the $-CH_2O$ group at indole C-4 is derived by methylation. It is noted, however, that the 2-carboxyl group of the indole moiety was labeled extensively by C-1 of serine. Since the alanine side chain of tryptophan is derived from L-serine,[11] this suggests that the indole moiety may arise by cyclization of tryptophan, connecting indole C-2 with the carboxyl group, followed by excision of the side-chain carbon atom 2 plus its attached nitrogen and methylation of indole C-4 (Figure 2). Consistent with this hypothesis, DL-[7a-^{14}C]tryptophan (0.5 mmol/L, 10% and 8% specific incorporation), L-[methylene-^{14}C]tryptophan (0.5 mmol/L, 7% and 12% specific incorporation) and [2-^{14}C]indole (1 mmol/L, 13 and 8% spec. incorp.) were efficiently incorporated into **1**. Nonincorporation of DL-4-methyl[methylene-^{14}C]tryptophan[12] suggests that methylation of the indole is not the first step in the reaction sequence.

On the basis of the above results and reasonable extrapolations, one may speculate that **1** arises from a dodecapeptide H_2N-L-Ser-L-Cys-L-Thr-(L?)-Thr-L-Cys-L-Glu-L-Cys-D-Cys-L-Cys-L-Ser-L-Cys-L-Ser-COOH through connection of the carbon atoms 3 of ser(3) and ser(12) and attachment of a (modified) tryptophan.

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(11) Miles, E. W. *Adv. Enzymol.* **1979**, *49*, 127.

(12) Synthesized from 4-methylindole and $^{14}CH_2O$ via the gramine route.[13]

(13) Weygand, F.; Linden, H. *Z. Naturforsch., B: Anog. Chem., Org. Chem., Biochem., Biophys., Biol.* **1954**, *9*, 682.

Gas-Phase Observation and CO Substitution Kinetics of *cis*-$Cr(CO)_4(C_2H_4)_2$ by Time-Resolved IR Absorption Spectrometry[†]

Bruce H. Weiller[‡] and Edward R. Grant*

Department of Chemistry, Purdue University
West Lafayette, Indiana 47907

Received September 11, 1986

Olefin complexes of metal carbonyl fragments have theoretical importance[1] and play a role in numerous catalytic systems.[2] Theory suggests an interesting trend in bond strengths for the bis-olefin and diene complexes of the 16-electron group VI (group 6) carbonyl fragments.[1d] Bis-olefin complexes of $M(CO)_4$ (M = Cr, Mo, W) are generally thought to be more stable than η^4-diene complexes. Experiments show that the mono- and bis-olefin complexes of molybdenum and tungsten carbonyls are quite stable[3] but such examples for chromium are rare. Only one $Cr(CO)_4(\text{olefin})_2$ complex is known and it is stabilized by relief of ring strain in the uncomplexed olefin.[4] Interestingly, the analogous η^4 complexes of nonconjugated dienes are generally quite stable for all three rows of group VI (group 6).[5]

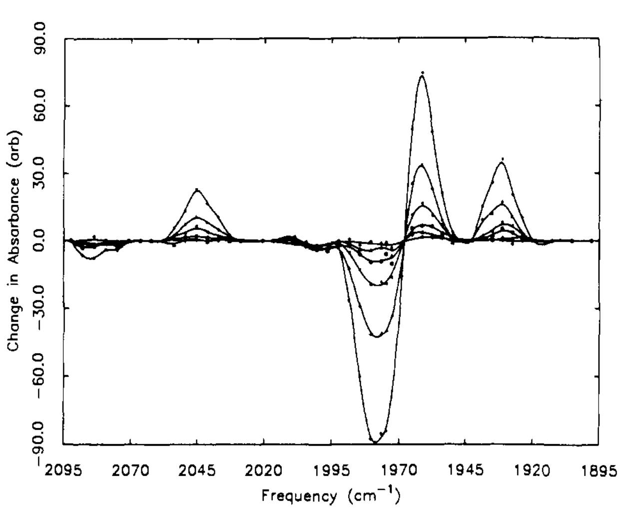

Figure 1. Transient IR absorption spectrum obtained following photolysis of a mixture of $Cr(CO)_5(C_2H_4)$ (0.12 torr), CO (0.56 torr), and C_2H_4 (500 torr). The initial spectrum (largest amplitude) corresponds to an observation time of 30 μs following the laser pulse. Subsequent spectra are separated in time by 13.7 ms. The instrumental resolution is 5 cm^{-1}.

