solvent, thus stabilizing addition intermediates, while, in the gas phase, the excess energy causes such an intermediate either to revert to reactants or to fragment in a different manner to products. There are several ways in the gas phase to remove this excess energy and obtain addition products: by collision with a third body,[16] by radiative emission,[14,17] and by using a single molecule of solvent.[18] The first two methods do not occur for the reactants and pressures used in this work; we have utilized monosolvation of the anion as a means of stabilizing the M + 31 ions.

Using the Riveros reaction

$$CH_3O^- + HCO_2CH_3 \rightarrow CO + \underset{\mathbf{2}}{CH_3O^-{\cdot\cdot}HOCH_3} \quad (5)$$

to generate a monosolvated methoxide,[19] we have reacted **2** with $CH_2{=}CHCN$, $CH_2{=}CHCHO$, and $CH_2{=}CHNO_2$. In all three cases, an M + 31 anion is the major product. Double resonance ejection indicates that it arises exclusively from **2**. Some M − 1 ion is also seen in these experiments, but it comes from reaction with bare methoxide, since reactions 1 and 5 proceed at comparable rates ($\sim 3 \times 10^{-10}$ cm molecule^{-1} s^{-1}). The basicity and $\Delta G_f°$ (298) of **2** may be estimated from literature values for the bonding energy of such cluster ions;[20] we obtain $\Delta G_f°$ (298) (**2**) = −135 ± 5 kcal/mol. This inplies that deprotonation of acrylonitrile by **2** is endergonic by 9 kcal/mol (the monosolvation reduces methoxide basicity by ~18 kcal/mol), but the observed addition of methoxide is near ergoneutral.

A true Michael addition involes a carbanionic nucleophile. Adding acetaldehyde to **2** results in an interchange of anions and production of monosolvated enolate **3**:

$$CH_3O^-{\cdot\cdot}HOCH_3 + CH_3CHO \rightarrow \underset{\mathbf{3}}{CH_2{=}CHO^-{\cdot\cdot}HOCH_3} + CH_3OH$$

Reaction of **3** with acrylonitrile gives only a trace of M + 43 anion at long times. This small yield is not necessarily due to the Michael addition being slow, but rather to it being the fourth reaction in the sequence, and simply commencing too late in the sequence to be observed, relative to collisional ion loss from the ICR cell.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

