C, 69.28; H, 8.36; N, 5.05. Found: C, 69.09; H, 8.37; N, 5.24.

(2*S*,5*R*)-1-(Carbobenzyloxy)-2-(1-hydroxypropyl)-5-methylpyrrolidine (8b). To the *trans*-amino alcohol **8a** (2.7 g, 19 mmol) in water (35 mL) containing $NaHCO_3$ (2 g, 24 mmol) was added benzyl chloroformate (3.22 g, 19 mmol). The reaction mixture was heated at 80 °C for 24 h, cooled, and extracted with $CHCl_3$ (3 × 30 mL). To the aqueous layer was added benzyl chloroformate (3.22 g, 19 mmol), and the mixture was heated at 80 °C for 24 h. The reaction mixture was then extracted with $CHCl_3$ (3 × 30 mL). The organic layers were joined, dried over Na_2SO_4, concentrated in vacuo, and distilled under reduced pressure to give **8b** (3.4 g, 65% yield): bp 175 °C (0.05 mmHg); $[\alpha]^{22}_D$ −55° (c = 1.36, chloroform); IR (neat) 3500, 1680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.50–7.20 (m, 5 H), 5.20–5.00 (m, 2 H), 4.05–3.70 (m, 2 H), 3.70–3.40 (m, 2 H), 2.70–2.50 (m, 1 H), 2.20–1.10 (m, 8 H), 1.15 (d, 1 H, *J* = 7 Hz), 1.10 (d, 2 H, *J* = 7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 154.7, 154.2, 136.9, 128.4, 127.9, 66.6, 62.4, 62.1, 57.4, 53.5, 30.5, 30.3, 29.60, 29.4, 29.1, 27.5, 26.9, 20.4, 19.3. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.28; H, 8.36; N, 5.05. Found: C, 69.28; H, 8.31; N, 5.14.

(2*S*,5*R*)-1-(Carbobenzyloxy)-2-(1-oxopropyl)-5-methylpyrrolidine (8c). Carbamate **8b** (2.77 g, 10 mmol) in CH_2Cl_2 (30 mL) was added to a solution of pyridinium chlorochromate (3.45 g, 16 mmol) in CH_2Cl_2 (40 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and then 3 h at room temperature. The solution was filtered over Celite, and the solvent was removed in vacuo. The brown residue was triturated with ether (4 × 30 mL). The organic layers were dried over Na_2SO_4 and concentrated in vacuo to give **8c** (2.28 g, 83% yield). An analytical sample was distilled under reduced pressure: bp (Kugelrohr) 220 °C (0.1 mmHg); $[\alpha]^{22}_D$ −56° (c = 0.95, chloroform); IR (neat) 1720, 1680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.85–9.75 (m, 0.7 H), 9.55–9.45 (m, 0.3 H), 7.35–7.15 (br s, 5 H), 5.20–5.00 (m, 2 H), 4.10–3.70 (m, 2 H), 2.50–1.40 (m, 6 H), 1.20 (d, 1 H, *J* = 7 Hz), 1.15 (d, 2 H, *J* = 7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.5, 201.0, 154.2, 154.1, 136.8, 128.4, 127.8, 66.5, 57.4, 53.6, 41.0, 40.9, 30.5, 29.6, 27.9, 27.5, 26.7, 26.5, 25.6, 20.4, 19.2. Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.95; H, 7.74; N, 5.10.

