single H → K substitutions to give unambiguous **HX$_3$H** (H29 → K), **HX$_5$H** (H27 → K), or **HXH** (H23 → K) metal-binding sites (the latter does not correspond to a pattern observed in nature). The metal-binding properties of these peptides were investigated by visible absorption (Co^{2+} complexes) and ^{1}H NMR (Zn^{2+} complexes) spectroscopy as follows. (i) The tetrahedral Co^{2+} ligand fields of the native and **HX$_3$H** peptides are identical, as indicated by d–d and thiolate charge-transfer transitions in their visible absorption spectra; these transitions differ from those of the **HX$_5$H** and **HXH** peptides (Figure 2A,B). (ii) Analysis of the thermodynamic stabilities of the peptide/Co^{2+} complexes by optical pH titration (Figure 2C) demonstrates that the native and **HX$_3$H** analogue are equally stable (pH midpoint approximately 6.2); the **HX$_5$H** analogue is significantly less stable (pH midpoint 6.8). The nonnative **HXH** analogue is least stable (pH midpoint 7.1) and is not to be considered further. (iii) The ^{1}H NMR spectrum of the native domain is essentially identical to that of the **HX$_3$H** analogue, whereas marked differences are observed in the ^{1}H NMR spectrum of the **HX$_5$H** analogue (Figure 2D). These results demonstrate that EBP-1 adopts an **HX$_3$H** structure rather than the **HX$_5$H** structure expected on the basis of sequence homologies.[13]

The Zn finger motif[1] provides a model of a sequence "template" that encodes a characteristic structure.[2-5] To define rules that relate sequence to structure, we and others have undertaken comparative studies of variant domains.[8,9] In this communication we have focused on alternative ligand spacings **HX$_3$H** and **HX$_5$H**, which (upon binding Zn^{2+}) encode a helical or looplike structure, respectively (Figure 1). The "ambiguous" metal-binding site (HX$_3$HXH) in a **HX$_5$H** gene family[13] is shown to follow the general Zn finger consensus (**HX$_3$H**) rather than that of homologous **HX$_5$H** domains. Ligand selection in this case may be rationalized by the presence of three peptide hydrogen bonds in a presumed **HX$_3$H**-associated 3_{10} helix that are absent or attenuated in the **HX$_5$H**-associated loop, as inferred from detailed comparison of representative NMR structures (Figure 1[16]). Such a mechanism would reflect the general thermodynamic coupling between metal binding and peptide folding.

Acknowledgment. We thank P. E. Wright for the coordinates of ref 3 and G. M. Glore and A. M. Gronenborn for the coordinates of ref 5. This work was supported by grants to M.A.W. from the NIH, the American Cancer Society, and Pfizer Scholars Program. M.A.M. is an NSF Predoctoral Fellow.

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(16) Possible hydrogen bonds were evaluated in the NMR structures shown in Figure 1 with the program XPLOR (Brunger, A. T. Yale University), which uses the CHARMM empirical energy function as described: Brooks, B. R.; Bruccoleri, R. E.; Olafson, B. O.; States, D. J.; Swaminathan, S.; Karplus, M. *J. Comput. Chem.* **1983**, *4*, 187-217.

Efficient Low-Temperature Thermal Functionalization of Alkanes. Transfer-Dehydrogenation Catalyzed by Rh(PMe$_3$)$_2$Cl(CO) in Solution under a High Pressure Dihydrogen Atmosphere

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The ability of soluble, low valent transition metal complexes to activate alkane carbon–hydrogen bonds has attracted intense interest for the past decade.[1,2] While numerous systems have been developed that undergo stoichiometric reactions with C–H bonds, progress toward the goal of catalytic alkane functionalization has been much more limited.[2] Dehydrogenation systems involving sacrificial hydrogen acceptors (transfer-dehydrogenation) represent one of the few reported classes of homogeneous alkane functionalization catalysts; however, they have hitherto displayed limited efficiency (under 70 turnovers) and have required severe reaction conditions (e.g., several days at 150 °C) to yield more than ca. 10 turnovers.[3-5]

