**Figure 1.** Relationship of specificity constants and ester substituents.

Because mutants of *S. cerevisiae* devoid of various components of the fatty acid synthetase complex had been prepared,[10] we envisaged that one of these mutants may be suitably used for the synthesis of **5**, a requisite intermediate for L-carnitine synthesis.[2] To test this supposition, **1** was exposed to two mutants of *S. cerevisiae*, ATCC 26403 (β-keto reductase negative) and ATCC 26404 (pantotheine free). As expected, the latter mutant behaved like the parent and afforded **2** (ee = 0.57) in 50% yield. In contrast, mutant ATCC 26403 gave indeed the desired **5** in 55%
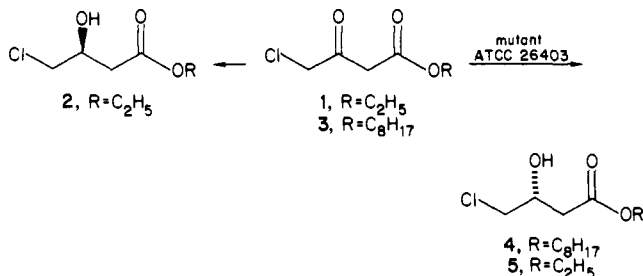


yield but the optical purity of the product was low[11] (ee = 0.16). Nevertheless, these results confirm the notion that the β-keto reductase component of the fatty acid synthetase complex is indeed a major competing enzyme engaged in the reduction of β-keto esters in vivo. Moreover, the successful prediction of the stereochemical outcome encouraged us to make further refinements. By taking maximal advantage of the differences in the $k_{cat}/K$[12] of the L and D reductases, **1** was continuously fed to a growing culture of mutant ATCC 26403 at a slow rate.[13] Under these

conditions, the optical purity of the desired **5** obtained after 72 h (53% yield) was enhanced markedly (ee = 0.90).

(13) The mutant ATCC 26403 was grown in 500 mL of medium (Schweizer, E.; Golling, H. *Proc. Nat. Acad. Sci. U.S.A.* **1970**, *67*, 660) in a 2 L Erlenmeyer flask for 24 h. Ethyl 4-chloroacetoacetate (**1**), diluted with two volumes of ethanol, was continuously fed to the culture at a rate of 3 mL/24 h. Simultaneously, a 30% sucrose solution was fed at a rate of 7 mL/24 h. The flask was incubated on a rotary shaker (250 rpm, 2 in. stroke) at 25 °C for 72 h.

## Synthesis and Structural Characterization of $Co(NO)_2[PhP(OCH_2CH_2)_2NH]Cl$: A Novel Carbon Dioxide Carrier

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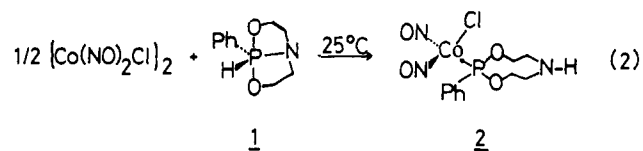
In the last decade, interest in the coordination chemistry of $CO_2$ has continued to grow.[1] Several $CO_2$–transition metal complexes, definitively characterized, point out different bonding modes for $CO_2$.[2]

This paper describes a novel mode of $CO_2$ coordination which involves, as the primary bonding site, a nucleophilic center located on a ligand of a metal complex. The oxophilic character of the metal center contributes to the stabilization of the adduct (eq 1).



$$ (1) $$
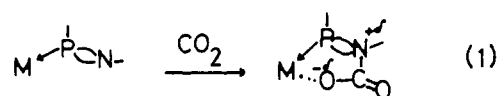
The reaction of $[Co(NO)_2Cl]_2$[3] with the bicyclic phosphorane[4] **1** affords the monomeric complex **2**[5] (eq 2). In this complex,



$$ (2) $$

(10) Kühn, L.; Castorph, H.; Schweizer, E. *Eur. J. Biochem.* **1972**, *24*, 492.

(11) The shift in the stereochemical pathway of reduction by the mutant ATCC 26403 is primarily due to the lack of β-keto reductase component of the fatty acid synthetase complex. The relative concentrations of β-keto ester oxidoreductases in a growing culture is different from those present in commercial Red Star bakers' yeast because some of these enzymes are inducible.