1-(Carbobenzyloxy)-2-(3-hydroxydecyl)-5-methylpyrrolidine (8d). Grignard reagent was prepared from Mg (2.9 g, 120 mmol) and heptyl bromide (19.7 g, 110 mmol) and then added to a cold (0 °C) solution of aldehyde **8c** (27.5 g, 100 mmol) in dry ether (100 mL). The reaction mixture was stirred 30 min at 0 °C then 3 h at room temperature, dropped to ice containing NH_4Cl, extracted with ether (4 × 60 mL), dried over Na_2SO_4, concentrated in vacuo, and purified by chromatography on silica gel (eluted with ether:pentane = 60:40, R_f = 0.2) to give alcohol **8d** (22.5 g, 62% yield): bp 204 °C (0.05 mmHg); IR (neat) 3500, 3200, 1680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.35–7.15 (m, 5 H), 5.15 (s, 2 H), 4.10–3.40 (m, 3 H), 2.40–1.70 (m, 4 H), 1.70–1.10 (m, 20 H). 0.95–0.75 (m, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 155.0, 137.0, 128.3, 127.7, 66.4, 52.9, 37.2, 31.7, 30.4, 29.6, 29.2, 27.4, 26.9, 25.6, 22.6, 20.4, 19.2, 14.0. Anal. Calcd for $C_{23}H_{37}NO_3$: C, 73.56; H, 9.93; N, 3.73. Found: C, 73.51; H, 9.54; N, 3.39.

(2*S*,5*R*)-1-(Carbobenzyloxy)-2-(3-oxodecyl)-5-methylpyrrolidine (8e). Alcohol **8d** (3.75 g, 10 mmol) in CH_2Cl_2 (30 mL) was added to a solution of pyridinium chlorochromate (3.45 g, 16 mmol) in CH_2Cl_2 (40 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and then 3 h at room temperature. The solution was filtered over Celite and solvent removed in vacuo. The brown residue was triturated with ether (4 × 30 mL). The organic layers were dried over Na_2SO_4, concentrated in vacuo, and purified by chromatography on silica gel (eluted with ether:pentane = 20:80, R_f = 0.20) to isolate ketone **8e** (2.2 g, 59% yield): bp 194 °C (0.05 mmHg); IR (neat) 1700 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.45–7.22 (m, 5 H), 5.25–5.03 (m, 2 H), 4.20–3.70 (m, 2 H), 2.55–2.18 (m, 4 H), 2.18–1.80 (m, 2 H), 1.75–1.40 (m, 4 H), 1.38–1.05 (m, 13 H), 1.00–0.80 (m, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.0, 155.1, 137.0, 128.5, 127.9, 66.5, 57.5, 57.2, 53.6, 53.3, 42.6, 39.9, 31.7, 31.0, 29.9, 29.2, 29.1, 28.5, 27.5, 27.2, 23.7, 22.6, 20.8, 19.6, 14.1. Anal. Calcd for $C_{23}H_{35}NO_3$: C, 73.95; H, 9.45; N, 3.75. Found: C, 73.85; H, 9.41; N, 3.74.

(3*S*,5*R*,8*S*)-3-Heptyl-5-methylpyrrolizidine (1). Carbamate **8e** (0.75 g, 2 mmol) in methanol (30 mL) was hydrogenated at atmospheric pressure over Pd–$BaSO_4$ (20 mg). When 2 equiv were absorbed, the solution was filtered and the solvent removed in vacuo. The crude product was distilled under reduced pressure to give **1** (0.36 g, 80% yield): bp 190 °C (25 mmHg); $[\alpha]^{22}_D$ +6.60° (c = 2.35, chloroform); IR (neat) 2860, 2790 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.65–3.55 (m, 1 H), 2.85–2.70 (m, 1 H), 2.70–2.55 (m, 1 H), 2.05–1.80 (m, 4 H), 1.55–1.15 (m, 16 H), 1.10 (d, 3 H, *J* = 7 Hz), 0.85 (t, 3 H, *J* = 7 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 66.5, 64.8, 61.6, 37.1, 34.4, 32.3, 32.0, 31.8, 31.6, 29.8, 29.3, 27.2, 22.6, 21.7, 13.9. MS (70 ev) *m/z* 223 (6) [$M^{+\cdot}$], 208 (9), 194 (3), 180 (2.5), 166 (1), 152 (1.5), 124 (100), 110 (4), 81 (21), 55 (10), 31 (7). Anal. Calcd for $C_{15}H_{29}N$: C, 80.64, H, 13.09; N, 6.27. Found: C, 80.52; H, 13.08; N, 6.22. The data show 2% less of the epimeric isomer at C-3.

