(DOH)_{pn}]I$. Following the method of Dolphin,[16a–d] $Co[C_2(DO)(DOH)_{pn}]I_2$ (5.0 g, 8.6 mmol), Et_3N (1.38 g, 14 mmol, freshly distilled), CH_2Cl_2 (165 mL), 95% ethanol (22 g), and ethyl vinyl ether (34 g, 0.47 mol, freshly distilled) were combined in a 1-L Erlenmeyer flask. The flask was stoppered and stored in the dark for 6 days. Rotary evaporation gave a black solid, which was purified on four 1000-μm silica plates. Elution with acetone gave two bands, green starting cobalt(III) diiodide (R_f 0.85), and an orange-brown substance (R_f 0.70). The orange-brown band was collected with acetone and evaporated to dryness to give dark orange, solid $(OHCCH_2)Co[C_2(DO)(DOH)_{pn}]I$ (0.84 g, 20% conversion of >95% yield, 80% recovered starting material): visible λ_{max} ($CHCl_3$) 392 nm; IR ($CHCl_3$) 1650, 1491 cm^{-1}; ^1H NMR ($CDCl_3$, vs. Me_4Si) δ 1.50 (t, J = 7.5 Hz, 6 H), 1.56 (d, J = 5.2 Hz, 2 H), 2.25 (br, 1 H), 2.38 (s, 6 H), 2.80 (br, 1 H), 2.90 (m, 4 H), 3.67 (br dd, 2 H), 4.14 (br dd, 2 H), 8.97 (t, J = 5.2 Hz, 1 H), 19.30 (s, 1 H). Anal. Calcd: C, 36.31; H, 5.28; N, 11.29. Found: C, 35.43; H, 4.75; N, 10.99. Ratios C:H:N, calcd 3.22:0.47:1.00; found, 3.22:0.43:1.00. Repeat analysis on an independently prepared sample gave C, 33.54; H, 4.93; N, 10.44. Recrystallization was attempted in ethanol/diethyl ether, ethanol/acetone, and carbon tetrachloride, all resulting in decomposition of the formylmethyl complex due to the heating required to overcome its relative insolubility. Care is necessary when working with solutions of **7** as it appears to be especially light sensitive. Repeating the synthesis using the dichloride, $Co[C_2(DO)(DOH)_{pn}]Cl_2$, led to a cleaner sample where a Cl^- replaced the I^- in **7**. Anal. Calcd. for $OHCCH_2Co[C_2(DO)(DOH)_{pn}]Cl$: C, 44.51; H, 6.47; N, 13.84. Found: C, 44.60; H, 6.57; N, 12.03.

Unsuccessful routes to **7** are provided as supplementary material.

(C) Physical Properties of 3. (i) Solubility. With gentle warming and stirring to overcome any possible kinetic insolubility, **3** was found to have a maximum solubility of ca. 11 mg/1.0 mL of methanol as well as reasonable solubility in acetonitrile, pyridine, 2-propanol, benzyl alcohol, and chloroform. Compound **3** was soluble to a lesser extent in ethanol, ethylene glycol, and THF.

(ii) Conductivity Determination of the Extent of Axial Chloride Dissociation in Methanol. Methanol solutions (5.5×10^{-4} M) of **3**, $Co[C_2(DO)(DOH)_{pn}]I_2$, $Et_3NH^+Cl^-$, and $[Ph_3P{=}N{=}PPh_3]^+Cl^-$ were prepared and their molar conductivities at 25 °C were found to be 6.2×10^{-3}, 8.5×10^{-3}, 8.5×10^{-3}, and 5.6×10^{-3} Ω^{-1} cm^{-1} M^{-1}, respectively, demonstrating that **3** is largely dissociated in methanol at 25 °C.

(iii) Axial 1,5,6-Trimethylbenzimidazole Binding Constant. A 1.60×10^{-4} M anhydrous methanol solution of the aquo PF_6^- complex (**5**) was prepared and the decrease in the λ_{max} 445 peak was monitored (an isosbestic point at 430 nm was observed) as 0, 50, 100, 150, 200, 400, 600, 800, and 1000 equiv of 1,5,6-trimethylbenzimidazole were added by use of a solution of 2.5 M 1,5,6-trimethylbenzimidazole in methanol. The data were graphically analyzed and the error bar was estimated by using Drago's method,[49] $K_{assoc} = 90 \pm 20$ M^{-1}.

