as ovalbumin (see Figure 2). The investigation of other 2-substituted bisalkylating quinonediimides (2-chloro, MeO and CF_3) having different redox potentials has so far revealed no advantages. However, this redox reaction does not appear to be a major drawback to cleavage of reduced, denatured proteins, where fragments may be easily separated from oxidized proteins. In addition, preliminary data suggest this redox pathway may be controlled by radical chain inhibitors such as 2,6-di-*tert*-butylphenol.

Further corroboration of the selectivity of this reagent was observed by automated amino acid analyses of substrates treated with **1**.[12] Compared to samples treated under the same conditions without reagent, the destruction of cysteine (observed as $CySO_3H$) in peptide and proteins treated with **1** was as follows: *N*-acetylcysteine (48%); reduced glutathione (42%); ovalbumin (12%); and partially reduced bovine pancreatic ribonuclease[7] (50%). The conditions for oxidative hydrolyses of these proteins are quite strenuous (24–48 h at 110 °C, 6.2 N HCl, excess Me_2SO) and preclude the precise evaluation of nonspecific reagent interactions with certain residues such as histidine, tyrosine, serine, and methionine. However, homoserine from methionine alkylation and cleavage was not observed, and both lysine and arginine residues were unaffected by the reagent in these cases. We do know that certain tryptophan (indole) residues can react. They do not seem to give cleavage of the protein chain. Ammonia production (above that produced by substrate or reagent alone) was clearly observed in the analyses of each of the reaction mixtures. This observation, the model studies, and our negative attempts to dansyl label[13] new N-termini produced in the fragmentation of ovalbumin using **1** support dehydroalanine formation and hydrolysis as the predominant pathway of degradation. The formation of dehydroalanine residues from cysteine sulfonium species has been observed previously by Gross to be favored over amide bond participation at elevated temperatures and, therefore, is not unexpected with reagent **1** under the prescribed conditions (80 °C).[14] The advantage of our reagent is that it can be employed under mild acidic reaction conditions and thus suppress the complications (particularly lysinoalanine formation) observed when DHA residues are generated under strongly alkaline conditions.[15] Further, the fragmentation does not occur at methionine and the pyruvoyl peptide fragments produced by hydrolysis are amenable to sequence analysis.[16] We believe reagents such as **1** will have significant application in protein modification and structure determination.

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(7) Reduction of bovine pancreatic ribonuclease (Worthington) as described by F. H. White, Jr., *J. Biol. Chem.*, **235**, 383 (1960), provided an enzyme with six free sulfhydryl functions according to DTNB assay.
(8) Reaction mixtures were applied directly to gels after quenching with aqueous 1% SDS–1% 2-mercaptoethanol and adjusting the pH to the bromophenol blue endpoint with ammonium hydroxide solution. Relatively large quantities of protein were employed to detect low levels of cleavage. Ovalbumin reactions were analyzed according to K. Weber and M. Osborn, *J. Biol. Chem.*, **244**, 4406 (1969); ribonuclease reactions were analyzed on "Biophore Gels" (Bio-Rad Laboratories). A variety of stepwise and individual schemes may be optimized to yield better cleavage and/or separations. This procedure required minimal sample manipulation and was used to allow the identification of cleavage with a range of substrates. A methodology of pH 7 for the initial addition, G-25 Sephadex separation of protein at pH 5 and hydrolysis with *p*-toluene sulfonic acid (0.1 M) 80 °C, 10 min, is convenient if the initial trials show cleavage.
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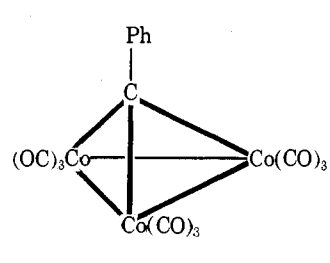
Metal Cluster Catalysis. 1. Hydroformylations of 1- and 2-Pentene Catalyzed by Two Cobalt Carbonyl Clusters: $Co_3(CO)_9(\mu_3\text{-}CC_6H_5)$ and $Co_4(CO)_8(\mu_2\text{-}CO)_2(\mu_4\text{-}PC_6H_5)_2$

Sir:

