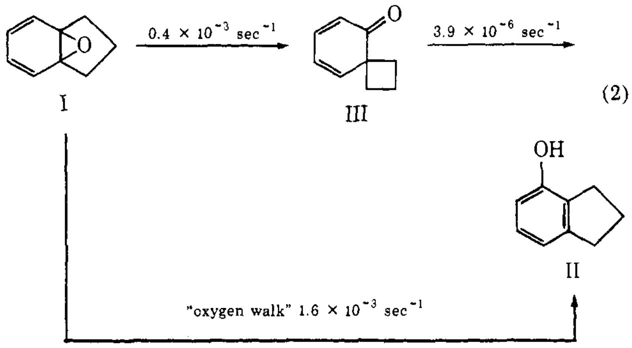
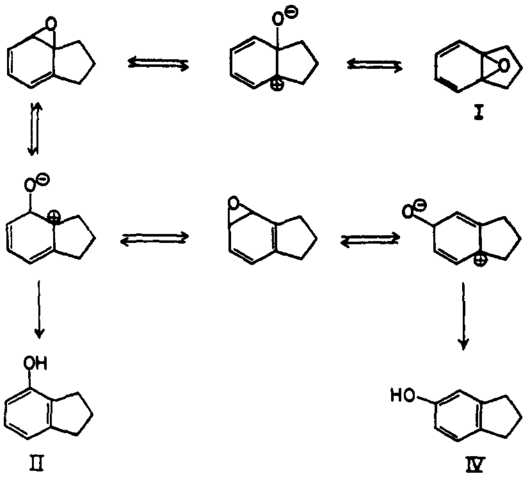
lack of deuterium solvent isotope effects,[3] establishment of great sensitivity to substituent electronic effects, plus lack of kinetic primary deuterium isotope effects for both benzene and naphthalene oxides, the rate-determining step for both k_0 and k_H has been established to be carbonium ion formation.[4] This being so, it might be anticipated that, for suitably favorable cases (stable carbonium ions), collapse of the carbonium ion to give an isomeric arene oxide could compete with collapse back to the original arene oxide prior to aromatization to a phenol. This would result in oxygen migration around the ring ("oxygen walk").

The isomerization of 8,9-indane oxide (I) to 4-indanol (II) was studied by Vögel and Günther,[5] who concluded from the isolation of a Diels–Alder adduct of the spiro ketone (III) that III was a requisite intermediate yielding II *via* dienone phenol rearrangement. We report herein kinetic studies (eq 2) which reveal that the path through III is a minor one and that the major portion of II arises from I *via* a requisite "oxygen walk." Repetitive scanning (30°, 50% dioxane–H_2O, v/v, μ = 0.1 with KCl, pH 7–12) reveals a pH-independent first-order (k_0 = 1.4 × 10^{-3} sec^{-1}) disappearance of I (250 mμ) with simultaneous appearance of II (285 nm (ϵ 3.42 × 10), 275 (6.19 × 10^2 M^{-1} cm^{-1}))[6] and the spiro ketone III (320 mμ).[7] After complete disappearance of I, first-order disappearance of III commences (k_1 = 3.9 × 10^{-6} sec^{-1}), and at t_∞ the only species present is II.[6] Only 30% of II is produced *via* I → III → II. (In a separate experiment, it was shown that pure III aromatizes to II at the same rate that III produced *in situ* aromatizes to II.) Since II is produced before a significant amount of III has formed and is produced more rapidly than III → II, II must also be produced from I (eq 2) *via* an "oxygen walk" (Scheme I). A second oxygen walk is possible and would account for the minor amounts of 5-indanol[6] observed during the isomerization of I. The decreased stability of the carbonium ion leading to 5-indanol accounts for only a small amount of that compound being produced.



I III II (2)

Scheme I



I II IV

97-100% 0-3%

Acknowledgment. This work was supported in part by grants to T. C. B. from the National Institutes of Health and the Cancer Research Fund of the University of California.

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(4) G. J. Kasperek, T. C. Bruice, H. Yagi, and D. M. Jerina, *J. Chem. Soc., Chem. Commun.*, 784 (1972).