(iv) Axial Chloride, Ion Pairing Effects in the ^1H NMR of 3 in CD_3OD. **3** (10 mg, 0.022 mmol) was dissolved in 1.0 mL of CD_3OD under N_2 and the 100-MHz ^1H NMR spectrum of the resulting solution was obtained (Figure 2B). In the drybox, 0.5 mL of the above solution was treated with a slight excess of $Ag^+BF_4^-$, the resulting AgCl was removed by filtration, and the 100-MHz ^1H NMR spectrum was recorded (Figure 2C). The remaining 0.5-mL CD_3OD solution used for the first ^1H NMR spectrum, but which was not treated with $Ag^+BF_4^-$, was evaporated to dryness under vacuum and redissolved in $CDCl_3$. The ^1H NMR spectrum (Figure 2D) was then obtained. This material also showed a single

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(49) Drago, R. S. "Physical Methods in Chemistry"; Saunders: Philadelphia, 1977; p 90.

TLC spot (SiO_2, acetone) identical with a fresh sample of **3**.

The lack of any detectable effect of Co(II) or other paramagnetic impurities on the ^1H NMR spectrum of **3** in CD_3OD was demonstrated by showing O_2 did not affect the ^1H NMR spectrum of **3** and that added toluene showed the usual sharp singlet for its methyl group.

(v) Thermal Stability of 3 in CD_3OD. A 0.022 M solution of **3** in CD_3OD was prepared, the ^1H NMR spectrum was recorded, and this material was left at room temperature in the dark. After 40 h, roughly 30% of the starting material remained. Similar experiments at 5 and −22 °C in the dark showed **3** also reacts or decomposes at these temperatures, often with the formation of a small amount of gray-green crystals. A more detailed study of the thermolysis of this complex is under investigation.[50]

(vi) Photochemical Stability of 3. No photochemical decomposition in the solid state of **3** was ever detected. However, like all analogous cobalt alkyls, it is quite sensitive in solution, especially at the concentrations used for UV–visible experiments. Since a knowledge of the photochemical stability of **3** was necessary prior to a study of its other reactions, it was briefly investigated with the following experiments (in CD_3CN rather than CD_3OD due to the more easily interpreted ^1H NMR spectrum of **3** in the former solvent).

A 0.22 M CD_3CN solution of **3** was prepared in a Pyrex ^1H NMR tube in the drybox. After an initial ^1H NMR spectrum was obtained, it was exposed for 10 min to diffuse fluorescent room lighting and then a second ^1H NMR spectrum was obtained that showed no detectable change. After 2 h more of room light, the intensities of the peaks due to starting material had decreased slightly and there was the appearance of a small singlet at δ (CD_3CN) 7.3 that was superimposable with the NMR spectrum of authentic vinylene carbonate. Within 24 h, about 50% of the starting material had decomposed, as estimated by the ^1H NMR spectrum. After 5 days in the drybox in the diffuse light, the solution was noticeably darker. The ^1H NMR spectrum showed that, relative to the HCD_2CN residuals, ca. 80% of the starting **3** had decomposed with the appearance of an intense δ 7.3 (s) peak, as well as the appearance of peaks at δ 3.45 (q, J = 7 Hz) and δ 1.1 (t, J = 7 Hz). These new peaks were not superimposable with the CH_3CH_2 group in free $C_2(DOH)_2pn$ ligand in CD_3CN. In a separate experiment, a 0.44 M NMR tube solution of **3** in CD_3CN was completely decomposed after 11 h of irradiation with a 275-W UV lamp and showed predominantly a broad, intense singlet, δ 7.7, and the sharp, δ 7.3, singlet attributed to vinylene carbonate.

(D) Physical Properties and Stability of the Formylmethyl Complex 7. (i) Conductivity Determination of the Extent of Axial Iodide Dissociation in Methanol. A 2.02×10^{-3} M anhydrous methanol solution of the formylmethyl complex **7** was prepared, and its molar conductivity at 26 °C was found to be $1.8 \times 10^{-2}\ \Omega^{-1}\ cm^{-1}\ M^{-1}$. Comparison of this value with those in part ii of section C clearly demonstrates that **7** is largely dissociated in methanol at 26 °C.

(ii) **Solution Stability of 7. (a) Stability in Basic Methanol.** A solution of 8.0 mg of the formylmethyl complex **7** in 1.0 mL of CD_3OD (1.6×10^{-2} M) was examined by ^1H NMR both before and 1 h after treatment with 0.6 equiv of KOH/CD_3OD. This was repeated for a 2.0×10^{-2} M solution in CD_3OD (10 mg/1.0 mL) and 1.0 equiv of KOH/CD_3OD. In both cases no loss of the formylmethyl signals (δ 8.97, 1.56) was observed.

