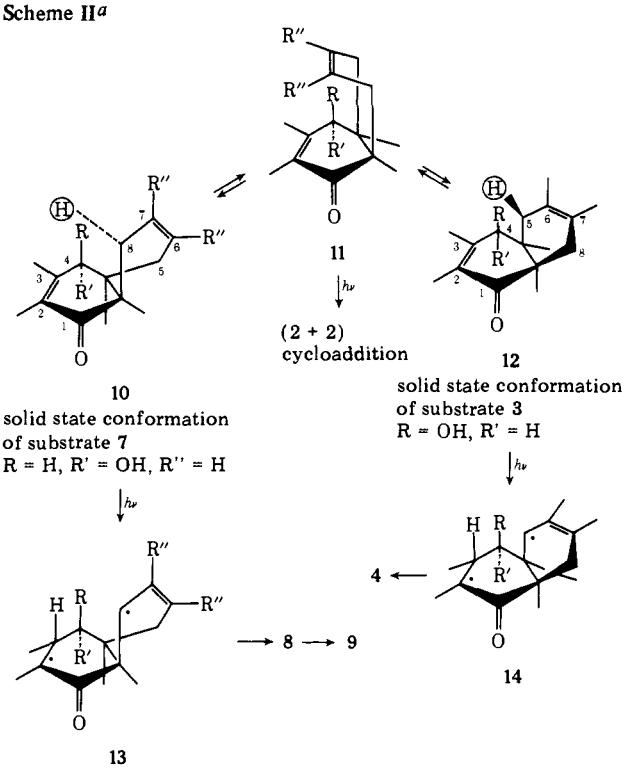
Scheme II[a]



adopt a conformation different from that adopted by **3** (hydroxyl group anti to bridgehead methyls). These differences are shown by structures **10** and **12** in Scheme II. With this information we are now in a position to understand the solid state photochemical results. Photoproduct **9** arises from conformer **10** via a six-membered transition state allylic hydrogen atom transfer from C(8) to C(3) followed by C(2) to C(8) bonding of the resulting biradical **13.** On the other hand, photoproduct **4** is formed through conformer **12** by means of a C(5) to C(3) hydrogen atom transfer (five-membered transition state![5]) and subsequent C(2) to C(5) bonding in **14.**

These processes are seen, as in our previous unimolecular solid state results,[6] to be least motion in character, that is, relatively little molecular reorganization is required to initiate product formation via carbon-carbon bonding following hydrogen abstraction. With regard to the abstraction processes themselves, the C(3) to H(5) distance in **12** is 2.72 (2) Å, and the C(3) to H(8) distance in **10** is 2.84(4) Å. Both values are within the suggested[6a] van der Waals radii sum limit of 2.90 Å for abstraction of hydrogen by carbon.[7] Significantly, substrate **6**, which is photochemically unreactive and exists in conformation **10** (R'' = CH_3), has a C(3) to H(8) interatomic distance of 2.92 (2) Å, just outside the suggested limit. For all three substrates the angle τ_c,[6a] the degree to which the abstracted hydrogen atom lies outside the mean plane of the C(2)-C(3) double bond, is very close to 50°. Similarly, Δ_c, the C(2)-C(3)···H_{abs} angle, is nearly constant at 75°. The conclusion is thus that these geometric factors are not responsible for the lack of solid state reactivity of substrate **6**.

Finally we turn to a discussion of the factors which give rise to the observed solution/solid state reactivity differences. We suggest that internal [2 + 2] photocycloaddition does not occur from conformers **10** and **12** owing to the relatively large double bond separations involved (≥4.37(2) Å in every case) as well as their nonparallel orientations. Parallel double bond approach at distances of less than ca. 4.1 Å is a well-established prerequisite for successful *inter*molecular [2 + 2] photocycloadditions.[6a,8] On the other hand, in solution, where conformational equilibration is facile, small amounts of conformers which better fulfill these requirements (e.g., **11**) will be present. It is thus reasonable to suggest that rapid [2 + 2] photocycloaddition from these minor, higher energy conformers can predominate in solution. Perusal of the photochemical literature reveals a number of additional examples of systems which likely react via nonminimum energy conformations in solution and which might therefore exhibit different photobehavior in the solid state. We plan to continue our investigations along these lines.