(5) E. Vögel and H. Günther, *Angew. Chem., Int. Ed. Engl.*, **6**, 385 (1967).

(6) Isolated from reaction mixture and shown to be identical with an authentic sample by glc, tlc, and nmr. Trace amounts (2–3%) of a glc peak corresponding to 5-indanol have been detected.

(7) Identification of spiro[3,5]nona-6,8-dien-5-one (III): the 100-MHz spectrum (CS_2 solution, line position in δ relative to TMS, and coupling constants in hertz) was assigned as six methylene cyclobutane hydrogens 1.70–3.10 and four vinyl hydrogens with 1 H_6 5.87, 1 H_7 6.86, 1 H_8 6.10, and 1 H_9 6.72; $^3J_{6,7}$ = $^3J_{8,9}$ = 9.5, $^3J_{7,8}$ = 6, $^4J_{6,8}$ = 1, $^4J_{7,9}$ = 1.75, and $^5J_{8,9}$ = 0.71 Hz. Concentration of the CS_2 solution resulted in formation of a Diels–Alder dimer whose melting point and ir, nmr, and mass spectra were identical with those of the dimer previously identified among the rearrangement products of 8,9-indane oxide: M. Wiesel, Ph.D. Thesis, Der Universitaté Köln, 1966, p 61. The σ_{max} 318 nm (ϵ 4305 M^{-1} cm^{-1}) (50% dioxane–H_2O) for the spiroketone was based on the weight of dimer produced after concentration.

Transition Metal Catalyzed [2 + 2] Cross-Addition of Olefins. Nickel(0)-Catalyzed Cycloaddition of Norbornadiene and Methylenecyclopropane

Sir:

One of the most intriguing natures of transition metal complexes is the ability to catalyze cycloaddition of olefins leading to cyclobutane derivatives, since the reaction mode is formally envisaged as a thermally forbidden [$_\pi 2_s$ + $_\pi 2_s$] process.[1] Although there exist

$$\| + \| \xrightarrow{M} \square$$

various examples of cyclodimerization reactions,[2,2i] only a few cases are known of coupling between two different olefins.[3,4] The essential intermediate in the cross-coupling reaction of olefins A and B is believed to be a

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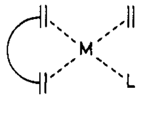
(1) R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969).

(2) For example: (a) C. W. Bird, R. C. Cookson, and J. Hudec, *Chem. Ind. (London)*, 20 (1960); (b) C. W. Bird, D. L. Colinese, R. C. Cookson, J. Hudec, and R. O. Williams, *Tetrahedron Lett.*, **No. 11**, 373 (1961); (c) P. W. Jolly, F. G. A. Stone, and K. MacKenzie, *J. Chem. Soc.*, 6416 (1965); (d) P. Heimbach and W. Brenner, *Angew. Chem.*, **79**, 813 (1967); (e) G. N. Schrauzer, *Advan. Catal.*, **18**, 373 (1968); (f) F. W. Hoover and R. V. Lindsey, Jr., *J. Org. Chem.*, **34**, 3051 (1969); (g) F. J. Weigert, R. L. Baird, and J. R. Shapley, *J. Amer. Chem. Soc.*, **92**, 6630 (1970); (h) P. Binger, *Angew. Chem.*, **84**, 352 (1972).

(2i) NOTE ADDED IN PROOF. Quite recently the intervention of a metallocyclic intermediate in metal catalyzed [2 + 2] cycloaddition reactions has been demonstrated: A. R. Fraser, P. H. Bird, S. A. Bezman, J. R. Shapley, R. White, and J. A. Osborn, *J. Amer. Chem. Soc.*, **95**, 597 (1973).

(3) A. Greco, A. Carbonaro, and G. Dall'Asta, *J. Org. Chem.*, **35**, 271 (1970); D. R. Coulson, *ibid.*, **37**, 1253 (1972).