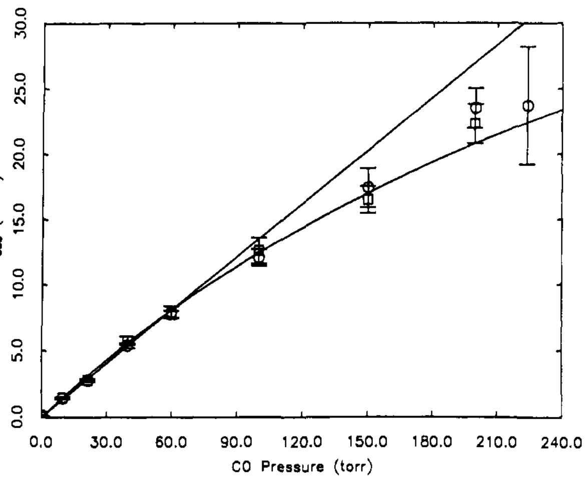

Figure 2. CO pressure dependence of k_{obsd} at 1975 (□) and 1961 cm^{-1} (○) for a constant C_2H_4 pressure of 300 torr. The straight line is the weighted fit to the data below 60 torr of CO. The curved line is the weighted nonlinear least-squares fit to all the data.

This paper reports the first gas-phase observation and infrared spectral characterization of $Cr(CO)_4(C_2H_4)_2$. This complex is unstable and reacts with CO by dissociative substitution. We follow the kinetics of this process by time-resolved IR absorption spectrometry, extracting a unimolecular decay constant orders of magnitude larger than the reported solution value for $Cr(CO)_4(\eta^4\text{-butadiene})$,[6] in an apparent conflict with elementary theory as cited above.

Our apparatus[7] and the technique of time-resolved IR absorption spectrometry as applied to organometallics[8] have recently

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[†] In this paper the periodic group notation in parentheses is in accord with recent actions by IUPAC and ACS nomenclature committees. A and B notation is eliminated because of wide confusion. Groups IA and IIA become groups 1 and 2. The d-transition elements comprise groups 3 through 12, and the p-block elements comprise groups 13 through 18. (Note that the former Roman number designation is preserved in the last digit of the new numbering: e.g., III → 3 and 13.)

[‡] Present address: Argonne National Laboratory, Chemistry Division, Argonne, IL 60439.

(1) (a) Dewar, M. J. S. *Bull. Soc. Chim. Fr.* **1951**, *18*, C79. (b) Chatt, J.; Duncanson, L. A. *J. Chem. Soc.* **1953**, 2939. (c) Ittel, S. D.; Ibers, J. A. *Adv. Organomet. Chem.* **1976**, *14*, 33. (d) Elian, M.; Hoffmann, R. *Inorg. Chem.* **1975**, *14*, 1058. (e) Albright, T. A.; Hoffmann, R.; Thibeault, J. C.; Thorn, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 3801. (f) Rosch, N.; Hoffmann, R. *Inorg. Chem.* **1974**, *13*, 2656. (g) Stockis, A.; Hoffmann, R. *J. Am. Chem. Soc.* **1980**, *102*, 2952 and references therein. (h) Bachman, C.; Demuynck, J.; Veillard, A. *J. Am. Chem. Soc.* **1978**, *100*, 2366. (i) Basch, H.; Newton, M. D.; Moskowitz, J. W. *J. Chem. Phys.* **1978**, *69*, 584. (j) Swope, W. L.; Schaefer, H. F., III *Mol. Phys.* **1977**, *34*, 1037. (k) J. Garcia-Prieto and O. Novaro, Molec. Phys. 41, 205 (1980).

