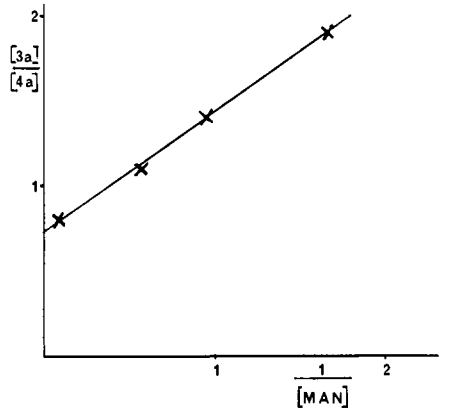
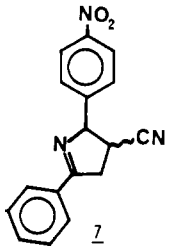


Figure 1.

or 1–5% EtOH, ruling out product dependence on radical chains, radical ions, intersystem crossing rates, or ionic intermediates. We propose that thermolysis of **1** (in the presence or absence of MAN) leads directly to the expected carbene **2** and that **2** reacts reversibly with MAN to yield a nitrile ylide intermediate (**6**).[13] In the presence of excess MAN this ylide may be captured by the double bond of a second MAN molecule to yield the stable diadduct **4a**. This process leading to adduct **4a** is in competition with the irreversible bimolecular cycloaddition of carbene **2** to MAN giving **3a**.

This mechanism is consistent with analogy, product ratio studies, and additional chemical evidence. Thus the formation of a halonium ylide during photolysis of diazo oxide **1** in the presence of 2,6-di-*tert*-butyl-4-bromophenol has been postulated.[14] Moreover, the regiochemistry of the trapping of our proposed ylide **6** by the acrylonitriles, to give **4a** or **4b**, conforms to that observed by Huisgen for the 1,3-dipolar addition of the electronically unsymmetrical benzonitrile 4-nitrobenzylylide to acrylonitrile yielding exclusively the regioisomer **7** (cis and trans).[15]



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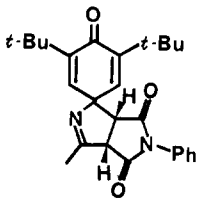

8

We have found that the molar product ratios ([**3a**]/[**4a**]) from thermolysis of **1** in MAN–heptane mixtures are proportional to 1/[MAN] as shown in Figure 1. These data give a linear plot of [**3a**]/[**4a**] vs. 1/[MAN] with an extrapolated intercept at 1/[MAN] = 0 of 0.7. Kinetic analysis of our proposed mechanism predicts that

$$\frac{d[3]/dt}{d[4]/dt} = \frac{k_3}{k_2} + \frac{k_{-2}k_3}{k_2k_4}(1/[MAN])$$

which should indeed be linear with 1/[MAN] and give a nonzero intercept corresponding to k_3/k_2. The observed variations of the product ratios with [MAN] are thus in accord with the suggested mechanism and clearly preclude the irreversible formation of **6** (which predicts [**3a**]/[**4a**] to be independent of [MAN]), as well as any alternative mechanism in which **3** and **4** mutually arise from some irreversibly formed 1:1 adduct by competing unimolecular vs. bimolecular closures (this would predict a zero intercept at 1/[MAN] = 0).

Compelling chemical evidence for the presence of the postulated nitrile ylide **6** derives from the reaction of carbene **2** in *acetonitrile solution containing a dipolarophile solute*. Thermolysis of **1** in CH_3CN at reflux or photolysis of **1** in CH_3CN at 15 °C in the presence of molar amounts of *N*-phenylmaleimide led in identical yields (48%) to a mixed diadduct shown by IR, ^1H NMR, and mass spectrometry to have the tricyclic spirodienone structure **8**.[16] We conclude that generation of carbene **2** in the presence of a saturated or unsaturated nitrile leads to a highly reactive nitrile ylide (cf. **6**) which can add to dipolarophiles. Although such chemistry will be more important for electrophilic carbenes, care must be taken in assuming that an aliphatic nitrile is an inert solvent for the spectroscopic studies of carbene structures and lifetimes.

