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Asymmetric Radical Reaction in the Coordination Sphere. III.[1] Asymmetric Addition of Trichloromethanesulfonyl Chloride and Carbon Tetrachloride to Olefins Catalyzed by a Ruthenium(II) Complex with Chiral Ligand

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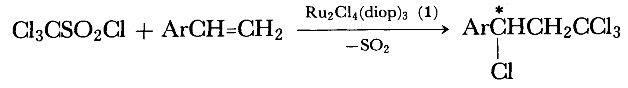
The asymmetric addition of trichloromethanesulfonyl chloride to styrene in the presence of a catalytic amount of a ruthenium(II) complex with chiral ligands, $Ru_2Cl_4[(-)\text{-diop}]_3$ or $Ru_2Cl_4[(+)\text{-diop}]_3$, proceeds under mild conditions to give optically active 1 : 1 adducts, 1,1,1,3-tetrachloro-3-phenylpropane (**2**), with the extrusion of sulfur dioxide. When (−)-DIOP or (+)-DIOP was used as a chiral ligand of the ruthenium(II) complex, (*R*)-(+)-(**2**) or (*S*)-(−)-(**2**), was obtained with about 10% enantiomeric excess, respectively. A reaction mechanism involving a radical redox transfer mechanism was proposed; the asymmetric induction was attributed to the restricted configuration of the radical intermediates confined in the coordination sphere of the ruthenium complex with chiral ligands.

We recently reported that the addition reaction of arene- and alkanesulfonyl chlorides with olefins catalyzed by a dichlorotris(triphenylphosphine)ruthenium(II) under mild conditions affords 2-chlorosulfones in high yield.[2] On the other hand, the addition of trichloromethanesulfonyl chloride to olefins catalyzed by the ruthenium(II) complex affords 1 : 1 adducts, 1,1,1,3-tetrachloropropanes, with the extrusion of sulfur dioxide.[3] A reaction mechanism involving a radical redox transfer process is proposed. The intermediate radicals generated by interactions of sulfonyl chlorides with the ruthenium(II) complexes are considered to be confined in the coordination sphere of the metal complexes and to have different features from such a free radical as that initiated by irradiation or decomposition of peroxides.

We suppose that the relation between a free radical and the radical in the coordination sphere of the metal complex closely resembles the relation between a carbene and a carbenoid. Nozaki and Noyori first reported that an asymmetric addition of alkyl diazoacetate with olefins catalyzed by a copper complex with chiral ligand gave optically active cyclopropanes.[4] This reaction involves a carbenoid intermediate generated by an interaction of the diazoacetate with the metal complex. The carbenoid was affected by the chiral ligand and differentiated the enantioface of the olefin in the addition step. Thus, an asymmetric induction is expected in the reaction of sulfonyl chloride with olefin, which proceeds by a radical reaction in the coordination sphere. In a preliminary paper, we reported that arene- and alkanesulfonyl chlorides reacted with styrenes in the presence of a ruthenium(II) complex with chiral ligand, $Ru_2Cl_4[(-)\text{-diop}]_3$ ((−)-**1**) or $Ru_2Cl_4[(+)\text{-diop}]_3$ ((+)-**1**), as a catalyst to give optically active 1 : 1 adducts.[5] We report, herein, an asymmetric radical addition of trichloromethanesulfonyl chloride to olefins catalyzed by the ruthenium(II) complex with chiral ligand **1**.

Results and Discussion

The reaction of trichloromethanesulfonyl chloride with olefin was carried out by using the ruthenium(II)-DIOP complex **1** as a catalyst. When $Ru_2Cl_4[(-)\text{-diop}]_3$ ((−)-**1**) was used, the reaction of trichloromethanesulfonyl chloride with styrene at 100 °C for 6 h in a degassed tube gave 1 : 1 adduct (**2a**) quantitatively with extrusion of sulfur dioxide. The adduct showed a specific rotation $[\alpha]_D$ +12° (*c* 12, benzene). Similarly, the reaction of trichloromethanesulfonyl chloride with styrene in the presence of $Ru_2Cl_4[(+)\text{-diop}]_3$ ((+)-**1**) was carried out; adduct **2a** was obtained quantitatively and showed $[\alpha]_D$ −10° (*c* 11, benzene).