(12) Most enzymes are not saturated with substrate [S] under physiological conditions (the ratio of [S]/K is in the range of 0.01–1.0). Hence the relative rates of enantioselective reduction by two competing enzymes in intact cells depends on the $V/K$ (first-order rate constant) ratio of the two enzymes, ee = $(V_L/K_L) - (V_D/K_D)/(V_L/K_L) + (V_D/K_D)$; see: Chen, C. S.; Zhou, B. N.; Girdaukas, G.; Shieh, W. R.; VanMiddleswroth, F.; Sih, C. J. *Biorg. Chem.* **1984**, *12*, 98.

(1) For a recent review, see: Darensbourg, D. J.; Kudaroski, R. A. *Adv. Organomet. Chem.* **1983**, *22*, 129–168.

(2) (a) Aresta, M.; Nobile, C. F.; Albano, V. G.; Forni, E.; Manassero, M. *J. Chem. Soc., Chem. Commun.* **1975**, 636–637. (b) Fachinetti, G.; Floriani, C.; Zanazzi, P. F. *J. Am. Chem. Soc.* **1978**, *100*, 7405–7506. (c) Braunstein, P.; Matt, D.; Dusausoy, Y.; Fischer, J.; Mitschler, A.; Ricard, L. *Ibid.* **1981**, *103*, 5115–5125. (d) Calabrese, J. C.; Herskovitz, T.; Kinney, J. B. *Ibid.* **1983**, *105*, 5914–5915.

(3) Prepared by the known method: Sacco, A.; Rossi, M.; Nobile, C. F. *Anal. Chim. (Rome)* **1967**, 499.

(4) (a) Houalla, D.; Brazier, J. F.; Sanchez, M.; Wolf, R. *Tetrahedron Lett.* **1972**, *29*, 2969–2970. (b) Houalla, D.; Mouheich, T.; Sanchez, M.; Wolf, R. *Phosphorus Relat. Group V Elem.* **1975**, *5*, 229–240. (c) Houalla, D.; Sanchez, M.; Gonbeau, D.; Pfister-Guillouzo, G. *Nouv. J. Chim.* **1979**, *3*, 507–509.
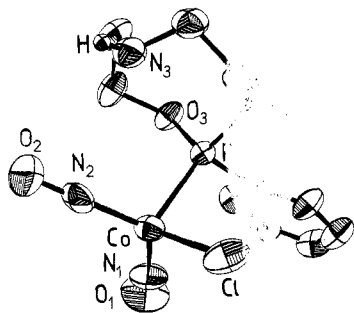
**Figure 1.** Molecular structure of $Co(NO)_2[PhP(OCH_2CH_2)_2NH]Cl$. Selected bond lengths (Å) and angles (deg): Co–Cl 2.262 (2), Co–P 2.244 (2), Co–N$_1$ 1.662 (6), Co–N$_2$ 1.662 (7), N$_1$–O$_1$ 1.142 (8), N$_2$–O$_2$ 1.142 (9), Co$\cdots$N$_3$ 3.682 (6), P$\cdots$N$_3$ 2.978 (7), Cl$\cdots$N$_3$ 3.522 (5), Cl–Co–P 97.39 (7), Cl–Co–N$_1$ 113.4 (3), Cl–Co–N$_2$ 115.8 (3), P–Co–N$_1$ 99.7 (2), P–Co–N$_2$ 108.8 (2), N$_1$–Co–N$_2$ 118.0 (3), Co–N$_1$–O$_1$ 162.7 (7), Co–N$_2$–O$_2$ 162.2 (8). Thermal ellipsoids represent 50% probability surfaces (H arbitrary scaled).

