and $[Fe(TIM)(CH_3NH_2)_2]^{2+}$ and $[Fe(TIM)(CH_3NH_2)(CO)]^{2+}$,[41] the carbon monoxide or cyanide derivative always has the smaller qs. Since the substitution of CO or CN^- for one of the trans donors would be expected to significantly enhance the net field strength of the trans ligands, the reduced magnitude of the qs which is observed for the CN^- or CO derivative is certainly in keeping with the model.

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References and Notes

(1) (a) G. M. Bancróft and R. H. Platt, *Adv. Inorg. Nucl. Chem.*, **15**, 59 (1972); (b) G. M. Bancroft, *Coord. Chem. Rev.*, **11**, 247 (1973).
(2) H. Eicher and A. Trautwein, *J. Chem. Phys.*, **50**, 2540 (1969).
(3) R. Ingalls, *Phys. Rev. A*, **133**, 787 (1964).
(4) G. M. Bancroft, M. J. Mays, and B. E. Pratter, *J. Chem. Soc. A*, 956 (1970).
(5) M. G. Clark, A. G. Maddock, and R. H. Platt, *J. Chem. Soc., Dalton Trans.*, 281 (1972).
(6) C. D. Pribula, T. L. Brown, and E. Münck, *J. Am. Chem. Soc.*, **96**, 4149 (1974).
(7) (a) R. M. Sternheimer, *Phys. Rev.*, **130**, 1423 (1963); (b) for a discussion of Sternheimer effects, see E. A. C. Lucken, "Nuclear Quadrupole Coupling Constants", Academic Press, New York, N.Y., 1969.
(8) W. A. Goddard III, and B. A. Olafson, *Proc. Natl. Acad. Sci. U.S.A.*, **72**, 2335 (1975).
(9) R. V. Parish, *Prog. Inorg. Chem.*, **15**, 101 (1972).
(10) R. L. Collins and J. C. Travis in "Mössbauer Effect Methodology", Vol 3, Plenum Press, New York, N.Y., 1967, pp 123–161.
(11) H. Eicher and A. Trautwein, *J. Chem. Phys.*, **50**, 2540 (1969).
(12) T. L. Brown, *Acc. Chem. Res.*, **7**, 408 (1974).
(13) A. J. Freeman and R. E. Watson, *Phys. Rev.*, **131**, 2566 (1963).
(14) R. Ingalls, *Phys. Rev.*, **128**, 1155 (1962).
(15) E. Clementi, *I.B.M. Corp. Syst., J.*, Table 37-01 (1965).
(16) C. F. Jackels, private communication.
(17) A. J. Nozik and M. Laplan, *Phys. Rev.*, **159**, 273 (1967).
(18) M. Pasternak, A. Simopoulous, and Y. Hazony, *Phys. Rev. A*, **140**, 1892 (1965).
(19) R. V. Parish and R. H. Platt, *Inorg. Chim. Acta*, **4**, 65 (1970).
(20) W. M. Reiff, *J. Am. Chem. Soc.*, **95**, 3048 (1973); private communication, to be submitted for publication.
(21) This value for the net charge or ligating sp^2 nitrogen atoms seems reasonable based on EXTENDED Hückel MO calculations on similar systems; unpublished results by S. C. Jackels and E. R. Davidson.
(22) Arguments have been advanced (M. A. Robinson, J. D. Curry, and D. H. Busch, *Inorg. Chem.*, **2**, 1178 (1963); P. Krumholtz, *Struct. Bonding (Berlin)*, **9**, 139 (1971)) which relate the lowest energy spin allowed transition in tris-α-diimine nickel(II) complexes to the ligand field strength of these ligands with respect to the analogous Fe(II) complex. In this context both py_3tame and py_3tren are similar to the symmetrical ligands bpy and pyridinalmethylimino (see L. J. Wilson and N. J. Rose, *J. Am. Chem. Soc.*, **90**, 6041 (1968), and E. Larsen, G. N. LaMar, B. E. Wagner, J. E. Parks, and R. H. Holm, *Inorg. Chem.*, **11**, 2652 (1972)). Thus, representing all the ligating atoms by a charge in these two cases seems justified. For, the PccBF ligand the arguments which justify the use of a single charge rather than two different charges are not as strong in view of the relatively low transition energy for the first spin allowed transition of $[Ni(PccBF)]^+$ (see Larsen et al.).
(23) The authors are grateful for the discussion of the referee concerning this point, also see ref 12.
(24) M. Dunaj-Jurco and E. C. Lingafelter, private communication.
(25) M. R. Churchill and A. H. Reis, Jr., *Inorg. Chem.*, **11**, 2299 (1972).
(26) V. L. Goedken, J. Pluth and S. Peng, Abstracts of the American Crystallographic Association Meeting, Summer, 1973, No. P2, p 189.
(27) A. Zalkin, D. H. Templeton, and T. Ukei, *Inorg. Chem.*, **12**, 1641 (1973).
(28) E. C. Lingafelter, private communication.
(29) C. Mealli and E. C. Lingafelter, *Chem. Commun.*, 885 (1970).
(30) E. B. Fleischer, A. E. Gebala, D. R. Swift, and P. A. Tasker, *Inorg. Chem.*, **11**, 2775 (1972).
(31) (a) C. K. Prout and T. J. Wiseman, *J. Chem. Soc.*, 497 (1964); (b) K. Bowman, A. P. Gaughan, and Z. Dori, *J. Am. Chem. Soc.*, **94**, 727 (1972).
(32) H. W. Smith and E. C. Lingafelter, private communication.
(33) D. A. Baldwin, R. M. Pfeiffer, D. W. Reichgott, and N. J. Rose, *J. Am. Chem. Soc.*, **95**, 5152 (1973).
(34) The TIM ligand provides its four nitrogen atoms in a plane containing the metal ion but some of the carbon atoms in this macrocyclic ligand are not in that plane. Thus, the ligating atoms in $[Fe(TIM)X_2]^{n+}$ complexes can possess D_{2h} symmetry but the entire complex cannot.
(35) B. W. Dale, R. J. P. Williams, P. R. Edwards, and C. E. Johnson, *Trans. Faraday Soc.*, **64**, 620, 3011 (1968).
(36) J. C. Dabrowiak, P. H. Merrell, J. A. Stone, and D. H. Busch, *J. Am. Chem. Soc.*, **95**, 6613 (1973).
(37) C. K. Jorgensen, "Modern Aspects of Ligand Field Theory", North-Holland Publishing Company, Amsterdam, 1971 Chapter 26.
(38) R. A. LaRossa and T. L. Brown, *J. Am. Chem. Soc.*, **96**, 2072 (1974).
(39) See ref 36 and 40 for a discussion concerning the placement in the spectrochemical series of planar macrocyclic ligands containing two α-diimine linkages.
(40) S. C. Jackels, K. Farmery, E. K. Barefield, N. J. Rose, and D. H. Busch, *Inorg. Chem.*, **11**, 2893 (1972).
(41) D. W. Reichgott and N. J. Rose, unpublished results.

Oxidative Addition of Benzyl Halides to Zero-Valent Palladium Complexes. Inversion of Configuration at Carbon

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Abstract: Inversion of configuration at carbon (90–100%) was observed during the oxidative addition of optically active α-phenethyl bromide and benzyl-α-*d* chloride to either tetrakis(triphenylphosphine)palladium(0) (**1**) in the presence of carbon monoxide or carbonyltris(triphenylphosphine)palladium(0) (**4**). The product acylpalladium(II) complex in each case was formed in high yield and was converted to the corresponding optically active ester. In the absence of carbon monoxide, benzyl-α-*d* chloride underwent oxidative addition to **1** to give a stable alkylpalladium(II) complex which was transformed into the acylpalladium complex via carbon monoxide insertion. The acylpalladium complex obtained in this manner yielded the corresponding optically active ester which did not contain as high a degree of optical purity (~75% net inversion). The cause of racemization was attributed to a nucleophilic exchange equilibrium process during the oxidative addition of benzyl-α-*d* chloride to **1**.

Three different types of mechanisms have been proposed for the oxidative addition of alkyl halides to low valent group 8 transition metal complexes: (a) nucleophilic displacement of halogen by attack of the metal at the carbon center,[1-8] (b) metal insertion into the carbon-halogen bond via a three-centered transition state,[9-12] and (c) homolytic carbon–halogen cleavage involving the intermediacy of carbon radicals.[13-20]

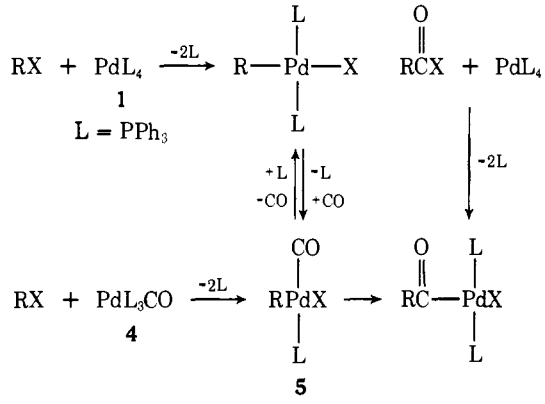
The isolation of racemized products and the retarding effect on the rate of reaction by radical scavengers have been offered as evidence for the involvement of radical intermediates in the oxidative addition of alkyl halides to d^8 iridium(I),[14] d^{10}

platinum(0),[18] and palladium(0)[19] complexes. The observation of CIDNP[21] in the reaction of certain alkyl halides with palladium(0) or platinum(0) complexes has been attributed to a radical oxidative addition process.[19]

The reactions of methyl iodide and benzyl halides with d^8 iridium(I), d^8 rhodium(I), and d^{10} platinum(0) complexes exhibit kinetics consistent with a nucleophilic type mechanism[2-5,9] and show no inhibition in the presence of galvanoxyl.[14] Similar oxidative additions of alkyl halides to d^8 cobalt(I) have been reported to occur with inversion of configuration at carbon.[7] In the oxidative additions of silicon compounds to d^8 and d^{10} platinum,[22-24] d^8 iridium,[24] and cobalt,[24] however, retention of configuration at silicon was observed exclusively. Recently, oxidative addition of an optically active allylic acetate to d^{10} palladium(0) has been shown to proceed with inversion of configuration at the chiral center.[25]

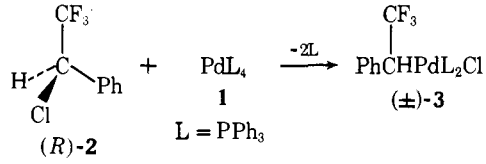
Results and Discussion

Stereochemistry. The oxidative addition of certain alkyl, aryl, vinyl, acyl, and aroyl halides to the d^{10} complex tetrakis(triphenylphosphine)palladium(0) (**1**) proceeds rapidly under mild conditions to give *trans*-haloalkyl- or *trans*-haloacyl(triphenylphosphine)palladium(II) complexes.[6,26,27] Since **1** exhibits nucleophilic character in its reactions with aryl



halides,[6] and reactions of benzyl halides with d^8 and d^{10} transition metal complexes exhibit second-order kinetics,[2] it seemed likely that the oxidative addition of benzyl halides to **1** would proceed by an SN2-type mechanism with inversion of configuration at the benzylic carbon.