References and Notes

(1) Brauman, J. I.; Blair, L. K. *J. Am. Chem. Soc.* **1968,** *90*, 5636–5637; **1970,** *92*, 5986–5992; **1971;** *93*, 3911–3914. Brauman, J. I.; Riveros, J. M.; Blair, L. K. *Ibid.* **1971,** *93*, 3914–3916.
(2) Nibbering, N. M. M. "Kinetics of Ion–Molecule Reactions", Ausloos, P., Ed.; Plenum Press: New York, 1979; pp 165–197.
(3) McIver, R. T., Jr. *Rev. Sci. Instrum.* **1970,** *41*, 555–558; **1978,** *49*, 111–118. McIver, R. T., Jr. "Ion Cyclotron Resonance Spectrometry", Hartman, H., Wanczek, K.-P., Eds.; Springer-Verlag: Berlin, 1978; pp 97–135. Hunter, R. L.; McIver, R. T., Jr. *Chem. Phys. Lett.* **1977,** *49*, 577–582.
(4) Jager, K.; Henglein, A. *Z. Naturforsch. A.* **1967,** *22*, 700–704.
(5) MacGregor, J. H.; Pugh, C. *J. Chem. Soc.* **1945,** 535–536.
(6) Oshima, K.; Shimoji, K.; Takahashi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1973,** *95*, 2694–2695. Biellman, J. F.; Vincens, J. J. *Tetrahedron Lett.* **1978,** 467–470. Eisch, J. J.; Galle, J. E. *J. Org. Chem.* **1979,** *44*, 3279–3280.
(7) Bierbaum, V. M.; DePuy, C. H.; Shapiro, R. H. 25th Annual Conference on Mass Spectrometry and Allied Topics, Washington, D.C., 1977, Paper FC-5.
(8) Bohme, D. K.; Lee-Ruff, E.; Young, L. B. *J. Am. Chem. Soc.* **1972,** *94*, 5153–5159.
(9) DePuy, C. H.; Bierbaum, V. M.; King, G. K.; Shapiro, R. H. *J. Am. Chem. Soc.* **1978,** *100*, 2921–2922.
(10) Cumming, J. B.; Kebarle, P. *Can. J. Chem.* **1978,** *56*, 1–9. Bartmess, J. E.; Scott, J. A.; McIver, R. T., Jr. J. Am. Chem. Soc. **1979,** *101*, 6046–6056, 6056–6063. Bartmess, J. E.; McIver, R. T., Jr. "Gas Phase Ion Chemistry", Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, Chapter 11.
(11) Walsh, A. D. *Dicuss. Faraday Soc.* **1947,** *2*, 18–25. Wells, P. R.; *Prog. Phys. Org. Chem.* **1968,** *6*, 111–145.
(12) DePuy, C. H.; Bierbaum, V. M.; Schmidt, R. J.; Shapiro, R. H. *J. Am. Chem. Soc.* **1978,** *100*, 2920–2921.
(13) Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley: New York, 1976. Shaw, R. *Int. J. Chem. Kinet.* **1973,** *5*, 261–269.
(14) Rains, L. J.; Moore, H. W.; McIver, R. T., Jr. *J. Chem. Phys.* **1978,** *68*, 3309–3311.
(15) Shiga, T.; Yamaoka, H.; Arakawa, K.; Sugiura, T. *Bull. Chem. Soc Jpn.* **1972,** *45*, 2065–2069.
(16) Henis, J. M. S. *J. Am. Chem. Soc.* **1968,** *90*, 844–851. Meot-Ner, M.; Field, F. H. *Ibid.* **1975,** *97*, 5339–5345. Olmstead, W. N.; Lev-On, M.; Golden, D. M.; Brauman, J. I. *Ibid.* **1977,** *99*, 992–998. Nielson, P. V.; Bowers, M. T.; Chau, M.; Davidson, W. R.; Sue, D. H. *Ibid.* **1978,** *100*, 3649–3658. Bass, L.; Hagler, A. T., Karpas, Z.; Klein, F. S. *Ibid.* **1979,** *101*, 2191–2196. Jasinski, J. M.; Rosenfeld, R. N.; Golden, D. M.; Brauman, J. I. *Ibid.* **1979,** *101*, 2259–2265. Chesnavich, W. J., Bowers, M. T. *Ibid.* **1979,** *101*, 5493–5502.
(17) Woodin, R. L.; Beauchamp, J. B. *Chem. Phys.* **1979,** *41*, 1–9.
(18) Asubiojo, O. I.; Blair, L. K.; Brauman, J. I. *J. Am. Chem. Soc.* **1975,** *97*, 6685–6688.
(19) Blair, L. K.; Isolani, P. C.; Riveros, J. M. *J. Am. Chem. Soc.* **1973,** *95*, 1057. Isolani, P. C.; Riveros, J. M. *Chem. Phys. Lett.* **1975,** *33*, 362–364. Faigle, J. F. G.; Isolani, P. C.; Riveros, J. M. *J. Am. Chem. Soc.* **1976,** *98*, 2049.
(20) Yamdagni, R.; Kebarle, P. *J. Am. Chem. Soc.* **1971,** *93*, 7139–7143. Such cluster ions in the ICR may have excess energy: Rosenfeld, R. N.; Jasinski, J. M.; Brauman, J. I. *Ibid.* **1979,** *101*, 3999–4000.

John E. Bartmess
Department of Chemistry, Indiana University
Bloomington, Indiana 47405

Received October 12, 1979

Clusters and Catalysis: On the Requirement for Multinuclear Centers to Catalyze the Hydrogenation of Carbon Monoxide

Sir:

Efficient homogeneous catalysis by mononuclear complexes of certain "difficult" reactions, such as methanation and Fischer–Tropsch synthesis, has not been achieved. It has been suggested that the lack of activity may be due to a requirement for multinuclear metal centers to activate the substrate sufficiently.[1] Early impetus in this direction was provided by experiments which showed that in toluene solution mononuclear carbonyl complexes were inactive for methanation, whereas some cluster complexes were active.[2] However, coordinatively unsaturated species in solution can readily oligimerize,[3] most carbonyls (including all of the mononuclear complexes) undergo decomposition[4] at temperatures below that expected for efficient catalysis of methanation,[5] and the activities of even the cluster complexes are extremely low;[6] so the results are not definitive. Further, in experiments similar to those used to test for methanation activity,[2] the mononuclear group 6b hexacarbonyls were found to be inactive for the hydrogenation of ethylene at 140 °C[7] and it has been previously reported that after photolysis these materials are inactive for the hydrogenation of monoolefins at 25 °C.[8,9] Since this reaction is facilely catalyzed by a number of homogeneous *mononuclear* complexes, the inability to catalyze the much more difficult reduction of CO may reflect the inactive form of the catalysts and not their mononuclear nature.