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Supplementary Material Available: Spectra of **4c**, **4d**, **6**, **7**, **3**, **8a**, **8b**, **8c**, **9b**, **8d**, **8e**, and **1** (27 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; seen any current masthead page for ordering information.

CsF-Promoted Esterification of Carboxylic Acids. A Practical Alternative to the Diazomethane Method and Direct Conversion of Organotin Carboxylates

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Esterification of carboxylic acids by reaction with alkyl halides is a fundamental transformation in organic synthesis.[1] Potassium and cesium salts have proved useful for this purpose. Clark et al., in their extensive studies, revealed KF to be effective, but unfortunately, the reaction usually required high temperature (110–130 °C).[2] In addition, KF[3] and $CsHCO_3$[4] were reported to promote solid-phase peptide synthesis. More recently, Cs_2CO_3 was employed in macrolactonization[5] and peptide synthesis.[6] However, little attention has been directed toward CsF[7]

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(2) (a) Clark, J. H.; Emsley, J. *J. Chem. Soc., Dalton Trans.* **1975**, 2129. (b) Clark, J. H.; Miller, J. M. *J. Chem. Soc., Chem. Commun.* **1976**, 229. (c) Clark, J. H.; Holland, H. L.; Miller, J. M. *Tetrahedron Lett.* **1976**, 3361. (d) Clark, J. H.; Miller, J. M. *J. Am. Chem. Soc.* **1977**, *99*, 498. (e) Clark, J. H.; Miller, J. M. *Tetrahedron Lett.* **1977**, 599. (f) Clark, J. H.; Emsley, J.; Hoyte, O. P. A. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1091. (g) Clark, J. H. *J. Chem. Soc., Chem. Commun.* **1978**, 789.

(3) Tam, J. P.; Kent, S. B. H.; Wong, T. W.; Merrifield, R. B. *Synthesis* **1976**, 955.

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(5) Kruizinga, W. H.; Kellog, R. M. *J. Am. Chem. Soc.* **1981**, *103*, 5183.

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Table I. Reaction of Benzoic Acid with Ethyl Iodide in the Presence of Alkali Metal Fluoride[a]

$$PhCOOH + EtI \xrightarrow{MF} PhCOOEt$$

M	solvent	yield of PhCOOEt,[b] %
Cs	DMF	100
	DMSO	92
	$ClCH_2CH_2Cl$	0
	C_6H_6	0
	THF	0
	CH_3CN	0
K	DMF	82
Na	DMF	2

[a] Reaction conditions: benzoic acid (1 mmol), ethyl iodide (2.9 mmol), MF (1.5 mmol), solvent (3 mL), room temperature, 24 h. [b] Based on GLC.

although Clark et al. briefly referred to the superiority of this reagent in the alkylation of phthalimide.[2c] We report herein that CsF promotes the alkylation of carboxylic acids smoothly under mild conditions. The present method offers an attractive way to avoid the use of diazomethane which is most commonly used in laboratories but is not suitable for large-scale reactions on account of its toxicity.

Additional significance of the CsF method lies in ester formation from organotin carboxylates. These compounds are masked carboxylic acids and frequently employed in amino acid synthesis.[1b] The direct organotin carboxylate-to-ester transformation, therefore, affords synthetic versatility.

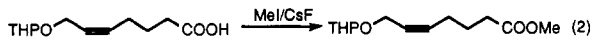
Alkylation of Free Carboxylic Acids. First, we screened solvents by employing the reaction between benzoic acid and ethyl iodide at room temperature (Table I). DMF gave the best result and DMSO the next best. Other less polar solvents were completely ineffective. Accordingly, DMF was our choice throughout this study. Table I also shows the results with other alkali metal fluorides. Under the same reaction conditions, NaF gave the ester in only 2% yield. While a good yield was obtained with KF, it is apparent that CsF is better.