Acknowledgment. We are grateful to Professor J. A. Kampmeier (University of Rochester) and Dr. R. Gallucci (General Electric Co.) for valuable discussions bearing on the reaction mechanism. Partial support of this work by Grant CA-11326 and postdoctoral fellowship CA-06787 (to B.H.T.) awarded by the National Cancer Institute, USPHS, is gratefully acknowledged.

Registry No. **1**, 955-02-2; **2**, 21205-90-3; **3a**, 82065-50-7; **3b**, 19510-09-9; **4a**, 82065-51-8; **4b**, 82065-52-9; methacrylonitrile, 126-98-7; acrylonitrile, 107-13-1.

Supplementary Material Available: Structure of **4a** and listings of positional and thermal parameters and of interatomic distances and angles (14 pages). Ordering information is given on any current masthead page.

(13) The half-lives for disappearance of **1** in heptane, in 10% MAN in heptane, and in neat MAN at 86 °C were found to be 30 ± 2, 35 ± 2, and 45 ± 3 min. These relatively small differences argue against the involvement of MAN in the decomposition of **1** (e.g., rate-determining formation of a pyrazoline) and are consistent with unimolecular formation of carbene **2** directly from **1**.

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(16) **8**: found *m/e* 418.2254 (M^+); ^1H NMR ($CDCl_3$) δ 1.18 (9 H, s), 1.23 (9 H, s), 2.22 (3 H, s), 3.20 (1 H, d, *J* = 8 Hz), 3.93 (1 H, d, *J* = 8 Hz), 5.88 (1 H, d, *J* = 3 Hz), 5.96 (1 H, d, *J* = 3 Hz), 7.15 (2 H, m), 7.35 (3 H, m); IR ($CHCl_3$) 1640, 1670, 1720 cm^{-1}; UV (hexane) λ_{max} 228 nm (ε 16 000). The ^{13}C NMR of **8** matches that of **4a** in appropriate respects. We thank Dr. T. Chang (Amer. Cyanamid Co.) for the high-resolution mass spectrum.

Synthesis and Electrophilic Reactivity of Dicarbonyl(cyclohexadienyl)nitrosylmanganese Cations

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Received February 1, 1982

A variety of nucleophiles are known[1] to add to the arene ring in (arene)$Mn(CO)_3^+$ to yield the corresponding cyclohexadienyl complex, from which the monofunctionalized arene can be obtained by oxidation or endo hydride abstraction in acid.[2] The addition of two nucleophiles to (arene)$Mn(CO)_3^+$ represents a possible route to difunctionalized 1,3-cyclohexadienes. Such double addition does not occur with most nucleophiles but is possible with strong hydride donors.[3,4] Double nucleophile addition to benzene has recently been shown[5] to occur with $(C_5H_5)Co(C_6H_6)^{2+}$, although in this case the usefulness is limited due to side reactions and the ready displacement of benzene by many nucleophiles.

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Table I. ^{1}H NMR[a] and IR Data for Cyclohexadienyl Complexes $[(C_6H_6R)Mn(CO)(NO)(L)]PF_6$[b]

R	L	ν_{CO}, cm^{-1}	ν_{NO}, cm^{-1}	H(3)	H(2,4)	H(1,5)	H(6)	CH_3
C_6H_5	CO	2111, 2078[c]	1843	6.99 (t, J = 6 Hz)[d]	6.22 (t, J = 6 Hz)	5.05 (t, J = 6 Hz)	4.22 (t)	
				7.6[e]	6.5 (t)	5.3 (t)	4.35 (t)	
CH_3	CO	2109, 2073[c]	1840	6.98 (t)[d]	6.02 (t)	4.81 (t)	2.94 (m)	0.78 (d, J = 6)
				7.3[e]	6.4	5.1	3.1	
CH_3	$P(OMe)_3$	2041[f]	1793	5.73 (q)[g]	5.35 (m)	3.75 (m)	2.60 (q)	0.64 (d, J = 6)
					5.04 (t)	3.56 (t)		3.83 (d, J = 11)