It has recently been demonstrated that temperature programmed decomposition (TPDE) of carbonyls *adsorbed on silica or alumina* leads to the formation of novel subcarbonyl species which are highly dispersed and which can be stable to >250 °C,[10-13] a temperature sufficient for catalysis of methanation over supported metals.[5] It was also shown that small amounts of CH_4 were formed during the TPDE in flowing He of some *mononuclear* carbonyls.[10-13] Further, both thermal activation (near 150 °C) as well as photolytic activation (near ambient) of the group 6b hexacarbonyls supported on alumina yields catalysts which are extremely active for olefin hydrogenation,[12,14] being far more active than "traditional"[15] heterogeneous catalysts of these metals. Hence, these catalysts should be especially well suited for the investigation of the reduction of CO. Since the above proscription on methanation

Table I. Methane Evolved per Metal Atom during TPDE to 600 °C in He as a Function of Carbonyl Nuclearity

mononuclear carbonyls			dinuclear carbonyls			polynuclear carbonyls		
carbonyl	loading, % M	CH_4/M	carbonyl	loading, % M	CH_4/M	carbonyl	loading, % M	CH_4/M
$V(CO)_6$	0.124	0.10	$Mn_2(CO)_{10}$	0.113	0.056	$Fe_3(CO)_{12}$	0.136	0.021
$Cr(CO)_6$	0.061	0.11	$Re_2(CO)_{10}$	0.627	0.050	$Ru_3(CO)_{12}$[a]	1.82	0.091
$Mo(CO)_6$	0.051	0.12	$Fe_2(CO)_g$[a]	0.297	0.035	$Os_3(CO)_{12}$[a]	0.376	0.073
$W(CO)_6$	0.228	0.22	$Co_2(CO)_8$	0.038	0.027	$Co_4(CO)_{12}$	0.119	0.035
$Fe(CO)_5$	0.116	0.03				$Rh_4(CO)_{12}$	0.098	0.078
$Ni(CO)_4$	0.06	0.01				$Rh_6(CO)_{16}$[a]	0.518	0.014
						$Ir_4(CO)_{12}$[a]	0.907	0.016
av		0.098			0.042			0.047

[a] Solventless run (mixed under He).

activity[1] should apply equally well to a stoichiometric reaction, a detailed study was undertaken of the dependence of CH_4 formation (during TPDE) on the nuclearity of the alumina supported complexes.

The complexes were adsorbed on γ-Al_2O_3 (previously calcined at 500 °C) from pentane solution or by sublimation using high purity techniques previously described.[11] The amounts of CH_4 evolved during TPDE are shown in Table I. Solventless runs with $Mo(CO)_6$, $W(CO)_6$, $Fe_3(CO)_{12}$, $Ru_3(CO)_{12}$, and $Os_3(CO)_{12}$ gave the same amounts of CH_4 as catalysts prepared by impregnation, indicating that the C and H in the CH_4 were derived from the carbonyl ligands and surface hydroxyl groups (σ-OH), respectively, and not from pentane. Table I clearly indicates that cluster complexes have no special propensity for the formation of CH_4 under these conditions.