On the basis of these results, we selected the following standard conditions: carboxylic acid:alkyl halide:CsF = 1:1.5:1.5; DMF; 10–15 °C, 24 h (eq 1). The results with

$$RCOOH + R'X \xrightarrow[DMF]{CsF} RCOOR' \qquad (1)$$

a variety of carboxylic acids and alkyl halides are summarized in Table II. The expected esters were generally obtained in reasonable yields except for *tert*-butyl and neopentyl iodides (entries 7 and 8). No restrictions were found with regard to the carboxylic acids. Bulky substituents do not affect the reaction (entries 11–13), and no isomerization was observed with α,β- and β,γ-unsaturated carboxylic acids (entries 14–16). The optical purities of the α-substituted acids were completely retained (entries 17–21). A variety of functional groups remained intact (entries 22–28).

The practical utility of this method was exemplified by large-scale O-methylation of 7-(tetrahydropyranyloxy)-5-heptynoic acid, an important intermediate for the α-side chain of prostaglandins[8] (eq 2). The reaction smoothly transformed the acid (6.0 g) to the methyl ester (5.0 g, 79%).[9]

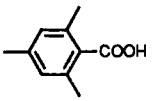
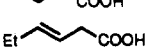
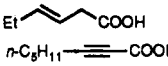
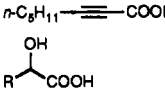
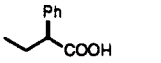
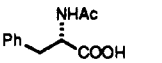
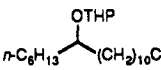
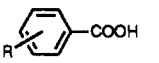


(2)

(7) For a review on alkali metal fluoride in organic synthesis, see: Yakobson, G. G.; Akhmetova, N. E. *Synthesis* **1983**, 169.

(8) For the diazomethane method: Corey, E. J.; Sachdev, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 8483.

Table II. CsF-Promoted Esterification of Carboxylic Acids[a]

entry	RCOOH	R'X	yield of ester,[b] %
1	PhCOOH	EtI	94 (94)
2		$EtOSO_2CH_3$	(81)
3		EtBr	(52)
4		$CH_2{=}CHCH_2Br$	95
5		$PhCH_2Br$	98
6		*i*-PrI[c]	(71)
7		*t*-BuI[c]	(3)
8		*t*-$BuCH_2I$	(0)
9	*n*-$C_{11}H_{23}COOH$	EtI[d]	(76)
10	*c*-$C_6H_{11}COOH$	EtI	(95)
11	*t*-BuCOOH	BuI	(87)
12	Ph_3CCOOH	EtI	83
13		EtI	(88)
14		MeI	80 (94)
15		MeI	74 (78)
16		MeI	90
17	R = CH_3 (*S*)	EtI	61 (78)
18	R = *c*-C_6H_{11} (*S*)	MeI[e]	97
19	R = *c*-C_6H_{11} (*R*)	MeI[e]	100
20		MeI[f]	(85)
21		EtI	90
22		MeI	70
23	$NCCH_2COOH$	EtI[d,g]	(79)
24	*t*-$BuMe_2SiO(CH_2)_{11}COOH$	MeI[h,i]	(87)[j]
			
25	R = 2-COPh	EtI[d]	98
26	R = 2-OAc	MeI	86
27	R = 4-OAc	MeI	79
28	R = 2-COOH	EtI[k]	70 (78)[l]

[a] Reaction conditions: RCOOH (1 mmol), R'X (1.5 mmol), CsF (1.5 mmol), DMF (3 mL), 10–15 °C, 24 h. [b] Isolated yields; GLC yields are given in parentheses. [c] At 40 °C. [d] EtI (2.9 mmol). [e] Reaction time (37 h). [f] MeI (3.4 mmol). [g] Reaction time (3 h). [h] MeI (6.8 mmol). [i] Reaction time (1 h). [j] $HO(CH_2)_{11}COOMe$ was formed in 2% yields. [k] EtI (3 mmol); CsF (3 mmol). [l] Yield of the diester.

