binding of the nucleophile to the acyl-enzyme, formation and subsequent decomposition of the tetrahedral intermediate, and product release.[9] The very fact that a substantial isotope effect is observed in subtilisin-catalyzed transesterification 1 indicates that the second step, namely, the abstraction of the proton from the hydroxyl group of the nucleophile by the catalytic triad's histidine,[10] is rate-limiting. Furthermore, since the magnitude of the primary deuterium kinetic isotope effect is related to the degree of proton transfer in the transition state,[11] the fact that this parameter is the same within experimental error for the subtilisin catalysis in different organic solvents (Table I) suggests a marked independence of the transition-state structure for the deacylation process on the nature of the reaction medium.

In order to test the generality of our findings with subtilisin, we have applied the deuterium kinetic isotope effect approach to transesterification 1 catalyzed by the lipase from *Pseudomonas fluorescens* in acetonitrile and in cyclohexane. As can be seen in the last two lines of Table I, for this (nonproteolytic) hydrolase, the magnitude of the isotope effect is nearly the same in both solvents, as is the case for the protease subtilisin. Therefore, combined with the results of Hammett analysis of the acylation of subtilisin,[4] the deacylation data obtained in this study support the notion of great similarities in the mechanism of enzymatic catalysis in different anhydrous solvents, whether the latter are miscible or immiscible with water and regardless of their chemical structure and physicochemical properties.

Supplementary Material Available: Analysis of kinetic expressions for reaction 1 and their implications (3 pages). Ordering information is given on any current masthead page.

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Highly Reduced Carbene Complexes: Formation of an Alkoxymalonate by Coupling of Carbon Dioxide with the Nucleophilic Carbene in $[Cr(CO_4)\{C(OMe)Ph\}]^{2-}$

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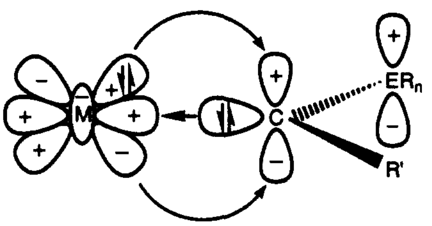
Received November 16, 1989
Revised Manuscript Received October 17, 1990

Fischer carbene complexes[1] can be described as complexes of singlet carbenes with transition-metal centers in which σ-donation from an sp^2 orbital is counterbalanced by π-donation into a vacant carbon p orbital (Scheme I).[1,2] In the archetypical carbene complexes of the group 6 metals, the carbene replaces an isolobal CO in a zero-valent hexacarbonyl to give a complex $[M(CO)_5\{C(ER_n)R'\}]$ (M = Cr, W; ER_n = heteroatomic substituent such as an alkoxy or amino group; R′ = alkyl or aryl group) whose reactivity is dominated by the electrophilicity of the carbenoid carbon.[1] We recently became intrigued by the possibility that the π-accepting ability of heteroatomic carbenes might be sufficient to allow formation of stable complexes in which carbene ligands replaced a CO within a carbonylmetalate (such as $[Cr(CO)_5]^{2-}$) and by the further possibility that the increased back-donation to the unsaturated carbon would then change the carbenoid carbon into a nucleophilic center (similar to the unsaturated carbon in a Schrock alkylidene complex[3]). We now report (Scheme II) that dianionic carbene complexes such as $[Cr(CO)_4\{C(OMe)Ph\}]^{2-}$ ($\mathbf{1}^{2-}$) *are* synthetically accessible, and that the anticipated umpolung[4] *does* induce a fundamentally new reactivity pattern.

Scheme I. Coordination of the Ligand in a Fischer Carbene Complex[a]



[a] E = O, N, or S.

The synthesis of $\mathbf{1}^{2-}$ utilizes a strategy similar to that which we have used to prepare phosphine-substituted,[5] arene-substituted,[6] and cyclopentadienyl-substituted[7] carbonylmetalates: one CO of the neutral carbene complex $[Cr(CO)_5\{C(OMe)Ph\}]$ (**2**) is replaced with an alkylphosphine,[8] and the substituted complex is reduced with an alkali-metal naphthalenide at −78 °C. Low-valent Cr complexes with π-acceptor ligands tend to obey the 18-electron rule, and we anticipated that electron transfer would lead to phosphine loss and give a dianionic carbene complex.