Although it can not be proved that CH_4 formation from mononuclear precursors was not preceded by agglomerization to clusters, if this were necessary for methane formation it is surprising that on these *very dilute* catalysts (fractional surface coverage ~0.008) the cluster complexes did not display considerably higher reactivity than the mononuclear complexes. Additional experiments with $Mo(CO)_6/Al_2O_3$ also indicate that sintering was probably not important. If a site of nuclearity n is required for CH_4 formation and the sites follow a random distribution, then at low loadings (w) the number of such sites (S_n) is given by

$$S_n = k_1 w^n \qquad (1)$$

The quantity of CH_4 formed (C) from these sites will be given by

$$C = k_2 S_n \qquad (2)$$

or

$$C = k_2 k_1 w^n \qquad (3)$$

Thus

$$\ln C = n \ln w + \ln (k_2 k_1) \qquad (4)$$

and a plot of ln C vs. ln w will have a slope ≥ 2 if any combination of multinuclear sites is necessary for CH_4 formation. Varying w over a range of 270-fold (maximum surface coverage was ~0.03) gave a slope of 1.1 ± 0.1 (Figure 1) and at the lowest loading the quantity of CH_4 formed was 75-fold greater than the calculated total number of multinuclear sites. These results are most consistent with the CH_4 being produced from mononuclear species. Although adherence to a strictly random distribution of the $Mo(CO)_6$ can not be proved, both carbonyl derived and traditional catalysts of supported Mo are believed to be close to 100% dispersed at even high loadings (up to ~10% Mo).[16,17] A selective clustering of the $Mo(CO)_6$ at a loading of 0.003% Mo would be most surprising and contrary to the usual entropic effect of decreased crystallite size with decreased loading.

Additional experiments have provided information on the nature of the CH_4 formation. Figure 2 indicates that during TPDE in He, $H_2(g)$ and CO(g) can coexist at high temperatures. The H_2 has been shown to be formed in a redox reaction between σ-OH and the carbonyl complex which may be approximated as[17]

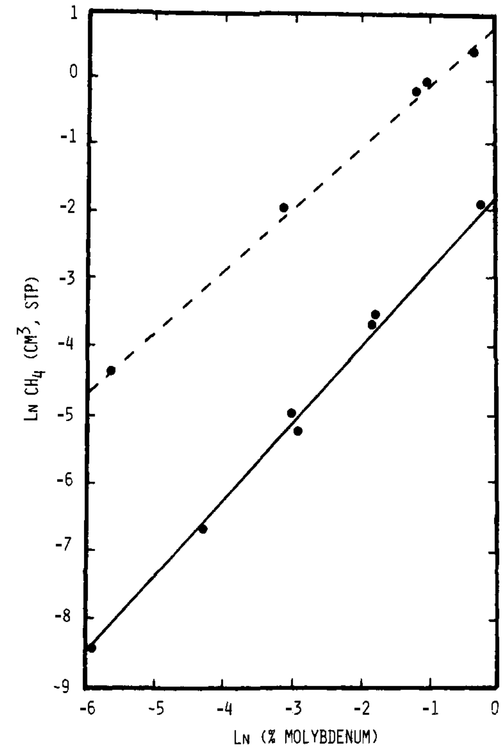

Figure 1. Variation of CH_4 formation with catalyst loading during the TPDE of $Mo(CO)_6/Al_2O_3$. The solid line is for TPDE in flowing He and has a slope of 1.11. The dashed line is for TPDE in flowing H_2 and has a slope of 0.93.

$$M(CO)_j\text{ads} + n(\sigma\text{-OH}) \xrightarrow{\Delta} (\sigma\text{-O}^-)_n M^{n+} + (n/2)H_2(g) + j CO \qquad (5)$$

Figure 2 also shows that the CH_4 is formed solely during the high temperature CO + H_2 peak. Hence, the CH_4 could be formed with either σ-OH or $H_2(g)$ acting as the source of H and either carbonyl ligands or CO(g) as the source of C. To differentiate between adsorbed species (which had never been in the gas phase) and gaseous precursors, the flow rate (F) of the He sweep gas was varied. If only adsorbed species are involved, then the quantity of methane formed should be independent of F. However, if gas-phase species are involved, then the amount of CH_4 formed will vary as $1/F^m$, where m is the overall order of the reaction, since the partial pressures of CO(g) and $H_2(g)$ are proportional to $1/F$. The data in Table II show that the amount of CH_4 formed is independent of F and hence independent of the reactant pressures. Since a zero-order reaction in H_2 at the high temperatures and very low H_2 pressures of these systems is extremely unlikely,[5,18] it

Table II. Effect of Sweep Gas on Methane Evolution during TPDE to 600 °C of $Mo(CO)_6/Al_2O_3$

sweep gas	flow rate, cm^3/min	CH_4/Mo
He	10	0.11
He	100	0.085
H_2	10	2.2
H_2	99	2.0