(2) (a) Parshall, G. W. *Homogeneous Catalysis*; Wiley: New York, 1980. (b) Moggi, L.; Juris, A.; Sandrini, D.; Manfrin, M. F. *Rev. Chem. Intermed.* **1981**, *4*, 171.

(3) Stolz, I. W.; Robson, G. R.; Sheline, R. K. *Inorg. Chem.* **1963**, *2*, 1264. Grevels, F. W.; Lindemann, M.; Benn, R.; Goddard, R.; Kruger, C. *Z. Naturforsch., B* **1980**, *35B*, 1298.

(4) Grevels, F. W.; Skibbe, V. *J. Chem. Soc., Chem. Commun.* **1984**, 681.

(5) (a) Bennett, M. A.; Pratt, L.; Wilkinson, G. *J. Chem. Soc.* **1961**, 2037. (b) Darensbourg, D. J.; Nelson, H. N., III; Murphy, M. A. *J. Am. Chem. Soc.* **1977**, *99*, 896. (c) Fischer, E. O.; Frohlich, W. *Chem. Ber.* **1959**, *92*, 2995. (d) Bennett, M. A.; Wilkinson, G. *Chem. Ind.* **1959**, 1516. (e) Manuel, T. A.; Stone, F. G. A. *Chem. Ind.* **1959**, 1349. (f) Leigh, G. J.; Fischer, E. O. *J. Organomet. Chem.* **1965**, *4*, 461. (g) Zingales, F.; Conziani, F.; Basolo, F. *J. Organomet. Chem.* **1967**, *7*, 461. (h) Zingales, F.; Granziani, M.; Belluco, U. *J. Am. Chem. Soc.* **1967**, *89*, 256.

(6) Dixon, P. T. ; Burkinshaw, P. M.; Howell, J. A. S. *J. Chem. Soc., Dalton Trans.* **1980**, 2237.

(7) Weiller, B. H.; Grant, E. R., submitted for publication in *J. Am. Chem. Soc.*

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been described in detail. In brief, a pulsed UV excimer laser beam crosses a broad-band IR beam (Nernst glower) in a static gas cell at 295 K. A monochromator resolves probe frequencies to 5 cm^{-1} and a digitizer captures transient IR absorptions from a 1-MHz InSb detector.

To observe $Cr(CO)_4(C_2H_4)_2$, we first convert $Cr(CO)_6$ into metastable $Cr(CO)_5(C_2H_4)$ by photolysis with excess C_2H_4. FTIR spectra show that $Cr(CO)_6$ (2000 cm^{-1}) decreases with photolysis while new bands at 2085 (~0.03), 1980 (0.82), and 1975 (1.00) cm^{-1} grow in along with lines for free CO. The new bands are assigned to $Cr(CO)_5(C_2H_4)$ and agree well with the few reported $Cr(CO)_5$(olefin) complexes[4] and with more numerous $M(CO)_5$(olefin) (M = Mo, W) complexes.[3]

After $Cr(CO)_6$ is converted to $Cr(CO)_5(C_2H_4)$, laser-induced transient IR absorptions are clearly observed. Figure 1 shows the complete transient absorption spectrum which consists of five bands at 2084, 2045, 1975, 1961, and 1931 cm^{-1}. The negative bands at 2084 and 1975 cm^{-1} are due to parent and match the absorption bands of $Cr(CO)_5(C_2H_4)$. We assign the remaining three positive bands to *cis*-$Cr(CO)_4(C_2H_4)_2$.

We reach this conclusion on the basis of the following observations. The new bands all display a decay constant equal to that for the recovery of $Cr(CO)_5(C_2H_4)$, which indicates a simple interconversion between two species. Coordinatively unsaturated species are excluded on the basis of the long lifetime of the new complex[9] and the inverse dependence of its observed decay constant on ethylene pressure (see below). The three new bands have an integrated intensity ratio of 1.0:2.5:1.4 which excludes the trans isomer. We suspect that the 1931-cm^{-1} band is an unresolved doublet giving a total of four bands.[10] Our observation of *cis*-$Cr(CO)_4(C_2H_4)_2$ is surprising in light of the trans structures for $M(CO)_4(C_2H_4)_2$ (M = Mo, W).[3]