Recently it was reported that RhL$_2$Cl(CO) (**1**; L = PMe$_3$) photochemically catalyzes alkane dehydrogenation with unprecedented efficiency.[6-8] Ford has shown that the major photoreaction of **1** is loss of CO and that the resulting fragment, RhL$_2$Cl, inserts into alkane C–H bonds.[9] Our photokinetic investigation of this system revealed that CO loss is the *only* photochemical step driving this uphill reaction; subsequent steps are thermal (nonphotochemical) and may be expressed as eqs 2a and 2b (each equation represents a multistep process).[7] The enthalpy of eq

$$\mathrm{RhL_2Cl(CO)} \xrightarrow{h\nu} \mathrm{RhL_2Cl} + \mathrm{CO} \tag{1}$$

$$\mathrm{RhL_2Cl} + \text{alkane} = \mathrm{RhL_2ClH_2} + \text{alkene} \tag{2a}$$

$$\mathrm{RhL_2ClH_2} + \mathrm{CO} = \mathrm{RhL_2Cl(CO)} + \mathrm{H_2} \tag{2b}$$

2 is the difference between the enthalpy of alkane dehydrogenation and that of Rh–CO bond dissociation. Given that disruption enthalpies of bonds between second-row transition metals and CO are less than 40 kcal/mol,[10] it might be expected that eq 2 is only slightly exothermic and therefore significantly reversible.[17] This

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(1) For reviews of alkane C–H bond activation by soluble, low valent transition metal complexes, see: (a) Bergman, R. G. *Science (Washington, D.C.)* **1984**, *223*, 902. (b) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (c) Halpern, J. *Inorg. Chim. Acta* **1985**, *100*, 41. (d) Jones, W. D.; Feher, F. J. *Acc. Chem. Res.* **1989**, *22*, 91 and ref 2.

(2) For a general review of homogeneous alkane functionalization with an emphasis on catalysis, see: *Activation and Functionalization of Alkanes*; Hill, C., Ed.; John Wiley and Sons: New York, 1989 and references therein.

(3) (a) Burk, M. J. Crabtree, R. H.; Parnell, C. P.; Uriarte, R. J. *Organometallics* **1984**, *3*, 816-817. (b) Burk, M. J.; Crabtree, R. H.; McGrath, D. V. *J. Chem. Soc., Chem. Commun.* **1985**, 1829-1830. (c) Burk, M. J.; Crabtree, R. H. *J. Am. Chem. Soc.* **1987**, *109*, 8025-8032.

(4) (a) Baudry, D.; Ephritikine, M.; Felkin, H.; Holmes-Smith, R. *J. Chem. Soc., Chem. Commun.* **1983**, 788-789. (b) Felkin, H.; Fillebeen-Khan, T.; Gault, Y.; Holmes-Smith, R.; Zakrzewski, J. *Tetrahedron Lett.* **1984**, *25*, 788-789. (c) Felkin, H.; Fillebeen-Khan, T.; Holmes-Smith, R.; Lin, Y. *Tetrahedron Lett.* **1985**, *26*, 1999-2000. (d) Cameron, C.; Felkin, H.; Fillebeen-Khan, T.; Forrow, N. J.; Guittet, E. *J. Chem. Soc., Chem. Commun.* **1986**, 801-802. (e) Sakakura, T.; Abe, F.; Tanaka, M. *Chem. Lett.* **1991**, 359-362.

(5) Thermal dehydrogenation (with no hydrogen acceptor) has been reported to be catalyzed by rhodium–phosphine complexes, although not with high efficiency, at elevated temperatures (e.g., 2.85 turnovers of cyclooctene from Rh(PPh$_3$)$_3$Cl after 48 h at 151 °C): Fujii, T.; Saito, Y. *J. Chem. Soc., Chem. Commun.* **1990**, 757-758.

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(8) Alkane photodehydrogenation has been previously reported for one other system: refs 3b,c.

(9) Spillet, C. T.; Ford, P. C. *J. Am. Chem. Soc.* **1989**, *111*, 1932-1933.

(10) For example, the first BDEs (kcal/mol) of the following second row metal carbonyls are as follows: Mo(CO)$_6$ (experimental,[11] 31.7; calculated,[12] 28.3); Ru(CO)$_5$ (experimental,[13] 27.9; calculated,[12] 21.9); Pd(CO)$_4$ (calculated,[12] 6.5). A lower limit of ca. 20 kcal/mol for the Rh–CO bond of Rh(PPh$_3$)$_2$(CO)Cl can be obtained from the fact that the equilibrium for the reaction $\mathrm{Rh(PPh_3)_3Cl + CO \rightleftharpoons Rh(PPh_3)_2(CO)Cl + PPh_3}$ lies very far to the right and from studies demonstrating that the Rh–P BDE of Rh(PPh$_3$)$_3$Cl is ca. 16 kcal/mol.[14-16] The Rh–CO bond of **1** is presumably stronger than that of Rh(PPh$_3$)$_2$(CO)Cl due to both steric and electronic factors.