Muetterties' studies of acetylene[1,2] and butadiene[1] cyclizations, catalyzed by $Ni_4(CNR)_4(\mu_3\text{-}CNR)_3$, and the reduction of synthesis gas to methane[3] by $Ir_4(CO)_{12}$ and $Os_3(CO)_{12}$ (along with Roundhill's[4] oxidations of carbon monoxide and cyclohexane to carbon dioxide and adipic acid, respectively) has focused attention on the use of discrete metal clusters as models for heterogeneous metal catalysis.[5] However, few organometallic clusters have ever been reported as homogeneous catalysts,[5] and systematic studies of clusters under a variety of catalytic conditions do not exist. Thus, we present the results of 1- and 2-pentene hydroformylations[6] (eq 1) catalyzed by two cobalt carbonyl clusters: $Co_3(CO)_9(\mu_3\text{-}CC_6H_5)$, **1**,[7] and $Co_4(CO)_8(\mu_2\text{-}CO)_2(\mu_4\text{-}PC_6H_5)_2$, **2**.[8]



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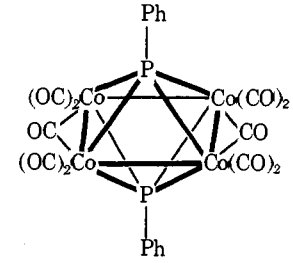


2

Hydroformylation of 1- and 2-pentene to aldehydes in high yields[9] with a fairly high normal-to-branched selectivity[10] was achieved under mild conditions. In addition, the hydrogenation of 1- and 2-pentyne and 1- and 2-pentene was effected.[11] Clusters **1** and **2** were recovered, unchanged,[12] in high yields from these reactions. Since **1** is bonded together by carbon-

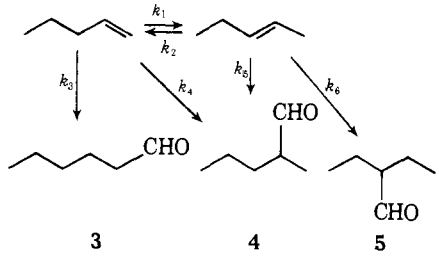
Table I. Hydroformylations of 1- and 2-Pentene Catalyzed by $Co_3(CO)_9(\mu_3\text{-}CC_6H_5)$, **1**, and $Co_4(CO)_8(\mu_2\text{-}CO)_2(\mu_4\text{-}PC_6H_5)_2$, **2**

Catalyst[a]	Substrate	Temp (°C)	Pressure[b] (psig)	Yield[c] (%)	Time (h)	Selectivity (3/4 + 5)
1	1-Pentene	90	875–800	57.5	104.0	5.4
		110	480–400	96.4	25.8	2.5
		110	715–620	92.7	49.5	3.8
		110	935–840	98.5	39.0	4.2
		110	1140–1040	94.2	32.5	4.7
		130	900–780	99.7	22.0	2.2
2	1-Pentene	130	490–420	65.0	63.5	1.5
		130	690–630	62.5	88.0	2.6
		130	900–805	100	23.0	2.7
		150	720–625	84.2	23.5	1.9
1	2-Pentene	110	230–150	83.1	26.0	0.8
		110	510–395	99.8	77.5	1.0
		110	705–635	82.2	44.0	1.1
		110	900–820	94.2	53.5	1.1
		130	270–150	98.7	47.5	0.7
		130	480–390	100	21.0	0.9
		130	735–635	100	18.0	1.1
		130	950–850	91.9	19.0	1.2
		130	1160–1020	99.3	50.8	1.1
2	2-Pentene	130	515–430	87.4	72.0	1.2
		130	940–850	88.7	70.5	1.3
		150	1120–990	95.2	22.5	0.6

[a] **1** is $Co_3(CO)_9(\mu_3\text{-}CC_6H_5)$ and **2** is $Co_4(CO)_8(\mu_2\text{-}CO)_2(\mu_4\text{-}PC_6C_5)_2$. [b] Pressure range refers to initial and final pressures (±5%) at the reaction temperature. [c] Reference 9.

cobalt bonds, as well as cobalt–cobalt bonds, and since **2** involves two C_6H_5P bridges, in addition to cobalt–cobalt bonds, these clusters cannot easily dissociate to give mononuclear cobalt centers. Dissociation of a metal fragment from either **1** or **2** would thereby lead to cluster decomposition. Furthermore, some hydroformylations were performed at milder conditions than those commonly required for $Co_2(CO)_8$. Taken together, this evidence is strongly indicative of catalysis by the intact cluster.