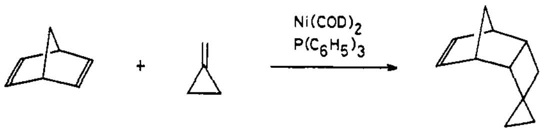
discrete metal complex containing both kinds of olefins. Therefore, crucially important for achieving the selective cross-addition is a proper choice of the olefin pair A and B; the metal coordination of A must in turn facilitate the coordination of B onto the same metal atom. When the olefins A and B are similar in type to each other, it is apparent that the specific formation of the mixed-ligand complex is thermodynamically and/or kinetically unfavorable. Conceptually, one of the most fruitful ways for gaining a high degree of selectivity may be the well-designed construction of the intermediary complexes of type **1** (M = four-coordinate metal atom;



1

L = auxiliary ligand) which bear a chelating diene and an olefin as substrate. On this assumption we have carried out a reaction of norbornadiene (**2**) and methylenecyclopropane (**3**) having a strained double bond with the aid of phosphine-modified nickel(0) catalysts and found a highly selective [2 + 2] cross-addition.

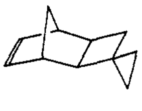
When a homogeneous, orange solution of **2** (4.0 mmol), **3** (4.0 mmol), bis(1,5-cyclooctadiene)nickel(0) [Ni(COD)$_2$] (0.2 mmol), and triphenylphosphine (0.22 mmol) in benzene (10 ml) was maintained at 20° for 24 hr under nitrogen, a single 1:1 cycloadduct **4** was obtained in 86% yield.[5] Cyclobutane dimers of **2** or **3**,



2 **3** **4**

which are known to form smoothly *via* the individual catalytic reactions,[2e,h] were produced in very small amounts.

Formation of **4** was suppressed by increasing the amount of triphenylphosphine ligand. No trace of **4** could be detected when bis(diphenylphosphino)ethane, a chelating bidentate ligand, was used. On the other hand, when no phosphine ligands were present in the catalyst system, a significant decrease in both stereoselectivity (endo/exo) and perispecificity (in a formal sense) of the cycloaddition resulted. Thus, reaction of **2** and **3** under the above described conditions afforded an isomeric mixture of 1:1 adducts, **4** (50%), **5** (3%), **6** (24%), and **7** (6%).[6] The cycloadducts **4** and **5** were independently prepared from *endo*- and *exo*-tricyclo-$[4.2.1.0^{2,5}]$non-7-en-3-one,[7] respectively, employing Wittig condensation with methylenetriphenylphosphorane followed by Simmons–Smith methylenation. The identity of **6** was confirmed by comparison with the authentic specimen obtained by Wittig reaction of tetracyclo$[4.3.0.0^{4,9}.0^{5,7}]$nonan-2-one and subsequent Simmons–Smith reaction. The independent synthesis of **7** was accomplished by the reaction of *endo*-tricyclo-$[5.2.1.0^{2,6}]$dec-8-en-3-one and methylenetriphenylphosphorane.



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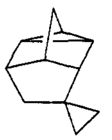

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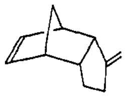

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A novel type of asymmetric cycloaddition was achieved by the use of a chiral, zerovalent nickel complex as the catalyst.[8,8c] When the reaction of **2** and **3** was carried out in the presence of Ni(COD)$_2$ and (−)-benzylmethylphenylphosphine[9] (optical purity 80%; 1:1.1 ratio) at 20° for 48 hr, **4** (48% yield) was obtained in an optically active form, $[\alpha]^{20}\text{D}$ −0.80° (*c* 10.6, CHCl$_3$). The absolute configuration and the optical purity have not yet been determined.