Reductions utilized a mixture of *cis*- and *trans*-$[Cr(CO)_4(PBu_3)\{C(OMe)Ph\}]$ (**3**) prepared in 61% yield by PBu_3 substitution of **2**.[8] Solution IR data suggested that potassium 1-methylnaphthalenide reduction (2.0 equiv of a 0.2 M THF solution) of **3** (0.62 g, 1.27 mmol in 30 mL of THF) at −78 °C resulted in formation of the desired dianionic carbene complex, since the carbonyl absorptions of the starting material at 2018 (s) and 1900 (vs) cm^{-1} were replaced by absorptions at 1859 (s) and 1737 (s, br)[9] cm^{-1}, consistent with the formation of a highly reduced carbonyl complex. This dianion was isolated by addition of 18-crown-6 (18-C-6) to complex the K$^+$ cation. After 12 h at room temperature the solvent was removed under vacuum to give a red oil, which solidified when washed with hexanes (2 × 30 mL). The solid was redissolved in THF (30 mL), and 60 mL of hexanes was mixed with the solution to give a purple precipitate. ^{13}C and ^{1}H NMR spectra of the product[10] could be obtained by dissolving the purple solid in CD_3CN at 240 K and recording spectra of the solution at 243 K.[11] These spectra are consistent with the proposed formulation of the reduction product as $[Cr(CO)_4\{C(OMe)Ph\}]^{2-}$ ($\mathbf{1}^{2-}$) and include a ^{13}C resonance at δ 171.7

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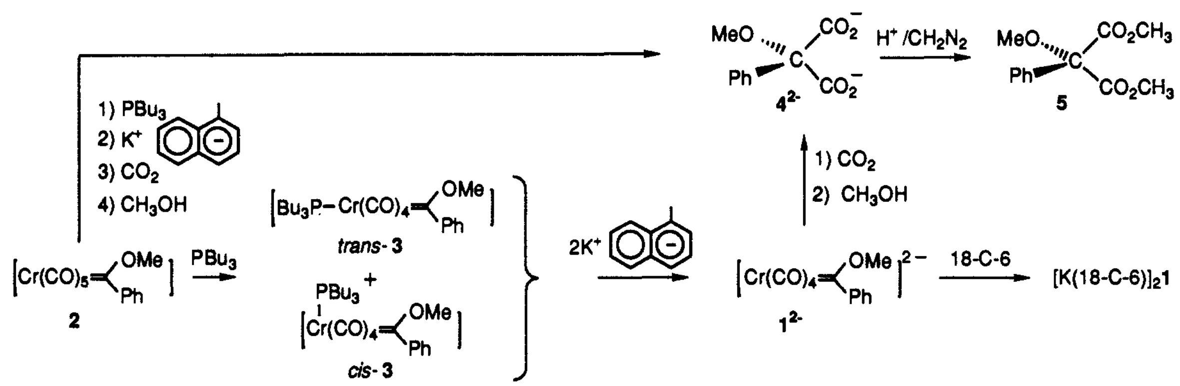
(9) (a) The broad 1737-cm^{-1} band is not Lorentzian and probably includes two absorptions (see mull spectral data of K(18-C-6)$^+$ salt below). Its shape probably reflects the presence of several ion pairs with somewhat different IR spectra: (b) Darensbourg, M. Y. *Prog. Inorg. Chem.* **1985**, *33*, 221.

