Hence this provides *the direct observation of the π-allyl-hydride exchange mechanism* proposed for 1,3 hydride shifts found in many metal catalyzed olefin reactions.

Acknowledgments. This work has been supported by the U.S. Army Research Office and the donors of the Petroleum Research Fund, administered by the American Chemical Society.

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(3) **1** can be also isolated by irradiating (350 nm) $Mo(diphos)_2(N_2)_2$ in benzene under C_2H_4 (1 atm) at 25°. Alternatively, under conditions used for the propylene reaction described herein, **1** is yielded when C_2H_4 is used.

(4) Pyrolysis (>100°) or reaction of **1** with CO, N_2, or TCNE yielded only C_2H_4; with Br_2, C_2H_4 and $C_2H_4Br_2$ were produced. In reactions at 25° with excess HCl or CF_3COOH both C_2H_6 and C_2H_4 are evolved.

(5) A. R. Fraser, P. H. Bird, S. A. Bezman, J. R. Shapley, R. White, and J. A. Osborn, *J. Am. Chem. Soc.*, **95**, 597 (1973).

(6) J. X. McDermott and G. Whitesides, *J. Am. Chem. Soc.*, **96**, 947 (1974).

(7) The tungsten analog behaves similarly but the hydride resonance is clearly resolved as a triplet of triplets ($J_{P_1-H} = 92$ Hz, $J_{P_2-H} = 17$ Hz) at −30°. Rapid rearrangement is thus not occurring (see also ref 9).

(8) A claim for this behavior in $Ni(acac)(PPh_3)(C_2H_5)$ has recently been shown to be in error: see F. A. Cotton, B. A. Frenz, and D. L. Hunter, *J. Am. Chem. Soc.*, **96**, 4820 (1974).

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(10) The only previously isolated π-allyl–hydride complex $HNi(\pi\text{-allyl})PPh_3$[11] is stable only below −30°. Although a temperature-dependent equilibrium was observed at −40 to −50°, the dynamics of the process were not observed.

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Electron-Transfer Reactions in Metalloporphyrins

Sir:

This report describes some experiments concerning electron-transfer reactions with metalloporphyrins that demonstrate that the path of electron transfer to the metal ion center can be via the porphyrin π-cloud and not via the fifth and sixth metalloporphyrin ligand positions.[1-4]

The reduction of the water-soluble tetra[*p*-sulfonatophenyl]porphinatocobalt(III), Co(III)-TPPS,[5-7] by chromous ion leads to the below rate law which is similar to the previously observed rate laws for the reduction of metalloporphyrins.[1,2,8]

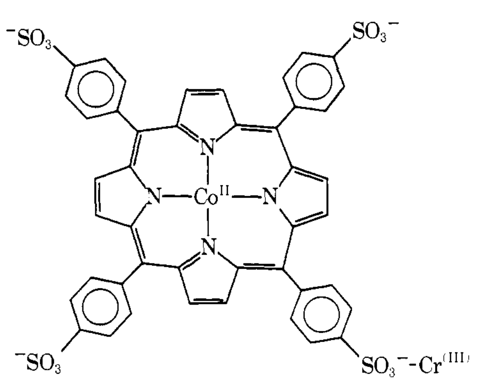
$$\text{rate of reduction} = \{k_1/[H^+] + k_2[Cl^-] + k_3[SCN^-]\}\,[Cr^{2+}][Co^{III}TPPS]$$

The rate constants in the above equation evaluated at 30° and an ionic strength of 0.25 ($NaClO_4$) are $k_1 = 4.9$ sec^{-1}, $k_2 = 2.9 \times 10^4\ M^{-2}$ sec^{-1}, and $k_3 = 1.3 \times 10^6\ M^{-2}$ sec^{-1}. The results are valid between pH 1.0 and 5.0.[9]

Since the rate of Co^{III}TPPS-SCN formation is slower than the electron transfer[10,11] a bridged Co(III)-N-C-S-Cr(II) reaction pathway can be ruled out. This is in agreement with the studies of Pasternack and Sutin.[2]

To further probe the mechanism of this reaction a product study was carried out which demonstrates that the reaction products have the Cr(III) bound to the Co(II)-TPPS moiety. This was verified by carrying out the reaction under stoichiometric conditions employing ^{51}Cr as a tracer[12] and using cation exchange columns to separate the products.[14]

We infer that the Cr(III) is attached to the sulfonate group as shown in structure I. These experiments imply that the electron-transfer goes via the porphyrin π-cloud and not via the fifth and sixth position[15] and also clearly demonstrate that the anion effects in these metalloporphyrin reductions are due to nonbridging ligand effects.