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References and Notes

(1) Appel, W. K.; Greenhough, T. J.; Scheffer, J. R.; Trotter, J.; Walsh, L. *J. Am. Chem. Soc.*, preceding paper in this issue.
(2) Photolyses were carried out either in the apparatus previously described[6a] or by coating the inner surface of a conventional immersion well vessel with a thin film of crystals and irradiating from the inside in an oxygen-free atmosphere. Conversions were generally kept below 50%. Low temperatures were employed to avoid development of liquid phases during irradiation. Solution photolyses at −70 °C gave results identical with those observed at ambient temperatures.[1]
(3) Scheffer, J. R.; Bhandari, K. S.; Gayler, R. E.; Wostradowski, R. A. *J. Am. Chem. Soc.* **1975,** *97,* 2178–2189.
(4) Greenhough, T. J.; Trotter, J., unpublished results. Full details of all X-ray crystal structure determinations will be published separately.
(5) This appears to be the first example of a five-membered transition state hydrogen abstraction process in which the abstracting atom is the olefinic carbon of a photoexcited alkene or enone chromophore. The corresponding six-membered transition state process, while rare in comparison with the Norrish type II reaction, is well established. (a) van Tamelen, E. E.; Whitesides, T. H. *J. Am. Chem. Soc.* **1971,** *93,* 6129–6140. (b) Scully, F.; Morrison, H. *J. Chem. Soc., Chem. Commun.* **1973,** 529–530. (c) Hornback, J. M. *J. Am. Chem. Soc.* **1974,** *96,* 6773–6774. (d) Hornback, J. M. *Tetrahedron Lett.* **1976,** 3389–3392; (e) Padwa, A.; Chiacchio, U.; Hatanaka, N. *J. Am. Chem. Soc.* **1978,** *100,* 3928–3930. (f) Herz, W.; Iyer, V. S.; Nair, M.; Saltiel, J. *Ibid.* **1977,** *99,* 2704–2713. (g) Hasegawa, T.; Aoyama, H.; Omote, Y. *Tetrahedron Lett.* **1975,** 1901–1902. (h) Smith, A. B., III; Agosta, W. C. *J. Am. Chem. Soc.* **1974,** *96,* 3289–3295. (i) Smith, A. B., III; Agosta, W. C. *Ibid.* **1973,** *95,* 1961–1968. (j) Wolff, S.; Schreiber, W. L.; Smith, A. B., III; Agosta, W. C. *Ibid.* **1972,** *94,* 7797–7806. (k) Gloor, J.; Schaffner, K. *Helv. Chim. Acta* **1974,** *57,* 1815–1845. (l) Nobs, F.; Burger, U.; Schaffner, K. *Ibid.,* 1977, *60,* 1607–1628; (m) Ayral-Kaloustian, S.; Wolff, S.; Agosta, W. C. *J. Am. Chem. Soc.* **1977,** *99,* 5984–5992.
(6) (a) Scheffer, J. R.; Dzakpasu, A. A. *J. Am. Chem. Soc.* **1978,** *100,* 2163–2173. (b) Appel, W. K.; Greenhough, T. J.; Scheffer, J. R.; Trotter, J. *Ibid.* **1979,** *101,* 213–215.
(7) Note that both hydrogen transfers found in this work involve abstraction by the β carbon of the α,β-unsaturated ketone system. This occurs despite the fact that the C(2)···H(8) distance (abstraction by the α carbon) in **10** is actually less [2.73 (4) Å] than the C(3)···H(8) distance of 2.84 Å corresponding to the observed β-abstraction process. For examples of photoreactions which involve intramolecular hydrogen abstraction by the α carbon of an α,β-unsaturated ketone system, see ref 5f, 5k, and 5l.
(8) Schmidt, G. M. J. *Pure Appl. Chem.* **1971,** *27,* 647–678. See also Irngartinger et al. (Irngartinger, H.; Acker, R.-D.; Rebafka, W.; Staab, H. A. *Angew. Chem., Int. Ed. Engl.* **1974,** *13,* 674–675) for an example of an intramolecular [2 + 2] photocycloaddition involving close (~3 Å) parallel approach of the reacting double bonds.