(10) ^{13}C NMR (CD_3CN, 240 K, 125.8 MHz): δ 247.1 (s, CO), 171.7 (s, Cr=C), 139.4–120.6 (c, C_6H_5), 69.9 (t, J = 142 Hz, OCH_2), 59.0 (q, J = 140 Hz, OCH_3). ^{1}H NMR (CD_3CN, 240 K, 300 MHz): δ 7.99 (d, J = 8 Hz, 2 H, ortho H), 7.17 (t, J = 8 Hz, 2 H, meta H), 6.83 (t, J = 7 Hz, 1 H, para H), 3.51 (s, 48 H, OCH_2), 3.37 (s, 3 H, OCH_3).

(11) IR spectra of a cold (ca. 240 K) CH_3CN solution of $[K(18\text{-}C\text{-}6)]_2\cdot\mathbf{1}$ are very similar to those of a THF solution, with bands at 1850 (s) and 1720 (vs) cm^{-1}. NMR spectra were recorded at 240 K because the complex undergoes a reaction or isomerization in CH_3CN at room temperature to generate two new species with bands at 1890 (s) and 1755 (s) cm^{-1} and at 1860 (s) and 1720 (vs) cm^{-1}. When CD_3CN solutions of $[K(18\text{-}C\text{-}6)]_2\cdot\mathbf{1}$ are warmed above 240 K, changes in ^{1}H and ^{13}C NMR spectra are observed which correlate with the changes in the IR spectra.

0002-7863/90/1512-9419$02.50/0

Scheme II



assigned to the carbenoid carbon. This is above the usual range for Fischer carbene complexes[12] (cf. δ 352.2 for the carbenoid carbon in **2**), as might be anticipated for an extremely electron rich carbene complex.[13] There is also a single carbonyl resonance, consistent with $\mathbf{1}^{2-}$ having a low barrier to rearrangement within a fluxional five-coordinate geometry.[15]

A crystalline salt of $\mathbf{1}^{2-}$ was obtained by redissolving the purple solid in THF (50 mL) and concentrating the filtered THF solution to give dark purple rectangular cubes of analytically pure $[K(18\text{-}C\text{-}6)]_2[Cr(CO)_4\{C(OMe)Ph\}]$[16] ($[K(18\text{-}C\text{-}6)]_2\cdot\mathbf{1}$, 0.59 g, 0.66 mmol ≡ 52%). These crystals would not redissolve in THF, but when dimethoxyethane (DME) was added the resulting solution had an IR spectrum with bands at 1860 (s) and 1730 (vs br) cm^{-1} similar to those of the freshly reduced THF solution and of the Nujol mull of the crystals.[9,16] This confirmed the identity of the crystals.

The dianion $\mathbf{1}^{2-}$ is the most highly reduced carbene complex reported to date. The only previous report of carbene complexes of a metal in a negative oxidation involved direct alkali-metal reduction of Fisher carbene complexes.[17] Reduction of **2**, for example, results in one-electron reduction to give unstable $[Cr(CO)_5\{C(OMe)Ph\}]^-$ ($\mathbf{2}^-$), but does *not* lead to addition of a second electron,[17] presumably because the π-acceptor CO ligands are tightly bound (this emphasizes the importance of the non-π-acceptor PR_3 ligand in the reduction of **3**). Winter has also reported the reduction of iodide-substituted carbene complexes: this led to highly reactive anionic carbene complexes of the type $[M(\eta\text{-}C_5H_5)(CO)_2(CRR')]^-$ (M = Mo, W), containing zero-valent metals.[18]

As anticipated, π-back-donation from the highly reduced metal center in $\mathbf{1}^{2-}$ renders the unsaturated carbon nucleophilic, as established by the reaction of K_2-**1** with CO_2. This electrophile was selected because CO_2 is not prone to single electron transfer reactions with highly reduced transition metal complexes,[19] and we have observed that excess CO_2 reacts readily with a solution of $\mathbf{1}^{2-}$ (prepared from 0.72 g, 1.48 mmol of **3**) at −78 °C. The solvent was removed under reduced pressure and CH_3OH added to the washed (hexanes) orange residue to give a white solid and an orange solution. The solid was collected by filtration to give 0.35 g (1.22 mmol ≡ 82%) of spectroscopically pure $K_2[Ph(MeO)C(CO_2)_2]$ ($K_2\cdot\mathbf{4}$).[20] This material was characterized by a conventional diazomethane esterification of the freshly prepared acid to give $Ph(MeO)C(CO_2Me)_2$ (**5**)[21] in 85% yield after chromatography. Neither $K_2\cdot\mathbf{4}$ nor **5** has been previously reported, and methoxy-substituted malonates and malonate esters would be difficult to synthesize by conventional deprotonation of malonate diesters.