I

Acknowledgment. This work was supported by a Grant from the National Science Foundation.

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(8) Our rate does differ in one respect from that of Sutin and Pasternack in that we have a zero intercept in the plot of $k_{obsd}/[Cr^{2+}]$ vs. $1/[H^+]$.

(9) The reactions were run under pseudo-first-order conditions in a Durrum-Gibson stopped-flow machine with Co(III)–TPPS concentration about $1 \times 10^{-5}\ M$ and $[Cr^{2+}]$ at $(3\text{-}6) \times 10^{-3}\ M$. The wavelengths at both 427 and 411 nms were employed to follow the course of the reaction.

(10) E. B. Fleischer and M. Krishnamurthy, *Ann. N.Y. Acad. Sci.*, **206**, 32 (1973).

(11) The rate constant k_3 is the same whether the SCN^- is placed with the Co(III)–TPPS solution or the Cr^{2+} solution.

(12) The chromium was also analyzed spectrally with the diphenylcarbohydrazide method.[13]

(13) E. B. Sandell, "Colorimetric Determination of Traces of Metals", Interscience, New York, N.Y., 1959, p 392.

(14) A stock solution of $^{51}Cr^{III}(H_2O)_6{}^{3+}$ (1949 (counts/min)/10 ml of $9 \times 10^{-5}\ M$ solution) was employed in these experiments. If 10.0 ml of the above solution was passed through an ion exchange column of Dowex 50W-X8 (9 × 1 in.) the eluent collected had an activity of 249 counts/min. A blank water solution had a counting rate of 236 counts/min. Thus the ion exchange resin caught 99% of the $Cr(H_2O)_6{}^{3+}$. If an equimolar mixture of $^{51}Cr(H_2O)_6{}^{3+}$ and Co(III)–TPPS was passed through the column the porphyrin containing eluent had a counting rate of 267 counts/min. On the other hand, when an equimolar mixture of $^{51}Cr(H_2O)_6{}^{2+}$ (produced by Zn(Hg) reduction of the radioactive chromic solution) and Co(III)–TPPS was passed through the column the porphyrin containing eluent now had a counting rate of 1951 counts/min. Thus the products of the reaction of chromous ion with the cobaltic porphyrin (chromic and cobaltous porphyrin) were completely eluted off the column. This demonstrates that the chromic ion is bound to the metalloporphyrin via the electron-transfer reaction. Interestingly, one can reoxidize the Cr(III)–Co(II)–TPPS with ferricyanide to the Cr(III)–Co(III)–TPPS and rereduce (with a different rate) the Co(III) center with $Cr(H_2O)_6{}^{2+}$ and isolate a $[Cr(III)]_2$–Co(II)–TPPS product.

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Nickel-Promoted Synthesis of Cyclic Biphenyls. Total Synthesis of Alnusone Dimethyl Ether

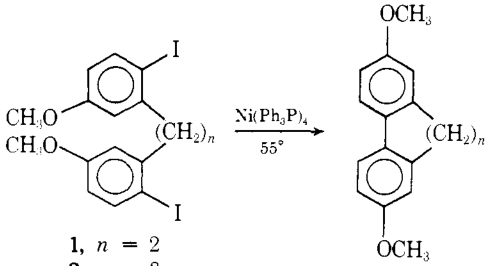
Sir:

Organotransition metal complexes are appearing with increasing frequency in synthetic methodology and in complex synthesis. Important advantages include the formation of carbon-carbon bonds selectively in the presence of a variety of functional groups and the formation of carbocyclic rings.[1] We have been concerned with the activation of aryl halides toward coupling with carbon units using transition metals[2,3] and were impressed with the high functional group compatibility of zerovalent nickel-promoted biphenyl synthesis.[3] At the same time, the set of naturally occurring bridged biphenyls has grown larger recently, including interesting structures[4,5] and exciting biological activity.[6] We wish to report that tetrakis(triphenylphosphine)nickel(0) is particularly effective in promoting the ring closure of 1,*n*-bis(iodoaryl)alkanes to form a variety of carbocyclic rings (bridged biphenyls). The method is successful for functionalized rings including a key intermediate in the synthesis of alnusone, a natural meta-bridged biphenyl.[5c]

The classic copper-promoted coupling of aryl halides is useful for intermolecular coupling of simple aryl halides but requires vigorous conditions and fails for rings larger than seven.[7] Electrooxidative phenol ether coupling is a promising new alternative but appears to require at least two alkoxy substituents on each arene ring, and the functional group compatibility has not been established.[8]