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Hydrolysis of Phenyl Acetates with Capped β-Cyclodextrins: Reversion from Meta to Para Selectivity

Sir:

Modeling of enzymic reactions by use of natural[1] and artificial[2] compounds has been extensively studied in the past decade. One notable advantage of the use of artificial com-

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Table I. Maximum Catalytic Rate Constants (k_c) and Dissociation Constants (K_d) for Reactions of Modified β-Cyclodextrins with Meta- and Para-Substituted Phenyl Acetates[a]

AcO–C$_6$H$_4$–X	X	k_c ($\times 10^2$ s^{-1})				K_d ($\times 10^3$ M)			
		1	**3**	**4**	**5**	**1**	**3**	**4**	**5**
6	*m*-NO_2	33.6[b] ± 5.0	57.2 ± 0.03	11.5 ± 2.4	3.00 ± 0.008	6.14[d] ± 1.00	6.64 ± 0.04	0.82 ± 0.03	0.11 ± 0.002
7	*p*-NO_2	5.37[c] ± 1.2	7.38 ± 1.87	5.50 ± 0.58	2.71 ± 0.004	4.80[e] ± 1.00	4.67 ± 1.58	0.33 ± 0.10	0.012 ± 0.0008
8	*m*-Me	0.97 ± 0.09	1.33 ± 0.39	0.61 ± 0.04	0.48 ± 0.07	3.50 ± 0.08	3.23 ± 1.25	0.32 ± 0.06	0.28 ± 0.012
9	*p*-Me	0.45 ± 0.04	0.45 ± 0.03	0.41 ± 0.07	0.31 ± 0.007	2.27 ± 0.75	2.33 ± 0.23	0.15 ± 0.03	0.053 ± 0.013

[a] In pH 10.60 (I = 0.15) $NaHCO_3$–Na_2CO_3 buffer, 25.0 °C, with 0.50–0.70% (v/v) CH_3CN added. [b] Reported[1b] 44.4 × 10^{-2} s^{-1}. [c] Reported[1b] 6.34 × 10^{-2} s^{-1}. [d] Reported[1b] 8.0 × 10^{-3} M. [e] Reported[1b] 6.1 × 10^{-3} M.

Table II. Selectivity in Reactions of Modified β-Cyclodextrins with Meta- and Para-Substituted Phenyl Acetates[a]

AcO–C$_6$H$_4$–X	X	k_c/K_d (M^{-1} s^{-1})				$(k_c/K_d)_{para}/(k_c/K_d)_{meta}$			
		1	**3**	**4**	**5**	**1**	**3**	**4**	**5**
6	*m*-NO_2	54.7[b]	86.1	140	272				
						0.21[d]	0.18	1.2	8.3
7	*p*-NO_2	11.2[c]	15.8	167	2260				
8	*m*-Me	2.7	4.1	19.1	17.1				
						0.70	0.46	1.43	3.4
9	*p*-Me	1.9	1.9	27.3	58.4				

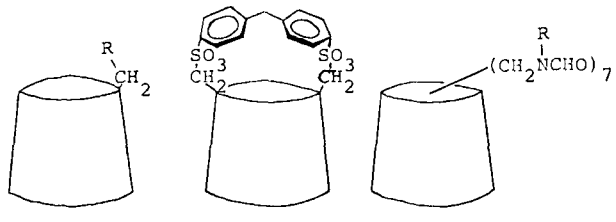
[a] 25 °C, pH 10.60. [b] Reported[1b] 55.5 M^{-1} s^{-1}. [c] Reported[1b] 10.3 M^{-1} s^{-1}. [d] Reported[1b] 0.19.

pounds is that the structure can be manipulated precisely for the study of a specific property. Cyclodextrins are one example of such a system.

Attachment of appropriate functional groups to cyclodextrins led to considerable enhancement of reactivity.[2c-e,3] Also, capping of the cyclodextrin cavity with a hydrophobic moiety[4] or a metal complex[5] dramatically strengthened the inclusion-binding ability of the cyclodextrin.

In the studies of the hydrolyses of substituted phenyl acetates by α- or β-cyclodextrins, meta-substituted phenyl esters were more rapidly hydrolyzed than the corresponding para isomers, a phenomenon termed "meta selectivity". This is apparently dependent on the depth of the cavity[6] and appropriate modifications of the cyclodextrins should alter this selectivity. In this communication, we report that very simple modifications of β-cyclodextrin lead to a conversion of the well-established meta selectivity to para selectivity.

