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Carbon Dioxide Chemistry of a Binuclear Iridium(0) Complex. Rapid and Reversible Oxygen Atom Transfer from Carbonate

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We report the activation of CO_2 by a binuclear complex of Ir(0). The activation and reduction of carbon dioxide are areas of potential importance for artificially recycling the products of combustion and respiration.[2,3] The activation of CO_2 may be accomplished by (i) chemical,[2-18] (ii) electrochemical,[19-21] or (iii) photochemical[22-26] means. A serious impediment to chemical or electrochemical reduction of CO_2, however, is the disproportionation of the single-electron-transfer product, $CO_2^{\bullet -}$ (eq 1).

$$2CO_2^{\bullet -} \xrightarrow{k_d} CO + CO_3^{2-} \tag{1}$$

Reactions of low-valent transition-metal complexes with CO_2 often result in the production of 1 equiv of CO_3^{2-} for each equivalent of CO_2 reduced to CO.[11-14,16] The resulting carbonate ligands are usually unreactive end products that serve to halve the overall efficiency of CO_2 reduction. We describe herein the preparation of the new iridium complexes $Ir_2(CO)_4(dmpm)_2$ (**1**) (dmpm = bis(dimethylphosphino)methane) and $Ir_2(CO)_3(dmpm)_2$ (**2**) and the reaction of **2** with CO_2(l) to form the μ-carbonate complex $Ir_2(\mu\text{-}CO_3)(CO)_2(dmpm)_2$ (**3**). The carbonate ligand of complex **3** shows unprecedented oxygen atom transfer reactivity and has been found to undergo rapid and reversible oxygen atom transfer to CO.

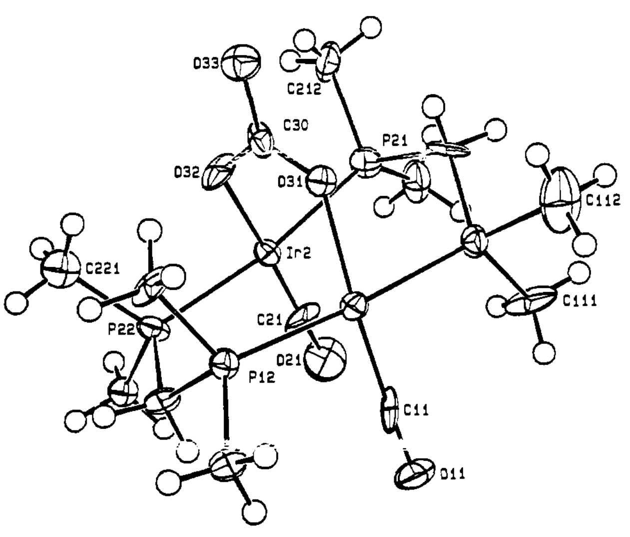
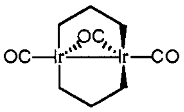


Figure 1. ORTEP drawing of $Ir_2(CO_3)(CO)_2(dmpm)_2$ (**3**). Selected bond distances and angles: Ir(1)–Ir(2), 2.965 (1) Å; Ir(1)–O(31), 2.08 (1) Å; Ir(2)–O(32), 2.09 (1) Å; O(31)–C(30), 1.29 (3) Å; O(32)–C(30), 1.29 (3) Å; C(30)–O(33), 1.27 (3) Å; Ir–P(av), 2.311 (6) Å; O(31)–C(30)–O(32), 123 (2)°; O(31)–C(30)–O(33), 118 (2))°; O(32)–C(30)–C(33), 119 (2)°; P(11)–Ir(1)–P(12), 176.4 (2)°; P(21)–Ir(2)–P(22), 171.4 (2)°; O(32)–Ir(2)–C(21), 177.8 (9)°; O(31)–Ir(1)–C(11), 176.4 (7)°.