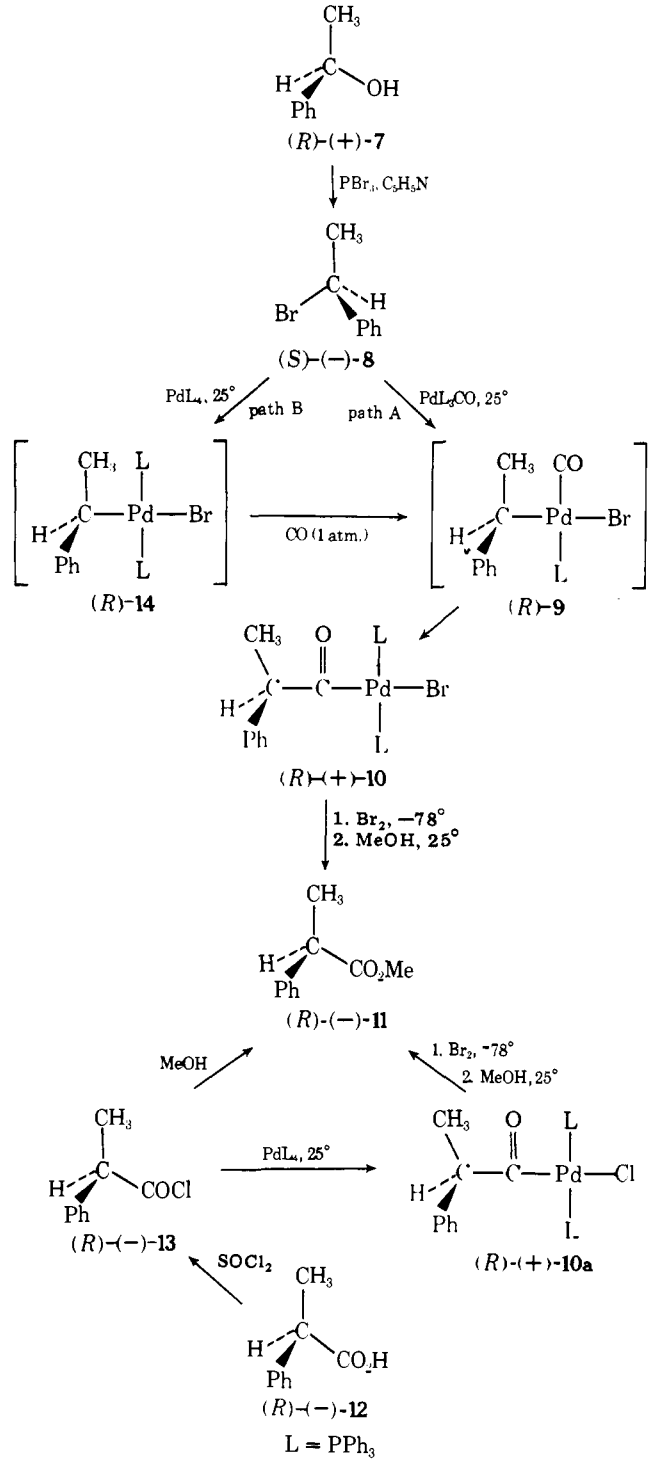
In a preliminary study[28] on the stereochemical details of the oxidative addition of alkyl halides to palladium(0), chiral 1-phenyl-2,2,2-trifluoroethyl chloride (**2**)[29] was chosen since it does not contain β-hydrogens which can undergo facile β-elimination[30] to give alkenes. The oxidative addition of **2** to **1** indeed gave an alkyl complex **3** but, unfortunately, it exhibited little or no optical rotation.



Carbonyltris(triphenylphosphine)palladium(0) (**4**)[31-34] undergoes oxidative addition reactions with a variety of organic halides to give acylpalladium(II) complexes, which can alternatively be prepared via the oxidative addition of acyl halides to **1**. It has been postulated[34] that the carbonyl–palladium complex **4** undergoes ligand dissociation in solution, leaving a coordinatively unsaturated palladium species which then allows facile oxidative addition to give **5**. A subsequent *intramolecular* carbonyl insertion affords the stable acyl complex.

α-Phenethyl Bromide. (*R*)-(+)-α-Phenethyl alcohol[35] was converted to its (*S*)-(−)-bromide (**8**)[36] which underwent oxidative addition to **4** to afford a dextrorotatory acylpalladium(II) complex **10** (Scheme I). In this example, β-elimination

Scheme I



was avoided by a relatively rapid intramolecular carbonyl insertion. The complex **10** was then converted to the known (*R*)-(−)-methyl α-phenylpropionate (**11**).[37] The chloro analogue (**10a**) of complex **10** was independently synthesized from chiral α-phenylpropionic acid (**12**)[37d,38] via the corresponding acid chloride (**13**).[38b] Since the reaction of **13** and **1** does not involve the chiral center, complex **10a** then unequivocally has the *R* configuration. In addition, since carbon monoxide inserts into the palladium–carbon bond with 100% retention of con-

Table I. Oxidative Addition of α-Phenethyl Bromide to Palladium(0) Complexes

Compound	Configuration	Obsd specific rotation	Rotation of pure compound	% optical purity
7	*R*(+)	$[\alpha]^{27}D$ +42.53 ± 0.02° (neat) $[\alpha]^{27}D$ +53.3 ± 0.8° ($CHCl_3$)	$[\alpha]^{27}D$ +43.43° (neat)[a] $[\alpha]^{27}D$ +54.4° ($CHCl_3$)	98.0
8 (for path A)	*S*(−)	$[\alpha]^{25}D$ −90.8 ± 0.7° ($CHCl_3$)	$[\alpha]^{27}D$ −125.1° (neat)[b] $[\alpha]^{27}D$ −111.5° ($CHCl_3$)[c]	81.4
10 (path A) (78.4% yield)	*R*(+)	$[\alpha]^{27}D$ +32 ± 2° ($CHCl_3$)		
11 (from **10**) (path A)	*R*(−)	$[\alpha]^{27}D$ −59.6 ± 1.1° ($CHCl_3$)	$[\alpha]^{26}D$ −88.20° ($CHCl_3$)[d,e]	67.6
12	*R*(−)	$[\alpha]^{25}D$ −69.8 ± 0.5° ($CHCl_3$) $[\alpha]^{25}D$ = −93.8 ± 0.2° (neat)	$[\alpha]^{25}D$ −75.8° ($CHCl_3$)[f] $[\alpha]^{25}D$ −101.9° (neat)	92.1
13	*R*(−)	$[\alpha]^{25}D$ −72.6 ± 0.3° ($CHCl_3$) $[\alpha]^{26.5}D$ −68.5 ± 0.4° ($CHCl_3$)		
10a	*R*(+)	$[\alpha]^{26.5}D$ +62.1 ± 0.8° ($CHCl_3$)		
11 (from **13**)	*R*(−)	$[\alpha]^{25}D$ −79.0 ± 0.7° ($CHCl_3$)	$[\alpha]^{26}D$ −88.20° ($CHCl_3$)	89.6
11 (from **10a**)	*R*(−)	$[\alpha]^{25}D$ −75.2 ± 1.0° ($CHCl_3$)	$[\alpha]^{26}D$ −88.20° ($CHCl_3$)	85.3
8 (for path B)	*S*(−)	$[\alpha]^{26}D$ −75.8 ± 0.3° ($CHCl_3$)	$[\alpha]^{27}D$ −111.5° ($CHCl_3$)	68.0
10 (path B) (92.0% yield)	*R*(+)	$[\alpha]^{27}D$ +36 ± 1° ($CHCl_3$)		
11 (from **10**) (path B)	*R*(−)	$[\alpha]^{27}D$ −55.3 ± 0.7° ($CHCl_3$)	$[\alpha]^{26}D$ −88.20° ($CHCl_3$)	62.7

[a] Calculated using the value of $[\alpha]^{25}D$ 43.45 ± 0.10° (neat)[35b] and assuming a linear relationship of $d[\alpha]^tD/dt = 0.012°/°C$: R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **99**, 45 (1911); *ibid.*, **105**, 1115 (1914). [b] Calculated from the value of 170°,[36b] allowing for the density of **8** ($d^{27}D$ 1.3584).[35b] [c] Calculated based on the observation that a synthetic sample of optically active (*S*)-**8** gave $[\alpha]^{27}D$ −78.7 ± 0.2° ($CHCl_3$) and $[\alpha]^{27}D$ −88.2 ± 0.1° (neat). [d] Determined by chiral NMR shift reagent method.[40-48] Enantiomeric ratios were calculated from peak areas of the methyl doublets. Area approximation was carried out comparatively by peak height and peak area measurements. Both methods agreed within 1%. [e] Values previously reported for optically pure **11** are as follows: $[\alpha]^{29}D$ 96.3° (neat),[37a] $[\alpha]^{27}D$ 109.2° (C_6H_6), $[\alpha]^{20}D$ 99.8° (ethanol), $[\alpha]^{23}D$ 98.8° (ethanol), $[\alpha]^{20}D$ 105.5° (neat),[37b] $[\alpha]^{21}D$ 99.4° (neat),[37c] $[M]^{25}D$ 170° (methanol), or $[\alpha]^{25}D$ 103.7° (methanol).[38d] [f] The highest reported values for the pure acid are $[\alpha]^{25}D$ 76.3° ($CHCl_3$)[38b] and $[\alpha]^{25}D$ 75.3° ($CHCl_3$).[38a] The average of these values is 75.8°.

figuration at carbon,[39] the oxidative addition step (**8** → **9**) must therefore involve an *inversion of configuration at carbon.* the absolute optical purity of **11** was determined by NMR analysis using a chiral chemical shift reagent[40-48] Eu(tfac)$_3$ [tfac = 3-trifluoroacetyl-*d*-camphorato anion]. A stereospecificity of 90% enantiomeric excess has been assigned to the conversion of **8** → **9**.[49]