Representative 1-pentene hydroformylations are summarized in Table I. The normal **5**-to-branched (**3** and **4**) selectivity



(1)

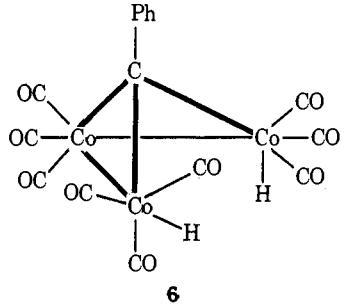
3 **4** **5**

was fairly high for catalysis by both clusters **1** and **2**.[13] A selectivity of 5.4 (90 °C, 840 psi 1:1, H_2:CO) was given by **1** vs. 2.7 (130 °C, 850 psi 1:1, H_2:CO) for **2**.[14] At equal pressures, the selectivity decreased as temperature increased when using either **1** or **2**. For example, the selectivity decreased from 5.4 to 2.2 for **1** as temperature increased from 90 to 130 °C at 840 psi. Similar decreases in selectivity with increasing temperature were reported for the hydroformylation of 1-pentene[15] and 1-hexene[16] with $Co_2(CO)_6(PR_3)_2$ catalysts (where R = alkyl or aryl). In those studies the catalytically active species was thought to be $HCo(CO)_3(PR_3)$.[16,17]

Selectivity increased with an increase in pressure with either **1** or **2** (Table I). For example, selectivity increased from 1.5 (455 psi) to 2.7 (850 psi) with **2** at 130 °C. Similarly, an increase in selectivity from 2.5 (440 psi) to 4.7 (1090 psi) at 110 °C was observed with **1**. A slight increase in selectivity with pressure has previously been observed for $Co_2(CO)_6(PR_3)_2$,[16] while decreases in selectivity occur with increasing pressure for $RhH(CO)(PR_3)_3$[18,19] and its polymer-anchored analogues.[19]

Starting with 1-pentene, product distribution studies as a function of conversion showed that significant amounts of 2-pentene were formed (30% of the remaining olefin was 2-pentene at 110 °C and 1000 psi after a 94.2% conversion with cluster **1** and 11% at 130 °C and 600 psi at 62.5% conversion with **2**).[20] Hydroformylation of the terminal double bond was faster than the internal isomer for **1** and **2**. Thus, if isomerization were fast, a selective route to terminal double bond hydroformylation from internal olefins could result. However, isomerization was not notably rapid. Thus, hydroformylations of 2-pentene did not yield more than 60% of **3** with either **1** or **2** as catalysts.

Hydroformylations of 2-pentene (Table I) gave more than 50% terminal product under a variety of temperatures and pressures with either of the clusters. Small increases in terminal



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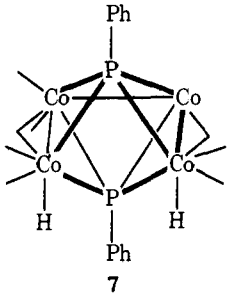

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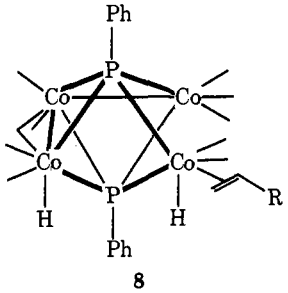

8

selectivity occur with an increasing pressure, while increasing temperature causes small selectivity decreases for both **1** and **2**. A selectivity of 56% terminal product, using **2** at 900 psi and 130 °C, is quite high when compared to recent patent claims using rhenium catalysts.[21]

Hydroformylations catalyzed by **1** and **2** are encouraging, not only because they are fairly selective but also because they are easily prepared,[7,8] relatively cheap, and air stable even in solution. Air-sensitive mononuclear cobalt[15,16,22-24] and rhodium[18,19,25-27] catalysts have now been widely studied.

In general, selectivity and reactivity may be varied greatly by the addition of phosphine or other ligands. Studies of the effect of added phosphine and cluster concentration on selectivity, reactivity, and cluster stability are underway.[28] Most importantly, these studies may shed light on possible catalytic mechanisms involving clusters that are not easily dissociated.[29] While it is not yet possible to provide definitive mechanistic information, the formation of intermediates such as **6**, **7**, and **8** is suggested.