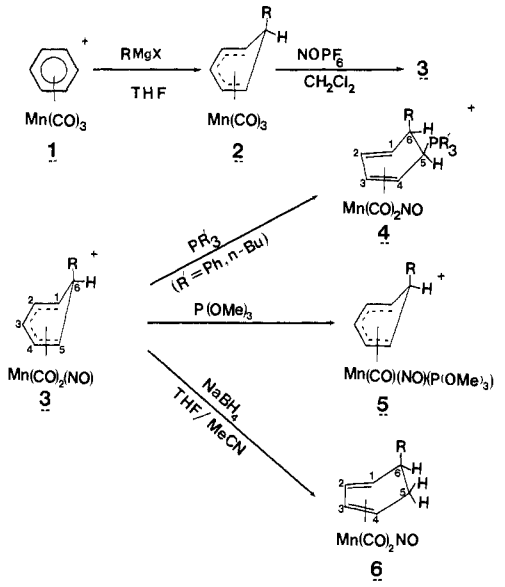
[a] δ scale. [b] Satisfactory elemental analysis was obtained for these compounds. [c] In CH_3NO_2. [d] In CD_3NO_2. [e] In CD_3COCD_3; slow decomposition occurs. [f] In CH_2Cl_2. [g] In CD_2Cl_2.

Table II. ^{1}H NMR[a] and IR Data for Cyclohexadiene Complexes 4 and 6[b]

R	nucleophile	ν_{CO}, cm^{-1}	ν_{NO}, cm^{-1}	H(2,3)	H(1,4)	H(6)	5-endo H	5-exo H	CH_3
CH_3	PPh_3	2047, 1998[c]	1761	5.66 (t)[d]	3.07	3.26	4.20 (t, J = 12 Hz)		0.83 (d, J = 7 Hz)
				5.55 (t)					
CH_3	$P(n\text{-}Bu)_3$	2043, 1992[c]	1755	5.76[d]	2.94	2.78	3.26		1.21 (d, J = 6 Hz)
				5.65					
C_6H_5	PPh_3	2048, 1999[c]	1762	5.85[d]	3.2	4.17	4.7		
CH_3	BH_4^-	2033, 1985[e]	1749	4.86 (t, J = 5.5 Hz)[f]	2.65 (m)	1.83 (m)	1.75 (m, J = 15,	1.01 (dm,	0.63 (d, J = 7 Hz)
				4.74 (t, J = 5.5 Hz)			10.5, 4 Hz)	J = 15)	
C_6H_5	BH_4^-	2035, 1987[e]	1750	4.96 (t, J = 5.5 Hz)[f]	2.76 (m)	3.06 (dt,	2.07 (m, J = 15,	1.58 (dm,	
				4.82 (t, J = 5.5 Hz)		J = 11, 3, 3)	11, 4 Hz)	J = 15)	

[a] δ scale. [b] Satisfactory elemental analysis was obtained for these compounds. [c] In CH_2Cl_2. [d] In CD_2Cl_2. [e] In hexane. [f] In C_6D_6.

Scheme I



Our strategy to effect the difunctionalization of coordinated arenes involves single nucleophile addition followed by reactivation of the cyclohexadienyl ring and then reaction with a second nucleophile, which need not be the same as the first. Reaction of $(C_6H_6)Mn(CO)_3^+$ (**1**) with Grignard reagents produced[2] high yields of the cyclohexadienyl complexes **2** (R = CH_3, C_6H_5). Compounds **2** were stirred with a stoichiometric amount of $NOPF_6$ in CH_2Cl_2 (N_2, 25 °C, 15 min), to give nearly quantitative yields of $[(C_6H_6R)Mn(CO)_2NO]PF_6$ (**3**, Scheme I). Interestingly, the same reaction with $(C_6H_6)Cr(CO)_3$ gives[6] only trace amounts of $(C_6H_6)Cr(CO)_2NO^+$. Table I gives the ^{1}H NMR (250 MHz) and IR data for compounds **3**.