Modifications of β-cyclodextrin (**1**) were carried out by the reactions of mercaptans with β-cyclodextrin 6-monotosylate (**2**).[7,8] The rigidly capped cyclodextrin (**5**) was prepared by a



1 R= OH **5** **10**

2 R= OTs

3 R= SMe

4 R= SC(Me)$_3$

procedure reported elsewhere.[4a,9] The modified cyclodextrins were purified by successive recrystallization from water and characterized by ^{1}H NMR and IR spectra and elemental analyses.[10]

The hydrolyses (pH 10.60) of *m*- and *p*-nitro- and methylphenyl acetates **6**–**9** were spectroscopically measured at 25 °C in the presence of an excess of the modified or native β-cyclodextrins and showed pseudo-first-order kinetics.[1b,11] From usual treatment[1b] of the kinetic data, the dissociation constants (K_d) and the maximum catalytic rate constants (k_c) were estimated (Table I).

While small structural change on β-cyclodextrin as in **3** caused only small changes in k_c and K_d of the phenyl acetates, the complete capping (**5**) led to a decrease in K_d of up to 300-fold and a decrease in k_c of up to 10-fold. The parameters of **4** fell between those of **3** and **5**. Capping of β-cyclodextrin decreased the rate constants for the para compounds less than those for the meta esters, such that their values became quite similar. Capping enhanced the binding of both the meta and para esters, but it enhanced binding of the para esters to a much greater degree. This trend is more clearly demonstrated in terms of ratios of selectivity factors, $(k_c/K_d)_{para}/(k_c/K_d)_{meta}$ (Table II). Although the well-known meta selectivity was conspicuous in **3**, little or no selectivity was observed in **4**. Conversion from meta-selective behavior to a para-selective one occurred in **5**. This para selectivity is mostly attributed to a large decrease in the dissociation constants of the para esters that was caused by the modification.

Thus, the selectivity exhibited by the capped β-cyclodextrin (**5**) was markedly different from that of the parent β-cyclodextrin where a far larger k_c of the meta ester determined the meta selectivity. The enhancement of binding demonstrated here that results from rigid capping with a hydrophobic moiety is quite different from the result obtained with a flexibly capped β-cyclodextrin (**10**).[3] This derivative showed a somewhat larger K_d and a far larger k_c for meta ester hydrolyses. This difference may be rationalized by an examination of the volumes of the cavities and the guest molecules. The binding of the esters by **5** would be deeper than that by **10**. This can be deduced from the better binding of the para esters than the corresponding meta isomers[12] and can be visualized by a CPK molecular model of **5** which showed a far larger hydrophobic pocket than those present in β-cyclodextrin and **10**.

Thus, the decrease in k_c by diphenylmethanesulfonate capping (**5**) is reasonable since deeper binding would result in a significant separation of the ester group from the reactive hydroxyl groups located on the cyclodextrin rim.

Thus, the well-known meta selectivity is not a general property of cyclodextrin catalyses; instead selectivity is apparently dependent on the depth of inclusion of the guest which can be easily varied by simple modifications of the cyclodextrin structure.

References and Notes

(1) (a) F. Cramer and W. Kampe, *J. Am. Chem. Soc.*, **87**, 1151 (1965); (b) R. L. van Etten, J. F. Sebastian, G. A. Clowes, and M. L. Bender, *Ibid.*, **89**, 3242 (1967); (c) D. L. Vander Jagt, F. L. Killian, and M. L. Bender, *Ibid.*, **92**, 1016 (1970); (d) T. S. Straub and M. L. Bender, *Ibid.*, **94**, 8875, 8881 (1972); (e) R. Breslow and P. Cambell, *Bioorg. Chem.*, **1**, 140 (1971); (f) H. J. Brass and M. L. Bender, *J. Am. Chem. Soc.*, **95**, 5391 (1973); (g) M. Komiyama and M. L. Bender, *Ibid.*, **100**, 4576 (1978); (h) I. Tabushi, K. Fujita, and H. Kawakubo, *Ibid.*, **99**, 6456, (1977); (i) I. Tabushi, H. Kuroda, K. Fujita, and H. Kawakubo, *Tetrahedron Lett.*, 2083 (1978); (j) I. Tabushi, K. Yamamura, K. Fujita, and H. Kawakubo, *J. Am. Chem. Soc.*, **101**, 1019 (1979).