The reaction of $Ir_2(CO)_4(dmpm)_2$ (**1**)[27] with Me_3NO produces 1 equiv of CO_2 and $Ir_2(CO)_3(dmpm)_2$ (**2**).[28] Complex **2** exhibits ν(CO) bands at 1902 (s) and 1846 cm^{-1}, indicative of terminal and semibridging CO ligands, respectively. The presence of two ν(P–C) dmpm bands at 942 (m) and 929 (m) cm^{-1} is a signature of a cis,cis or cis,trans $(dmpm)_2$ conformation.[29] The variable-temperature $^{31}P\{^1H\}$ NMR spectrum of **2** shows a single resonance at −42.9 ppm at 25 °C, coalescence at −10 °C, and an AA′XX′ multiplet extending from −22.3 to −61.4 ppm ($J_{P_AP_X}$ = 74.3 Hz) at −70 °C. The exchange rate at −10 °C is calculated to be extremely rapid, 5000 s^{-1}, with a free energy of coalescence of 11 kcal/mol.[31,32] The dynamic $^{31}P\{^1H\}$ data together with IR evidence in the ν(P–C) region establish a cis,trans diphosphine conformation for **2**. These data suggest that **2** possesses the "non-A-frame" M_2L_7 geometry, analogous to the structurally characterized complex $Rh_2(CO)_3(dppm)_2$.[30]



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(27) Complex **1** was prepared from $[Ir(COD)Cl]_2$ (1.41 g, 2.10 mmol) and dmpm (0.57 g, 4.20 mmol) at 0 °C in toluene. The resulting cream-colored slurry was stirred for 5 min at which time CO was added, causing the mixture to turn dark red. The reaction was warmed to room temperature and the solution was stirred 2 h, resulting in a pale yellow solution and a light yellow solid. This product was reduced in situ over an excess of Na/Hg under an atmosphere of CO for 5 days. The yellow solution was filtered and reduced in volume. Precipitation of yellow crystalline material was accomplished by slow addition of hexanes to give 1.34 g (83% yield) of $Ir_2(CO)_4(dmpm)_2$ (**1**). Anal. Calcd for $C_{14}H_{28}P_4O_4Ir_2$: C, 21.87; H, 3.68. Found: C, 21.94; H, 3.64. ^{1}H NMR (CD_3CN): δ 3.46 (m, 4 H), δ 1.80 (s, 24 H). $^{31}P\{^1H\}$ NMR ($CD_3C_6D_5$): δ −65.4 (s). IR ($CH_3C_5H_5$): ν(CO) 1956 (m), 1930 (s), 1890 (s), 1865 (w). Complex **1** was also characterized by a single-crystal X-ray diffraction study, the results of which will be reported separately.

(28) Complex **2** was prepared from **1** (0.025 g, 0.32 mmol) and Me_3NO (0.024 g, 0.32 mmol) at 70 °C in toluene. The solvent was removed to give 0.20 g (83% yield) of red-brown $Ir_2(CO)_3(dmpm)_2$ (**2**). Anal. Calcd for $C_{13}H_{28}P_4O_3Ir_2$: C, 21.08; H, 3.82. Found: C, 21.41; H, 4.06. ^{1}H NMR (C_6D_6): δ 2.63 (m, 4 H), 1.45 (s, 24 H). $^{31}P\{^1H\}$ NMR (C_6D_6): δ −42.9 (s). IR (KBr): ν(CO) 1902 (vs), 1846 (m); ν(P–C) 942 (m), 929 (m).