To test the ring size limitations on the formation of ortho-bridged biphenyls by aryl iodide coupling with zerovalent nickel, we prepared the 1,*n*-bis(iodoaryl)alkanes **1-5** and the 14-membered ring precursor, **6**, using conventional methodology.[9] Treatment of **1** with 1.0 mol equivalent of bis(1,5-cyclooctadiene)nickel[10] in DMF under argon failed to give dihydrophenanthrene **7** in more than 15-20% yield; generally, the Ni(0) reagent suffered side reactions and left the bulk of diiodide **1** unreacted. Addition of 1 or 2 mol equivalents of a phosphine (Et_3P, Ph_3P, diphos, etc.) failed to give significant improvement in conversion. However, tetrakis(triphenylphosphine)nickel(0)[11] reacted with **1** at 55° over 20 hr in DMF to produce **7** as colorless crystals after preparative layer chromatography, 81% yield.

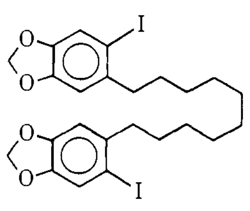
Under identical conditions ($Ni(Ph_3P)_4$, 44-45°, DMF), the higher homologs of **1** were converted to the cyclic products **8**, **9**, **10**, and **11** in yields of 83, 76, 85, and 35-45%, respectively. The reactions proceeded smoothly and reproducibly except for the case where *n* = 6 (**5** → **11**). For diiodide **5**, complete conversion was generally observed, but the yields were variable over seemingly identical experiments. The concentration in these reactions was about 2.6 m*M*; no attempt was made to consider higher dilution conditions. The bisbenzocycloheptane **8** was also obtained efficiently (74% yield) by heating **2** at 240° with copper bronze (no solvent), but larger rings could not be obtained (yields <20%) by this technique.



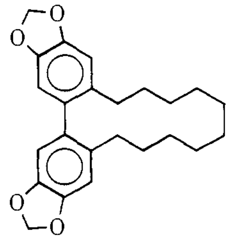
1, *n* = 2
2, *n* = 3
3, *n* = 4
4, *n* = 5
5, *n* = 6

7, *n* = 2, 81%
8, *n* = 3, 83%
9, *n* = 4, 76%
10, *n* = 5, 85%
11, *n* = 6, 38%

The bis(iodoaryl)alkane **6** was obtained by Wittig condensation of 1,6-bis(triphenylphosphonium)hexane diiodide with (4,5-methylenedioxyphenyl)acetaldehyde, hydrogenation of the resulting diene, and iodination with silver trifluoroacetate-iodine.[12] As before, tetrakis(triphenylphosphine)nickel(0) converts **6** to the macrocyclic biphenyl **12**; the colorless crystalline product (mp 112-113.5°) was obtained in 58% yield. The general functional group compatibility of the nickel reactions[3] allows efficient cyclizations of functionalized substrates. For example, ketone **14** was obtained from the benzyl bromide **13** (via coupling-carbonylation with nickel carbonyl[13] and iodination as before[12]) and converted to the bisbenzocycloheptanone **15** (80% yield) using any of several nickel(0)-phosphine combinations.



6



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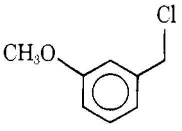

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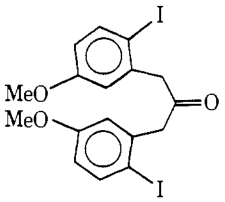

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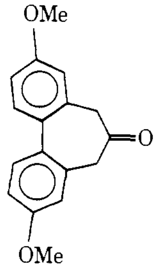
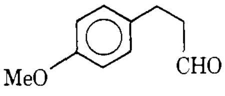


15

Alnusone (**16**), along with its close relatives alnusonol and alnusoxide, appears in the wood of *Alnus japonica Steud*[5] and shares the skeleton of several other plant constituents.[5] The pseudo-symmetry of the alnusones (as indicated in **16**) suggests a simple strategy for total synthesis where the intramolecular coupling of aryl halide units (i.e., in **17**) is a key step. The enone **17** is viewed as two (methoxyphenyl)propyl units linked by a single carbon, and 3-(*p*-methoxyphenyl)propanol (**18**)[14] serves as precursor to both aryl units. The carbon link is added by formation of epoxide **19**,[15] and the units are joined by attack of the anion[16] from dithiane **20**. Conventional hydrolysis[17] of the dithiane unit



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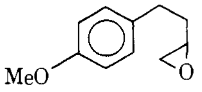