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(12) Ziegler, T.; Tschinke, V.; Ursenbach, C. *J. Am. Chem. Soc.* **1987**, *109*, 4825-4837.

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Table I. Results of Reaction 3 with Various Saturated Hydrogen Donors and Unsaturated Acceptors[a]

satd substrate	hydrogen acceptor (concn, M)	dehydrogenated product (mol/mol of **1**)	hydrogenated product (mol/mol of **1**)
cycloheptane	norbornene (1.35)	cycloheptene (53)	norbornane (230)
cyclohexane	norbornene (1.35)	cyclohexene (1.7)	norbornane (330)
tetrahydrofuran	norbornene (1.35)	2,3-dihydrofuran (106) 2,5-dihydrofuran (18) furan (6)	norbornane (340)
n-hexane	norbornene (1.35)	hexenes (9.6)[b]	norbornane (250)
cyclooctane	norbornene (1.35)	cyclooctene (59)	norbornane (360)
cyclooctane	cyclohexene (1.58)	cyclooctene (106)	cyclohexane (360)
cyclooctane	cycloheptene (1.35)	cyclooctene (53)	cycloheptane (1400)
cyclooctane	*tert*-butylethylene (1.24)	cyclooctene (4)	*tert*-butylethane (60)
cyclooctane	ethylene (200 psi)	cyclooctene (12)	ethane

[a] Conditions: [**1**] = 0.4 mM; P_{H_2} = 1000 psi; 60 °C; 100-min reaction time. All products and concentrations determined by gas chromatography in comparison with authentic (commercial) samples. The identity of the cyclooctene and norbornane products from a run with cyclooctane substrate and norbornene acceptor was confirmed by GC/MS. [b] We have not yet successfully determined the isomeric distribution of the hexenes.

would imply that **1** might act as an alkene hydrogenation catalyst and, more significantly, that the reaction fragment RhL_2Cl could be catalytically generated without light. Note that the mechanism of eqs 1 and 2 implies that the formation of RhL_2Cl is sufficient to effect alkane dehydrogenation.

In accord with the above reasoning we find that, under those conditions that should favor the back reaction of eq 2 (most notably high hydrogen pressure), both alkene hydrogenation and alkane dehydrogenation are observed.

$$RCH_2CH_2R + R'CH{=}CHR' \xrightarrow[>30\ ^\circ C\ (dark)]{1,\ H_2} RCH{=}CHR + R'CH_2CH_2R' \quad (3)$$

In the absence of added H_2 no reaction is observed.

The system of eq 3 is extremely reactive. For example, under 1000 psi of H_2 at 60 °C for 25 h, a cyclooctane solution of **1** (0.40 mM) and norbornene (3.8 M) yielded 560 turnovers of cyclooctene (0.22 M) and norbornane (1.7 M). The reaction rate increases dramatically with temperature; at 100 °C a similar solution of **1** (0.20 mM) afforded 950 turnovers of cyclooctene (0.19 M) and norbornane (1.2 M) *in under 15 min.*

Notably, even the very high turnover numbers obtained are not limited by catalyst decomposition but rather by complete hydrogenation of the alkene hydrogen acceptor. IR spectroscopy of reaction solutions after several hundred turnovers reveals no diminution of the characteristic C–O stretch of **1** (1956 cm^{-1}). UV–visible observation of the solutions during (under 1000 psi of H_2) and after catalysis shows no change in the spectrum, and there is no visible loss of clarity. The reaction is unaffected by the addition of mercury to the reaction mixture, implying that the active catalytic species is not colloidal.[19]

Preliminary mechanistic and screening studies have been conducted at 60 °C. Cyclooctane, which has an anomalously low enthalpy of dehydrogenation (23.3 kcal/mol[18]), is a particularly reactive substrate. Note, however, that comparably high turnover numbers for cycloheptane dehydrogenation (26.3 kcal/mol[17,18]) can also be obtained (Table I). The reaction rate is independent of norbornene (acceptor) concentration above ca. 0.3 M. The nature of the alkene acceptor seems much less critical than with previously reported transfer-dehydrogenation systems;[3,4] a wide variety of olefins including ethylene are suitable (Table I). Figure 1 reveals a linear dependence of the dehydrogenation on hydrogen pressure.