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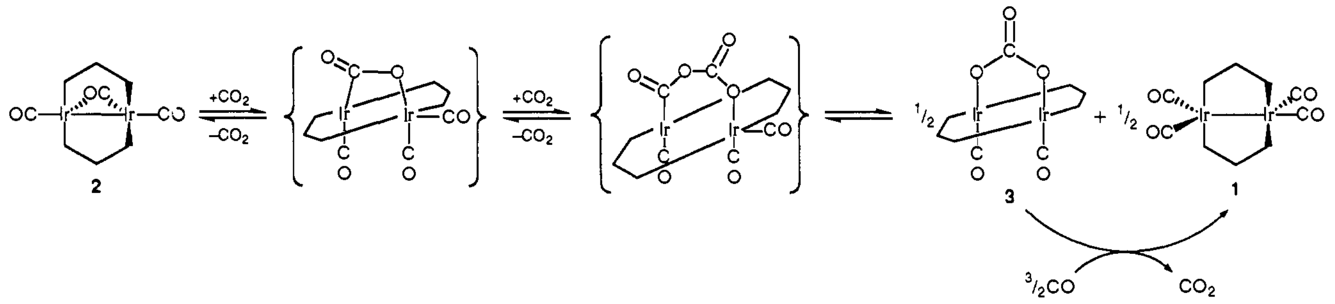
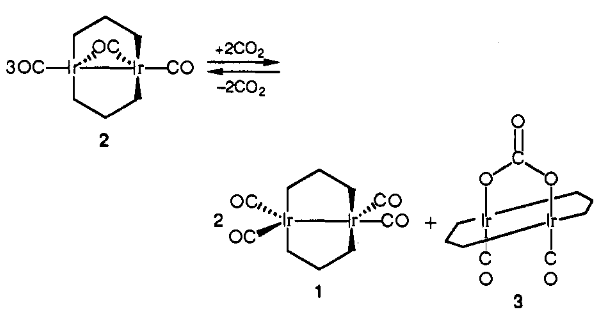
Scheme I. Reversible Carbonate Oxygen Atom Transfer from **3** to CO



Complex **2** reacts with both CO_2 and CO. The reaction of **2** with liquid CO_2 affords a mixture of **1** and the new carbonate complex $Ir_2(CO_3)(CO)_2(dmpm)_2$ (**3**).[36] The reaction of **2** with 1 equiv of CO leads back to **1**. The structure of **3** was determined by single-crystal X-ray diffraction.[37] An ORTEP drawing of **3** together with selected bond angles and distances appears in Figure 1. Complex **3** possesses an essentially planar bridging carbonate, torsionally canted at 20° with respect to the Ir–Ir vector. The Ir–Ir separation of 2.965 (1) Å, deep purple color, and overall structure are consistent with a weakly Ir···Ir interacting, d^8–d^8 face-to-face bi-square-planar system.

The formation of **3** and **1** in the reaction of **2** with CO_2(l) appears to result from reductive disproportionation of $2CO_2$ to CO_3^{2-} and CO (eq 2). Isolated yields of **3** are typically ~40%,



(2)

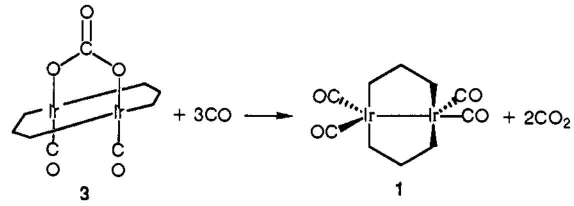
indicating that some of the CO produced by CO_2 disproportionation is lost to the vapor phase in equilibrium with CO_2 liquid under reaction conditions.

The reaction of **2** with $^{13}CO_2$ (99% ^{13}C) leads to a surprising result. Comparison of the IR bands of **3** produced from $^{13}CO_2$ with those of **3** from CO_2 (natural abundance) reveals new $\nu(^{13}CO)$ at 1896, 1878, 1523, and 1226 cm^{-1}. The disproportionation of $^{13}CO_2$ to ^{13}CO and $^{13}CO_3$ was verified by $^{13}C\{^1H\}$ NMR. The sample of **3** prepared from $^{13}CO_2$ showed $^{13}C\{^1H\}$ NMR signals at δ 177 (^{13}CO) and δ 164 ($^{13}CO_3$). However, there are also intense $\nu(^{12}CO_3)$ bands evident at 1561 (s) and 1257 (m) cm^{-1} (Table I).[38] The key observation from this labeling experiment is that a significant portion of the CO_3^{2-} groups contain ^{12}C! This suggests that CO from **2** is used to produce some of the CO_3^{2-}. The significance of this result lies in the fact that *the products are not consistent with simple disproportionation of two* $^{13}CO_2$ *molecules to produce* ^{13}CO *and* $^{13}CO_3^{2-}$.