(b) Stability toward 1,5,6-Trimethylbenzimidazole. A solution of 10 mg of the formylmethyl complex **7** in 1.0 mL of CD_3OD (2.0×10^{-2} M) was treated with 5.0 mg (1.0 equiv) of $AgPF_6$. After removal of AgI by filtering through glass wool, 20 equiv of 1,5,6-trimethylbenzimidazole and 1 equiv of KOH/CD_3OD were added. The ^1H NMR spectrum, taken after 1 h, showed >90% of **7** remaining, and a slight upfield shift in the formylmethyl signal (δ 8.82 (t, J = 5 Hz, 1H), 1.40 (d, J = 5 Hz, 2H)).

(c) Stability toward Cobalt(II). To 1.0 mL of a 1.1×10^{-2} M solution of $Co[C_2(DO)(DOH)_{pn}]Cl$ in methanol containing 1 equiv of KOH 5 mg (0.92 equiv) of the formylmethyl complex **7** was added. The formylmethyl complex was shown to be completely stable under these conditions for at least 10 min (by visible and IR spectroscopy).

(E) Methanolysis of 3 and Resultant Stoichiometry. (i) General. The methanolyses of **3** were generally performed at a concentration of 5.0 mg of **3** per 1.0 mL of dry ($Mg(OMe)_2$), degassed methanol (1.1×10^{-2} M), well below the maximum solubility of **3** in methanol of approximately 2.2×10^{-2} M. Samples of **2a** were weighed (±0.3 mg) into 2-dram vials, brought into the drybox, and dissolved in methanol. Solution vials were septum capped to exclude air, aluminum foil wrapped to exclude light, and were removed from the drybox along with septum-capped vials containing the base catalyst.

Standard KOH/methanol solutions were prepared from 1.50 g of $KOH{\cdot}X(H_2O)$ (85% KOH, 15% H_2O) and 25 mL of degassed methanol. The addition of a known amount of acid followed by base back-titration to a phenolphthalein end point confirmed the base molarity was 0.92 M. Under the usual conditions of 5.0 mg of **3** in 1.0 mL of CH_3OH, 12 μL of the 0.92 M KOH/MeOH solution corresponds to 1.0 equiv of base. The CH_3O^-/HO^- ratio is 4000:1 under these conditions (calculated by using pK_w = 15.7, pK_a (CH_3OH) = 15.5).[51]

(ii) The Methanolysis of Ethylene Carbonate $\overline{OCH_2CH_2OC{=}O}$, as a Control Reaction. To establish the conditions and rate at which carbonate methanolysis of the carbonate group occurs, ethylene carbonate was examined in a model reaction. A 2.2×10^{-3} M ethylene carbonate solution in CH_3OH was prepared. Within 1 min of the addition of 1.0 equiv of the standard KOH/MeOH solution at 22 °C, the starting IR bands at 1805 and 1780 cm^{-1} had almost completely disappeared, and a new band at 1755 cm^{-1}, that superimposed with that of authentic $CH_3OCO_2CH_3$, had appeared. In a similar experiment, 0.2 equiv of KOH/MeOH catalytically removed ca. 90% (IR) of the carbonate group in ethylene carbonate in 2 min.

The presence of $DOCH_2CH_2OD$ was established in a ^1H NMR experiment where 25 mg (0.28 mmol) of ethylene carbonate in 1.0 mL of CD_3OD treated with 1.0 equiv of KOD/CD_3OD gave a singlet at δ 3.58, superimposable with that of authentic $HOCH_2CH_2OH$ in CD_3OD.

(iii) Methanolysis of 3 with Anhydrous $KOCH_3$, as a Control Reaction. In the drybox, an anhydrous $KOCH_3/CH_3OH$ solution was prepared by cautiously combining 852 mg of elemental potassium and 25.0 mL of CH_3OH. One equivalent of this $KOCH_3/CH_3OH$ solution was used to initiate a 10 mg of **3**/1.0 mL of CH_3OH reaction. The burgundy-red color appeared with the usual, ca. 0.5 min, half-life, and the product analysis with the usual, ca. 0.5 min, half-life, and the product analysis as described below showed 56% CH_3CHO, 98% Co(II), and 50% each of $CH_3OCO_2^-$ and $CH_3OCO_2CH_3$; i.e., the normal methanolysis reaction was observed.