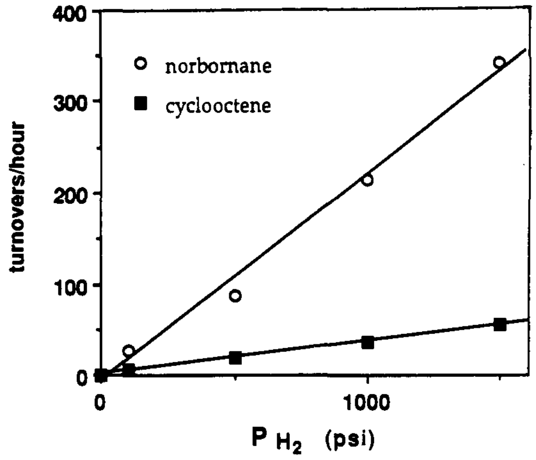


Figure 1. Plot of rate of formation of products of reaction 3 (turnovers/hour) versus dihydrogen pressure. Reaction conditions: cyclooctane solvent; [**1**]^0 = 0.4 mM; 60 °C; [norbornene]^0 = 1.35 M.

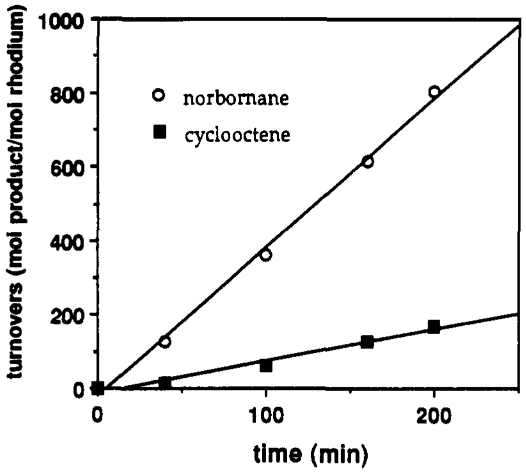
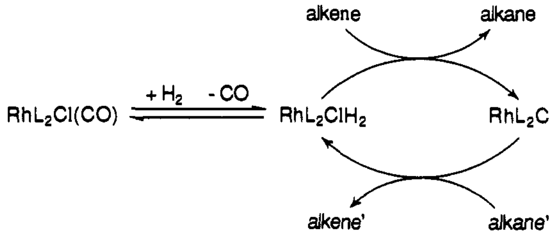


Figure 2. Plot of formation of products of reaction 3 versus time. Reaction conditions: cyclooctane solvent; [**1**]^0 = 0.4 mM; 60 °C; [norbornene]^0 = 1.35 M; P_{H_2} = 1000 psi.

Scheme I



Reaction 3 is completely suppressed by even low pressures of added carbon monoxide (50 Torr) or by added PMe_3 (0.4 mM). Monitoring the progress of the reaction at various time intervals reveals that within the limits of experimental error a constant reaction rate is reached within 40 min at 60 °C (Figure 2). An

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(17) Enthalpies of alkane dehydrogenation range from that of cyclooctane (23.3 kcal/mol) to that of *tert*-butylethane (34.0 kcal/mol). For typical examples, the formation of alkenes from *n*-butane, the following enthalpies (kcal/mol) can be calculated: *trans*-2-butene, 27.5; *cis*-2-butene, 28.5; 1-butene, 30.1.[18]

(18) Stull, D. R.; Westrum, E. F.; Sinke, G. C. *The Chemical Thermodynamics of Organic Compounds*; Robert E. Kreiger Publishing: Malabar, FL, 1987.

(19) Anton, D. R.; Crabtree, R. H. *Organometallics* **1983**, *2*, 855–859.

apparently lower initial rate may be attributable to the time necessary for the system to reach an equilibrium in which CO is partitioned between ligand, solution, and atmospheric CO.

The above observations in conjunction with our studies of the photochemical system suggest a mechanism of the type shown in Scheme I.

Scheme I is undoubtedly a highly simplified representation of a very complex system. For example, the dimerization of RhL_2Cl or its addition to olefin may be expected[20] (followed in either case by a reaction with CO to regenerate **1**). Addition of RhL_2Cl to olefin can be invoked as one possible explanation for the observation of saturation in norbornene concentration above ca. 0.3 M. We also note that the H_2/CO substitution reactions may proceed via an indirect route. The observed inhibition by added PMe_3 is consistent with our photokinetic studies, which indicate that H_2 elimination from $RhL_2Cl(CO)H_2$ proceeds via phosphine loss;[21] by the principle of microscopic reversibility, H_2 addition to **1** should also involve prior loss of phosphine. This is well precedented by studies of H_2 addition to $Rh(PPh_3)_3Cl$.[16]

In summary, an efficient catalytic system for alkane dehydrogenation is reported which requires an added hydrogen atmosphere. Our explanation for this almost paradoxical observation is that the thermodynamic barrier to CO loss from **1** is overcome by its being coupled with alkene hydrogenation. This affords the reactive fragment RhL_2Cl, which thermally dehydrogenates alkanes in accord with studies of its photocatalytic behavior. Further studies of mechanism and selectivity are in progress as are attempts to develop more effective routes to the fragment RhL_2Cl.