$Cr(CO)_4(C_2H_4)_2$ is expected to relax to $Cr(CO)_5(C_2H_4)$ by a dissociative substitution process:[11]

$$Cr(CO)_4(C_2H_4)_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Cr(CO)_4(C_2H_4) + C_2H_4 \qquad (1)$$

$$Cr(CO)_4(C_2H_4) + CO \xrightarrow{k_3} Cr(CO)_5(C_2H_4) \qquad (2)$$

The assumptions of a steady state for $Cr(CO)_4(C_2H_4)$ and time-independent densities of excess CO and C_2H_4 predict a simple exponential decay for $Cr(CO)_4(C_2H_4)_2$ and recovery for $Cr(CO)_5(C_2H_4)$ with identical time constants. All of the time-dependent absorptions in Figure 1 are well fit by single exponentials and the time constants match under all conditions.

The above kinetics predict the observed decay constants (k_{obsd}) to depend on CO and C_2H_4 pressures:

$$k_{obsd} = \frac{k_1 k_3 [CO]}{k_2 [C_2H_4] + k_3 [CO]} \qquad (3)$$

Figure 2 shows that k_{obsd} increases with CO at constant $[C_2H_4]$ becoming nonlinear at high [CO] in accordance with eq 3. Equation 3 also indicates that k_{obsd}^{-1} should be linear with $[C_2H_4]$. This is observed when $[C_2H_4]$ is varied from 300 to 900 torr with CO constant at 0.56 torr. A vanishing intercept is found, but this is expected for $[CO] << [C_2H_4]$. Furthermore, the CO dependence (0.12–1.5 torr) at 700 torr of C_2H_4 is linear, which confirms this supposition.

Under conditions where $k_2[C_2H_4] >> k_3[CO]$, the quantity k_1k_3/k_2 can be determined from the linear dependencies of k_{obsd} on [CO] and $1/k_{obsd}$ on $[C_2H_4]$. The three separate data sets give an average value of $k_1k_3/k_2 = (44.4 \pm 5.1) \times 10^3$ s^{-1}. From the weighted, nonlinear least-squares fit to the data of Figure 2, separate values of k_1 and k_3/k_2 are found to be $k_1 = (6 \pm 2) \times 10^4$ s^{-1} and $k_3/k_2 = 0.7 \pm 0.2$. These combine to give a value of $k_1k_3/k_2 = (46 \pm 18) \times 10^3$ s^{-1}, in good agreement with the linear fits.

The fast gas-phase unimolecular decay constant obtained for *cis*-$Cr(CO)_4(C_2H_4)_2$ (k_1) establishes the instability of this complex. This behavior differs drastically from that of $Mo(CO)_4(C_2H_4)_2$ and $W(CO)_4(C_2H_4)_2$, which are stable trans isomers.[3] We see no evidence for *trans*-$Cr(CO)_4(C_2H_4)_2$.

The unimolecular decay constant of $Cr(CO)_4(C_2H_4)_2$ is 3×10^7 larger than the reported 300K solution value for $Cr(CO)_4$(η^4-butadiene).[6,12] Complexes of $Cr(CO)_4$ with nonconjugated dienes are more stable than with conjugated dienes,[5a,b,6,13] but our results show that *$Cr(CO)_4$(olefin)$_2$ complexes decay orders of magnitude faster than both.* This result has important implications for the theory of bonding in these complexes.

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Note Added in Proof. After this paper was submitted we became aware of new work by Gregory et al.[14] reporting formation of *cis*-$Cr(CO)_4(C_2H_4)_2$ in xenon solution. The assigned IR spectrum of the cis isomer, as well as crude kinetic observations confirming its formation as the primary photosubstitution product, are in good agreement with the present work. Gregory et al. also report the slower appearance of *trans*-$Cr(CO)_4(C_2H_4)_2$ in their system, which is not observed in our gas-phase experiments (possibly due in our case to pulsed irradiation and the scavenging effect of added CO).