The cyclohexadienyl ring in **2** is at best very weakly electrophilic, but the ring in **3** is readily attacked by nucleophiles to give coordinated dienes. Thus a slurry of **3** in CH_2Cl_2 rapidly reacts with tertiary phosphines to give a solution of the phosphonium salt **4**. Addition of ethyl ether precipitated the products. Table II gives ^{1}H NMR and IR data. $P(OMe)_3$ reacted with **3** (R = CH_3) to yield a mixture of **4** and **5**, as judged from IR spectra. An analytically pure sample of **5** (R = Me) was obtained by chromatography through alumina and is characterized in Table I. Phosphine addition to **1** has been studied previously,[7] and a comparison with results presented herein shows that the ring in **3** is more electrophilic than in **1** in a thermodynamic sense. For example, the relatively weak base triphenylphosphine does not add to **1** but readily adds to **3**. Similarly, the equilibrium constant for tri-*n*-butylphosphine addition is small[7] with **1** and semiquantitatively determined to be much greater with **3**.

Hydride addition to **3** was effected by adding $NaBH_4$ to a solution of **3** in THF/CH_3CN (2:1) at −5 °C. Solvent evaporation, pentane extraction, and elution with ethyl ether through neutral alumina gave pure products **6** (see Scheme I, Table II). The ^{1}H NMR spectrum of **6**, Figure 1, is typical[5,8-15] for a coordinated

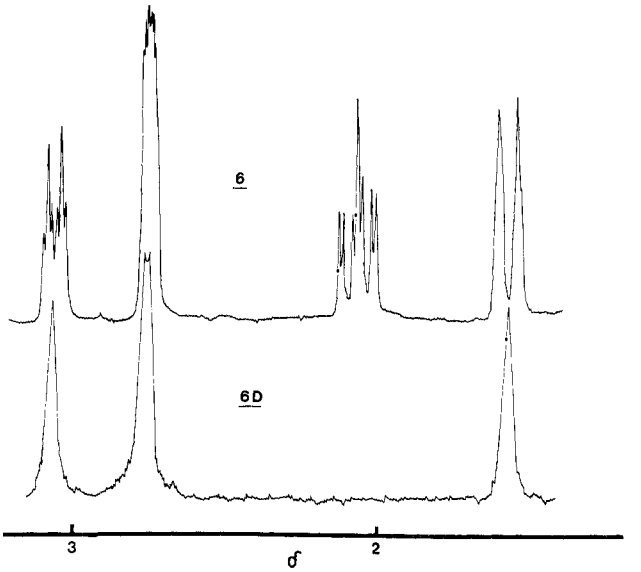


Figure 1. ^{1}H NMR spectra (250 MHz) in C_6D_6 of dicarbonyl(1–4-η-6-*exo*-phenylcyclohexa-1,3-diene)nitrosylmanganese (**6**) and the deuterated analogue (**6D**).

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cyclohexadiene. Generally in cyclic π-hydrocarbon complexes such as **6** the 5-exo hydrogen appears as a doublet at higher field than 5-endo H, which shows a more complicated splitting pattern due to coupling to the olefinic hydrogens as well as 5-exo H. For compounds **6** one also expects[16] the vicinal coupling between 5-endo H and H-6 to be quite large and that between 5-exo H and H-6 to be small. Coupling of 5-exo H to the olefinic hydrogens should be small because of its nearly perpendicular orientation. For example, Figure 1 shows that for **6** ($R = C_6H_5$), J (5-exo H, 5-endo H) = 15 Hz, J (5-endo H, H-6) = 11 Hz, and J (5-endo H, H-4) = 4 Hz. Only the 15-Hz coupling could be resolved with 5-exo H.

Much to our surprise the preparation of **6** ($R = C_6H_5$) using $NaBD_4$ gave endo addition of deuteride (**6D**). Figure 1 shows that the 5-endo H is absent in the deuteride; the same result was obtained with **6D** ($R = CH_3$). The coupling constant arguments given above make it highly unlikely that the NMR assignments of 5-exo H and 5-endo H are incorrect. In particular the collapse of the 11-Hz coupling in the H-6 resonance in the deuteride is strong evidence that the addition was endo. $^2H\{^1H\}$ spectra of **6D** ($R = CH_3$, C_6H_5) confirmed that the selectivity was 100%, with no exo product being formed. Since at equilibrium the distribution of exo and endo deuteride should be near 1:1, it follows that the observed results refer to the kinetic product. Endo addition of nucleophiles to coordinated cyclic π hydrocarbons is very unusual. There are reported examples of initial exo products that can transform to endo species upon standing,[17,18] and some complexes of Pt(II) and Pd(II) are known to undergo endo addition via an initial ligand displacement step followed by migration to the ring.[19–21] Borodeuteride addition to (tropylium)$Mo(CO)_3^+$ is reported to yield a mixture of exo and endo products, with the exo predominating.[22,23] To our knowledge, the reaction reported herein is the first example of exclusive endo addition as the kinetic product. Experiments are underway to search for the obvious possible intermediates in this reaction, i.e., a species containing a M–H or M–CHO bond.