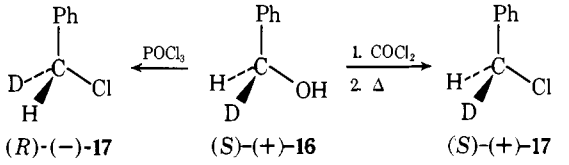
The reaction (path B, Scheme I) between (*S*)-(−)-**8** and complex **1** in a carbon monoxide atmosphere also led to the formation of the dextrorotatory acylpalladium(II) complex **10**, which was then converted to the ester (*R*)-(−)-**11**. This reaction proceeds via the initial oxidative addition of **8** to **1** affording the alkylpalladium complex **14** which undergoes carbon monoxide insertion to give **10**. The insertion of carbon monoxide in this case also takes place more rapidly than β-elimination. Since the insertion step occurs with 100% retention of configuration at carbon, the addition of **8** to **1** must take place with *inversion* of configuration at carbon. The stereospecificity of the oxidative addition step (**8** → **14**) was determined to be 95%.[49]

The isolation of the intermediate alkylpalladium(II) complex **14** from the reaction of **8** and **1** was not possible. Oxidative addition of **8** to **1** in the absence of carbon monoxide afforded styrene, ethylbenzene, and dibromobis(triphenylphosphine)-palladium(II) (**15**).[50]

$$\underset{\mathbf{8}}{PhCH(CH_3)Br} + \underset{\mathbf{1}}{PdL_4} \longrightarrow PhCH{=}CH_2 + PhCH_2CH_3 + \underset{\mathbf{15}}{PdL_2Br_2}$$

L = PPh_3

Benzyl-α-*d* Chloride. (*S*)-(+)-Benzyl-α-*d* alcohol (**16**)[51] was converted to its corresponding chloride **17** of either the same[52-54] or the opposite configuration, depending on the reagent chosen. Treatment of (*S*)-(+)-**17** with complex **1** afforded the alkylpalladium(II) complex **18** which upon carbonylation yielded the acylpalladium(II) complex **19**. The intrinsically small optical rotatory power of **18** and **19** rendered polarimetric measurements extremely difficult. The acyl complex **19** was converted to (*R*)-(−)-methyl phenylacetate-α-*d* (**20**) which was correlated with the known (*R*)-(+)-2-deuterio-2-phenylethanol (**21**).[55]



(*R*)-(−)-**17** (S)-(+)-**16** (*S*)-(+)-**17**

Neither the halogen cleavage of the acyl complex **19** nor the reduction of the ester **20** would lead to inversion of configuration at the chiral center; therefore both **19** and **20** have the *R* configuration. Since the carbonylation of palladium–carbon σ bonds occurs with 100% retention of configuration,[39] the oxidative addition of **17** to **1** (Scheme II, path A) must proceed with *inversion of configuration at the benzylic carbon.* The optical purities of **17**, **20**, and **21** have been determined (vide infra) to be 81.0 ± 4.0%, 59.8 ± 3.6%, and 57.0 ± 3.0%, respectively, allowing then the determination of the degree of stereospecificity of the oxidative addition of **17** to **1** to be 74%.

The loss of stereochemistry in the oxidative addition of **17** to **1** can be accounted for in part by the partial racemization of **17** under the reaction conditions since unreacted (*S*)-(+)-**17** recovered from the oxidative addition reaction suffered a 10% loss of its optical activity.[56] The racemization of the alkyl complex **18** cannot occur by a reversible σ–π rearrangement[57] unless the benzyl group rotates to present its opposite face to palladium. This inversion is unlikely since optically active π-allyl palladium complexes retain their configuration.[25] A nucleophilic exchange process[3b,49] between **18** and a palladium(0) species (Scheme III) is more plausible. Rapid transformation of the alkyl complex **18** to the acyl complex **19** would suppress either the rearrangement or the nucleophilic exchange process.

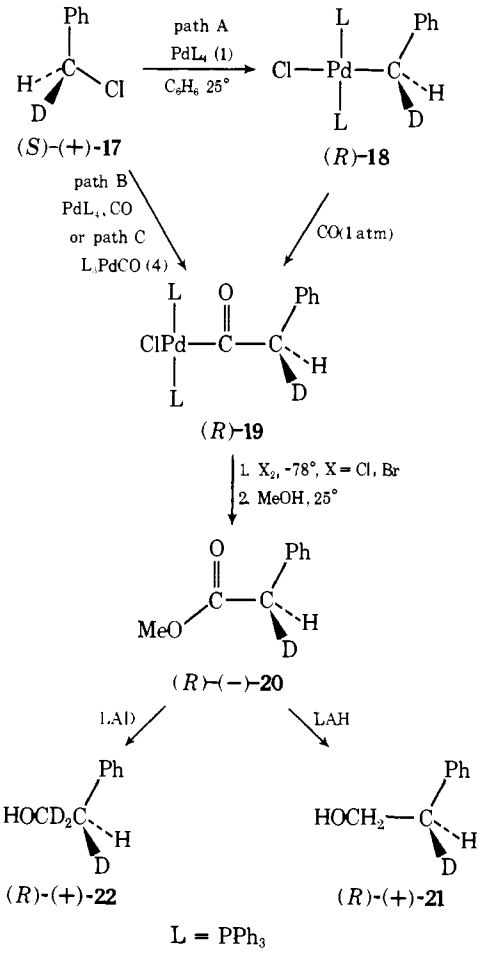
As expected, when (*S*)-(+)-**17** was allowed to react with complex **1** in the presence of carbon monoxide (Scheme II, path B), the acylpalladium(II) complex **19** could be isolated in a single step and converted to (*R*)-(−)-**20** and (*R*)-(+)-**21** of substantially higher optical rotations. Similar oxidative

Table II. Oxidative Addition of Benzyl-α-*d* Chloride to Palladium(0) Complexes in Benzene at 25 °C

Starting chloride[b]	Specific rotation[a] (% enantiomeric excess)	Palladium(0) used (L = Ph_3P)	Derived product ester	Specific rotation[a] (% enantiomeric excess)	Overall stereospecificity
(*S*)-(+)-**17**	$[\alpha]^{28}D$ +1.24° (81.0 ± 4.0%)[c]	1. PdL_4[d] 2. CO	(*R*)-(−)-**20**	$[\alpha]^{28}D$ −0.52° (59.8 ± 3.6%)[c]	74%
(*S*)-(+)-**17**	$[\alpha]^{28}D$ +1.24° (81.0 ± 4.0%)	PdL_3CO	(*R*)-(−)-**20**	$[\alpha]^{28}D$ −0.73° (83.9 ± 4.0%)	100%
(*S*)-(+)-**17**	$[\alpha]^{30}D$ +1.12° (73.1 ± 3.8%)	PdL_4, CO	(*R*)-(−)-**20**	$[\alpha]^{28}D$ −0.64° (73.5 ± 4.0%)	100%

[a] Rotations were taken on the neat liquid in a 1.000-cm cell. [b] Prepared from the alcohol (*S*)-(+)-**21** by the reaction with phosgene.[52] [c] The values for maximum rotation of these compounds are presented in Table IV. [d] Unreacted (*S*)-(+)-**17** recovered from the reaction mixture suffered a 10% loss of optical activity $[\alpha]^{28}D$ +1.12° (neat, *l* = 0.1).

Scheme II



addition of (*S*)-(+)-**17** to the carbonyl-palladium complex **4** also afforded complex **19,** contrary to the reported[33] lack of reactivity of **4** towards benzyl chloride. The recovered (*S*)-(+)-**17** in the reactions was not appreciably racemized. In contrast, when (*S*)-(+)-**17** (3 equiv) and the palladium(0) complex **1** were stirred in degassed benzene for 5 days, the unreacted **17** recovered from the reaction mixture was 100% racemized. From the available data on the optical purities of compounds **17, 20,** and **21,** the oxidative addition of **17** to the palladium(0) complexes (**1** and **4**) proceeded with 100% inversion of configuration at carbon.

Determination of Optical Purity. While the addition of the chiral chemical shift reagent Eu(tfac)$_3$ [tfac = 3-trifluoroacetyl-*d*-camphorato anion] to a deuteriochloroform solution of methyl α-phenylpropionate (**11**) caused significant enantiomeric separation in the NMR spectrum so as to allow direct determination of optical purity,[49] the same treatment to either methyl phenylacetate-α-*d* (**20**) or 2-deuterio-2-phenylethanol (**21**) in deuteriochloroform did not produce any enantiomeric separation in the NMR spectrum.[56] The NMR analysis with a more effective chiral europium shift reagent, Eu(dcm)$_3$ (dcm = *d,d*-dicampholylmethanato anion),[58] on a deuteriochloroform solution of the trideuterated alcohol, 1,1,2-trideuterio-2-phenylethanol, (*R*)-(+)-**22,** which was obtained from lithium aluminum deuteride reduction of (*R*)-(−)-**20,** caused substantial separation of the absorption peaks due to the enantiomers.[59] Measurement of the areas under the absorption peaks allowed the determination of optical purity for (*R*)-(+)-**22.** The maximum rotations for the ester **20** and the alcohols **21** and **22** were calculated (Table III). The absolute rotation of chiral chloride **17**[60] was determined on the basis of the stereospecific conversion from the alcohol (*S*)-(+)-**16**[51] by phosphorus oxychloride.

These assignments of optical purity were further confirmed by the following reaction sequence (Scheme IV, Table III).