All the foregoing findings are rationalized in terms of the intervention of the Ni(0) complexes having the general structure **1** in the product-determining step. The observed clean cross-coupling is the result of the specific order of coordination tendency of the substrates, *i.e.*, L $\gg$ diene as bidentate ligand > olefin > diene as unidentate ligand.[10] Certain nonconjugated dienes, including **2**, are known to form the stable chelate complexes.[11] Secondly, strained olefins have a tendency to form rather stable metal complexes due to partial strain relief upon complexation.[12,13] The relative ease with which these olefins form the corresponding metal complexes could be inferred by comparing the strain energies involved in the carbon–carbon double bond, $SE_{\text{C=C}}$.[14] Thus, the highly strained olefin **3** ($SE_{\text{C=C}}$ = 13 kcal/mol) is anticipated to afford a complex with greater stability compared with that containing **2** ($SE_{\text{C=C}}$ = 7.5 kcal/mol) as an exo,[15] unidentate ligand. Notably, attempted cycloaddition of **2** to methylenecyclobutane ($SE_{\text{C=C}}$ = 1.8 kcal/mol) or cyclobutene ($SE_{\text{C=C}}$ = 3.7 kcal/mol) resulted in only dimerization of **2**. Due to the decrease in $SE_{\text{C=C}}$ in these cases, complexes bearing two molecules of **2** would be formed

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(4) After submission of this paper, Ti-catalyzed reaction of 1,3-butadiene and ethylene forming vinylcyclobutane was reported: L. G. Cannell, *J. Amer. Chem. Soc.*, **94**, 6867 (1972).

(5) All new compounds gave correct elemental analyses and spectral data (ir, nmr, and mass) consistent with the assigned structure.

(6) For the $[{}_{\sigma}2 + {}_{\pi}2]$ type reaction involving **3**, see R. Noyori, T. Odagi, and H. Takaya, *J. Amer. Chem. Soc.*, **92**, 5780 (1970); R. Noyori, Y. Kumagai, I. Umeda, and H. Takaya, *ibid.*, **94**, 4018 (1972).

(7) R. D. Miller and V. Abraitys, *ibid.*, **94**, 663 (1972). We thank Dr. Miller for informing us of the detailed procedure for the preparation of the cyclobutanones.

(8) Asymmetric induction in homogeneous catalysis forming carbon–carbon bonds: (a) (carbenoid reactions) H. Nozaki, H. Takaya, S. Moriuti, and R. Noyori, *Tetrahedron*, **24**, 3655 (1968); R. Noyori, H. Takaya, Y. Nakanisi, and H. Nozaki, *Can. J. Chem.*, **47**, 1242 (1969); W. R. Moser, *J. Amer. Chem. Soc.*, **91**, 1135 (1969); (b) (hydroformylation) M. Tanaka, Y. Watanabe, T. Mitsudo, A. Yamamoto, and Y. Takegami, *Chem. Lett.*, 483 (1972); I. Ogata and Y. Ikeda, *ibid.*, 487 (1972).

(8c) NOTE ADDED IN PROOF. Asymmetric oligomerization of olefins has been reported: B. Bogdanović, B. Henc, B. Meister, H. Pauling, and G. Wilke, *Angew. Chem.*, **84**, 1070 (1972).

(9) K. Naumann, G. Zon, and K. Mislow, *J. Amer. Chem. Soc.*, **91**, 7012 (1969).

(10) The order is referred to only roughly. The concentration of each component is to be considered.

(11) E. O. Fischer and H. Werner, "Metal π-Complexes," Vol. 1, Elsevier, Amsterdam, 1966, p 81.

(12) For example, (a) J. G. Traynham and J. R. Olechowski, *J. Amer. Chem. Soc.*, **81**, 571 (1959); (b) M. A. Muhs and F. T. Weiss, *ibid.*, **84**, 4697 (1962); (c) J. P. Visser, A. J. Schipperijn, J. Lukas, D. Bright, and J. J. de Boer, *Chem. Commun.*, 1266 (1971).

(13) Recently a stable Ni complex of **3** was reported: M. Englert, P. W. Jolly, and G. Wilke, *Angew. Chem.*, **83**, 84 (1971).

(14) *Cf.* P. v. R. Schleyer, J. E. Williams, and K. R. Blanchard, *J. Amer. Chem. Soc.*, **92**, 2377 (1970).