(2) (a) F. Cramer and G. Mackensen, *Angew. Chem.*, **78**, 641 (1966); (b) F. Cramer and G. Mackensen, *Chem. Ber.*, **103**, 2138 (1970); (c) R. Breslow and L. E. Overmann, *J. Am. Chem. Soc.*, **92**, 1075 (1970); (d) W. B. Gruhn and M. L. Bender, *Bioorg. Chem.*, **4**, 219 (1975); (e) R. Breslow, J. B. Doherty, G. Guillot, and C. Lipsey, *J. Am. Chem. Soc.*, **100**, 3227 (1978); (f) I. Tabushi, Y. Kuroda, and Y. Kimura, *Tetrahedron Lett.*, 3227 (1976); (g) I. Tabushi, H. Sasaki, and Y. Kuroda, *J. Am. Chem. Soc.*, **98**, 5727 (1976); (h) I. Tabushi, Y. Kimura, and K. Yamamura, *ibid.*, **100**, 1304 (1978); (i) I. Tabushi, Y. Kuroda, and K. Shimokawa, *ibid.*, **101**, 1615 (1979); (j) A. Ueno, H. Yoshimura, R. Saka, and T. Osa, *ibid.*, **101**, 2779 (1979).

(3) J. Emert and R. Breslow, *J. Am. Chem. Soc.*, **97**, 670 (1975).

(4) (a) I. Tabushi, K. Shimokawa, N. Shimizu, H. Shirakata, and K. Fujita, *J. Am. Chem. Soc.*, **98**, 7855 (1976); (b) I. Tabushi, K. Shimokawa, and K. Fujita, *Tetrahedron Lett.*, 1527 (1977); (c) I. Tabushi, L. C. Yuan, and K. Fujita, *ibid.*, 2503 (1977).

(5) I. Tabushi, N. Shimizu, T. Sugimoto, M. Shiozuka, and K. Yamamura, *J. Am. Chem. Soc.*, **99**, 7100 (1977).

(6) A modified cyclodextrin with a shallow cavity exhibited a marked enhancement of the hydrolysis rate of *m*-nitro- and *tert*-butylphenyl acetates. See ref 3.

(7) L. D. Melton and K. N. Slessor, *Carbohydr. Res.*, **18**, 29 (1971).

(8) The procedure of the present modification was similar to that described elsehwere. See ref 4b.

(9) The capped cyclodextrin (**5**) was very stable in alkaline solution (pH 11, aqueous Na_2CO_3, 25 °C, >12 h), in marked contrast to the unstable monotosylate **2**. The capping positions were discussed in ref 2e and 2i.

(10) **3**: ^1H NMR (D_2O) δ 2.0 (3 H, CH_3, s), 2.8 (2 H, CH_2S), 3.2–4.1 (40 H, cyclodextrin protons other than C_1 H), 4.90 (7 H, C_1 H); IR spectrum was very similar to that of β-cyclodextrin. Found: C, 43.55; H, 6.22. Calcd for $C_{43}H_{72}O_{34}S\cdot H_2O$: C, 43.64; H, 6.30. **4**: ^1H NMR (D_2O–Me_2SO-d_6) δ 1.18 (9 H, CH_3, s), 2.9 (2 H, CH_2S), 3.15–4.0 (40 H, cyclodextrin protons other than C_1 H), 4.81 (7 H, C_1 H); IR spectrum was very similar to that of β-cyclodextrin. Found: C 45.08; H, 6.38. Calcd for $C_{46}H_{78}O_{34}S\cdot H_2O$: C, 45.09; H, 6.58.

(11) When fast reactions were being followed, the time necessary to complete the mixing of the reactants and to begin recording of the spectral change did not exceed 6 s.

(12) Although the methyl-substituted ester was bound by β-cyclodextrin more strongly than the nitro-substituted ester, the former was bound by the capped cyclodextrin (**5**) more weakly than the latter. This may indicate the importance of an interaction between the nitro group and the capping moiety by London dispersion force. The significance of London dispersion forces of a nitro group in guest bindings by α-cyclodextrin was discussed: R. J. Bergeron, M. A. Channing, G. Gibeily, and D. M. Pillor, *J. Am. Chem. Soc.*, **99**, 5146 (1977).