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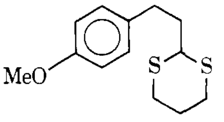
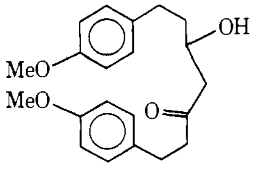
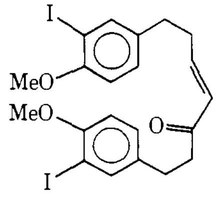


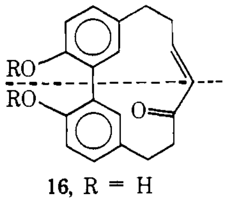
20



21



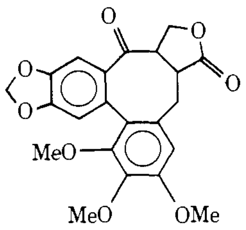
17



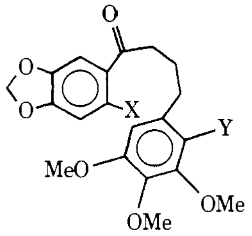
16, R = H
22, R = CH_3

produces **21**, which is converted in three steps[18] to the enone **17**. Then reaction with tetrakis(triphenylphosphine)nickel(0) in DMF at 50° for 40 hr produces the dimethyl ether (**22**) of alnusone (**16**), which is isolated as a colorless solid in high purity (52% yield).[19] The product is identical in comparison of ir, mass, and ^{1}H NMR spectral data, and TLC behavior with a sample of **22** prepared by O,O-dimethylation of alnusone (**16**) from natural sources.[24]

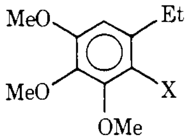
Hindered aryl halides provide the most important general limitation on the method. Direct approaches to the bisbenzocyclooctadienone structures as in steganone (**23**)[20] have not succeeded. For example, the related system **24** reacts with zerovalent nickel reagents at 40-50° to give rapid insertion into the aryl-bromide bond followed by slower insertion into the aryl-iodide bond. However, no aryl-aryl coupling is observed either inter- or intramolecularly; the products from hydrogen substitution for halogen (i.e., **25** and **26**) are obtained in yields of 39 and 24%, respectively. Tetrahydrofuran as solvent produces **25** in 93% yield; addition of D_2SO_4-D_2O during isolation leads to unlabeled **25**.[21] The failure to achieve aryl-aryl coupling is general for compounds with serious steric hindrance around the aryl iodide substituent. For example, aryl iodide **27** gave only the reduction product **28** when treated with zerovalent nickel (70-100% yield, depending on solvent and phosphine ligands). Further definition of the ring size and steric limitations on biaryl coupling with nickel(0) reagents will be presented in the full paper describing this work.



23



24, X = Br; Y = I
25, X = H; Y = I
26, X = H; Y = H



27, X = I
28, X = H

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Institutes of Health for financial support of this work. We also wish to thank Professor Paul Helquist for assistance in the early stages of this study.

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(4) Meta-bridged biphenyl alkaloids from *Lythraceae:* (a) lythranine, R. J. McClure and G. A. Sim, *J. Chem. Soc., Perkin Trans. 2*, 2073 (1972); (b) lythrancine, M. J. Barrow, P. D. Chadwick, and G. A. Sim, *ibid.*, 1812 (1974), E. Fujita and Y. Saeki, *J. Chem. Soc., Perkin Trans. 1*, 2141 (1972) and 297 (1973), and references therein; (c) lythrumine, H. Wright, J. Clardy, and J. P. Ferris, *J. Am. Chem. Soc.*, **95,** 6467 (1973); (d) decinine, J. P. Ferris, R. C. Briner, and C. B. Boyce, *ibid.*, **93,** 2953 (1971).

(5) Meta-bridged biphenyls from *japonica:* (a) asadanin, M. Yasue, *Mokuzai Gakkaishi*, **11,** 146 and 152 (1965); (b) myricanone and myricanol, R. V. M. Campbell, L. Crombie, B. Tuck, and D. A. Whiting, *Chem. Commun.*, 1206 (1970), and M. J. Begley and D. A. Whiting, *ibid.*, 1207 (1970); (c) alnusone, alnusonol, alnusoxide, M. Nomura and T. Tokoroyama, *J. Chem. Soc., Chem. Commun.*, 65 (1974).