Scheme III

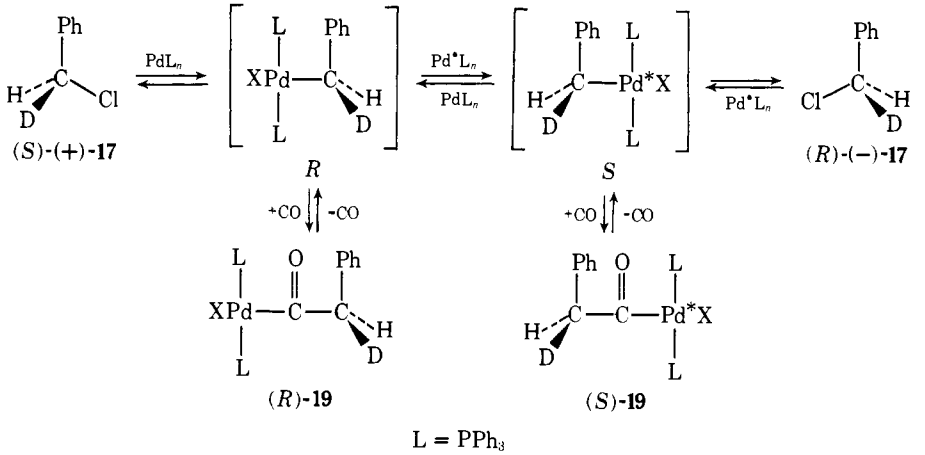
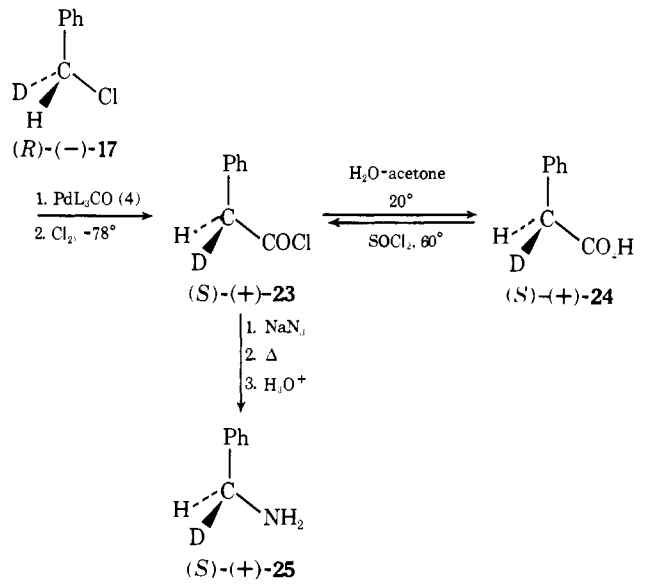


Table III. Stereochemistry of the Oxidative Addition of Chiral Benzyl-α-*d* Chloride to Palladium(0)

PhC*HDCl (**17**)			Oxidative addition in C_6H_6 at 25°						Derived products			
Configuration	Specific rotation[a]	% ee[b]	Pd(0)[c] system used	Molar ratio **17** to **1** or **4**	Reaction time (h)	Yield (%) of acyl complex **19**	Recovered **17** Specific rotation	% ee	Product	Configuration	Specific rotation	% ee
S	$[\alpha]^{28}D$ +1.24° (±0.02°)	81.0 (±4.0)	1. PdL_4 (**1**)[d] 2. CO	2.26	72	100	$[\alpha]^{30}D$ +1.12° (±0.02°)	73.1 (±2.1)	**20**	*R*[e]	$[\alpha]^{27}D$ −0.52° (±0.02°)	59.8[f] (±3.6)
									21	*R*	$[\alpha]^{28}D$ +0.86° (±0.02°)	57.0 (±3.0)
S	$[\alpha]^{28}D$ +1.24° (±0.02°)	81.0 (±4.0)	PdL_3CO (**4**)	2.30	65	85	$[\alpha]^{25}D$ +1.19° (±0.02°)	77.8 (±2.3)	**20**	*R*	$[\alpha]^{28}D$ −0.73° (±0.02°)	83.9 (±4.0)
S	$[\alpha]^{30}D$ +1.12° (±0.02°)	73.1 (±3.8)	**1** and CO^2	2.38	90	–	$[\alpha]^{30}D$ +1.10° (±0.02°)	71.9 (±2.2)	**20**	*R*	$[\alpha]^{28}D$ −0.64° (±0.02°)	73.5 (±4.0)
									21	*R*	$[\alpha]^{28}D$ +1.11° (±0.02°)	73.5 (±4.0)
S	$[\alpha]^{25}D$ +1.15° (±0.02°)	75.2 (±4.0)	**4**	1.98	108	69	—	—	**20**	*R*	$[\alpha]^{24}D$ −0.65° (±0.02°)	75.0 (±5.0)
									22	*R*	$[\alpha]^{25}D$ +1.06° (±0.02°)	75.0 (±5.0)
R	$[\alpha]^{25}D$ −1.28° (±0.02°)	83.5 (±1.9)	**4**	2.44	67	96	—	—	**23**	*S*[h]	$[\alpha]^{25}D$ +2.14° (±0.02°)	73.8 (±10.0)
R	$[\alpha]^{25}D$ −1.16° (±0.02°)	75.8 (±4.0)	**4**	2.34	72	–	$[\alpha]^{25}D$ −1.13° (±0.02°)	73.8 (±2.2)	**23**	*S*	$[\alpha]^{26}D$ +2.22° (±0.03°)	75.7 (±10.0)
									24	*S*[i]	$[\alpha]^{26}D$ +1.52° (±0.20°)	75.7 (±10.0)
									25	*S*	$[\alpha]^{26}D$ +1.37° (±0.18°)	75.7 (±10.0)

[a] All rotations, unless otherwise specified, were value for the neat liquids taken using the Perkin-Elmer Model 141 polarimeter with a polarimetric cell of path length 1.000 cm. [b] Calculated from the absolute rotation $[\alpha]^{25}D \pm 1.53 \pm 0.06°$ (neat, $l = 0.1$) and the density for $PhCH_2Cl$, d^{25}_4 1.10. The previously extrapolated values[52,53] for the absolute rotation, $[\alpha]^{25}D \pm 1.36°$, seemed low. The absolute rotation was determined from the observation that a sample of (*S*)-(+)-PhCHDOH ($[\alpha]^{25}D$ +1.32 ± 0.02° (neat, $l = 0.1$), 83.5 ± 1.9% ee) gave (*R*)-(−)-PhCHDCl ($[\alpha]^{26}D$ −1.28 ± 0.02° (neat, $l = 0.1$), assuming 100% stereospecific inversion at carbon during the chlorination reaction with $POCl_3$). The samples of the alcohol and the chloride contained 1.00 ± 0.05 deuterium per molecule based on NMR analysis. [c] L = PPh_3. [d] The intermediate alkylpalladium complex was isolated. [e] The configuration of the ester **20** was assigned on the basis of chemical correlation with **21** where configuration was known.[55] [f] Calculated from the absolute rotation $[\alpha]^{24\text{-}28}D \pm 0.87 \pm 0.08°$ (neat, $l = 0.1$). and the density for $PhCH_2CO_2CH_3$: d^{25}_4 1.03. The absolute rotation was calculated on the basis that the stereospecific reduction of a sample of (*R*)-(−)-$PhCHDCO_2CH_3$ (**20**) ($[\alpha]^{24}D$ −0.65 ± 0.02° (neat, $l = 0.1$)) by $LiAlD_4$ gave (*R*)-(+)-$PhCHDCD_2OH$ (**22**) ($[\alpha]^{25}D$ +1.06 ± 0.02° (neat, $l = 0.1$)) whose optical purity was determined to be 75 ± 5% by NMR analysis using the chiral shift reagent, Eu(dcm)$_3$.[59] [g] The intermediate alkylpalladium complex was formed in situ and carbonylated immediately. [h] The configuration of the acid chloride **23** was assigned on the basis that the synthetic sequence leading to its formation from (*R*)-(−)-**17** involves *one stereochemical inversion at carbon.* The % enantiomeric excess of **23** was calculated from the absolute rotation $[\alpha]^{26}D \pm 2.92 \pm 0.40°$ (neat, $l = 0.1$) and the density of $PhCH_2COCl$: d^{20}_4 1.17. The absolute rotation of **23** was determined from the chemical correlation with $PhCHDNH_2$ (**25**). [i] The configuration of the carboxylic acid **24** was assigned on the basis that the direct hydrolysis of the acid chloride **23** to **24** did not involve the chiral carbon.

Scheme IV



Chiral (*R*)-(−)-**17** (75.8 ± 4.0% ee) was converted to the corresponding acid chloride (*S*)-(+)-**23** whose product of hydrolysis, (*S*)-(+)-**24**, underwent chlorination with thionyl chloride to regenerate the acid chloride without loss of optical purity. The subsequent formation of the acyl azide and its rearrangement led to the synthesis of the corresponding isocyanate which underwent hydrolysis to yield (*S*)-(+)-benzylamine-α-*d* (**25**).[61] The optical purity of **25** was determined to be 75.7 ± 10%. In only two of the steps was the asymmetric carbon involved in the transformation, and the Curtius rearrangement has been known to proceed with complete *retention* of configuration at carbon.[62,63] Thus, the oxidative addition of (*R*)-(−)-**17** to complex **4** proceeds with 100% net inversion of configuration at carbon. Results obtained from this study enabled the assement of maximum specific rotation for a few chiral compounds whose dissymmetry is due to deuterium substitution (Table IV).

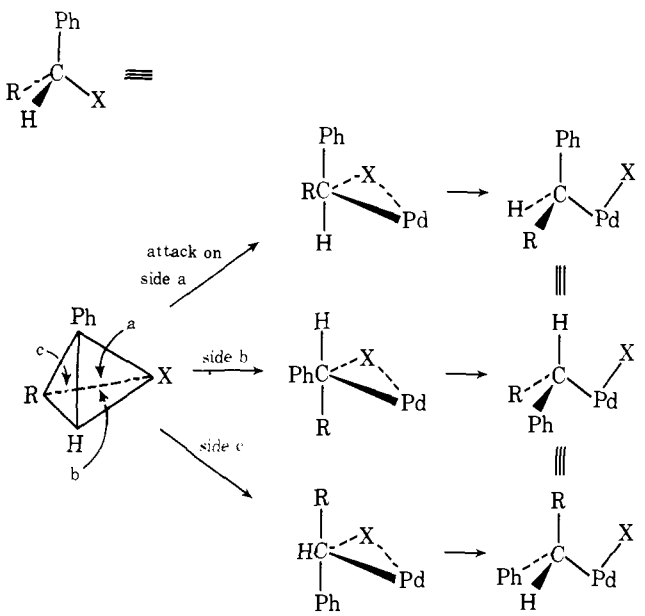
Stereospecific inversion of configuration at the chiral carbon during the oxidative additions of α-phenethyl bromide (**8**) and benzyl-α-*d* chloride (**17**) to either of the palladium(0) complexes (**1** or **4**) suggests an SN2-type mechanism in which palladium(0) serves as a nucleophile. In the reaction of the

Table IV. Absolute Rotations of Chiral Compounds Where Dissymmetry Is Due to Deuterium Substitution