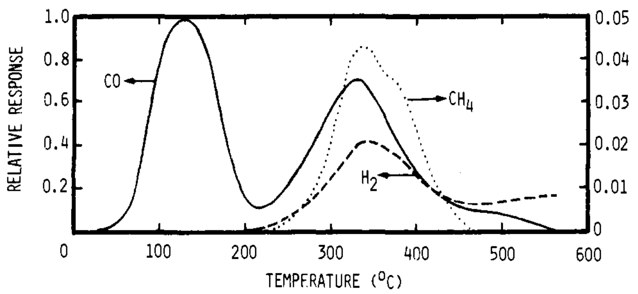

Figure 2. The TPDE in flowing He of $Mo(CO)_6/Al_2O_3$.

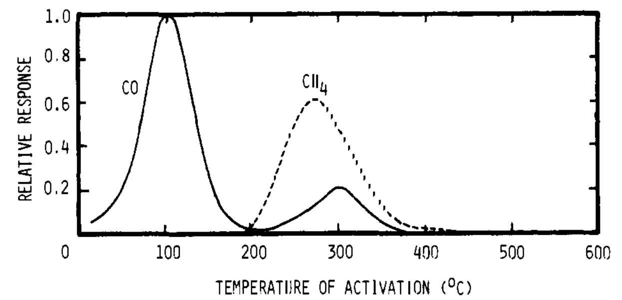

Figure 3. The TPDE in flowing H_2 of $Mo(CO)_6/Al_2O_3$.

is highly probable that *only adsorbed species are responsible for the formation for CH_4*.

TPDE in flowing H_2 affords a quasicatalytic reaction [the $H_2(g)$ functions as a normal reactant, but the only source of CO is the carbonyl] (Figure 3). As in the case with He as the sweep gas, the amount of CH_4 formed did not change significantly with nuclearity (1.4, 1.7, and 1.7 CH_4/M for mononuclear, dinuclear, and cluster complexes, respectively) even though the average amount of methane formed increased ~30-fold.[20] CH_4 formation again varies linearly with loading (Figure 1) and is independent of flow rate (Table II), again suggesting reaction at mononuclear sites and only involving adsorbed species. Hydrogenation apparently did not proceed via the Boudouard reaction

$$2CO = C_{ads} + CO_2 \qquad (6)$$

followed by hydrogenation of Cads since an average of only $0.1 CO_2/Mo$ was detected in these experiments. It is also unlikely that hydrogenation was preceded by dissociation of the CO since, in the absence of H_2, CO(g) is evolved at a similar temperature. These results and the similarity of the TPDE spectra in carriers of He and H_2 strongly suggest the *direct hydrogenation of carbonyl ligands*.

Activation of $Mo(CO)_6/Al_2O_3$ at 100 °C in flowing He is known to result in the evolution of 3.00 CO/Mo and the quantitative formation of $Mo(CO)_3$ads which is probably *molecularly* isolated on the surface.[17,21,22] A salient feature supporting this description is the steric requirement of the reversible reaction[22]

$$Mo(CO)_5ads \rightleftarrows Mo(CO)_3ads + 2CO(g) \qquad (7)$$

The TPDE in flowing H_2 of $Mo(CO)_3$ads is shown in Figure 4. When this was compared with Figure 3, it is clear that CH_4 formation was not affected and in fact ~73% of the carbonyl ligands of this stoichiometrically well-defined, *mononuclear species* were hydrogenated to CH_4 before they could desorb as CO(g). Although hydrogenation of carbonyl-like intermediates has long been considered a possible step in methanation (and Fischer-Tropsch synthesis),[23] to our knowledge this is the first demonstration of this reaction,[24] a significant new feature being the requisite thermal stability of supported subcarbonyl species compared with the lower temperature decomposition of the bulk carbonyls.[11,26] By adding He or CO to the H_2 carrier gas it is also now found that the quantity of CH_4 formed is approximately first order in $H_2(g)$ and zero order in CO(g). Further, alternating pulses of H_2 and D_2 at 225 °C over a catalyst prepared by heating $Mo(CO)_6/Al_2O_3$ at 225 °C in He shows no kinetic isotope effect. These kinetics are the same as usually found for catalytic methanation[5,27] suggesting possible similarities in mechanism although we have no definitive information on this point.