(iv) Methanolysis of the (Aquo) Hexafluorophosphate Complex, 4, and of 3 in the Presence of Excess Cl^- or I^-. A Control Probing the Effect of Ion Pairing. Since Cl^- ion pairing in **3** was shown to affect the ^1H NMR spectrum of **3** in MeOH, a control reaction using **4** was done to show that **3** and **4** gave identical methanolysis stoichiometries.

A solution of 12.8 mg (0.022 mmol) of analytically pure **4** in 1.0 mL of degassed CH_3OH was treated with 24 μL (1.0 equiv) of the standard KOH/CH_3OH solution. The usual orange to burgundy-red color change was observed, and product analysis showed 100% Co(II), 51% CH_3CHO, and ca. 50% each of $CH_3OCO_2CH_3$ and $CH_3OCO_2^-$.

To 1.0-mL aliquots of a solution of 10.0 mg of **3** in 2.0 mL of MeOH were added $(CH_3)_4NCl$ (122 mg, 100 equiv), and $(n\text{-}C_4H_9)_4NI$ (113 mg, 20 equiv). Deprotection with 12 μL (1.0 equiv) of standard KOH/MeOH and product analysis showed 100% Co(II), 55% CH_3CHO, and ca. 50% each of $CH_3OCO_2CH_3$ and $CH_3OCO_2^-$ in both cases.

(v) CH_3CHO Identification and Yield. Twenty standard (5 mg of **3**/1.0 mL of degassed CH_3OH) solutions were prepared as above. Each orange solution was, in turn, treated with 1.0 equiv (12 μL) of the standard KOH/CH_3OH solution and the burgundy-red product mixture was analyzed after 2 min by GC on a 21-ft 10% Carbowax 20 M on 80–100 mesh Chromosorb W-Hp column run isothermally at 70 °C. A sharp peak was observed which coincided with authentic CH_3CHO in CH_3OH or in THF. This and the GC–MS experiment (vide infra) show that the compound detected is CH_3CHO, even though a ^1H NMR experiment in CD_3OD showed that (0.011 M CH_3CHO in CD_3OD exists completely, as expected, as its hemiacetal: δ 1.37 (d, J = 7 Hz, $CH_3CH(OD)(OCD_3)$), 4.8 (q, J = 7 Hz, $CH_3CH(OD)(OCD_3)$). Rapid methanol loss from the hemiacetal to yield CH_3CHO must be occurring on the GC injector port or column. The observed yield of CH_3CHO, and its standard deviation, 61 ± 6%, was obtained from cut-and-weigh quantification in comparison to an equal number of injections of independently prepared 1.1×10^{-2} M CH_3CHO (freshly distilled)/CH_3OH solutions). In a control experiment where 1.0 mL of the standard CH_3CHO/CH_3OH solution was placed in a septum-capped, 2-dram vial with a large N_2 volume above the solution and then injected into the GC, it was shown that the volatile CH_3CHO is not lost to vaporization. In an experiment performed in CD_3OD, the CH_3CHO was found to be identical with that in CH_3OH.

The identity of the volatile product as CH_3CHO was confirmed in a GC–MS experiment, and by isolation of a 2,4-dinitrophenylhydrazone derivative. In the GC–MS experiment, a solution of 5.0 mg of **3** in 1.0 mL of CH_3OH was treated with 12 μL of standard KOH/CH_3OH and injected after 2 min. The following m/e values, % of the base peak, and (literature % of the base peak) were observed: 44, 70% (77%); 43, 40% (42%); 42, 12% (12%); 41, 7% (5%); 29, 100% (100%). Rapid H/D

(50) Finke, R. G.; Hay, B. P., work in progress.

(51) Reference 30b, p 62.

(52) "CRC Atlas of Spectral Data and Physical Constants for Organic Compounds"; Graselli, J. G., Ritchey, W. M., Eds.; CRC Press: Cleveland, 1975; Vol. II, p 3.

exchange between basic methanol and acetaldehyde rendered GC–MS experiments with deuterium-labeled methanol useless.

In the 2,4-DNP experiment, a solution of 400 mg of **3** in 40 mL of methanol was treated with 160 μL (0.17 equiv) of standard KOH/CH_3OH. After 15 min the burgundy-red solution was poured into 16 mL of freshly prepared 2,4-DNP reagent, and the reaction mixture was evaporated to dryness. Possible products were separated by TLC (1000 μm of silica, repeatedly eluted with 90% CCl_4/10% pyridine)[53] to give five distinct bands (R_f values): orange (0.95); red-orange (0.80); yellow (0.55); red-orange (0.2); purple (0.1), turned colorless over 1 h. Only the yellow band (R_f 0.55) was unambiguously identified, and was shown to be identical with authentic acetaldehyde 2,4-dinitrophenylhydrazine by TLC and ^1H NMR (δ 1.50 (br s, 1H), 2.04 (d, J = 6 Hz, 3H), 7.45 (m, 1H), 7.84 (d, J = 9 Hz, 1H), 8.20 (m, 1H), 9.01 (d, J = 3 Hz, 1H).