Compound	Maximum rotation	Method of determination
PhCHDOH[a]	$[\alpha]^{25}D$ 1.58 ± 0.01° (neat, l = 0.1)	Enzymatic reduction of benzaldehyde-α-d[51]
PhCHDCl[a]	$[\alpha]^{25}D$ 1.53 ± 0.06° (neat, l = 0.1)	Highest rotation obtainable from $POCl_3$ chlorination of PhCHDOH
$PhCHDCO_2Me$[a]	$[\alpha]^{25}D$ 0.87 ± 0.08° (neat, l = 0.1)	Chemical correlation with $PhCHDCD_2OH$
PhCHDCOCl[c]	$[\alpha]^{26}D$ 2.92 ± 0.40° (neat, l = 0.1)	Chemical correlation with $PhCHDNH_2$
$PhCHDCO_2H$[c]	$[\alpha]^{26}D$ 2.01 ± 0.50° (c 25.72, $CHCl_3$, l = 0.1)	Chemical correlation with $PhCHDNH_2$
$PhCHDNH_2$[b]	$[\alpha]^{26}D$ 1.81 ± 0.07° (neat, l = 1.0)	NMR analysis of derivatives[61]
$PhCHDCH_2OH$[a]	$[\alpha]^{28}D$ 1.51 ± 0.10° (neat, l = 0.1)	Chemical correlation with $PhCHDCO_2Me$
$PhCHDCD_2OH$	$[\alpha]^{25}D$ 1.41 ± 0.11° (neat, l = 0.1)	NMR analysis using chemical shift reagent Eu(dcm)$_3$[59]

[a] Deuterium content was determined by NMR analysis. [b] Deuterium content was not determined. [c] Deuterium content was determined by mass spectral analysis.

alkyl halides with **4**, an alternative mechanism involving direct nucleophilic attack by the carbonyl group seems unlikely since metal carbonyls are known to be poor nucleophiles and are reactive towards bases.[64] An alternative mechanism requires concerted attack of palladium at the carbon-halogen bond from any one of three of the tetrahedral faces common to the carbon-halogen bond through a trigonal bipyramidal transition state. In the case of α-phenethyl bromide (R = CH_3) face b may be preferred on steric grounds. If carbon-halogen bond



scission occurs always with least motion of the equatorial group *in one preferred direction*, i.e., towards palladium, then the same enantiomorph is always obtained, having the net effect of a configurational inversion at carbon. Mechanistically, a cis palladium complex would be predicted. The failure to observe the cis isomer could be a consequence of fast cis to trans isomerization in palladium complexes.

Experimental Section

The preparation of and reactions involving air sensitive tetrakis(triphenylphosphine)palladium(0) (**1**) and carbonyltris(triphenylphosphine)palladium(0) (**4**) were carried out under appropriate inert atmosphere (nitrogen or carbon monoxide). All solvents used for oxidative addition reactions were purified and degassed.

Oxidative Addition of Benzyl Chloride to Carbonyltris(triphenylphosphine)palladium(0) (4). Synthesis of Chloro(phenylacetyl)bis(triphenylphosphine)palladium(II). Carbonyltris(triphenylphosphine)palladium(0)[31b] (2.56 g, 3.04 mmol) was dissolved in 50 ml of carbon monoxide-saturated benzene and an excess of benzyl chloride (1.65 g, 13.0 mmol) was introduced. After 18 h of stirring under carbon monoxide at 25 °C, the initial orange solution changed to a yellow slurry. The reaction mixture was diluted with 100 ml of hexane and filtered and the isolated white complex was washed thoroughly with ether and dried in vacuo. The complex was identified as chloro(phenylacetyl)bis(triphenylphosphine)palladium(II) by comparison of its ir spectrum to that of an authentic sample synthesized by the oxidative addition of phenylacetyl chloride to tetrakis(triphenylphosphine)palladium(0): ir ($CHCl_3$) 1670 cm^{-1} (RCO-Pd). The yield of this reaction, which was not optimized, was 36.9%. Anal. Calcd for $C_{44}H_{37}ClOP_2Pd$: C, 67.27; H, 4.75. Found: C, 67.74; H, 4.72.

Oxidative Addition of Benzyl Bromide to Carbonyltris(triphenylphosphine)palladium(0) (4). Synthesis of Bromo(phenylacetyl)bis(triphenylphosphine)palladium(II). To a solution of 1.38 g (1.50 mmol) of carbonyltris(triphenylphosphine)palladium(0) in 50 ml of carbon monoxide-saturated anhydrous benzene was added 0.273 g (1.60 mmol, 5% excess) of benzyl bromide. After 17 h of stirring at 25 °C, the reaction mixture was mixed with hexane and a white complex was isolated by filtration. It was thoroughly washed with ether and dried in vacuo. The complex was identified as bromo(phenylacetyl)bis(triphenylphosphine)palladium(II) by its ir spectrum (ir ($CHCl_3$) 1670 cm^{-1}) which is virtually superimposable with that of chloro(phenylacetyl)bis(triphenylphosphine)palladium(II) in the 4000–300-cm^{-1} region and by its conversion to methyl phenylacetate in refluxing methanol. The yield of the complex was 1.11 g (1.34 mmol, 89.3%). Anal. Calcd for $C_{44}H_{37}BrOP_2Pd$: C, 63.43; H, 4.52. Found: C, 62.99; H, 4.40.

Preparation and Transformation of Optically Active Bromo(α-phenylpropionyl)bis(triphenylphosphine)palladium(II) (10). Formation of (*R*)-(−)-Methyl α-Phenylpropionate (11). Path A: Via Carbonyltris(triphenylphosphine)palladium(0) (4). To a 50 ml carbon monoxide-saturated benzene solution containing 1.87 g (2.22 mmol) of carbonyltris(triphenylphosphine)palladium(0) was added 1.44 g (7.78 mmol, 3.51 equiv) of chiral α-phenethyl bromide, $[\alpha]^{25}D$ −90.8° (c 2.81, $CHCl_3$, l = 0.1).[36] The mixture was stirred under carbon monoxide at 25 °C for 60 h. Dilution of the mixture with hexane and filtering afforded an orange yellow complex (1.47 g, 1.74 mmol, 78.4%): ir ($CHCl_3$) 1670 (C=O), (Nujol) 283 cm^{-1} (Pd-Br, trans to acyl); $[\alpha]^{27}D$ +32° (c 1.00, $CHCl_3$, l = 0.1).

A second run of the same reaction using only a 40% excess of the alkyl bromide for 90 h afforded a yellow complex whose ir spectrum indicated the presence of both the expected acyl complex (1670 cm^{-1}) and the extraneous tripalladium cluster complex, $Pd_3(CO)_3(PPh_3)_3$ (1870 cm^{-1}).[31b,34] This batch of complex gave a smaller optical rotation: $[\alpha]^{27}D$ + 16° (c 1.00, $CHCl_3$, l = 0.1).

The complex obtained above was dissolved in 20 ml of methylene chloride and the solution was cooled to −78 °C before adding 244 mg (1.52 mmol, 0.876 equiv) of bromine. The addition of bromine caused heavy precipitation of a bright yellow complex. The mixture was then warmed to 25 °C and 5 ml of anhydrous methanol was introduced. After 15 min, the mixture was diluted with an equal volume of hexane and was filtered. The complex isolated was thoroughly washed with methanol and ether in succession. The filtrate was concentrated and extracted with six 10-ml portions of pentane. The pentane extracts were combined and concentrated. GLC analysis (175 °C, 10 ft × 0.375 in., 20% DEGS on Chromosorb W 60/80) showed the presence of methyl α-phenylpropionate as the only volatile product. The crude product (40.0 mg 0.244 mmol, 16%) was shown to have optical activity: $[\alpha]^{27}D$ −54.3° (c 2.34, $CHCl_3$, l = 0.1). Preparative GLC (150 °C, DEGS column) yielded 32.3 mg of pure methyl α-phenyl propionate: ir (neat) 1745 cm^{-1} (RCOOR); NMR ($CDCl_3$) 7.34 (s, 5H, C_6H_5), 3.74 (q, 1 H, J = 7.5 Hz, -CHCO), 3.64 (s, 3 H, CO_2CH_3),

and 1.48 ppm (d, 3, J = 7.5 Hz, CH_3CH); mass spectrum (70 eV) m/e (rel intensity) 164 (20.4), 105 (100.0); $[\alpha]^{27}D$ −59.6° (c 1.83, $CHCl_3$, l = 0.1), 67.6% optically pure. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.24; H, 7.26.

Path B: Via Tetrakis(triphenylphosphine)palladium(0) (1). As soon as complete solubilization of 1.86 g (1.61 mmol) of tetrakis(triphenylphosphine)palladium(0) in 50 ml of carbon monoxide-saturated anhydrous benzene was achieved, 0.605 g (3.27 mmol, 2.03 equiv) of α-phenethyl bromide, $[\alpha]^{26}D$ −75.8° (c 6.20, $CHCl_3$, l = 0.1), was added to the solution. A color transition from greenish yellow to orange was observed. The reaction was allowed to proceed for 96 h before the isolation of an orange-yellow complex (1.25 g, 1.48 mmol, 92.0%): ir ($CHCl_3$) 1670 cm^{-1} (RCOPd); $[\alpha]^{27}D$ +36° (c 1.54, $CHCl_3$, l = 0.1).

The complex was allowed to react with 160 mg (1.00 mmol, 0.676 equiv) of bromine at −78 °C in methylene chloride. The mixture was warmed to 25 °C and 5 ml of methanol was added. Filtering and concentrating the filtrate gave a brown residue which was carefully extracted with fifteen 10-ml portions of pentane. All pentane extracts were combined and concentrated. Preparative GLC (150 °C, 10 ft × 0.325 in., 20% DEGS on Chromosorb W 60/80) of the residual oil afforded 30.4 mg (18.5%) of chiral methyl α-phenylpropionate: ir ($CHCl_3$) 1740 cm^{-1} (RCO_2R'); mass spectrum (70 eV) parent ion at m/e 164; $[\alpha]^{27}D$ −55.3° (c 3.04, $CHCl_3$, l = 0.1), 62.7% optically pure.

Synthesis of Optically Active Chloro(α-phenylpropionyl)bis(triphenylphosphine)palladium(II) (10a) by the Oxidative Addition of Optically Active α-Phenylpropionyl Chloride to Tetrakis(triphenylphosphine)palladium(0) (1). α-Phenylpropionyl chloride,[38b] $[\alpha]^{26.5}D$ −68.5° (c 8.04, $CHCl_3$, l = 0.1), was synthesized by the conventional method from chiral l-phenylpropionic acid (Norse Labs, $[\alpha]^{25}D$ −69.8° (c 4.47, $CHCl_3$, l = 0.1), 92.1% optically pure).