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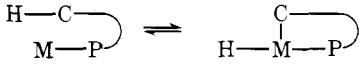
Activation of Carbon–Hydrogen Bonds by $[Rh(diphos)_2]^0$

Sir:

The activation of carbon–hydrogen bonds poses an interesting and important challenge. Despite the apparent similarity to H_2 in terms of bond energy and polarity, the C–H bond, unlike H_2, does not readily undergo activation via oxidative addition. Most examples are restricted to intramolecular metalations[1] (eq 1), in which entropic effects undoubtedly play



(1)

a major role. While C–H bond activation is also indicated by H/D exchange reactions of arenes[2,3] using catalysts such as $PtCl_4^{2-}$ in D_2O/DOAc and NbH_3Cp_2 under D_2, the mechanism of the exchange and details of the activation process remain uncertain. In the present paper, we describe an approach to the activation of C–H bonds which is based on the notion that a highly energetic odd-electron complex can react with C–H bonds to form organic radicals by eq 2, and we demonstrate that this reaction does indeed occur. Implicit in this approach to C–H bond activation is the view that the more energetic the M· species, the more stable the resultant M–H bond, and, when the bond dissociation energies for M–H and C–H are of similar value, reaction 2 may proceed at a useful rate.[4]

$$M\cdot + R\text{-}H \rightarrow M\text{-}H + R\cdot \qquad (2)$$

Previously, we reported[5] the electrochemical reduction of $[Rh(diphos)_2]^+$ in CH_3CN, Me_2SO, and DMA and subsequent formation of the hydride, $RhH(diphos)_2$; the overall reaction consumes two e^-. Through a combination of electrochemical and chemical techniques, we established that the reduction proceeds in one-electron steps, initially yielding $[Rh(diphos)_2]^0$ which reacts with a solvent molecule to form the product hydride and a reducible solvent radical which undergoes the second electron transfer. This sequence is shown in eq 3–5 and represents an ECE mechanism for the reduction. Since eq 4 represents a subset of eq 2, thereby demonstrating its feasibility, we next focused on using a solvent that would preclude (4) and permit us to study the reaction of the Rh^0 species with added substrates.

$$Rh^+ + e^- \rightarrow Rh\cdot \qquad (3)$$

$$Rh\cdot + Sol\text{-}H \rightarrow Rh\text{-}H + Sol\cdot \qquad (4)$$

$$Sol\cdot + e^- \rightarrow Sol^- \qquad (5)$$

To this end, we examined the electrochemical reduction of $[Rh(diphos)_2]^+$ in benzonitrile. Cyclic voltammetry (CV) of $[Rh(diphos)_2](ClO_4)$ in this solvent at a hanging Hg drop electrode (HMDE) shows a reversible one-electron couple at −2.10 V vs. an Ag/0.1 M $AgNO_3$ in benzonitrile reference. Constant potential coulometry (CPC) at −2.20 V yields, as before,[5] a coulometric n value of 2 and the hydride, $RhH(diphos)_2$, as the sole inorganic product. Analysis of the organic distillate by GC–MS reveals that tributylamine is formed in 80–95% conversion with respect to the initial amount of Rh complex. 1-Butene is also produced, although a quantitative analysis of the yield was not obtained because of evaporation.[6] In the previous electrolyses[5] the source of the hydrogen atom was demonstrated to be the solvent. In benzonitrile, however, the primary source of the hydrogen atom for Rh hydride formation is the electrolyte, tetrabutylammonium perchlorate, and not the solvent. The formation of Hofmann degradation products from the reaction of electrochemically generated anionic intermediates with tetraalkylammonium salts is not uncommon.[7] We envision this to be a similar process involving initial attack of Rh^0 on a C–H bond of the electrolyte followed by an electron transfer and subsequent elimination to yield tributylamine and 1-butene.

The viability of a competition between added C–H bond substrates and the electrolyte was demonstrated by the generation of $[Rh(diphos)_2]^0$ in a mixed solvent system. Electrolysis of $[Rh(diphos)_2]^+$ in benzonitrile containing 1.0 M CD_3CN and 0.1 M (n-Bu_4N)ClO_4 yields an 1:1 mixture of $RhH(diphos)_2$ and $RhD(diphos)_2$.[8] Both a statistical correction for available hydrogens and an isotope effect should favor reaction with (n-Bu_4N)ClO_4 and compensate for the differences in molar concentrations of the two substrates. Thus, the observed 1:1 RhH–RhD product composition indicates no dramatic preference of the Rh^0 intermediate for reaction with either substrate.

It was, therefore, of primary interest to explore the reactivity of this Rh^0 complex with *unactivated* C–H bonds. Electrochemical reduction of $[Rh(diphos)_2]^+$ in a 1:1 by volume solution of benzonitrile and cyclohexane containing 0.1 M (n-Bu_4N)ClO_4 reveals[10] the formation of cyclohexyl radical as

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