(vi) $CH_3OCO_2CH_3$ and $CH_3OCO_2^-$ Identification and Yields. Using ten 5.0 mg of **3**/1.0 mL of CH_3OH solutions, each treated with 12 μL (1.0 equiv) of KOH/CH_3OH, the IR yield and standard deviation of $CH_3OCO_2CH_3$ (ν_{CO} 1755 cm^{-1}, ϵ 2.5 ± 0.1 × 10^2 M^{-1} cm^{-1}) was 50 ± 10% in comparison to authentic material. Similarly, $CH_3OCO_2^-$ (ν_{CO} 1655 cm^{-1}, ϵ 3.4 ± 0.3 × 10^2 M^{-1} cm^{-1}) was detected in 48 ± 10% yield by IR. The IR standards of $CH_3OCO_2^-$ were prepared by the addition of 1.0 equiv of CO_2 via gas tight syringe to 0.022 M KOH/CH_3OH solutions to give samples with reproducible IR spectra. A simple control showed that the addition of 1 equiv of KOH/CH_3OH to a 0.022 M dimethylcarbonate in CH_3OH solution gave no reaction, i.e., that $CH_3OCO_2^-$ is not formed from the dimethylcarbonate product and OH^- present in the reaction.

(vii) $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$ Identification and Yield. The treatment of orange CH_3OH solution of **3** with base causes the rapid formation of a burgundy-red, air-sensitive solution of $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$. This cobalt(II) material was independently prepared by the Cl atom transfer reduction of 122 mg (0.3 mmol) of $Co[C_2(DO)(DOH)_{pn}]Cl_2$ with 80 mg (0.31 mmol) of $[Cr(acac)_2]_2$ in 100 mL of CH_3OH. Alternatively, the cobalt(II) complex was prepared by a Co(I) + Co(III) → 2Co(II) redox reaction. Fifty milligrams (0.13 mmol) of $Co[C_2(DO)(DOH)_{pn}]Cl_2$ and 44.5 mg (0.13 mmol) of $(CO)Co[C_2(DO)(DOH)_{pn}]$ were combined in 25 mL of CH_3OH to give the desired burgundy-red product. The product showed a λ_{max} (CH_3OH) of 520 nm, obeyed Beer's law with an ϵ_{max} (CH_3OH) of 3.6 ± 0.2 × 10^3 M^{-1} cm^{-1}, and exhibited the expected[54] eight-line (I(Co) = $^7/_2$) ESR spectrum under N_2, identical with that observed for the Co(II) methanolysis product of a 2.2 × 10^{-2} M solution of **3**. The yield and standard deviation of $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$, 100 ± 5%, were determined from 20 methanolysis experiments using the measured extinction coefficient. In the drybox, solutions of 5.0 mg of **3**/1.0 mL of CH_3OH were treated with 12 μL (1.0 equiv) of standard KOH/CH_3OH, and the products were analyzed and quantified by visible spectroscopy in a septum-capped, 0.10-mm pathlength quartz cell.

(viii) Methanolysis Product Yields vs. Equivalents of KOMe. Aliquots (1.0 mL) of a 1.1 × 10^{-2} M **3**/CH_3OH solution were treated with 25, 10, 3.8, 1.0, 0.4, 0.17, 0.13, and 0.08 equiv of the standard KOH/CH_3OH solution and the products were identified as above. For ≥1 equiv of base, analyses were performed 2 min after addition of base. For <1 equiv of base, analyses were performed after a period of time inversely proportional to the amount of base added. Cobalt(II) yields of 100 ± 5% were determined for each of the base concentrations. Yields of 50% each for $CH_3OCO_2CH_3$ and $CH_3OCO_2^-$ were observed in each case, except for <<1 equiv of base, where only trace $CH_3OCO_2^-$ and 50% $CH_3OCO_2CH_3$ were detected. In the samples giving <50% $CH_3OCO_2^-$, addition of 1 equiv of KOH/CH_3OH after completion of the methanolysis regenerated 50% $CH_3OCO_2^-$, consistent with the equilibrium $CH_3O^- + CO_2 \rightleftharpoons CH_3OCO_2^-$. Observed acetaldehyde yields (equiv of base) were the following: 13% (25), 25% (10), 42% (3.8), 60% (1), 67% (0.4), 80–88% (0.17), 84% (0.13), 84% (0.08). That the base-dependent acetaldehyde yields were a consequence of base-catalyzed decomposition of acetaldehyde was supported by a control experiment. A freshly prepared 1.1 × 10^{-2} M solution of acetaldehyde in methanol was divided into 1.0-mL aliquots in septum-capped 2-dram vials. To the aliquots 0, 0.08, 0.13, 0.17, 0.40, 1.0, 3.8, 10, and 25 equiv of KOH/CH_3OH were added and the solutions were examined by GLC after a period of time analogous to that used for the methanolysis reaction. The number of equivalents of base used, observed % acetaldehyde remaining (and corrected **3** methanolysis yields) are the following: 25, 15% (87%); 10, 35% (70%); 3.8, 65% (65%); 1.0, 80% (75%); 0.4, 80% (85%); 0.17, 90% (89–98%); 0.13, 95% (90%); 0.08, 95% (90%); 0, 100% (95% by extrapolation).