To a degassed benzene solution of 1.73 g (1.50 mmol) of tetrakis(triphenylphosphine)palladium(0) was added 0.261 g (1.55 mmol) of chiral α-phenylpropionyl chloride. After 12 h of stirring under nitrogen, the solution yielded a creamy white complex which was isolated by filtration and washed with ether. The complex, $[\alpha]^{26.5}D$ +62.1° (c 2.69, $CHCl_3$, l = 0.1), had an ir spectrum (($CHCl_3$) 1670 cm^{-1}) virtually identical with that of bromo(α-phenylpropionyl)bis(triphenylphosphine)palladium(II). Yield: 0.978 g (1.22 mmol, 81.6%).

Bromine Cleavage of Optically Active Chloro(α-phenylpropionyl)bis(triphenylphosphine)palladium(II) (10a) and Subsequent Methanolysis of Chiral α-Phenylpropionyl Bromide. Formation of Optically Active Methyl α-Phenylpropionate (11). (a) With Equimolar Quantity of Bromine. Optically active chloro(α-phenylpropionyl)bis(triphenylphosphine)palladium(II) (0.978 g, 1.22 mmol) was dissolved in methylene chloride, the solution was cooled to −78 °C and 196 mg (1.22 mmol) of bromine was added. Upon warming to 25 °C, the mixture was allowed to react with 5 ml of anhydrous methanol. Routine workup afforded a yellow complex and an oil. Purification of the oil by preparative GLC (150 °C, 10 ft × 0.375 in., 20% DEGS on Chromosorb W 60/80) yielded 24.6 mg (12.2%) of methyl α-phenylpropionate: ir ($CHCl_3$) 1740 cm^{-1} (RCO_2R'); NMR ($CDCl_3$) identical with that of an authentic sample; mass spectrum (70 eV) parent ion at m/e 164; $[\alpha]^{26}D$ −60.6° (c 2.13, $CHCl_3$, l = 0.1), 68.7% optically pure. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found, C, 72.90; H, 7.59.

The yellow complex was identified as bromochlorobis(triphenylphosphine)palladium(II) by its high melting point (250–270 °C), ir spectrum which was superimposable with that of dichlorobis(triphenylphosphine)palladium(II) in the 4000–1000 cm^{-1} region, and elemental analysis. Anal. Calcd for $C_{36}H_{30}BrClP_2Pd$: C, 57.91; H, 4.05. Found: C, 57.41; H, 4.19.

(b) With Limited Quantity of Bromine. A second sample (0.926 g, 1.16 mmol) of chloro(α-phenylpropionyl)bis(triphenylphosphine)-palladium(II), $[\alpha]^{26.5}D$ +62.1° (c 2.69, $CHCl_3$, l = 0.1), was treated with 160 mg (1.00 mmol, 0.862 equiv) of bromine at −78 °C in methylene chloride. Subsequent methanolysis of the mixture and routine workup afforded a yellow complex and an oil. Preparative GLC (150 °C, 10 ft × 0.375 in., 20% DEGS on Chromosorb W 60/80) of the oil yielded 20.6 mg (0.126 mmol, 12.6%) of methyl α-phenylpropionate: mass spectrum (70 eV) parent ion at m/e 164; $[\alpha]^{25}D$ −75.2° (c 2.06, $CHCl_3$, l = 0.1), 85.3% optically pure.

Direct Methanolysis of Optically Active α-Phenylpropionyl Chloride (13). To 100 mg (0.595 mmol) of α-phenylpropionyl chloride, $[\alpha]^{26.5}D$ −68.5° (c 8.04, $CHCl_3$, l = 0.1), was added 1 ml of anhydrous methanol at 25 °C. The mixture was concentrated to give an oil which after purification by preparative GLC (150 °C, DEGS column) yielded 28.6 mg (0.174 mmol, 29.3%) of methyl α-phenylpropionate: mass spectrum (70 eV) parent ion at m/e 164; $[\alpha]^{25}D$ −79.0° (c 2.86, $CHCl_3$, l = 0.1), 89.6% optically pure.

Bromine Cleavage of Chloro(α-deuteriophenylacetyl)bis(triphenylphosphine)palladium(II) (19) and Subsequent Methanolysis of the Acid Bromide. Formation of (*R*)-(−)-Methyl α-Deuteriophenylacetate (20). To a vigorously stirred solution of 7.70 g (9.79 mmol) of chloro(α-deuteriophenylacetyl)bis(triphenylphosphine)palladium(II) in 250 ml of methylene chloride was added 1.48 g (9.25 mmol, 0.945 equiv) of bromine at −78 °C. The reaction mixture was stirred for 5 min at −78 °C and was allowed to warm to 25 °C. The precipitated bromochlorobis(triphenylphosphine)palladium(II) was removed by filtration and was washed with 20 ml of methanol. The combined filtrates were stirred at 25 °C for 30 min and concentrated under reduced pressure. The residue was distilled to give 1.1 g (7.3 mmol, 78%) of chiral (*R*)-(−)-methyl α-deuteriophenylacetate (**20**): bp 55–56 (0.75 mmHg); $[\alpha]^{28}D$ −0.50° (neat, l = 0.1); NMR ($CDCl_3$) 7.25 (s, 5 H, C_6H_5), 3.65 (s, 3 H, OCH_3), and 3.58 ppm (t, 1 H, PhC*H*D, J = 2.2 Hz).

Oxidative Addition of Optically Active Benzyl-α-*d* Chloride (17) to Tetrakis(triphenylphosphine)palladium(0) (1). Formation of Chloro(α-deuteriobenzyl)bis(triphenylphosphine)palladium(II) (18). To a solution of 13.0 g (11.3 mmol) of tetrakis(triphenylphosphine)palladium(0) in 250 ml of degassed benzene was added 3.0 g (2.4 mmol) of (*S*)-(+)-benzyl-α-*d* chloride,[52] $[\alpha]^{28}D$ +1.24° (neat, l = 0.1), under nitrogen. The reaction mixture was stirred at 25 °C for 72 h and then concentrated under reduced pressure. To the residue was added 100 ml of ether and then 200 ml of pentane. The yellow complex was isolated by filtration and washed with 100 ml of pentane to afford 8.0 g (11 mmol, 94%) of chloro(α-deuteriobenzyl)bis(triphenylphosphine)palladium(II) (**18**): mp 140–144 °C dec; NMR ($CDCl_3$) 7.9–6.3 (m, 38 H, aromatic) and 2.70 ppm (bs, 1 H, PhC*H*D). Anal. Calcd for $C_{43}H_{36}ClDP_2Pd$: C, 68.08; H, 5.01. Found: C, 67.12; H, 4.92.

The combined filtrates were concentrated by distillation through a 10-cm Vigreux column. Short path distillation afforded 0.7 g of the unreacted benzyl-α-*d* chloride: bp 47–50 °C (4 mmHg); $[\alpha]^{28}D$ +1.12° (neat, l = 0.1). GLC analysis indicated a 98% purity.

Carbonylation of Chloro(α-deuteriobenzyl)bis(triphenylphosphine)palladium(II) (18). Formation of Chloro(α-deuteriophenylacetyl)bis(triphenylphosphine)palladium(II) (19). A slurry of 8.0 g (11 mmol) of chloro(α-deuteriobenzyl)bis(triphenylphosphine)palladium(II) in 150 ml of anhydrous ether was stirred under 1 atm of carbon monoxide at 25 °C for 20 h. The creamy white complex was isolated by filtration and washed with 100 ml of pentane to give 7.9 g (10 mmol, 94%) of chloro(α-deuteriophenylacetyl)bis(triphenylphosphine)palladium(II) (**19**): ir (KBr) 1670 cm^{-1} (RCOPd).

Lithium Aluminum Hydride Reduction of (*R*)-(−)-Methyl α-Deuteriophenylacetate (20). Formation of (*R*)-(+)-2-Deuterio-2-phenylethanol (21). To a slurry of 0.414 g (10.9 mmol) of lithium aluminum hydride in 10 ml of anhydrous ether was added dropwise an ethereal solution of 1.14 g (7.57 mmol) of (*R*)-(−)-methyl α-deuteriophenylacetate, $[\alpha]^{28}D$ −0.71° (neat, l = 0.1). The mixture was stirred at 25 °C for 36 h and then hydrolyzed by the addition of 30 ml of 10% aqueous hydrochloric acid. The ether layer was separated and the aqueous layer was extracted with three 50-ml portions of ether. The combined ethereal extracts were dried over magnesium sulfate and concentrated. The residual oil was distilled to yield 0.644 g (5.24 mmol, 69.2%) of 2-deuterio-2-phenylethanol: bp 60 °C (0.6 mmHg); $[\alpha]^{28}D$ −1.13° (neat, l = 0.1); NMR ($CDCl_3$) 7.22 (s, 5 H, aromatic), 3.80 (d, 2 H, CH_2OH, J = 6.5 Hz), 2.80 (tt, 1 H, C*H*D, J = 6.5 Hz, 2.0 Hz), and 1.76 ppm (s, 1 H, O*H*); mass spectrum (40 eV) parent ion at m/e 123. NMR, GLC, and mass spectrometric analyses indicated that the sample was >99% pure and contained 0.92 ± 0.01 deuterium per molecule.

One-Step Preparation and Subsequent Reaction of Optically Active Chloro(α-deuteriophenylacetyl)bis(triphenylphosphine)palladium(II) (19). Formation of (*R*)-(−)-Methyl α-Deuteriophenylacetate (20). Path A: Via Carbonyltris(triphenylphosphine)palladium(0) (4). To a carbon monoxide-saturated benzene solution containing 10.5 g (11.4 mmol) of carbonyltris(triphenylphosphine)palladium(0) was added 3.35 g (26.2 mmol, 2.30 equiv) of benzyl-α-*d* chloride, $[\alpha]^{28}D$ +1.24° (neat, l = 0.1). The mixture was stirred under carbon monoxide at 25 °C

for 65 h. Mixing with 100 ml of hexane and filtering afforded 7.66 g (9.74 mmol, 85.5%) of chloro(α-deuteriophenylacetyl)bis(triphenylphosphine)palladium(II): ir ($CHCl_3$) 1670 cm^{-1} (RCOPd).

The hexane filtrate was concentrated by distillation at 80 °C. The residual oil was distilled to afford 0.782 g (5.22 mmol, 35.3%) of benzyl-α-*d* chloride: bp 26 °C (0.55 mmHg); $[\alpha]^{28}D$ +1.19° (neat, *l* = 0.1).