(15) C. F. Wilcox, Jr., and W. Gaal, *ibid.*, **93**, 2453 (1971), and references cited therein.

in preference to the desired mixed ligand complexes.[16] Thus, a difference in $SE_{C=C}$ of the olefinic substrates proved to play a crucial role in the construction of the key intermediate **1**. The exclusive production of the adduct **4** having endo stereochemistry,[17] as well as the efficient inhibitory effect of bis(diphenylphosphino)ethane, provides definite evidence for the existence of the complex **1** in which **2** is acting as an endo bidentate ligand. With the chiral phosphine ligand present in the coordination sphere, two orientations of the substrates **2** and **3** are possible. Preferential formation or further reaction of one of these diastereomeric intermediates could lead to the observed enantioselective cyclobutane formation.

The exact factors which maintain the balance of the stability and the reactivity of the intermediary metal complexes, and which control the reaction course, remain to be elucidated. Attempts to characterize the reactive intermediates by physical methods are now in progress.

[16] Cyclopropene and 1-methylcyclopropene containing the extraordinarily high $SE_{C=C}$ (26 kcal/mol) polymerized violently under the present catalytic conditions (even at −60°).

[17] The major dimer of **2** has an endo,trans,exo structure.[2e]

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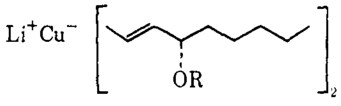
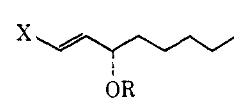
Total Synthesis of Prostaglandins. IV.[1] A Completely Stereospecific Synthesis of Prostaglandin E_1

Sir:

In a previous communication[2] we disclosed a concise novel route for the synthesis of prostaglandin E_1 (PGE_1, **8**) in its naturally occurring form. The prostanoic acid nucleus was constructed *via* conjugate addition of the cuprate **1a**, derived from (*S*)-*trans*-3-(1-ethoxyethoxy)-1-iodo-1-octene (**2b**), to (±)-2-(6-carboethoxyhexyl)-4-(2-tetrahydropyranyloxy)-2-cyclopenten-1-one (ethyl ester corresponding to **3b**). Since the attack by **1a** proceeded virtually exclusively from the least hindered side of **3b**, the configuration of the alkoxy function at C-4 in **3** is therefore of the utmost importance in dictating the eventual stereochemistry of the prostanoic acid skeleton at C-8 and C-12. We herein record an efficient method for the preparation of 2-(6-carbomethoxyhexyl)-4(*R*)-hydroxy-2-cyclopenten-1-one (**3a**)[3] and a refined procedure for the synthesis of (*S*)-*trans*-3-hydroxy-1-iodo-1-octene (**2a**).[4] The assembly of these two synthons[5] thus constitutes a completely stereospecific synthesis of PGE_1 (**8**).



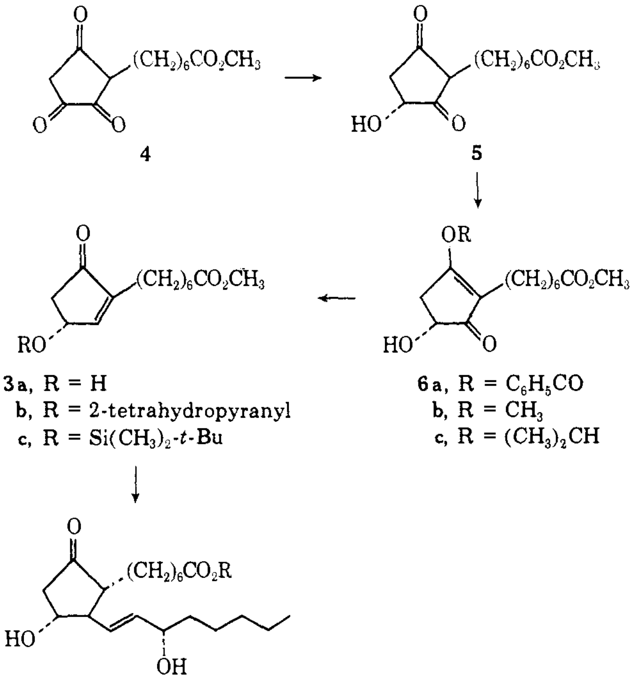
1a, R = $CH(CH_3)OCH_2CH_3$
b, R = $Si(CH_3)_2$-*t*-Bu