(F) The H· Source. (i) Oxidation of the $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$ Product and Its Characterization as Intact $Co^{III}[C_2(DO)(DOH)_{pn}]X_2$. Although the identical visible and ESR spectra of the Co(II) methanolysis product, in comparison to authentic $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$ (section E, (vii)), seemed to rule out the macrocyclic ligand as the H· source, this was confirmed by I_2 or $BrCCl_3$ oxidation to $Co^{III}[C_2(DO)(DOH)_{pn}]X_2$, followed by visible, TLC, and 360-MHz ^1H NMR analysis.

A solution of 5.0 mg of **3**/1.0 mL of CH_3OH was treated with 12 μL (1 equiv) of standard KOH/CH_3OH, and after 2 min was titrated with a solution of 200 mg of I_2/4.0 mL of CH_3OH (0.20 M), monitoring loss of λ_{max} 520 nm in the visible spectrum. To completely consume the Co(II) 27 μL of the I_2 solution (0.50 ± 0.05 equiv of I_2) was required. The resultant orange Co(III) solution was evaporated to dryness, and the ^1H NMR spectrum of the residue ($CDCl_3$) showed 100 ± 10% of each of the ligand positions to be intact and identical with those of authentic $Co^{III}[C_2(DO)(DOH)_{pn}]X_2$: δ 1.2 (t, 6H), 2.6 (s, 6H), 2.7 (m, 2H), 3.1 (q, 4H), 4.2 (m, 4H), 19.4 (s, 1H, O···H···O). In addition to the NMR signals assigned to the ligand system, several small, unidentified peaks at δ 9.63 (s), 4.69 (s), 3.85 (d), and 3.79 (s) were observed. These peaks were not generated in control reactions of 1.1 × 10^{-2} M solutions of CH_3CHO and/or H_2CO in methanol with I_2 or $BrCCl_3$.

A solution of 5.0 mg of **3**/1.0 mL of CH_3OH was oxidized with 5 μL of $BrCCl_3$, and the reaction mixture was evaporated to dryness. Purification of the residue by TLC (silica/acetone) gave one major band which cospotted with authentic Co(III) dihalides. The ^1H NMR spectrum ($CDCl_3$) of the green Co(III) product was similar to that obtained in the I_2 oxidation above, showed 100 ± 10% of all ligand positions to be intact, and also included the same small, unidentified peaks.

(ii) Attempted Detection of ·CH_2OH Derived Products H_2CO and $HOCH_2CH_2OH$. The potential ·CH_2OH derived products, H_2CO and $HOCH_2CH_2OH$, were searched for among the methanolysis products of **3**. Control experiments were also done to determine the reported levels of detectability of these substances under the reaction conditions.

(a) $HOCH_2CH_2OH$. A solution of 34 mg of $HOCH_2CH_2OH$/10 mL of CH_3OH was prepared (5.5 × 10^{-3} M), a 1.0-mL aliquot of this solution was treated with 12 μL (2 equiv) of the standard KOH/CH_3OH, and the solution was evaporated to dryness. The ^1H NMR spectrum of the residue (CD_3OD) showed $DOCH_2CH_2OD$, δ 3.56, to be detectable at concentrations as low as 5.5 × 10^{-4} M in the reaction mixture.

A solution of 5.0 mg of **3**/1.0 mL of CH_3OH was treated with 12 μL (1 equiv) of the standard KOH/CH_3OH, air oxidized to Co(III) after 2 min, and evaporated to dryness. The ^1H NMR spectrum (CD_3OD) of the residue showed no (<5%) $HOCH_2CH_2OH$.