The complex obtained above was dissolved in 100 ml of methylene chloride and the solution was cooled to −78 °C before the addition of 1.43 g (8.94 mmol) of bromine. Heavy precipitation of a yellow complex was immediate. The mixture was warmed to 25 °C and 20 ml of anhydrous methanol was added. After 15 min, the mixture was filtered and the filtrate was concentrated. The residue was extracted four times with pentane, and the combined filtrates were concentrated to an oil which was purified by distillation at 0.20 mmHg. The purified product (0.750 g, 5.00 mmol, 55.6%) was identified as (*R*)-(−)-methyl α-deuteriophenylacetate: NMR ($CDCl_3$) 7.24 (s, 5 H, aromatic), 3.62 (s, 3 H, CO_2CH_3), and 3.56 ppm (m, 1 H, CD*H*); $[\alpha]^{28}D$ −0.74° (neat, *l* = 0.1). GLC analysis (150 °C, 10 ft × 0.375 in., 20% FFAP on Chromosorb W 60/80) indicated >99% purity.

Path B: Via Tetrakis(triphenylphosphine)palladium(0) (1). Upon solubilization of tetrakis(triphenylphosphine)palladium(0) (10.0 g, 8.67 mmol) in 100 ml of carbon monoxide-saturated benzene, 2.64 g (20.7 mmol, 2.39 equiv) of chiral benzyl-α-d chloride, $[\alpha]^{28}D$ +1.12° (neat, *l* = 0.1), was added to the solution. The reaction was allowed to proceed for 90 h before the isolation (by filtration) of chloro(α-deuteriophenylacetyl)bis(triphenylphosphine)palladium(II): ir ($CHCl_3$) 1670 cm^{-1} (RCOPd). The yield was 3.33 g (4.23 mmol, 48.8%).

From the filtrate 0.733 g (5.75 mmol) of optically active benzyl-α-*d* chloride was recovered by distillation (28 °C (0.55 mmHg)): $[\alpha]^{28}D$ +1.10° (neat, *l* = 0.1).

The complex obtained above was dissolved in 100 ml of methylene chloride and the solution was cooled to −78 °C before the addition of 0.640 g (4.00 mmol) of bromine. The mixture was brought to 25 °C and 20 ml of anhydrous methanol was added. After 15 min, the mixture was worked up by the routine procedure. Filtration, concentration of the filtrate, extraction with pentane (six times), concentration of the combined pentane extracts, and finally distillation under reduced pressure were effected. The purified product was identified as methyl α-deuteriophenylacetate by comparison of its GLC retention times with an authentic sample and by mass spectral analysis: mass spectrum (70 eV) parent ion at *m/e* 151, $[\alpha]^{28}D$ −0.65 (neat, *l* = 0.1). The yield was 0.388 g (2.57 mmol, 64.3%).

Racemization of Benzyl-α-*d* Chloride. A solution of 0.499 g (3.91 mmol) of (*R*)-(−)-benzyl-α-*d* chloride, $[\alpha]^{25}D$ −0.38° (neat, *l* = 0.1), and 1.17 g (1.02 mmol) of tetrakis(triphenylphosphine)palladium(0) in 20 ml of degassed anhydrous benzene was stirred under nitrogen at 30 °C for 5 days. Dilution of the mixture with pentane precipitated chloro(α-deuteriobenzyl)bis(triphenylphosphine)palladium(II) and the filtrate was concentrated by distillation through a 5-cm Vigreux column. The residual oil was purified by distillation using a molecular still. The recovered benzyl-α-*d* chloride was racemic: $[\alpha]^{28}D$ +0° (neat, *l* = 0.1).

Lithium Aluminum Deuteride Reduction of (*R*)-(−)-Methyl α-Deuteriophenylacetate (20). Formation of (*R*)-(+)-1,1,2-Trideuterio-2-phenylethanol (22). A solution of 0.435 g (2.89 mmol) of (*R*)-(−)-methyl α-deuteriophenylacetate, $[\alpha]^{24}D$ −0.65° (neat, *l* = 0.1), in 10 ml of anhydrous ether was added dropwise to a slurry of 0.286 g (6.81 mmol) of lithium aluminum deuteride in 25 ml of anhydrous ether at 0 °C. The mixture was stirred at 25 °C for 42 h. Hydrolytic workup with 10% aqueous hydrochloric acid followed by extraction of the aqueous phase with four 10-ml portions of ether and drying and concentration of the combined ethereal extracts afforded an oil which was purified by distillation at 0.7 mmHg to yield 0.233 g (1.87 mmol, 64.7%) of product: $[\alpha]^{25}D$ −1.06° (neat, *l* = 0.1); NMR ($CDCl_3$) 7.20 (s, 5 H, aromatic), 2.75 (bs, 1 H, PhC*H*D) and 2.57 ppm (bs, 1 H, O*H*); mass spectrum (70 eV) parent ion at *m/e* 125. NMR integration ratios indicated 100 ± 5% monodeuteration at the benzylic carbon.

Synthesis and Hydrolysis of Optically Active α-Deuteriophenylacetyl Chloride (23). Formation of Optically Active α-Deuteriophenylacetic Acid (24). A sample of 3.00 g (3.81 mmol) of chloro(α-deuteriophenylacetyl)bis(triphenylphosphine)palladium(II) was prepared by the oxidative addition of 1.94 g (15.2 mmol) of chiral benzyl-α-*d* chloride, $[\alpha]^{26}D$ −1.16° (neat, *l* = 0.1), to 5.99 g (6.50 mmol) of carbonyltris(triphenylphosphine)palladium(0).

The acyl complex in 100 ml of methylene chloride was allowed to react at −78 °C with 3.5 ml of a 1.05 M solution of chlorine (3.7 mmol, 0.97 equiv) in carbon tetrachloride. The mixture was stirred at −78 °C for 15 min and then warmed to 25 °C. Dilution of the mixture with twice its volume of pentane and filtering under nitrogen yielded a light yellow filtrate which was concentrated under nitrogen. The residue was extracted with ten 20-ml portions of pentane. The pentane extracts were combined and concentrated to an oil which was purified by distillation to give 180 mg (1.16 mmol, 31.4%) of optically active α-deuteriophenylacetyl chloride. Mass spectral analysis indicated 0.901 ± 0.003 deuterium per molecule. The rotation of this sample was determined by mixing the product with a known quantity of phenylacetyl chloride and taking the measurement of the neat liquid mixture.

The amount of phenylacetyl chloride added was 0.216 g. The mole percent of active material in the mixture was then 45.3%. The observed rotation was $\phi^{26}D$ +0.106 ± 0.002° (neat, *l* = 0.1) which was extrapolated to $\phi^{26}D$ +0.234 ± 0.004° for 100% active material. Allowing for the density (d^{20}_4 1.17) and the deuterium content of the sample of acid chloride, the specific rotation of α-deuteriophenylacetyl chloride was calculated to be $[\alpha]^{26}D$ +2.22 ± 0.03° (neat, *l* = 0.1).

The acid chloride mixture was treated at 20 °C with 15 ml of a 1:1 water–acetone mixture. The combined solutions were stirred for 5 min and the solvents were removed under reduced pressure to afford a white solid which was recrystallized from pentane at −78 °C. Filtering, washing with pentane which was chilled at −78 °C, and drying in vacuo for 14 h yielded 0.283 g (2.07 mmol, 80.7%) of a mixture of phenylacetic acid and α-deuteriophenylacetic acid: mp 75 °C; mass spectrum (70 eV) parent peaks at *m/e* 136 and 137. The observed rotation was $\phi^{26}D$ +0.016 ± 0.002° (*c* 25.72, $CHCl_3$, *l* = 0.1). Allowing for the presence of undeuterated material and the deuterium content of the deuterated material (assuming no loss during the hydrolysis), the specific rotation of α-deuteriophenylacetic acid was calculated to be $[\alpha]^{26}D$ +1.52 ± 0.20° (*c* 25.72, $CHCl_3$, *l* = 0.1).

The Stereospecific Curtius Rearrangement of Optically Active α-Deuteriophenylacetyl Chloride in the Presence of Sodium Azide. Formation of Optically Active Benzylamine-*d* (25). A 0.283 g (2.07 mmol) mixture of 45.3% α-deuteriophenylacetic acid in phenylacetic acid was treated with 0.840 g (7.06 mmol, 3.41 equiv) of thionyl chloride in 10 ml of chloroform under nitrogen at reflux for 1 h. Volatile materials were removed at reduced pressure, and the oil was purified by distillation (55–60 °C (0.25 mmHg)) to afford 0.304 g (1.95 mmol, 94.4%) of a colorless mixture of 45.3% α-deuteriophenylacetyl chloride in phenylacetyl chloride, assuming no loss of deuterated material. An additional 0.266 g of purified phenylacetyl chloride was added to facilitate polarimetric measurements. The observed rotation was $\phi^{26}D$ +0.056 ± 0.002° (neat, *l* = 0.1) which was converted to $[\alpha]^{26}D$ +2.21 ± 0.03° by allowing for the undeuterated material and the density factor.

The acid chloride mixture (0.570 g, calculated to be 24.0% of active α-deuteriophenylacetyl chloride) was dissolved in 5 ml of toluene and was added dropwise to a vigorously stirred heterogeneous mixture of 0.584 g (8.98 mmol, 2.00 molar equiv) of sodium azide in 10 ml of water and 2 ml of toluene at 0–5 °C. After stirring for 2.5 h, the toluene phase was removed and the aqueous phase was extracted twice with 5-ml portions of toluene. The toluene extracts were combined, dried over magnesium sulfate, and then slowly heated at the rate of 1°/min. Gas evaluation began at ca. 45 °C and diminished at 60 °C. The solution was then heated at 80 °C for 0.5 h.[65] Removal of toluene by distillation at 110 °C through a Vigreux column left a residue which was mixed with 10 ml of 20% aqueous hydrochloric acid and heated at reflux for 1.5 h. The solution was neutralized with 5 N aqueous sodium hydroxide and continuously extracted with ether. The ethereal layer was dried over magnesium sulfate and the solvent was removed at reduced pressure. Distillation at 10 mmHg afforded 0.152 g of a mixture of benzylamine and chiral benzylamine-α-*d*. Assuming no loss in the deuterated material and no racemization during the Curtius rearrangement step, the sample was 24.0% benzylamine-α-*d*.

An additional 0.125 g of benzylamine was added to facilitate polarimetric measurements. The mixture of amines had an observed rotation of $\phi^{26}D$ +0.016 ± 0.002° (neat, *l* = 0.1). Allowing for the presence of undeuterated material and the density factor (d^{20}_4 0.98 for benzylamine), the specific rotation for benzylamine-α-*d* was calculated to be $[\alpha]^{26}D$ +1.37 ± 0.18° (neat, *l* = 0.1).