$$\mathrm{Cl_3CSO_2Cl} + \mathrm{ArCH{=}CH_2} \xrightarrow[-\mathrm{SO_2}]{\mathrm{Ru_2Cl_4(diop)_3}\ (\mathbf{1})} \mathrm{Ar}\underset{\mathrm{Cl}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CCl_3}$$

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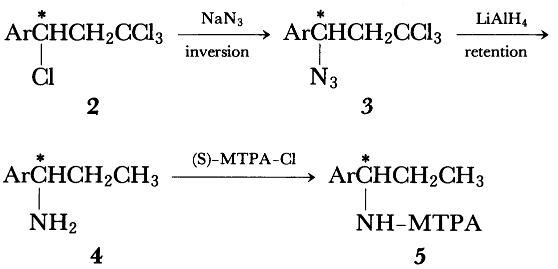
The enantiomeric excess and absolute configuration of products **2** in the present reactions were estimated by converting to a known optically active compound. The adduct (−)-**2a**, which showed $[\alpha]_D$ −10° (*c* 11, benzene), was treated with sodium azide to give 3-azido-1,1,1-trichloro-3-phenylpropane (**3a**),[6] which was reduced with lithium aluminum hydride to afford 1-amino-1-phenylpropane (**4a**).[7] Amine **4a** showed $[\alpha]_D$ +2.1° (*c* 2.3, benzene) and was determined to be 10% enantiomeric excess and (R)-configuration. In a similar way, the adduct (+)-**2a** ($[\alpha]_D$ +12° (*c* 12, benzene)) was converted to amine **4a**, which showed $[\alpha]_D$ +3.1° (*c* 1.7, benzene) and corresponded to 14% ee of (S)-isomer.

The optical yield of **2a** was also determined by a HPLC analysis of the diastereomer (**5a**) derived from the amine **4a**. Amine **4a** was treated with (*S*)-MTPA-Cl,[8] prepared by the reaction of (*S*)-MTPA (MTPA=2-methoxy-2-trifluoromethylphenylacetic acid) with thionyl chloride, to give the diastereomeric MTPA-



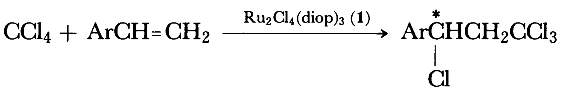
$$\mathrm{Ar}\underset{\underset{\displaystyle\mathrm{Cl}}{|}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CCl_3}\ (\mathbf{2}) \xrightarrow[\text{inversion}]{\mathrm{NaN_3}} \mathrm{Ar}\underset{\underset{\displaystyle\mathrm{N_3}}{|}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CCl_3}\ (\mathbf{3}) \xrightarrow[\text{retention}]{\mathrm{LiAlH_4}}$$

$$\mathrm{Ar}\underset{\underset{\displaystyle\mathrm{NH_2}}{|}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CH_3}\ (\mathbf{4}) \xrightarrow{\mathrm{(S)\text{-}MTPA\text{-}Cl}} \mathrm{Ar}\underset{\underset{\displaystyle\mathrm{NH\text{-}MTPA}}{|}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CH_3}\ (\mathbf{5})$$

amide (**5a**). The diastereomer **5a** was separated into two isomer peaks by HPLC. Thus, the optical yield of adduct **2a** was estimated to be 14% ee. Similarly, the addition of trichloromethanesulfonyl chloride to several styrenes was carried out, and the optical purity of the products (**2b**—**d**) was also determined by HPLC analysis of the diastereomeric MTPA-amide. The results are summarized in Table 1.