The phosphine nucleophiles reported in this study are believed to add exo as shown in **4**. Proof of this must await X-ray structure determination but is strongly indicated by the similarities in the NMR spectra to other coordinated cyclohexadiene phosphonium complexes.[15,24] The complexes **4** generally gave somewhat broadened NMR resonances due to trace paramagnetic impurities, but the complex **4** ($R = CH_3$; $PR_3' = PPh_3$) showed a well-resolved spectrum (Table II) with H-5 split into a triplet. This triplet probably arises from coupling of H-5 to phosphorus (J = 12 Hz) and to H-6 ($J \approx 12$ Hz). Thus, the reasoning given above to show that deuteride adds endo suggests that PPh_3 adds exo, as expected.

In conclusion, this communication shows that double nucleophile addition to coordinated arene is facile provided the hydrocarbon ring is reactivated by substitution of CO by NO^+ after the first nucleophile addition. The second addition is regioselective and stereoselective, with borodeuteride forming the endo product exclusively while other nucleophiles form exo products. Preliminary results show that simple carbanions such as $CH(CO_2Me)_2^-$ readily add to **3**, suggesting that the procedures reported herein may find usefulness in organic synthesis. X-ray structural determinations of **2**, **3**, and **4** are in progress.[25]

Acknowledgment. Valuable discussions with Dr. S. D. Ittel and Professor P. G. Williard are gratefully acknowledged. This work was supported by a grant from the National Science Foundation (No. CHE-8023964).

Registry No. 3 ($R = C_6H_5$), 81971-52-0; **3** ($R = CH_3$), 81971-54-2; **4** ($R = CH_3$; $PR_3' = PPh_3$), 81971-56-4; **4** ($R = CH_3$; $PR_3' = P(n\text{-}Bu)_3$), 81971-58-6; **4** ($R = C_6H_5$; $PR_3' = PPh_3$), 81987-39-5; **5** ($R = CH_3$), 81971-60-0; **6** ($R = CH_3$), 81971-61-1; **6** ($R = C_6H_5$), 81971-62-2.

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Equilibrium and Kinetic CO Binding Parameters of T- and R-State Hemoglobin Chains Using Iron–Manganese Hybrids

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Received March 12, 1982

An understanding of hemoglobin (Hb) cooperativity requires knowledge of the protein's ligand affinity and binding rates, both in its low affinity (T) and high affinity (R) forms.[1] However, only indirect determinations of T-state CO binding properties have been available to date,[2–4] and there are no measurements of CO binding to the individual chains within R-state Hb. We report here the first directly obtained values of the CO affinities and on and off rate constants for CO binding to the individual chains within T- and R-state HbA. Comparison of the T- and R-state parameters gives unambiguous values for the amount by which the T state lowers the affinity of a chain, as well as for the relative contributions of the on and off rates in achieving the affinity reduction. The results, along with our recent kinetic study,[5] provide a complete set of parameters with which those of model compounds can be compared.[6]

We have measured CO binding to the ferrous iron subunits within mixed-metal [Mn, Fe] hybrid hemoglobins.[7] T-state hemoglobin binding parameters are obtained through the use of [Mn^{II}, Fe^{II}] hybrids, whereas the R-state parameters are obtained from the [Mn^{III}, Fe^{II}] hybrids. In both valency states of the hybrids the two ferrous iron chains bind CO, but the manganese-containing chains do not. Structural[8] and functional[9–11]

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