the open form of **1**, as exemplified by the appearance of a $\nu$(NH) band in the IR, behaves as a monodentate P-coordinated ligand.[7] The molecular structure of **2** was established by single X-ray diffraction (Figure 1). A crystal of 0.25 × 0.40 × 0.50 mm was selected to collect intensities on a Nonius CAD-4 diffractometer with $\omega^{-1}/_3\theta$ scan and $1° < \theta < 35°$, using Mo K$\alpha$ radiation (graphite monochromator). The unit cell was orthorhombic of space group $P2_12_12_1$ with $a$ = 7.031 (2) Å, $b$ = 12.950 (3) Å, $c$ = 16.254 (4) Å, $V$ = 1480 (1) Å$^3$, and $Z$ = 4. The structure was solved by means of the Patterson function and the heavy-atom method, and refined to final anisotropic agreement indice of $R$ = 0.040 for the 1395 independent reflections for which $I > 1.3I$ (background) and $I > 1.4\sigma(I)$. Hydrogen atoms were located by difference Fourier maps.

The cobalt is basically tetrahedrally coordinated with interligand angles ranging from 97.39 (7)° for P–Co–Cl to 118.0 (3)° for N$_1$–Co–N$_2$. The bond distances Co–N$_{1,2}$ (1.662 Å) and Co–P (2.244 Å) agree with those reported for Co(NO)$_2$PPh$_3$I (1.664 and 2.238 Å) and Co(NO)$_2$(PPh$_2$R)I (1.68 and 2.260 Å).[8] The Co–N$_1$–O$_1$ and Co–N$_2$–O$_2$ bond angles deviate from 180° in accordance with previous findings in pseudotetrahedral {M(NO)$_2$}$^{10}$ complexes.[9] The Co$\cdots$N$_3$ distance (3.682 Å) excludes the possibility of bonding between Co and N of ligand **1**. Moreover the P$\cdots$N$_3$ distance (2.978 Å) is not compatible with a P–N bond (1.986 Å in [HP(OCH$_2$CH$_2$)$_3$N]BF$_4$).[10]

While the structural parameters described above are not unusual, the monodentate coordination of ligand **1** through the P atom leads to an interesting reactivity of complex **2** toward CO$_2$ with the participation of the free >NH group.

When a THF solution of **2** was saturated with CO$_2$ at –30 °C, a dark brown solid corresponding to Co(NO)$_2$[PhP-(OCH$_2$CH$_2$)$_2$NH](CO$_2$)Cl (**3**) could be isolated. This complex

released CO$_2$ when stored under argon giving back **2**. In solution, the reversibility **2** $\rightleftharpoons$ **3** was checked over several cycles. Complex **3** displays a strong IR band due to the bonded CO$_2$ at 1655 cm$^{-1}$ (Nujol mull) as confirmed by isotope labeling ($^{13}$CO$_2$, 1612 cm$^{-1}$). Ligand **1** absorptions masked the other CO$_2$ bands. The two $\nu$(NO) are slightly shifted to higher frequencies ($\Delta\nu$ = 10 cm$^{-1}$) with respect to **2**, while the $\nu$(NH) at 3350 cm$^{-1}$ has disappeared. These data point out that the reversible coordination of CO$_2$ involves the >NH function of **1**. The simplest formulation of this novel CO$_2$ complex is depicted in as a carbamato-like derivative.



**3**
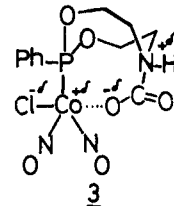
The assistance of Co as an oxophilic center for the bifunctional coordination of CO$_2$ was revealed by the difference in the diffuse reflectance spectra of **2** and **3**. The absence in the spectrum of **3** of a 450-nm absorption occurring for **2** indicates electronic pertubation in the coordination sphere of the metal. However, in solution (CH$_2$Cl$_2$) **2** and **3** exhibit the same spectrum meaning that solvatation has weakened the Co$\cdots$OCO interaction.[12]