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(9) Yields are based on pentene consumed. The major products were the linear aldehyde, **3**, hexanal, and two branched aldehydes, **4**, 2-methylpentanal, and **5**, 2-ethylbutanal. Only small amounts of pentane (≤3%) were formed during the reactions. The corresponding linear and branched alcohols were formed at higher temperatures but in small yields (≤8%) and only in trace amounts if the reaction was stopped before 100% of the pentene was consumed. The formation of high molecular weight compounds, presumably due to aldehyde condensation reactions, becomes noticeable at higher reaction temperatures and long reaction times.
(10) The ratio of hexanal, **3**, to 2-methylpentanal, **4**, and 2-ethylbutyral, **5**, was determined by analytical GLC on a 10 ft × ⅛ in. 20% Carbowax 20M/Chromosorb W column (programmed from 100 °C for 4 min to 130 °C at 16°/min) using electronic integration and normalization techniques.
(11) Both 1- and 2-pentyne are reduced at 90 °C and 400 psi hydrogen to a mixture of pentene and pentane with **2**. For example, 1-pentyne gave pentane (14%), 1-pentene (72%), and 2-pentene (14%) after 21 h at these conditions. The reduction of both 1- and 2-pentene is slow even at 140 °C and 400 psi where pentane was obtained in 89% (90 h) and 27% (40 h) from the 1- and 2-isomers, respectively. Fairly selective reduction of enzynes to dienes is thus possible.
(12) The melting point and IR spectra were identical.
(13) These reactions were carried out at constant volume. Thus, the pressure dropped during the reaction (see Table I).
(14) The pressure given refers to the average between the starting and final pressures observed.
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(29) Cluster catalysis has never been definitively proved. Clusters, generally, could reversibly dissociate, under catalytic conditions, to smaller fragments which, in turn, could catalyze the observed reaction. One method to prove catalysis by a cluster would be to synthesize a cluster which itself is optically active (e.g., $FeCoNi(CO)_9(\mu_3\text{-CR})$ where R = alkyl or aryl group. Here there are four different groups attached to the carbon bridging the cluster), then use the chiral cluster to carry out asymmetric catalytic reactions. If the product is optically active, then cluster catalysis is established.

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(Acetylacetonato)[(−)-*N*-alkylephedrinato]dioxomolybdenum, a New Class of Chiral Chelate Complexes Which Catalyze Asymmetric Epoxidation of Allylic Alcohol

Sir:

In asymmetric synthesis,[1] the use of an asymmetric catalyst is considered the most efficient way to minimize a loss of a precious chiral source. Although Wynberg et al.[2] have recently succeeded in asymmetric epoxidation of α,β-unsaturated ketones by employing chiral phase transfer agents as oxidation catalysts, no attempts have been made in the area of asymmetric epoxidations which can be catalyzed by chiral transition metal complexes.

While Sharpless et al.[3] have reported highly stereo- and regioselective epoxidation of allylic alcohols (**1**) by using achiral vanadium and molybdenum complexes as catalysts, we have now found, as shown in Scheme I, that **1** can be asymmetrically oxidized with cumene hydroperoxide, giving optically active epoxy alcohols (**2**), in the presence of chiral molybdenum catalyst, MoO_2 (acac)[(−)-*N*-alkylephedrinate] (**3**).[4]

Since the high stereo- and regioselectivity achieved by Sharpless et al.[3] are seemingly due to the coordination of **1** to the metal catalysts in the transition state, complexes such as **3**, which can fulfill the following two postulates, are expected to act as catalysts for asymmetric epoxidation of **1**: (a) the catalyst should contain the chiral ligand which behaves as a fixed ligand and does not dissociate from a central metal atom during a reaction; (b) the catalyst should contain two labile ligands both of which can be readily replaced by reactants under an influence of the fixed chiral ligand. We selected (−)-*N*-alkylephedrine (**4**) as ligands which fulfilled the former criterion because amine complexes of Mo had been known to be catalytically less active for epoxidation of olefins.[5] Acetylacetone was chosen as a replaceable ligand because $MoO_2(acac)_2$ was catalytically active for epoxidation of olefins.[6]

By employing our novel chiral complexes (**3**), it has become possible for the first time to produce **2** whose optical yields