Alkylation of Organotin Compounds.[10] Organotin carboxylates were prepared by heating an equimolar mixture of carboxylic acid and hexabutyldistannoxane in refluxing benzene for 3 h. The tributyltin carboxylates obtained by evaporating the benzene were subjected to the alkylation without purification (eq 3).[11] A DMF solution

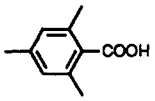
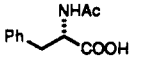
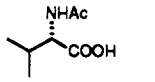
$$RCOOH + \tfrac{1}{2}Bu_3SnOSnBu_3 \xrightarrow{\text{benzene}} Bu_3SnOCOR \xrightarrow[DMF]{R'X/CsF} RCOOR' \qquad (3)$$

(9) Conversion of the THP acid to the hydroxy methyl ester by use of *p*-toluenesulfonic acid in MeOH resulted in contamination of an allenyl compound (10%) shown below: Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1988**, *110*, 4726.

(10) For a related study, see: Sato, T.; Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1989**, *30*, 2959.

(11) Similar results were obtained when the pure, isolated tributyltin benzoate was used: see Experimental Section.

Table III. Ester Formation from Tributyltin Carboxylates (eq 3)[a]

RCOOH	R'X	reactn time[b]	yield of ester,[c] %
PhCOOH	EtI	18	94 (99)
	CH_2=$CHCH_2Br$	18	96 (100)
c-$C_6H_{11}COOH$	EtBr	24	(91)
PhCH=CHCOOH	EtI	20	91
	EtBr	19	89
	EtI	30	91
	EtI	25	85

[a] Reaction conditions: RCOOH (1 mmol), $(Bu_3Sn)_2O$ (0.55 mmol), benzene, reflux, 3 h; R'X (1.5 mmol), CsF (1.5 mmol), DMF (3 mL), 30 °C. [b] Time for reaction between tributyltin carboxylate and alkyl halide. [c] Isolated yields; GLC yields are given in parenthese.

of the carboxylate (1 equiv) and the alkyl halide (1.5 equiv) was stirred in the presence of CsF (1.5 equiv) at 30 °C for 18–30 h. Aqueous workup afforded the esters in good to excellent yields as shown in Table III. It is particularly noteworthy that no racemization was detected with the organotin carboxylates derived from amino acids. The crucial role of CsF is apparent from the observation that exposure of $Bu_3SnOCOPh$ to EtI in the absence of CsF under similar conditions failed to afford the ethyl ester.[12]

In summary, CsF is a versatile promoter for the alkylation of carboxylic acids. Although the use of rather long reaction times (24 h usually) and the DMF solvent are necessary, it is evident that the CsF method can replace the diazomethane-based esterification in many cases. The mechanism of this reaction is not yet clear, but it is reasonable to assume that hydrogen bonding plays a key role in the reaction of free carboxylic acids as proposed for KF.[2] Since CsF is a good scavenger of hydrogen halides,[13] a wide spectrum of acid-sensitive functions is tolerant of the reaction conditions. On the other hand, the attack of the fluoride ion on the tin atom seems to drive the reaction of the organotin carboxylates. Since protection is a process which deactivates functional groups, direct transformation of protected functions needs special activation.[14] The overall driving force in the present case is presumably the strong interactions between the fluorine and tin atoms. The strong affinities of fluorine for hydrogen and tin enable these unique alkylation reactions of carboxylic acids.

Experimental Section

All solvents were purified by standard methods before use. CsF, (*E*)-2-hexenoic acid, (*E*)-3-hexenoic acid, 2,2-dimethylpropyl iodide, 12-hydroxydodecanoic acid, 2,4,6-trimethylbenzoic acid, 2-octynoic acid, triphenylacetic acid, (*S*)-2-phenylbutanoic acid, tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]europium(III) [Eu(hfc)$_3$] were obtained from Aldrich Chemical Co. (*S*)-*N*-Acetylvaline and 2-methyl-2-propyl iodide were purchased from Tokyo Kasei Kogyo. (*S*)- and (*R*)-2-Cyclohexyl-2-hydroxyacetic acid and (*S*)-2-hydroxypropanoic acid were products of Sigma, and other reagents were obtained from Wako Chemicals. These commercially available reagents were used without purification. The following compounds were prepared: 4-acetoxybenzoic acid,[15] tributyltin benzoate,[16] 12-(*tert*-butyldimethylsiloxy)dodecanoic acid [from 12-hydroxydodecanoic acid and *tert*-butyldimethylsilyl chloride:[17] IR (neat) 3050, 1708 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 6 H), 0.88 (s, 9 H), 1.22–1.34 (m, 14 H), 1.45–1.65 (m, 4 H), 2.33 (t, J = 7.33 Hz, 2 H), 3.59 (t, J = 6.72 Hz, 2 H), 9.80 (br, 1 H)], 7-(tetrahydropyranyloxy)-5-heptynoic acid,[8] 12-(tetrahydropyranyloxy)octadecanoic acid [from 12-hydroxyoctadecanoic acid in 3 steps (i. CH_2N_2, ii. DHP-H$^+$, iii. 1 N NaOH): IR (neat) 3050, 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.71 Hz, 3 H), 1.2–1.9 (m, 34 H), 2.33 (t, J = 7.33 Hz, 2 H), 3.50 (m, 1 H), 3.60 (m, 1 H), 3.92 (m, 1 H), 4.67 (m, 1 H), 8.90 (br, 1 H)].