Further support for the carbamato-like structure was obtained from $^{31}$P and $^{13}$C NMR spectroscopies. $^{31}$P NMR spectrum of **3** under CO$_2$ (THF or CH$_2$Cl$_2$, 200 K) shows a singlet at 177 ppm (166 ppm for **2**, H$_3$PO$_4$).[13] Evacuation of the solution or warming up to 300 K decreased the 177 ppm resonance while the 166 ppm peak appeared. This phenomenon is reversible and could be repeated several times in the presence of CO$_2$. The $^{13}$C NMR spectrum of **3** under CO$_2$ shows a singlet at 159.6 ppm (CH$_2$Cl$_2$, 180 K, Me$_4$Si) assigned to bound CO$_2$. This signal disappeared upon warming the solution to 300 K. This $^{13}$C chemical shift differs from those observed for $\eta^1$- and $\eta^2$-CO$_2$ complexes ($\sim$200 ppm)[14] but is very close to those reported for a carbamato group either bonded to a porphinato–zinc system (157.2 ppm)[15] or formed from the reaction of **1** with CO$_2$ (161.4 ppm).[16]

In conclusion, the results described here provide spectroscopic evidence for a new mode of reversible CO$_2$ coordination using a transition-metal system with a ligand bearing a free amino group. Interestingly the carbamato-like derivative thus formed can mimic one of the proposed modes of action of biotin,[17] a reversible CO$_2$ carrier involved in biosynthetic carboxylation reactions.

(5) In a typical procedure, a toluene solution (15 mL) of 1.06 g (5 mmol) of **1** was added dropwise to a stirred suspension of 0.770 g (2.5 mmol) of [Co(NO)$_2$Cl$_2$]$_2$ in toluene (5 mL) under argon at 25 °C. After 2 h of reaction, the solvent was evaporated and the dark brown solid was recrystallized from acetone–pentane at –20 °C (1.34 g, yield 72%). Anal. Calcd for Co(NO)$_2$[PhP(OCH$_2$CH$_2$)$_2$NH]Cl: C, 32.85; H, 3.86; N, 11.49; Cl, 9.70. Found: C, 33.23; H, 3.86; N, 11.34; Cl, 9.68. $^{31}$P NMR $\delta$ 166 (200 K); IR 3350 ($\nu$(NH)), 1822, 1755 cm$^{-1}$ ($\nu$(NO)) in Nujol mull.

(6) Complexes containing bridging or chelating ligand **1** have also been isolated: (a) Ballivet-Tkatchenko, D.; Bonnet, M. C.; Faure, R.; Loiseleur, H. *Phosphorus Sulfur* **1983**, *18*, 468. (b) Mordenti, L.; Roustan, J. L.; Riess, J. G. *Organometallics* **1983**, *2*, 843–845. (c) Agbossou, S.; Bonnet, M. C.; Tkatchenko, I. *Nouv. J. Chim.* **1985**, in press.

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(11) In a typical procedure, a THF solution (40 mL) of 1.0 g (2.7 mmol) of **2** was saturated with dry CO$_2$ at –30 °C (atmospheric pressure). After 1 h, pentane (20 mL) was added. After 2 days at –25 °C a dark brown microcrystalline compound was formed. It was filtered off and dried under CO$_2$ (0.49 g, yield 40%). Anal. Calcd for Co(NO)$_2$[PhP-(OCH$_2$CH$_2$)$_2$NH]Cl(CO$_2$)·0.5C$_4$H$_8$O: C, 34.93; H, 3.84; N, 9.41, Cl, 7.94; P, 6.94; Co, 13.21. Found: C, 35.08; H, 4.03; N, 9.35; Cl, 8.06; P, 7.50; Co, 12.99. CO$_2$ determination (a) by iodine addition 9.7, (b) by sulfuric acid addition 9.2, calcd 9.85. $^{31}$P NMR $\delta$ 177 (200 K); $^{13}$C NMR $\delta$ 159.6 (CO$_2$) (180 K); IR 1830 and 1765 ($\nu$(NO)), 1655 cm ($\nu$(C=O)) in Nujol mull.

(12) The UV-visible spectrum of **2** in CH$_2$Cl$_2$ (7.1 × 10$^{-3}$ M) shows absorption maxima at 320, 380, 440, and 660 nm. Conductivity data for **2** and **3** in MeCN ((1–8) × 10$^{-3}$ M) in the temperature range 0–25 °C indicated a nonelectrolyte behavior for both complexes.

(13) The observed value should be compared with that found for the cationic complex [Co(NO)$_2$(PNH)]$^+$ClO$_4^-$ where ligand **1** is chelating (186 ppm).[6a]

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