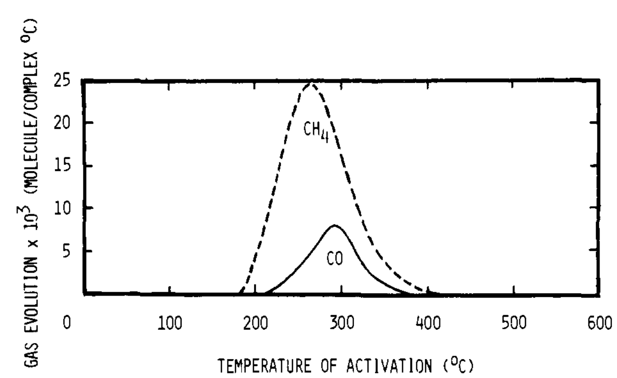

Figure 4. The TPDE in flowing H_2 of $Mo(CO)_3(ads)$.

Photolysis of $Mo(CO)_6/Al_2O_3$ at 30 °C in flowing H_2 results in a remarkable and selective reaction: the evolution of ~3CO/Mo followed by nearly pure CH_4. (The catalyst is very active for the hydrogenation of ethylene.[26]) At this temperature sintering is especially unlikely since the surface species are probably molecularly isolated at 100 °C.[17] These data strongly support the results of the thermal studies suggesting that the ligands in $Mo(CO)_3$ads are highly active for methane formation and reaction is occurring on mononuclear sites.

Our results suggest a novel reaction sequence for catalytic methanation:

$$M + CO \rightarrow M(CO)ads \qquad (8)$$

$$4\sigma\text{-}OH + M(CO)ads \rightarrow MO_3 + 2\sigma\text{-}O^- + CH_4 \qquad (9)$$

$$3H_2 + MO_3 \rightarrow M + 3H_2O \qquad (10)$$

$$2H_2O + 2\sigma\text{-}O^- \rightarrow 4\sigma\text{-}OH \qquad (11)$$

$$CO + 3H_2 \rightarrow CH_4 + H_2O \qquad (12)$$

Reactions 8, 10, and 11 are well known. Reaction 9 simply expresses the known stoichiometry of CH_4 formation during the TPDE of carbonyls in flowing He.[28] Reaction 9 presumedly represents a sequence of steps which would cycle with reactions equivalent to 10 and 11 so that M only gets slightly oxidized during reaction. A unique feature of this scheme is that CH_4 is formed by reaction with σ-OH, the role of the H_2 being to rereduce the metal. High reactivity for catalytic methanation of $Mo(CO)_6$ and $W(CO)_6$ supported on Al_2O_3 has also been discovered, the activities being roughly 100-fold higher than for analogous "traditional"[15] heterogeneous catalysts.[29] However, we currently do not know if the catalytic species remain mononuclear under reaction conditions.

Acknowledgment. Support of this research by the Department of Energy is gratefully acknowledged.