The reaction products, 1,1,1,3-tetrachloro-3-arylpropanes, in the reaction of trichloromethanesulfonyl chloride with olefins corresponded to the adducts obtained by the addition of carbon tetrachloride to olefins. Matsumoto and Nagai have reported that a radical addition reaction of carbon tetrachloride with olefin catalyzed by the ruthenium(II) complex proceeds by a radical redox transfer mechanism and the intermediate radicals are considered to be confined in the coordination sphere of the ruthenium complex.[9] Thus, an asymmetric radical addition of carbon tetrachloride to olefins can also be expected by using the ruthenium(II) complex with chiral ligands as a catalyst.

When the ruthenium(II)-(−)-DIOP complex (−)-**1** was used as a catalyst, the addition reaction of carbon tetrachloride with styrene at 100 °C for 6 h gave 1 : 1 adduct (**2a**) in 73% yield.



$$\mathrm{CCl_4 + ArCH{=}CH_2} \xrightarrow{\mathrm{Ru_2Cl_4(diop)_3\ (1)}} \mathrm{Ar}\underset{\underset{\displaystyle\mathrm{Cl}}{|}}{\overset{*}{\mathrm{C}}}\mathrm{HCH_2CCl_3}$$

2

Adduct **2a** showed a specific rotation $[\alpha]_D$ +12° (*c* 6.1, benzene). Similarly, when (+)-**1** was used as a catalyst, adduct **2a** was obtained in 68% yield and showed $[\alpha]_D$ −10° (*c* 5.3, benzene). The optical yields and absolute configurations of products **2** were determined by comparing the optical rotation of **4**, which was derived

Table 1. Reaction of Trichloromethanesulfonyl Chloride with Styrene Derivatives

Ar	DIOP	Product	$[\alpha]_D$/° (*c*, in PhH)	Chemical yield/%	Optical yield/%ee[a]	Absolute configuration
C_6H_5	(−)	**2a**	+12 (12)	97	13 (14)	R
C_6H_5	(+)	**2a**	−10 (11)	100	7 (10)	S
p-$CH_3C_6H_4$	(−)	**2b**	+11 (24)	98	—[c]	R
p-$CH_3C_6H_4$	(+)	**2b**	− 9 (23)	100	—[c]	S
p-ClC_6H_4	(−)	**2c**	+ 7 (23)	89	13	R
p-ClC_6H_4	(+)	**2c**	− 7 (23)	87	9	S
m-$O_2NC_6H_4$	(−)	**2d**	+ 7 (36)[b]	79	—[d]	R
m-$O_2NC_6H_4$	(+)	**2d**	− 7 (39)[b]	87	—[d]	S

a) Optical yields were estimated by HPLC of MTPA-amides and optically pure sample reported as $[\alpha]_D$+21.7° (PhH) in parentheses. b) The reaction was carried out for 24 h. c) The amine **4b**, which was converted from the adduct **2b**, did not show any optical rotation. Racemization in the reaction of **2b** with sodium azide may be caused. d) The azide **3d** was reduced by sodium borohydride to the amine **4d** remaining trichloromethyl moiety. However, the diastereomer **5d** formed from **4d** did not show a pure chromatogram by HPLC analysis.