(b) H_2CO. Solutions of H_2CO (5.5 × 10^{-3} M, generated from either paraformaldehyde or aqueous solutions) in CH_3OH were used in control experiments. While H_2CO could be detected in 1.0-mL aliquots of these soluions by the chromotropic acid test (detectability level 10%) and by isolation of the dimedon and 2,4-DNP derivatives, treatment of the H_2CO/CH_3OH solution with 0.25–1.0 equiv of standard KOH/CH_3OH resulted in solutions which gave negative results to all three tests. These results suggest that a 50% yield of H_2CO in the methanolysis of **3** would not be detectable.

In keeping with the control experiments, methanolysis products from solutions of 5.0 mg **3**/1.0 mL CH_3OH and 3 μL (0.25 equiv) of standard KOH/CH_3OH gave a negative chromotropic acid test and failed to give dimedon or 2,4-DNP derivatives of H_2CO.

(c) $^{13}CH_3OH$ Methanolysis of 3. In an attempt to observe solvent derived products, the methanolysis of **3** in ^{13}C-labeled CH_3OH was performed.

In a mixture of 0.5 mL of $^{13}CH_3OH$, 1.0 mL of CD_3OD, and 1.5 mL of CH_3OH was dissolved 17 mg of **3**, and 12 μL (0.4 equiv) of standard KOH/CH_3OH was added. After 10 min the Co(II) solution was air oxidized and the ^{13}C NMR spectrum of the products was obtained. After 18 000 transients, only methanol was observed in the ^{13}C NMR spectrum.

(iii) $PhCH_2OH$ Solvent. Using carefully prepared $PhCH_2OH$ solvent, which gave a negative PhCHO test (section A (iv)), PhCHO produced in the deprotection of **3** was detected as its 2,4-DNP derivative.

To a solution of 5 mg of **3**/0.9 mL of $PhCH_2OH$ was added 12 μL (1 equiv) of standard KOH/CH_3OH. After 5 min the deep red-brown, air-sensitive solution was examined by GC (21-ft 10% Carbowax on 80–100 mesh Chromosorb W-HP run isothermally at 150 °C) and the amount of PhCHO produced was determined to be 52 ± 15%. Air oxidation of the Co(II) solution gave an orange solution, but no change in the GC-observed PhCHO concentration. (The PhCHO yields determined by GC are suspect, as a background concentration corresponding to 180 ± 10% (based on **3**) was generated from $PhCH_2OH$ by, apparently, an injection port phenomenon. For this reason, the PhCHO yield was independently determined by a 2,4-DNP experiment). The Co(III) solution was added to 10 mL of the 2,4-DNP reagent and evaporated to

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dryness, and the ^1H NMR spectrum of the residue dissolved in $CDCl_3$ showed ca. 40% PhCHO, DNP derivative: δ 9.05 (d, 1 H), 8.66 (br s, 1 H), 8.28 (m, 1 H), 8.06 (m, 2 H), 7.68 (m, 2 H), 7.39 (m, 3 H), identical with authentic material.

(iv) Other Solvents. (a) Ethanol. To a heterogeneous mixture of 5.0 mg of **3** and 1.0 mL of ethanol was added 5 μL (0.5 equiv) of 1.1 M sodium ethoxide in ethanol. After 4 min the acetaldehyde yield was measured by GC (55 ± 10%, corrected for base-catalyzed decomposition).

In a 0.1-mm pathlength visible cell, 1.0 mL of a solution of 5 mg of **3** in 5.0 mL of ethanol was treated with 1.0 equiv of NaOEt/EtOH, and growth of cobalt(II), λ_{max} 520 nm, was followed vs. time. The reaction required 4800 s to go to completion, and after 5300 s the reaction products were examined by visible and IR spectroscopy and by GC. The observed products were the following: cobalt(II), 95 ± 5%; diethyl carbonate, IR 1760 cm^{-1}, assigned by analogy to dimethyl carbonate (1755 cm^{-1}); acetaldehyde 60 ± 20%, after correction for base-catalyzed decomposition over 5300 s.

Solutions of 5 mg of **3** in 1.0 mL of MeOH/EtOH (7:3 and 3:7) were prepared and 0.5 equiv of standard base was added. The acetaldehyde yields were determined by GC to be 63 ± 10 and 66 ± 10%, after 5 and 6 min, respectively.