Table I. Comparison of IR Data for **3** Prepared from CO_2 vs $^{13}CO_2$ (cm^{-1})

3 (CO_2)	3 ($^{13}CO_2$)	assignment[38]
1942 (vs)	1942 (vs)	$\nu(^{12}CO)$
	1896 (m)	$\nu(^{13}CO)$
1920 (sh)	1920 (w)	$\nu(^{12}CO)$
	1878 (m)	$\nu(^{13}CO)$
1561 (vs)	1561 (s)	$\nu(^{12}CO_3)$
	1523 (s)	$\nu(^{13}CO_3)$
1257 (m)	1257 (m)	$\nu(^{12}CO_3)$
	1226 (m)	$\nu(^{13}CO_3)$

Our results suggest that the μ-CO_3 group of **3** undergoes reversible oxygen atom transfers with CO. This conclusion is supported by additional experimental evidence. A mixture of **1** and **3** reacts at 25 °C in acetonitrile to give **2** and CO_2, establishing the reversibility of eq 2. Complex **3** reacts rapidly with CO to give **1** and CO_2 (eq 3).



(3)

The presence of $^{12}CO_3^{2-}$ in the reaction of **2** with $^{13}CO_2$ therefore is explained by reverse oxygen atom transfer from coordinated $^{13}CO_3^{2-}$ to ^{12}CO to produce $^{13}CO_2$ and $^{12}CO_2$, either of which can disproportionate. Indeed, in the reaction of **3** with ^{13}CO (99% ^{13}C), the products are 50% $^{13}CO_2$, 50% $^{12}CO_2$, as determined by GC/MS, and **1** (50% ^{13}CO) (eq 4). The insertion

$$\underset{\mathbf{3}}{Ir_2(CO_3)(CO)_2(dmpm)_2} + {}^{13}CO \rightarrow Ir_2(CO)_2({}^{13}CO)_2(dmpm)_2 + \underset{1:1}{{}^{13}CO_2 + {}^{12}CO_2} \quad (4)$$

of CO into the μ-CO_3 Ir–O bond of **3** to afford a C_2O_4 intermediate is implied by the oxygen atom transfer to CO. The fact that equal $^{13}CO_2/^{12}CO_2$ isotope partitioning is observed in the reaction of **3** with ^{13}CO (eq 4), suggests that the C_2O_4 intermediate rapidly collapses to 2 equiv of CO_2 (Scheme I).[39] The reverse

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(36) Complex **3** was prepared from **2** and CO_2(l) in a LECO-MRA-114R pressure reactor at 25 °C. Typically, 3 L of CO_2 gas was condensed into a 5-mL reactor containing 0.12 g (0.16 mmol) of **2**, resulting in an average pressure of 1700 psi. The mixture was vented and then opened in an inert-atmosphere box to collect solid products. Solids were washed with ~10 mL of Et_2O followed by ~1 mL of toluene to remove unreacted **2** and **1**, formed as a coproduct. $Ir_2(CO_3)(CO)_2(dmpm)_2$ (**3**) was dried under vacuum to yield 0.051 g (41%) of purple solids. X-ray quality crystals of **3** were obtained by the diffusion of Et_2O into an acetonitrile solution of **3**. Anal. Calcd for $C_{13}H_{28}P_4O_5Ir_2$: C, 20.21; H, 3.66. Found: C, 19.53; H, 4.16. ^1H NMR (CD_3CN): δ 3.32 (m, J_{PH} = 4.0 Hz, 4 H), 1.76 (s, 24 H). $^{31}P\{^1H\}$ NMR (CD_3CN): δ −6.2 (s). $^{13}C\{^1H\}$ NMR (CD_3CN): δ 177 (s, ^{13}CO), 164 (s, $^{13}CO_3$). IR (KBr): ν(CO) 1942 (s), 1920 (sh), 1602 (sh), 1561 (s), 1257 (m); ν(P–C) 941 (s).