Table 2. Reaction of Carbon Tetrachloride with Styrene Derivatives

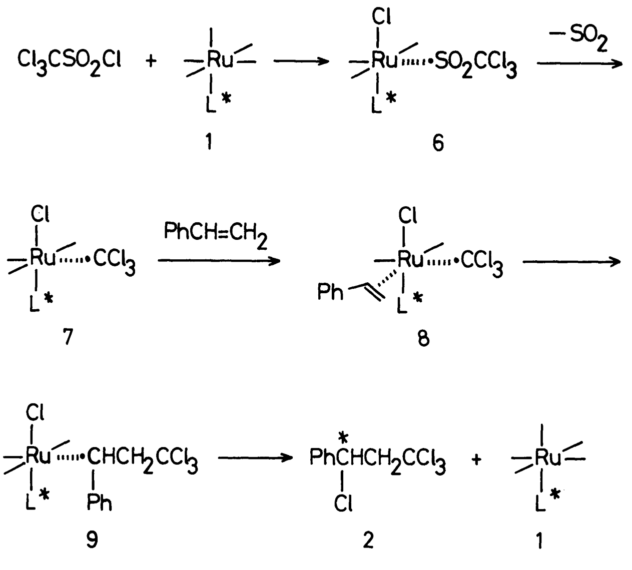
Ar	DIOP	Product	$[\alpha]_D$/° (*c*, in PhH)	Chemical yield/%	Optical yield/%ee[a]	Absolute configuration
C_6H_5	(−)	**2a**	+12 (6.1)	73	13 (13)	R
C_6H_5	(+)	**2a**	−10 (5.3)	68	7 (11)	S
p-$CH_3C_6H_4$	(−)	**2b**	+10 (3.4)	79	—[c]	R
p-$CH_3C_6H_4$	(+)	**2b**	− 7.8 (3.0)	80	—[c]	S
p-ClC_6H_4	(−)	**2c**	+ 5.2 (3.9)	70	10	R
p-ClC_6H_4	(+)	**2c**	− 4.9 (2.9)	68	6	S
m-$O_2NC_6H_4$	(−)	**2d**	+ 5.2 (1.9)	54[b]	—[d]	R
m-$O_2NC_6H_4$	(+)	**2d**	− 3.7 (2.6)	57[b]	—[d]	S

a) Optical yields were estimated by HPLC of MTPA-amides and optically pure sample reported as $[\alpha]_D$+21.7° (PhH) in parentheses. b) The reaction was carried out for 24 h. c) The amine **4b**, which was converted from the adduct **2b**, did not show any optical rotation. Racemization in the reaction of **2b** with sodium azide may be caused. d) The azide **3d** was reduced by sodium borohydride to the amine **4d** remaining trichloromethyl moiety. However, the diastereomer **5d** formed from **4d** did not show a pure chromatogram by HPLC analysis.

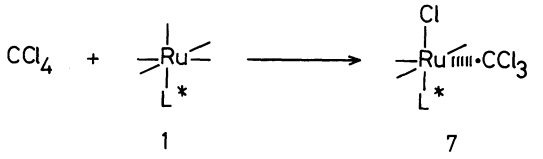
from **2**, with that of known optically active amine and by HPLC analysis of the MTPA-amides **5**. The reaction of carbon tetrachloride with various styrenes was carried out in a similar way and the results are summarized in Table 2.

There are a few reports in an asymmetric addition of polyhaloalkane to olefin. Boutevin and Dongala have reported the addition of carbon tetrachloride to an optically active olefin, menthyl acrylate, catalyzed by iron or copper salts.[10] Murai and Sonoda studied the asymmetric addition of bromotrichloromethane to styrene catalyzed by RhCl[(−)-diop].[11] They obtained optically active (*S*)-(−)-3-bromo-1,1,1-trichloro-3-phenylpropane with 32% ee when the rhodium-DIOP complex was employed as the catalyst. However, no mechanistic aspects are described.

The addition reaction catalyzed by the ruthenium(II) complex can be explained by the following mechanism involving a radical redox transfer process in the coordination sphere of the ruthenium(II) complexes (Scheme 1). In the case of the reaction of trichloromethanesulfonyl chloride, the ruthenium(II) catalyst **1** selectively activates a sulfur-chlorine bond of trichloromethanesulfonyl chloride, which is weaker than a carbon-chlorine bond, to give a trichloromethanesulfonyl radical confined to the coordination sphere of the ruthenium(III) species (**6**). The intermediate **6** readily loses sulfur dioxide to give a trichloromethyl radical confined to the ruthenium(III) species (**7**). Then, the intermediate **7** forms a π-complex (**8**) with styrene and the coordinated styrene reacts with the confined carbon radical to give 3,3,3-trichloro-1-phenylpropyl radical confined to the ruthenium(III) species (**9**). The carbon radical in **9** abstracts the chlorine atom from the ruthenium(III) species containing chiral ligands to give the adduct **3** and regenerate the ruthenium(II) catalyst **1**. It also may be probable that **7** directly reacts with styrene to give **9** without forming the intermediate **8**. As shown in Scheme 1, the trichloromethanesulfonyl, trichloromethyl, and 3,3,3-trichloro-1-phenylpropyl radical are considered to be confined in the coordination sphere of the ruthenium complexes containing chiral ligands. An enantioface differentiation may be occurred in the last step in Scheme 1, abstracting the chlorine atom from the ruthenium(III) species **9** with chiral ligand by the carbon radical. The asymmetric addition in the reaction of carbon tetrachloride with olefin will be similar to that of the reaction of trichloromethanesulfonyl chloride with olefin. Carbon tetrachloride reacts with the ruthenium(II) complex **1** to give the intermediate **7**, (Scheme 2) which reacts with styrene and to afford optically active **2** in a similar way as shown in Scheme 1.