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[8] Poliakoff, M.; Weitz, E. In *Advances in Organometallic Chemistry*; Stone, F. G. A., Ed.; Academic: New York, 1986; Vol. 25, p 277.

[9] The gas-phase CO recombination rate constants for metal carbonyl fragments are generally on the order of 10^{10} M^{-1} s^{-1}: Seder, T. A.; Church, S. P.; Weitz, E. *J. Am. Chem. Soc.* **1986**, *108*, 4721.

[10] Note that the 1980- and 1975-cm^{-1} bands of $Cr(CO)_5(C_2H_4)$ are unresolved in Figure 1.

[11] (a) Darensbourg, D. J. *Adv. Organomet. Chem.* **1982**, *21*, 113. (b) Howell, J. A. S.; Burkinshaw, P. M. *Chem. Rev.* **1983**, *83*, 557. (c) Angelici, R. J. *Organomet. Chem. Rev.* **1968**, *3*, 173.

[12] Reference 6 reports a solution rate constant for the reaction (η^4-butadiene)$Cr(CO)_4$ $\rightarrow$ (η^2-butadiene)$Cr(CO)_4$, which we compare to our gas-phase value for k_1. However, the data of ref 6 can be interpreted by an alternate mechanism that does not give an elementary rate constant (see ref 5g,h). Efforts are under way in this laboratory to study the gas-phase kinetics of (η^4-butadiene)$Cr(CO)_4$.

[13] (a) Fischler, I.; Budzwait, M.; Koerner von Gustorf, E. A. *J. Organomet. Chem.* **1976**, *105*, 325. (b) Koerner von Gustorf, E. A.; Jaenicke, D.; Polansky, O. E. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 532.

[14] Gregory, M. F.; Jackson, S. A.; Poliakoff, M.; Turner, J. J. *J. Chem. Soc., Chem. Commun.* **1986**, 1175.

Macrolide Biosynthesis. Tylactone Formation Involves the Processive Addition of Three Carbon Units

Stephen Yue, Janice S. Duncan, Yoshikuni Yamamoto, and C. Richard Hutchinson*

School of Pharmacy and Department of Bacteriology
University of Wisconsin, Madison, Wisconsin 53706

Received August 18, 1986

An important question in the biosynthesis of macrolide antibiotics like erythromycin A and tylosin concerns the biochemistry of macrolactone formation.[1] It is clear that simple carboxylic acids—acetate, butyrate, and propionate—are the source of all the carbon and oxygen atoms of the erythronolide[2,3] and tylonolide[4,5] macrolactones and very probable that the α-carboxyl de-

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[1] Seno, E. T.; Hutchinson, C. R. In *Antibiotic Producing Streptomyces, Vol. IX. The Bacteria: A Treatise on Structure and Function*; Day, L. E., Queener, S. W., Eds.; Academic: New York, 1986; pp 231–279.

[2] (a) Kaneda, T.; Butte, J. C.; Taubman, S. B.; Corcoran, J. W. *J. Biol. Chem.* **1962**, *237*, 322–328. (b) Friedman, S. M.; Kaneda, T.; Corcoran, J. W. *J. Biol. Chem.* **1964**, *239*, 2386–2391.

[3] Cane, D. E.; Hasler, H.; Taylor, P. B.; Liang, T.-Y *Tetrahedron* **1983**, *39*, 3449–3455.

[4] (a) Omura, S.; Nakagawa, A.; Takeshima, H.; Miyazawa, J.; Kitao, C. *Tetrahedron Lett.* **1975**, *50*, 4503–4506. (b) Omura, S.; Takeshima, H.; Nakagawa, A.; Kanemoto, N.; Lukacs, G. *Bioorg. Chem.* **1976**, *5*, 451–454. (c) Omura, S.; Takeshima, H.; Nakagawa, A.; Miyazawa, J.; Piriou, F.; Lukacs, G. *Biochemistry* **1977**, *16*, 2860–2866.

[5] O'Hagan, D.; Robinson, J. A.; Turner, D. L. *J. Chem. Soc., Chem. Commun.* **1983**, 1337–1340.

0002-7863/87/1509-1253$01.50/0