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References and Notes

(1) C. D. Cook and G. S. Jauhal, *Can. J. Chem.*, **45**, 301 (1967).
(2) (a) P. B. Chock and J. Halpern, *J. Am. Chem. Soc.*, **88**, 3511 (1966); (b) *Proc. Int. Conf. Coord. Chem.*, **10** 135 (1967).
(3) (a) J. P. Collman, D. M. Murphy, and G. Dolcetti, *J. Am. Chem. Soc.*, **95**, 2687 (1973); (b) J. P. Collman and M. R. MacLaury, *ibid.*, **96**, 3019 (1974).
(4) J. C. Douek and G. Wilkinson, *J. Chem. Soc. A*, 2604 (1969).
(5) (a) A. J. Hart-Davis and W. A. G. Grahm, *Inorg. Chem.*, **10**, 1651 (1971); (b) *ibid.*, **9**, 2658 (1970).
(6) P. Fitton and E. A. Rick, *J. Organomet. Chem.*, **28**, 287 (1971).
(7) F. R. Jensen, V. Madan, and D. H. Buchanan, *J. Am. Chem. Soc.*, **92**, 1414 (1970).
(8) D. Dodd and M. D. Johnson, *J. Chem. Soc. D*, 571 (1971).
(9) R. Ugo, A. Pasini, A. Fusi, and S. Cenini, *J. Am. Chem. Soc.*, **94**, 7364 (1972).
(10) R. G. Pearson and W. R. Muir, *J. Am. Chem. Soc.*, **92**, 5519 (1970).
(11) J. F. Harrod, C. A. Smith, and K. A. Than, *J. Am. Chem. Soc.*, **94**, 8321 (1972).
(12) M. F. Semmelhack and L. Ryono, *Tetrahedron Lett.*, 2967 (1973).
(13) J. S. Bradley, D. E. Connor, D. Dolphin, J. A. Labinger, and J. A. Osborn, *J. Am. Chem. Soc.*, **94**, 4043 (1972).
(14) J. A. Labinger, A. V. Kramer, and J. A. Osborn, *J. Am. Chem. Soc.*, **95**, 7908 (1973).
(15) S. Otsuka, A. Nakamura, T. Yoshida, M. Naruto, and A. Ataka, *J. Am. Chem. Soc.*, **95**, 3180 (1973).
(16) J. P. Birk, J. Halpern, and A. J. Pickard, *J. Am. Chem. Soc.*, **90**, 4491 (1968).
(17) R. G. Pearson and J. Rajaram, *Inorg. Chem.*, **13**, 246 (1974).
(18) A. V. Kramer, J. A. Labinger, J. S. Bradley, and J. A. Osborn, *J. Am. Chem. Soc.*, **96**, 7145 (1974).
(19) A. V. Kramer and J. A. Osborn, *J. Am. Chem. Soc.*, **96**, 7832 (1974).
(20) D. Hopgood and R. A. Jenkins, *J. Am. Chem. Soc.*, **95**, 4461 (1973).
(21) A. R. Lepley and G. L. Closs, "Chemically Induced Magnetic Polarization", Wiley, New York, N.Y., 1973.
(22) C. Eaborn, D. J. Tune, and D. R. M. Walton, *J. Chem. Soc., Chem. Commun.*, 1223 (1972).
(23) C. Eaborn, P. N. Kapoor, D. J. Tune, C. L. Turpin, and D. R. M. Walton, *J. Organomet. Chem.*, **34**, 153 (1972).
(24) L. H. Sommer, J. E. Lyons, and H. Fujimoto, *J. Am. Chem. Soc.*, **91**, 7051 (1969).
(25) B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.*, **98**, 630 (1976).
(26) (a) P. Fitton, M. P. Johnson, and J. E. McKeon, *Chem. Commun.*, 6 (1968); (b) P. Fitton, J. E. McKeon, and B. C. Beam, *ibid.*, 370 (1969).
(27) K. Suzuki and M. Nishida, *Bull. Chem. Soc. Jpn.*, **46**, 2887 (1973).
(28) J. K. Stille, L. F. Hines, R. W. Fries, P. K. Wong, D. E. James, and K. S. Y. Lau, *Adv. Chem. Ser.*, **No. 132**, 90 (1974).
(29) J. K. Stille and R. W. Fries, *J. Am. Chem. Soc.*, **96**, 1514 (1974).
(30) J. Schwartz and J. B. Cannon, *J. Am. Chem. Soc.*, **96**, 2276 (1974).
(31) (a) A. Misono, Y. Uchida, M. Hidai, and K. Kudo, *J. Organomet. Chem.*, **20**, P7 (1969); (b) K. Kudo, M. Hidai, and Y. Uchida, *ibid.*, **33**, 393 (1971).
(32) K. Kudo, M. Hidai, T. Murayama, and Y. Uchida, *Chem. Commun.*, 1701 (1970).
(33) K. Kudo, M. Sato, M. Hidai, and Y. Uchida, *Bull. Chem. Soc. Jpn.*, **46**, 2820 (1973).
(34) M. Hidai, M. Kokura, and Y. Uchida, *J. Organomet. Chem.*, **52**, 431 (1973).
(35) (a) P. E. Verkade, K. S. deVries, and B. M. Wepster, *Recl. Trav. Chim., Pays-Bas*, **83**, 1149 (1964); (b) H. J. Dauben, Jr., and L. L. McCoy, *J. Am. Chem. Soc.*, **81**, 5404 (1959).
(36) (a) W. Gerrard, *J. Chem. Soc.*, 848 (1945); (b) H. M. R. Hoffmann and E. D. Hughes, *ibid.*, 1245 (1964).
(37) (a) W. A. Bonner and J. A. Zderic, *J. Am. Chem. Soc.*, **78**, 3218 (1956); (b) H. Pracejus, *Justus Liebigs Ann. Chem.*, **634**, 9 (1960); (c) D. B. Denney and W. F. Beach, *J. Org. Chem.*, **24**, 108 (1959); (d) K. Pettersson, *Ark. Kemi*, **10**, 283 (1956).
(38) (a) A. Fredge, *Ark. Kemi*, **7**, 241 (1954); (b) S. P. Bakshi and E. E. Turner, *J. Chem. Soc.*, 171 (1961); (c) V. Prelog and H. Scherrer, *Helv. Chim. Acta*, **42**, 2227 (1959); (d) B. Sjöberg, *Acta Chem. Scand.*, **14**, 273 (1960).
(39) L. F. Hines and J. K. Stille, *J. Am. Chem. Soc.*, **94**, 485 (1972).
(40) (a) G. M. Whitesides and D. W. Lewis, *J. Am. Chem. Soc.*, **92**, 6979 (1970); (b) *ibid.*, **93**, 5914 (1971).
(41) (a) H. L. Goering, J. N. Eikenberry, and G. S. Koermer, *J. Am. Chem. Soc.*, **93**, 5913 (1971); (b) H. L. Goering, J. N. Eikenberry, G. S. Koermer, and C. J. Lattimer, *ibid.*, **96**, 1493 (1974).
(42) E. B. Dongala, A. Solladie-Cavallo, and G. Solladié, *Tetrahedron Lett.*, 4233 (1972).
(43) P. G. Duggan and W. S. Murphy, *J. Chem. Soc., Chem. Commun.*, 263 (1973).
(44) R. S. Hansen and W. S. Trahanovsky, *J. Org. Chem.*, **39**, 570 (1974).
(45) A. Rahm and M. Pereyre, *J. Organomet. Chem.*, **88**, 79 (1975).
(46) V. Schurig, *Tetrahedron Lett.*, 3297 (1972).
(47) A. Claesson, L. J. Olsson, G. R. Sullivan, and H. S. Mosher, *J. Am. Chem. Soc.*, **97**, 2919 (1975).
(48) D. F. Evans, J. N. Tucker, and G. C. de Villardi, *J. Chem. Soc., Chem. Commun.*, 205 (1975).
(49) K. S. Y. Lau, R. W. Fries, and J. K. Stille, *J. Am. Chem. Soc.*, **96**, 4983 (1974).
(50) J. K. Stille and K. S. Y. Lau, *J. Am. Chem. Soc.*, following paper in this issue.
(51) V. E. Althouse, D. M. Feigl, W. A. Sanderson, and H. S. Mosher, *J. Am. Chem. Soc.*, **88**, 3595 (1966).
(52) J. L. Kice, R. H. Engebrecht, and N. E. Pawlowski, *J. Am. Chem. Soc.*, **87**, 4131 (1965).
(53) E. G. Miller, D. R. Rayner, H. T. Thomas, and K. Mislow, *J. Am. Chem. Soc.*, **90**, 4861 (1968).
(54) A. Streitwieser, Jr., and J. R. Wolfe, Jr., *J. Am. Chem. Soc.*, **81**, 4912 (1959).
(55) The earlier reported highest value for the chiral alcohol **21** was $[\alpha]^{25.6}_{D}$ +1.74°: C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, *J. Am. Chem. Soc.*, **88**, 3347 (1966).
(56) P. K. Wong, K. S. Y. Lau, and J. K. Stille, *J. Am. Chem. Soc.*, **96**, 5956 (1974).
(57) R. R. Stevens and G. D. Shier, *J. Organomet. Chem.*, **21**, 495 (1970).
(58) M. D. McCreary, D. W. Lewis, D. L. Wermick, and G. M. Whitesides, *J. Am. Chem. Soc.*, **96**, 1038 (1974).
(59) NMR measurement on (*R*)-(+)-**22** was performed on a SL-FT-100 NMR spectrometer. We wish to thank Professor H. S. Mosher and Mr. G. R. Sullivan, Department of Chemistry, Stanford University for the NMR spectrum.
(60) The value of 1.36° was extrapolated previously for chiral benzyl-α-*d* chloride.[52,53]
(61) The absolute rotation of **25** has been determined to be $[\alpha]^{25}_{D}$ 1.80 ± 0.07° (neat, l = 1.0) by NMR analysis of its derivatives, (+)-(4*R*)- and (−)-(4*S*)-3(benzyl-α-*d*)-4-phenyloxazolidin-2-thione: H. Gerlach, *Helv. Chim. Acta*, **49**, 2481 (1966).
(62) P. A. S. Smith, *Org. React.*, **3**, 337 (1946).
(63) C. F. H. Allen and A. Bell, *Org. Syn.*, **24**, 94 (1944).
(64) E. O. Fischer and A. Maasböl, *Angew. Chem.*, **76**, 645 (1964).
(65) Y. Iwakura, K. Hayashi, and K. Iwata, *Makromol. Chem.*, **89**, 214 (1965).