Scheme 1.



Scheme 2.

In conclusion, asymmetric induction was definitely observed in the addition of sulfonyl chloride or carbon tetrachloride to olefin catalyzed by the ruthenium(II) complex containing chiral ligand such as (−)-DIOP or (+)-DIOP. The results support our assumption that the radicals generated by interaction of the ruthenium(II) complexes are confined in the coordination sphere of the metal complexes. The radical in the coordination sphere should be called "RADICALOID" since a carbene-metal complex is called a carbenoid. The enantiomeric excess of the products obtained in the present reaction was not satisfied, while high enantioselective addition was achieved in the chiral copper carbenoid reaction and applied to the synthesis of industrially valuable chrysanthemic acid.[12] This suggests that the "RADICALOID" coordinates to the metal complex more loosely compared with that of carbenoid.

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Experimental

Measurement. Melting points and boilng points were uncorrected. The infrared absorption spectra were determined on a Hitachi Model 260-10 spectrophotometer with samples as either neat liquids or KBr disks. The proton magnetic resonance spectra were recorded at 60 MHz by using a JNM-PMX 60 SI spectrometer with Me_4Si as an internal standard in $CDCl_3$. The optical rotations were measured with a JASCO DIP-140 polarimeter. The high-performance liquid chromatography system consisted of a

Hitachi 655 liquid chromatograph equipped with a Rhedyne 7125 sample injector. Elutions were monitored at 260 nm using a Hitachi 638-41 variable-wavelength UV monitor. The gel permeation chromatography was performed by using a JAI LC-08 liquid chromatograph with a JAIGEL-1H column (20ϕ×600 mm×2, chloroform as an eluent). Mass spectra were determined with a JEOL JMX-DX 300 mass spectrometer with JEOL JMA 5000 Mass Data System at an ionizing voltage of 20—70 eV.

Materials. The ruthenium(II) complexes such as $Ru_2Cl_4[(-)\text{-diop}]_3$ ((−)-**1**) and $Ru_2Cl_4[(+)\text{-diop}]_3$ ((+)-**1**) were prepared by the methods described in the literature.[13] Trichloromethanesulfonyl chloride, carbon tetrachloride, styrene, *p*-methylstyrene, *p*-chlorostyrene (Tokyo Kasei Chemicals), and *m*-nitrostyrene (Aldrich Chemicals) were purified by distillation under nitrogen prior to use.

General Procedure for the Reaction of Trichloromethanesulfonyl Chloride with Olefins. A solution containing of 5.0 mmol of trichloromethanesulfonyl chloride, 7.5 mmol of olefin, 0.05 mmol of **1** in 10 cm^3 of benzene was degassed and heated in a sealed tube at 100 °C for 6—24 h. The reaction mixture was chromatographed on silica gel using benzene as an eluent. The products were identified by their infrared absorption spectra, proton magnetic resonance spectra, mass spectra, and high-resolution mass spectra. The physical and spectral data of the compounds (**2a—d**) are as follows.

(*R*)-(+)-1,1,1,3-Tetrachloro-3-phenylpropane (2a): Bp 85—88 °C/0.3 mmHg† (Kugelrohr); IR (neat) 1490, 1450, 1420, 1200, and 970 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=3.49 (2H, d, J=6.0 Hz), 5.17 (1H, t, J=6.0 Hz), and 7.25 (5H, s); MS *m/z* 256 (M$^+$); HRMS *m/z* 255.9428 ($C_9H_8Cl_4$ requires 255.9380).