2a, X = I; R = H
b, X = I; R = $CH(CH_3)OCH_2CH_3$
c, X = I; R = $Si(CH_3)_2$-*t*-Bu
d, X = Li; R = $Si(CH_3)_2$-*t*-Bu

The scheme adopted for the preparation of the key intermediate **3**[6] and its reaction with the cuprate reagent **1** is summarized in Scheme I. The readily available 2-(6-carbomethoxyhexyl)cyclopentane-1,3,4-trione[7] (**4**) was best converted to 2-(6-carbomethoxyhexyl)-4(*R*)-hydroxycyclopentane-1,3-dione (**5**) by microbial reduction. A wide variety of microorganisms was found to be capable of performing the asymmetric reduction of **4** to **5**; the most suitable of these microbes was *Dipodascus uninucleatus* which gave completely stereospecific reduction to the 4(*R*) alcohol **5**. Exposure of 1 g of **4**, mp 79–81°, to this organism for 24 hr in a soybean-glucose medium gave 750 mg of **5**:[8] mp 89–91°; uv max (CH_3OH) 272 nm (ϵ 23,500); $[\alpha]^{24}D$ +16.1° (c 0.76, CH_3OH); CD (C 1.61 × 10^{-5}, CH_3OH),

Scheme I



3a, R = H
b, R = 2-tetrahydropyranyl
c, R = $Si(CH_3)_2$-*t*-Bu

6a, R = C_6H_5CO
b, R = CH_3
c, R = $(CH_3)_2CH$

7, R = CH_3
8, R = H

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[1] Paper III of this series: C. J. Sih, R. G. Salomon, P. Price, R. Sood, and G. Peruzzotti, *Tetrahedron Lett.*, 2435 (1972).

[2] C. J. Sih, P. Price, R. Sood, R. G. Salomon, G. Peruzzotti, and M. Casey, *J. Amer. Chem. Soc.*, **94**, 3643 (1972).

[3] Compound **3a** has been synthesized previously as the racemic modification: (a) L. Heslinga, M. van Gorkom, and D. A. van Dorp, *Recl. Trav. Chim. Pays-Bas*, **87**, 1421 (1968); see also F. S. Alvarez, D. Wren, and A. Prince, *J. Amer. Chem. Soc.*, **94**, 7823 (1972); (b) C. J. Sih, R. G. Salomon, P. Price, G. Peruzzotti, and R. Sood, *Chem. Commun.*, 240 (1972); (c) R. Pappo and P. W. Collins, *Tetrahedron Lett.*, 2627 (1972).

[4] The procedure for the preparation of hydroxyvinyl iodide **2a** reported herein is a variant of a previously described procedure (ref 2). An alternate synthesis of **2a** has been published: (a) E. J. Corey and D. J. Beams, *J. Amer. Chem. Soc.*, **94**, 7210 (1972); (b) for the resolution of **2a**, see A. F. Kluge, K. G. Untch, and J. H. Fried, *ibid.*, **94**, 7827 (1972)].

[5] E. J. Corey, *Pure Appl. Chem.*, **14**, 19 (1967).

[6] The approach described in this communication parallels that of Pappo and Collins.[3c]

[7] Prepared in 75–80% yield by the sodium ethoxide catalyzed condensation of methyl 9-ketodecanoate with ethyl oxalate; *cf.* J. Katsube and M. Matsui, *Agr. Biol. Chem.*, 33, 1078 (1969). In turn 9-ketodecanoic acid was prepared in 95% yield from 8-carbomethoxyoctanoic acid *via* condensation of the corresponding acid chloride with ethoxymagnesiomalonic ester; *cf.* R. E. Bowman, *J. Chem. Soc.*, 322 (1950).

[8] Satisfactory infrared, nuclear magnetic resonance, and mass spectra were obtained.