The biscarboxylation of $\mathbf{1}^{2-}$ is unique, but the mechanistic details of the reaction remain unclear. The reaction most probably involves an initial carbon dioxide/carbene coupling similar to that reported by Bergman[22] (in which CO_2 addition to an electron-rich iridium methylidene complex leads to a metalloheterocycle), but in our system the initial coupling product is still so electron rich that the carbenoid-derived carbon adds a second CO_2 to form a second C–C bond. A second model for the initial CO_2 addition comes from Fischer's report of metalloheterocycle formation by CO_2 addition to an anionic carbyne complex.[23] The only other report of a reaction of CO_2 with a carbene or alkylidene complex involves a reaction manifold complementary to that in Scheme II: Schrock has briefly stated that $[Ta({=}CHCMe_3)(CH_2CMe_3)_3]$ gives bis-*tert*-butylallene with CO_2[24] in a reaction that is probably driven by the oxophilicity of the high-valent Ta.

Our observation that $\mathbf{1}^{2-}$ is synthetically accessible and can be biscarboxylated significantly extends the known reactivity of Fischer carbene complexes. The carboxylation is an interesting addition to the reactions of carbene complexes with potential applications in organic synthesis,[25] and we have already established that $K_2\cdot\mathbf{4}$ can be prepared from readily available **2** in a single pot (without isolation of **3**) in good (53%) overall yield. The synthetic implications of this reaction are currently being explored in our laboratories.

Acknowledgment. We thank the NSF for financial support through Grant CHE-8722424 and the Office of Naval Research for partial support of preliminary experiments.

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(13) Using Fenske's model,[14] increased back-donation decreases paramagnetic deshielding of the carbenoid carbon by decreasing the percent C character of the LUMO and by moving the energy of the LUMO away from that of the occupied orbitals and toward that of the other virtual orbitals.

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(16) IR (Nujol mull, $\nu_{C{\equiv}O}$) 1855 (s), 1728 (vs), 1715 (vs) cm^{-1}. Anal. Calcd for $C_{36}H_{56}CrK_2O_{17}$: C, 48.53; H, 6.33; K, 8.78. Found (Dornis u. Kolbe, Mülheim a.d. Ruhr, FRG): C, 48.40; H, 6.40; K, 8.60.

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(20) IR (Nujol mull, selected): 1611 cm^{-1} (carboxylate). ^{1}H NMR (D_2O, 300 MHz): δ 7.56–7.35 (m, 5 H, C_6H_5), 3.26 (s, 3 H, OCH_3). ^{13}C NMR ($D_2O + CO(CD_3)_2$, 75.45 MHz, multiplicities from gated spectra): δ 176.14 (s, 2 $\mathit{C}O_2K$), 139.62–127.32 (c, C_6H_5), 90.90 (s, quaternary C), 53.07 (s, $O\mathit{C}H_3$).

(21) IR (selected, neat): 1746 cm^{-1} (ester C═O). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.55–7.35 (m, 5 H, C_6H_5), 3.79 (s, 6 H, 2 CO_2CH_3), 3.41 (s, 3 H, OCH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75.45 MHz, multiplicities from gated spectra): δ 168.34 (s, 2 $\mathit{C}O_2CH_3$), 134.69 (s), 128.84 (d), 128.23 (d), 123.38 (d) (all C_6H_5), 86.36 (s, quaternary C), 54.50 (q, $O\mathit{C}H_3$), 53.01 (q, 2$CO_2\mathit{C}H_3$). Exact mass calcd for $C_{12}H_{14}O_5$: 238.0841. Found: 238.0837.

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