Acknowledgment. We thank the Division of Chemical Sciences, Office of Basic Energy Sciences, Office of Energy Research, U.S. Department of Energy, for support of this work. Loans of rhodium trichloride from Johnson-Matthey are gratefully acknowledged. A.S.G. thanks the Camille and Henry Dreyfus Foundation for a Distinguished New Faculty Grant.

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(20) Our photochemical studies indicate that reaction of RhL_2Cl with CO is not competitive with its reaction with cyclooctane under P_{CO} < ca. 50 Torr. The first-order rate dependence on P_{H_2} of reaction 3 indicates that the addition of H_2 to RhL_2Cl is also not competitive with the reaction with alkane. This is an unsurprising conclusion given that (a) the concentration of H_2 is ca. 1/1000 that of C–H bonds even under 1500 psi of H_2 and (b) on the basis of Ford's flash photolysis studies[9,15] we would expect the reaction of RhL_2Cl with H_2 to be much slower than its reaction with olefin. For a detailed description of the chemistry of $Rh(PPh_3)_2Cl$, which is very relevant to this work, see refs 15 and 16.

(21) Maguire, J. A.; Goldman, A. S., to be submitted for publication.

Additions and Corrections

Tethered Oligonucleotide Probes. A Strategy for the Recognition of Structured RNA [*J. Am. Chem. Soc.* **1991**, *113*, 5109–5111]. PAUL L. RICHARDSON and ALANNA SCHEPARTZ*

Pages 5110 and 5111: The sequence of one of the oligonucleotides used in this study was reported incorrectly. The sequence written as AAAUUUUGGA in the caption to Figure 2 and on lines 36–37 of page 5111 should read UCGGGCUUUGGG.

Computer Software Reviews

ESR, ESR II, ESR^a and ESR^a II. Calleo Scientific Software Publishers: 1300 Miramont Drive, Fort Collins, CO 80524. List prices: $175.00, $245.00, $225.00, and $295.00.

ESR and ESR II are first-order isotropic electron spin resonance spectral simulation programs designed for the Apple MacIntosh family of computers. ESR II is a variant of ESR which takes advantage of the math coprocessor in the MacIntosh II computers (with considerable timesavings). With these programs, users can simulate spectra for systems with one unpaired electron containing up to 24 nuclear spin sets, and for $\sum I$ up to 90 for each set. In addition to varying hyperfine coupling constants, nuclear spin, and the number of equivalent nuclei, the user can define nuclear abundances, *g* value, spectrometer frequency, line width, spectrum width, plot resolution, and plot dimensions. All naturally occurring nuclei for the first 103 elements are included.

ESR^a and ESR^a II are companion programs similar to those described above except that they can additionally simulate first-order anisotropic spectra with anisotropic *g* or *A* tensors or both, as well as spectra with Gaussian or Lorenzian line shapes. Spectra generated by all four programs can be displayed and plotted in derivative and absorption modes, and with inverted phase and sweep. The software is not copy protected.

Those familiar with the standard Mac user-interface will find ESR and ESR^a easy to learn and use. In this regard, the programs seem ideal for instructional purposes. They may be somewhat less ideal, however, for users who want to use the programs for fitting experimental spectra. The plotting routine, for example, only allows one to specify the plot dimensions in inches. Additionally, there is no option to save a spectrum as a data-array. This would be useful for a variety of purposes, such as transferring the spectral data to other machines for comparison with experimental spectra and for simulating superposition spectra.

Most unfortunately, pasting spectra generated by ESR and ESR^a into word processing and graphics programs (e.g. Microsoft Word, ChemDraw, ChemIntosh, Pagemaker, and Cricket Draw) presents serious difficulties. Spectra copied onto the Clipboard are invariably clipped due to the programming means by which the ESR creates high-resolution spectra. To get around this problem, one must first create a plotfile using ESR and then use a program capable of handling large drawing sizes (e.g. MacDraw) to read the plotfile and resize it. Only after this resizing operation can a spectrum be cut and pasted into other programs. Users who lack such a program will likely find this a serious inconvenience.

In summary, for the simulation of standard electron spin resonance spectra, ESR and ESR^a are convenient programs to both learn and use. For more demanding users, these programs lack a number of features that might otherwise make them much more attractive.

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