(37) Crystal data for **3**·MeCN: $Ir_2P_4O_5NC_{15}H_{31}$, fw = 813.71, monoclinic, space group $P2_1/n$ (No. 14), a = 11.823 (2) Å, b = 14.166 (3) Å, c = 14.807 (4) Å, β = 96.13 (2)°, V = 2465 (2) Å^3, Z = 4, d_{calc} = 2.192 g cm^{-3}. The structure was solved by MULTAN least-squares Fourier methods and was refined to R and R_w values of 0.041 and 0.047 for 214 variables and 1875 unique observations with $I > 3\sigma(I)$ with Mo Kα radiation. Data were corrected for absorption empirically.

(38) The $\nu(^{13}CO)$ and $\nu(^{12}CO)$ bands of CO and CO_3^{2-} ligands in complex **3** do not appear to be mixed appreciably. The relative intensities of all $\nu(^{13}CO)$ and $\nu(^{12}CO)$ bands in the IR spectrum of **3** are directly proportional to the total $^{13}C/^{12}C$ ratio. Moreover, $^{13}C\{^1H\}$ NMR verifies incorporation of ^{13}C into both CO and CO_3^{2-}.

(39) A μ-C(O)OC(O) intermediate formed by CO_2 insertion with **2**[18] is also possible but is not consistent with the formation of carbonate. An Ir_2-(μ-O) intermediate[40] has been considered but eliminated on the grounds that the μ-CO_3^{2-} carbon of **3** does not equilibrate with $^{13}CO_2$.

process, head-to-tail dimerization of CO_2, has often been invoked in the disproportion of CO_2. Oxygen atom transfer to CO from CO_2,[11] NO,[33] NO_2,[34] and O_2[35] has been reported. The present system is the first to display facile oxygen atom transfer from carbonate. Our studies of oxygen atom transfer from **3** to other substrates are continuing.

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Supplementary Material Available: Tables consisting of crystal data and data collection parameters (Table 1), positional parameters (Table 2), temperature factor expressions (Table 3), bond distances (Table 4), and bond angles (Table 5) for **3** (10 pages); a table of observed and calculated structure factors for **3** (14 pages). Ordering information is given on any current masthead page.

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Total Synthesis and Evaluation of (±)-*N*-(*tert*-Butyloxycarbonyl)-CBI, (±)-CBI-CDPI$_1$, and (±)-CBI-CDPI$_2$: CC-1065 Functional Agents Incorporating the Equivalent 1,2,9,9a-Tetrahydrocycloprop[1,2-*c*]benz[1,2-*e*]indol-4-one (CBI) Left-Hand Subunit