(*S*)-(−)-1,1,1,3-Tetrachloro-3-phenylpropane (2a): Bp 88—90 °C/0.3 mmHg (Kugelrohr); IR (neat) 1490, 1450, 1420, 1200, 970 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=3.49 (2H, d, J=6.0 Hz), 5.17 (1H, t, J=6.0 Hz), and 7.25 (5H, s); MS *m/z* 256 (M$^+$), HRMS *m/z* 255.9356 ($C_9H_8Cl_4$ requires 255.9380).

(*R*)-(+)-1,1,1,3-Tetrachloro-3-(*p*-tolyl)propane (2b): Bp 90—95 °C/0.3 mmHg (Kugelrohr); IR (neat) 1510, 1420, 1200, and 970 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=2.30 (3H, s), 3.50 (2H, d, J=6.0 Hz), 5.17 (1H, t, J=6.0 Hz), and 6.97—7.30 (4H, m); MS *m/z* 270 (M$^+$); HRMS *m/z* 269.9496 ($C_{10}H_{10}Cl_4$ requires 269.9537).

(*S*)-(−)-1,1,1,3-Tetrachloro-3-(*p*-tolyl)propane (2b): Bp 90—95 °C/0.3 mmHg (Kugelrohr); IR (neat) 1515, 1420, 1200, and 970 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=2.30 (3H, s), 3.50 (2H, d, J=6.0 Hz), 5.18 (1H, t, J=6.0 Hz), and 6.97—7.30 (4H, m); MS *m/z* 270 (M$^+$); HRMS *m/z* 269.9464 ($C_{10}H_{10}Cl_4$ requires 269.9537).

(*R*)-(+)-1,1,1,3-Tetrachloro-3-(*p*-chlorophenyl)propane (2c): Mp 41—42 °C; Bp 105—110 °C/0.4 mmHg (Kugelrohr); IR (neat) 1500, 1420, 1200, 1100, and 970 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=3.40—3.50 (2H, m), 5.17 (1H, t, J=6.0 Hz), and 7.25 (4H, s); MS *m/z* 290 (M$^+$); HRMS *m/z* 289.9010 ($C_9H_7Cl_5$ requires 289.8990).

(*S*)-(−)-1,1,1,3-Tetrachloro-3-(*p*-chlorophenyl)propane (2c): Mp 41—42 °C; bp 103—105 °C/0.3 mmHg (Kugelrohr); IR (neat) 1500, 1425, 1210, 1100, and 970 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=3.40—3.50 (2H, m), 5.17 (1H, t, J=6.0 Hz), and 7.25 (4H, m); MS *m/z* 290 (M$^+$); HRMS *m/z* 289.9045 ($C_9H_7Cl_5$ requires 289.8990).

(*R*)-(+)-1,1,1,3-Tetrachloro-3-(*m*-nitrophenyl)propane (2d): IR (neat) 1530 and 1350 cm^{-1}; ^{1}H NMR (CCl$_4$) δ= 3.50—3.62 (2H, m), 5.32 (1H, t, J=6.0 Hz), and 7.34—8.30 (4H, m); MS *m/z* 301 (M$^+$); HRMS *m/z* 300.9243 ($C_9H_7O_2NCl_4$ requires 300.9231).

(S)-(−)-1,1,1,3-Tetrachloro-3-(*m*-nitrophenyl)propane (2d): IR (neat) 1530 and 1350 cm^{-1}; ^{1}H NMR (CCl$_4$) δ= 3.50—3.62 (2H, m), 5.33 (1H, t, J=6.0 Hz), and 7.36—8.30 (4H, m); MS *m/z* 301 (M$^+$); HRMS *m/z* 300.9200 ($C_9H_7O_2NCl_4$ requires 300.9231).