References and Notes

(1) Muetterties, E. L. *Science* **1977,** *196*, 839.
(2) Thomas, M. G.; Beier, B. F.; Muetterties, E. L. *J. Am. Chem. Soc.* **1976,** *98*, 1296.
(3) Grubbs, R.; Lau, C. P.; Cukier, R.; Brubaker, C., Jr. *J. Am. Chem. Soc.* **1977,** *99*, 4517.
(4) Wender, I.; Pino, P. "Organic Synthesis Via Metal Carbonyls"; Interscience: New York, 1968; Vol. 1, Chapter 1.
(5) Vannice, M. A. *J. Catal.* **1975,** *37*, 449.
(6) The most active cluster complex, $Ir_4(CO)_{12}$, had a turnover frequency of $N = 1 \times 10^{-5}$ s^{-1} at 140 °C.[2]
(7) C_2H_4 and H_2 (0.5 atm each) were added to an ampule containing 2 cm^3 of toluene and 50 mg of complex before heating; the turnover frequency was $<10^{-9}$ s^{-1}. CO(g) may inhibit reaction. However, activation of $Mo(CO)_6$ in toluene near 140 °C with removal of CO followed by treatment at 90 °C also gave no reaction (turnover frequency $<10^{-8}$ s^{-1}).
(8) Wrighton, M. S.; Schroeder, M. A. *J. Am. Chem. Soc.* **1973,** *95*, 5764. The turnover frequency for the hydrogenation of monoolefins is apparently $<10^{-5}$ s^{-1}.
(9) Wrighton, M. S.; Ginley, D. S.; Schroeder, M. A.; Morse, D. L. *Pure Appl. Chem.* **1975,** *41*, 671.
(10) Brenner, A.; Hucul, D. A.; Hardwick, S. J. *Inorg. Chem.* **1979,** *18*, 1478.
(11) Brenner, A.; Hucul, D. A. *Inorg. Chem.* **1979,** *18*, 2836.
(12) Brenner, A. *J. Mol. Catal.* **1979,** *5*, 157.
(13) Brenner, A.; Hucul, D. A. *J. Catal.*, **1980,** *61*, 216.
(14) Turnover frequencies are between 0.1 and 5 s^{-1} at 25 °C for the hydrogenation of ethylene.
(15) A "traditional" catalyst is made by impregnation with an aqueous solution of the appropriate metal salt followed by calcination and reduction.
(16) Massoth, F. E. *J. Catal.* **1973**, *30*, 204.
(17) Brenner, A.; Burwell, R. L., Jr. *J. Catal.* **1978,** *52*, 353.
(18) Even at subambient temperatures and several hundred Torr of H_2, the hydrogenation of ethylene remains about first order in H_2.[19]
(19) Bond, G. C. "Catalysis by Metals"; Academic: New York, 1962; Chapter 11.
(20) Experiments were done as those given in Table I except to avoid possible complications from hydrogenolysis of residual pentane all runs [except for $V(CO)_6$ and $Fe(CO)_5$] were done as dry mixes and neither $Ni(CO)_4$ nor $Co_4(CO)_{12}$ have been run in H_2.
(21) Burwell, R. L., Jr.; Brenner, A. *J. Mol. Catal.* **1976,** *1*, 77.
(22) Brenner, A.; Burwell, R. L., Jr. *J. Am. Chem. Soc.* **1975,** *97*, 2565.
(23) Anderson, R. B. *Catalysis* **1956,** *4*, 29.
(24) Hydrocarbon synthesis has been reported for several carbonyl cluster complexes supported on hydroxylated alumina and heated for several hours at ~300 °C in closed ampules.[25] The H_2(g) is supplied by the water gas shift reaction [the H_2O(g) is produced by heating the hydroxylated Al_2O_3]. In this system the long contact times do not allow one to either identify the primary reaction products or discriminate between hydrogenation of subcarbonyl species or reaction with CO(g).
(25) Smith, A. K.; Theolier, A.; Basset, J. M.; Ugo, R.; Commereuc, D.; Chauvin, Y. *J. Am. Chem. Soc.* **1978,** *100*, 2590.
(26) Brenner, A., unpublished results.
(27) Dalla Betta, R. A.; Shelef, M. *J. Catal.* **1977,** *49*, 383.
(28) Direct measurements of oxidation state for several supported carbonyls have established that for each mole of CH_4 formed during TPDE in He the metal is oxidized by six units [letting the oxidation state of C be 2, this is equivalent to the oxidation state of the four hydrogens changing from +1 (in σ-OH) to −0.5 (in CH_4)].[10,11,13,17]
(29) At 250 °C, $H_2/CO = 3$, and $P = 1$ atm; the initial turnover frequency for $Mo(CO)_6/Al_2O_3$ was 3×10^{-2} s^{-1} and $E_a = 92$ kJ/mol, giving an extrapolated activity of $N = 5 \times 10^{-5}$ s^{-1} at 140 °C.[30,26] For $W(CO)_6/Al_2O_3$, $N = 2 \times 10^{-3}$ s^{-1} at 250 °C.[28]
(30) Brenner, A.; Hucul, D. A. *Proc. Int. Conf. Chem. Uses Molybdenum, 3rd, 1979*, in press.

Alan Brenner,* Dennis A. Hucul
Department of Chemistry, Wayne State University
Detroit, Michigan 48202

Received September 17, 1979

Sequence Dependent Binding of *cis*-Dichlorodiammineplatinum(II) to DNA

Sir:

cis-Dichlorodiammineplatinum(II) (*cis*-DDP) is an anticancer drug of clinical importance.[1] The site of cytotoxic action of *cis*-DDP is generally believed to be DNA.[2] We previously reported that covalent binding of *cis*-DDP to DNA unwinds and shortens the double helix.[3] Here we present evidence that the drug binds selectively to the $(dG)_n \cdot (dC)_n$, $n \leq 4$, sequence in DNA and discuss a possible recognition site for this interaction.