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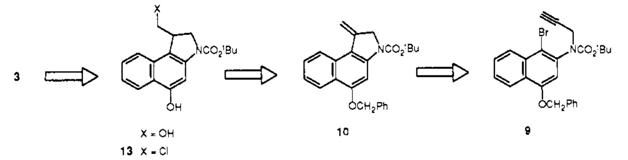
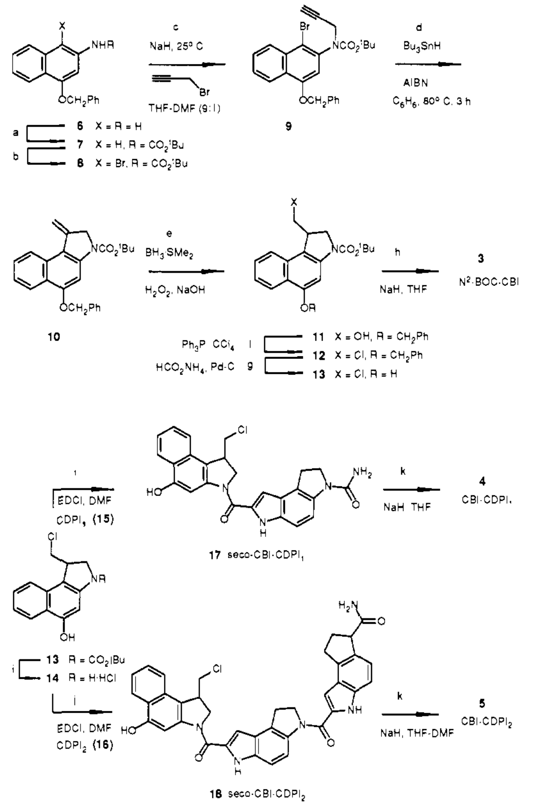
(+)-CC-1065 (**1**, NSC-298223), an antitumor antibiotic isolated from cultures of *Streptomyces zelensis*, possesses exceptionally potent in vitro cytotoxic activity, broad spectrum antimicrobial activity, and confirmed in vivo antitumor activity.[2-3] In a series of extensive investigations the site and mechanism of the (+)-CC-1065 antitumor activity have been related to its irreversible covalent alkylation of sequence-selective B-DNA minor groove sites [5′-d(A/GNTTA)-3′ and 5′-d(AAAAA)-3′] that has been demonstrated to proceed by 3′-adenine *N*-3 alkylation of the electrophilic cyclopropane present in the left-hand (CPI) subunit of (+)-CC-1065.[4,5] The demonstration that simplified agents including CDPI$_3$[6] methyl ester exhibit a substantial preference for A–T rich noncovalent minor groove binding[7] attributable to preferential stabilization of a noncovalent complex within the narrower, sterically more accessible A–T rich minor groove[8] (*accessible hydrophobic binding*) has suggested that CC-1065 is best represented as a selective[9] alkylating agent superimposed on the CDPI$_3$ skeleton and derives its properties in part from the effective delivery of a selective alkylating agent to accessible adenine N-3 alkylation sites. The additional demonstration that agents possessing the exceptionally reactive, parent 1,2,7,7a-tetrahydrocycloprop[1,2-*c*]indol-4-one (CI) left-hand subunit, e.g., CI-CDPI$_x$ (x = 1, 2),[10] or the unnatural enantiomer of the CC-1065 left-hand subunit (CPI), e.g., (−)-CPI-CDPI$_2$[11,12] and

Scheme I



Scheme II[a]



[a] (a) 2.0 equiv of $(tBuO_2C)_2O$, dioxane, 95 °C, 3 h, 96%; (b) 1.2 equiv of *N*-bromosuccinimide, catalytic H_2SO_4, THF, −60 °C, 5 h, 98%; (c) 1.3 equiv of NaH, 3.0 equiv of 3-bromopropyne, 24 °C, 3 h, 100%; (d) 2.0 equiv of Bu_3SnH, 0.2 equiv of AIBN, benzene, 80 °C, 1 h; (e) 6.3 equiv of $Me_2S{\cdot}BH_3$, THF, 0–25 °C, 3 h; 2 N NaOH, 30% H_2O_2, 0–25 °C, 1 h, 45 °C, 20 min, 62% from **9**; (f) 2.0 equiv of Ph_3P, 6 equiv of CCl_4, CH_2Cl_2, 24 °C, 10 h, 99%; (g) 25% aqueous HCO_2NH_4/THF 1:5, 10% Pd/C, 0 °C, 2.5 h, 97%; (h) 3 equiv of NaH, THF, 24 °C, 2 h, 93%; (i) 3 N anhydrous HCl/EtOAc, 24 °C, 10 min, 100%; (j) for **17**, 3 equiv of EDCI, 1.0 equiv of **15**, 5 equiv of $NaHCO_3$, DMF, 24 °C, 3 h, 86%; for **18**, 3 equiv of EDCI, 1.0 equiv of **16**, DMF, 24 °C, 5 h, 78%; (k) for **4**, 5 equiv of NaH, THF, 24 °C, 2 h, 74%; for **5**, 2 equiv of NaH, 2:1 THF–DMF, 0 °C, 1 h, 84%.

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(1) (a) National Institutes of Health career development award recipient, 1983–1988 (CA 01134), Alfred P. Sloan fellow, 1985–1989. (b) On leave from Kyorin Pharmaceutical Co., Ltd., Tochigi, Japan. (c) American Cancer Society postdoctoral fellow (ACS no. PF-3311).

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