(b) Isopropyl Alcohol. In the manner described above, 5 mg of **3** in 1.0 mL of MeOH/*i*-PrOH (7:3 and 3:7) were prepared and deprotected with 0.5 equiv of base. The acetaldehyde yields were determined by GC to be 47 ± 10% and 36 ± 5% after 5 and 45 min, respectively. No acetone was detected among the products.

This procedure was repeated in 7:3 *i*-PrOH/CD_3OD. After 10 min the acetaldehyde yield was determined to be 50 ± 5%. Again, no acetone was detected among the products (by GC).

(c) Ethylene Glycol. To a solution of 5 mg of **3**/1.0 mL of ethylene glycol was added 22 μL (1.0 equiv) of a 0.5 M KOH/ethylene glycol solution, and the products were analyzed after 3 min. The burgundy-red solution was determined to contain 80% Co(II) (λ_{max} 520 nm) and 40% CH_3CHO (GC). Acidification of the solution with 4 μL (4.3 equiv) of concentrated HCl resulted in the conversion of acetaldehyde and ethylene glycol into 2-methyl-1,3-dioxolane (40% yield based upon starting **3**, determined by GC by comparison to a standard solution; δ ($CDCl_3$) 1.25 (d, J = 5 Hz, 3 H), 3.8 (m, 4 H), 4.82 (q, J = 5 Hz, 1 H) (lit.[55] δ 1.26, 3.8) by the well-known[56] dehydration reaction. The acetaldehyde yields were not greatly increased by reducing the amount of base catalyst used in the deprotection of ethylene glycol solutions of **3**. When 0.17 equiv of KOH/ethylene glycol was used, an acetaldehyde yield of ca. 45% was detected. In order to confirm the structure of the Co(II) product in the above reactions, a $BrCCl_3$ oxidation of the solvolysis product followed by ^1H NMR analysis was used. A solution of 5 mg of **3**/1.0 mL of ethylene glycol was treated with 22 μL (1.0 equiv) of 0.5 M KOH/ethylene glycol. After 15 min, the burgundy-red solution was treated with 5 μL (4.6 equiv) of $BrCCl_3$, and the resultant orange solution was evaporated to dryness. The ^1H NMR ($CDCl_3$) spectrum of the residue, δ 1.2 (t, 6H), 2.6 (s, 6H), 3.1 (q, 4 H), was identical with that of authentic $Co^{III}[C_2(DO)(DOH)_{pn}]X_2$ added to the solution. Clearly, catalytic CH_3CHO formation or H· abstraction from the ligand are not taking place.

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Registry No. 3, 75504-42-6; **3** (PG = –B(OBu-*t*)), 87728-43-6; **3** (PG = BPh), 87738-96-3; **3** (PG = $-C(CH_3)OCH_3$), 87728-44-7; **3** (PG = $(-SiMe_3)_2$), 87728-45-8; **3** (PG = $-CPh_2$), 87728-46-9; **3** (PG = P(O)OPh), 87728-47-0; **4**, 87728-37-8; **5**, 87728-39-0; **6**, 87728-41-4; **7**, 87728-42-5; $(CO)Co[C_2(DO)(DOH)_{pn}]$, 75504-41-5; $Co[C_2(DO)(DOH)_{pn}]Cl_2$, 75962-19-5; $Co[C_2(DO)(DOH)_{pn}]I_2$, 75962-04-8; $Co^{II}[C_2(DO)(DOH)_{pn}]Cl$, 75504-43-7; $Co^{II}[C_2(DO)(DOH)_{pn}]Br$, 75962-16-2; $Co[C_2(DO)(DOH)_{pn}]I(PF_6)$, 87728-35-6; Bz-Me, 1128-27-4; $\overline{OCH_2CH_2OC{=}O}$, 96-49-1; CH_3CHO, 75-07-0; $CH_3OCO_2CH_3$, 616-38-6; CH_3OCO_2H, 7456-87-3; $ClCH_2CHO$, 107-20-0; $CH_2CHO^-Li^+$, 67285-39-6; $CH_2{=}CHOSn(n\text{-}Bu)_3$, 66031-94-5; ethyl vinyl ether, 109-92-2; trimethylsilyl vinyl ether, 6213-94-1; diol dehydratase, 9026-90-8; 4-chloro-2-dioxolanone, 3967-54-2.

Supplementary Material Available: A tabulation of the data from the five decoupling experiments on **3**, details and ORTEP plot from the X-ray diffraction structural study of **3**, experimental details on the unsuccessful routes to the formylmethyl complex **7**, and a summary on other diol protecting groups for analogs of **3** that were examined (12 pages). Ordering information is given on any current masthead page.

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