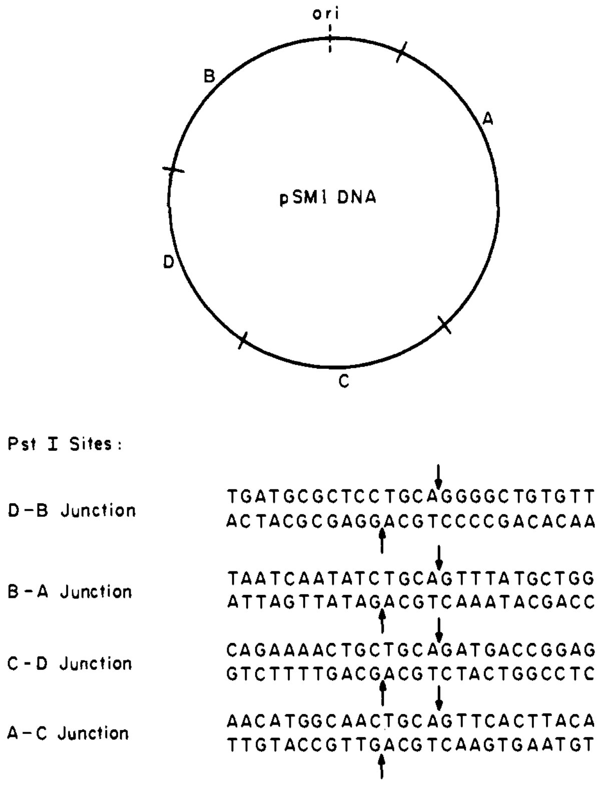

Figure 1. Map of bacterial plasmid pSM1 DNA showing the origin of replication (ori) and cleavage pattern by the restriction endonuclease Pst I. Fragments A, B, C, and D are 1.80, 1.60, 1.19, and 1.09 kilobases in length, respectively. The sequence of bases at each of the four cutting sites is also shown.

Closed and nicked circular pSM1 DNAs and *cis*-DDP were incubated at 37 °C in 5 mM NaCl, 1 mM sodium phosphate buffer (pH 7.4), as described previously.[3] The final concentration of *cis*-DDP was 0.023 mM and the formal ratio (r_f) of Pt to DNA phosphate was 0.075. At various times, samples were removed from the reaction mixture, brought to 0.2 M in NaCl, and frozen to stop the reaction,[3] and spin dialyzed[4] for subsequent analysis by restriction endonuclease cleavage, gel electrophoresis, and atomic absorption (AA) spectroscopy. The spin dialysis step removes unbound platinum and excess salt to facilitate restriction endonuclease cleavage and the determination of the mole ratio of platinum bound per DNA phosphate (r) by carbon arc AA spectroscopy.

The restriction endonuclease Pst I (New England Biolabs) cleaves the circular pSM1 DNAs at four sequence specific loci to produce four fragments designated A-D in order of decreasing size (Figure 1). The fragments are separable by agarose gel electrophoresis (Figure 2, control channels C). Cleavage of DNA that had been incubated with *cis*-DDP produces partially fragmented pieces that are readily identified on the gels because of their greater length. These partials include the four "dimers" BA, AC, DB, and CD and the four "trimers" DBA, BAC, ACD, and CDB (Figure 1), all of which eventually appear over the time course of the experiment (Figure 2). Since *cis*-DDP unwinds the double helix, it is not surprising that the Pst I enzyme would be unable to cut the platinated DNA. It is significant, however, that fragments B and D are the first to disappear over the incubation time course, concomitant with the appearance of the DB dimer on the gels (Figure 2). This result indicates that, at low levels of platination (t = 20 min, r = 0.004), the restriction endonuclease Pst I can cleave the DNA at three of the four normal cutting sites but not at the D-B junction.[5] At comparable binding levels, *trans*-dichlorodiammineplatinum(II) did not produce this effect.

Since all four cutting sites have the same six-base-pair se-