General Procedure for the Reaction of Carbon Tetrachloride with Olefins. A solution containing 5.0 mmol of carbon tetrachloride, 20.0 mmol of olefin, 0.05 mmol of **1** in 10 cm^3 of benzene was degassed and heated in a sealed tube at 100 °C for 6—24 h. The reaction mixture was chromatographed on silica gel using benzene as an eluent. The products were identified by comparing their boiling points, IR spectra, ^{1}H NMR spectra, mass spectra with that of the products **2** obtained by the reaction of trichloromethanesulfonyl chloride with olefins.

Preparation of 1-Amino-1-arylpropane (4). A solution of 1.4 g (5.4 mmol) of 1,1,1,3-tetrachloro-3-phenylpropane (**2a**) which showed $[\alpha]_D$ −10° (*c* 11, benzene) and 1.0 g (15 mmol) of sodium azide in 15 cm^3 of ethanol-water=4 : 1 (v/v) was heated at 70—75 °C for 5 d. After cooling, 50 cm^3 of water and 100 cm^3 of ether were added to the reaction mixture. The organic layer was extracted and dried over sodium sulfate. The solvent was removed to give 1.0 g of an oil which was found to contain a starting material **2a** by TLC analysis. Purification by gel permeation liquid chromatography using chloroform as an eluent gave 0.75 g (65%) of 3-azido-1,1,1-trichloro-3-phenylpropane (**3a**) as a yellow oil: IR (neat) 2100 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=3.07—3.14 (2H, m), 4.90 (1H, t, J=6.0 Hz), 7.29 (5H, s); MS *m/z* 263 (M$^+$).

A solution of 0.69 g (2.6 mmol) of the azide **3a** in 60 cm^3 of dry dibutyl ether was added dropwise to a stirred suspension of 2.0 g (53 mmol) of lithium aluminum hydride in 40 cm^3 of dry dibutyl ether at room temperature. After the addition was completed, the mixture was heated at 100 °C for 24 h, then cooled in an ice bath, and treated with 2.0 cm^3 of 15% sodium hydroxide, and 6.0 cm^3 of water. After stirring for additional 30 min, the mixture was filtered, and the precipitate was washed with ether. The combined ethereal solution was washed with 15% hydrochloric acid, the acidic aqueous layer was made basic with 15% sodium hydroxide, and the aqueous layer was extracted with ether. The organic layer was dried over sodium sulfate and the solvent was removed to give 0.15 g (43%) of 1-amino-1-phenylpropane (**4a**): $[\alpha]_D$ +2.1° (*c* 2.3, benzene); IR (neat) 3300 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.84 (3H, t, J=6.0 Hz), 1.45—1.92 (4H, m), 3.64—3.86 (1H, m), and 7.22 (5H, s); MS *m/z* 134 (M$^+$−1).

Preparation of 2-Methoxy-2-trifluoromethylphenylacetic Acid (MTPA) Amides (5). The sample of optically active (*R*)-(+)-1-amino-1-phenylpropane **4a** (45 mg, 0.33 mmol) was added to a solution of 42 mg (0.17 mmol) of (*S*)-(−)-2-methoxy-2-trifluoromethylphenylacetyl chloride (MTPA-Cl), which was prepared by refluxing (*S*)-(−)-MTPA, excess thionyl chloride, and sodium chloride in 3 cm^3 of dichloromethane for 2 d and then removing the excess thionyl chloride in vacuo. The mixture was stirred at room temperature for 24 h. The amine hydrochloride precipitated was filtered off and the solvent was removed under reduced pressure to give 75 mg of the crude MTPA amide (**5a**) as a yellow oil: IR (neat) 3400, 3300, 2950, 1690, 1510, 1270, 1170, and

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† 1 mmHg=133.322 Pa.

1110 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.73—1.05 (3H, m), 1.50—2.00 (2H, m), 3.29—3.40 (3H, m), 4.68—5.07 (10H, m); MS m/z 351 (M$^+$+1).

Separation of the MTPA Amides (5). The HPLC separation of the MTPA amides **5** was performed with a Waters Radial PAK Cartridge Silica Column (8mm×10 cm, particle size 10 μm) using hexane-ethyl acetate=30 : 1 (v/v) as an eluent at a flow rate of 1.0 cm^3 min^{-1}.

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