(6) Certain ortho-bridged biphenyls have significant in vivo antileukemia activity and in vitro antitumor activity. For example, the bisbenzocyclooctadiene derivatives in the steganone series: S. M. Kupchan, R. W. Britton, M. F. Ziegler, C. J. Gilmore, R. J. Restivo, and R. F. Bryan, *J. Am. Chem. Soc.*, **95,** 1335 (1973). Other bisbenzocyclooctadiene compounds have been observed in nature: N. K. Kochetkov, A. Khorlin, O. S. Chizov, and V. I. Sheichenko, *Tetredron Lett.*, 730 (1961).

(7) For a review, see P. E. Fanta, *Synthesis*, **9,** 1 (1974).

(8) For examples and references, see A. Ronlan and V. C. Parker, *J. Org. Chem.*, **39,** 1014 (1974).

(9) All new compounds showed ir, ^{1}H NMR, and mass spectral data consistent with their structure. Compounds **1** (mp 110–111°), **6** (mp 111–112°), and **13** are known: J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 684 (1942). Compounds **2** (mp 133–135°), **3** (mp 115–116°), **4** (mp 81–82°), **5** (mp 80–81°), **7** (mp 87–88°), **8** (mp 99.5–101°), **9** (mp 139.5–141°), **10** (mp 99.5–101°), **11** (mp 98–100°), **12** (mp 112–113.5°), **14** (mp 157–158°), **15** (mp 129–130°), **20** (mp 46–47°), and **22** (mp 150–151°) gave acceptable results from combustion analysis. Compounds **13, 17, 18, 19, 21, 24, 25, 26, 27,** and **28** were oils; after purification by distillation or preparative layer chromatography, they were characterized by ir, ^{1}H NMR, and mass spectral data.

(10) B. Bogdanovic, M. Kroner, and G. Wilke, *Justus Liebigs Ann. Chem.*, **699,** 1 (1966). For detailed modified procedures, see M. F. Semmelhack, *Org. React.*, **19,** 178 (1972), and R. A. Schunn, *Inorg. Synth.*, **15,** 5 (1974).

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(13) (a) M. F. Semmelhack, Doctoral Thesis, Harvard University, 1967; (b) E. Yoshisato and S. Tsutsumi, *J. Org. Chem.*, **33,** 869 (1968).

(14) The aldehyde **18** was prepared from commercial 3-(*p*-methoxyphenyl)propionic acid by reduction ($LiAlH_4$, 98% yield) to the alcohol followed by oxidation (CrO_3, 83%).

(15) The yield of **19** is 86%; bp 82° (0.02 Torr); cf. E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87,** 1353 (1965).

(16) The dithiane derivative **20** was prepared from **18** and 1,3-propanedithiol in 94% yield; cf. E. J. Corey and D. Seebach, *J. Org. Chem.*, **40,** 231 (1975).

(17) D. Seebach and D. Steinmüller, *Angew. Chem., Int. Ed. Engl.*, **7,** 619 (1968).

(18) Acetylation of **21** followed by base-promoted elimination of acetic acid (diazabicyclononene–chloroform, 25°, 0.5 hr) and then silver(I) promoted iodination[12] gives **17** in 62% yield overall from **19** and **20.**

(19) The major by-products appear to be high molecular weight products, presumably from intermolecular aryl–aryl coupling.

(20) For a clever alternative approach to the steganone skeleton, see D. Becker, L. Hughes, and R. Raphael, *J. Chem. Soc., Chem. Commun.*, 430 (1974).

(21) Efficient reduction of an aryl iodide with a bulky ortho substituent was shown to occur by hydrogen atom transfer from tetrahydrofuran.[2b] We assume a similar process is operating with **24** and **27.**

(22) Fellow of the Alfred P. Sloan Foundation (1973–1975) and recipient of a Camille and Henry Dreyfus Teacher–Scholar Grant (1973–1978).

(23) National Science Foundation Predoctoral Trainee (1970–1974).

(24) We are grateful to Professor T. Tokoroyama (Osaka City University, Oaska, Japan) for providing generous samples of natural alnusone.

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Received April 9, 1975

Specific Enrichment with ^{13}C of the Methionine Methyl Groups of Sperm Whale Myoglobin[1]

Sir:

The value of ^{13}C NMR spectroscopy to the study of protein structure and mobility is substantially increased when single carbon resonances can be observed; under favorable conditions such resonances from proteins have been studied at natural abundance.[2] Efforts to enrich protein samples with respect to ^{13}C have facilitated the study of a number of proteins.[3,4] We report here a selective method to enrich in ^{13}C the methyl group of the two methionyl residues, 55 and 131, in covalently intact sperm whale myoglobin. In the ^{13}C NMR spectrum of this protein sample, which possessed in