The NMR and IR spectra of the following esters were in complete agreement with those of the authentic samples: ethyl benzoate, ethyl cyanoacetate, diethyl phthalate, ethyl cinnamate (Wako Chemicals), ethyl (*S*)-2-hydroxypropanoate (Aldrich), benzyl benzoate, isopropyl benzoate, ethyl dodecanoate (Tokyo Kasei Kogyo), allyl benzoate, methyl 2-octynoate (Pfaltz & Bauer), ethyl (*S*)-*N*-acetylphenylalanine (Sigma), ethyl cyclohexylcarboxylate,[15] ethyl triphenylacetate,[15] ethyl 2,4,6-trimethylbenzoate,[15] ethyl 2-benzoylbenzoate,[15] methyl 2-acetoxybenzoate,[15] methyl 4-acetoxybenzoate,[15] butyl 2,2-dimethylpropanoate,[18] methyl 7-(tetrahydropyranyloxy)-5-heptynoate,[8] and ethyl (*S*)-*N*-acetylvaline.[19] Methyl (*E*)-2-hexenoate, methyl (*E*)-3-hexenoate, methyl (*S*)-2-cyclohexyl-2-hydroxyacetate, methyl (*S*)-2-phenylbutanoate, methyl 12-(tetrahydropyranyloxy)octadecanoate, and 12-(*tert*-butyldimethylsiloxy)dodecanoate were obtained from the corresponding carboxylic acids and CH_2N_2. Physical data of these methyl esters are given below.

Physical Data. Methyl (*E*)-3-hexenoate: IR (neat) 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.99 (t, J = 7.33 Hz, 3 H), 2.05 (m, 2 H), 3.03 (dd, J = 1.10, 6.59 Hz, 2 H), 3.68 (s, 3 H), 5.51 (dtt, J = 1.10, 6.59, 15.0 Hz, 1 H), 5.61 (dtt, J = 1.10, 6.23, 15.0 Hz, 1 H). Methyl (*E*)-2-hexenoate: IR (neat) 1722, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J = 7.33 Hz, 3 H), 1.48 (m, 2 H), 2.18 (m, 2 H), 3.72 (s, 3 H), 5.82 (d, J = 15.7 Hz, 1 H), 6.97 (dt, J = 6.97, 15.7 Hz, 1 H). Methyl (*S*)-2-cyclohexyl-2-hydroxyacetate: $[\alpha]^{28}_D$ 29.0° (*c* 1.02, $CHCl_3$); IR (neat) 3490, 1732 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.1–1.5 (m, 6 H), 1.6–1.8 (m, 5 H), 2.66 (d, J = 6.59 Hz, 1 H), 3.79 (s, 3 H), 4.03 (dd, J = 3.30, 6.59 Hz, 1 H). Methyl (*S*)-2-phenylbutanoate: $[\alpha]^{19}_D$ 82.3° (*c* 1.0, $CHCl_3$); IR (neat) 1730 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 7.32 Hz, 3 H), 1.80 (m, 1 H), 2.09 (m, 1 H), 3.45 (t, J = 7.69 Hz, 1 H), 3.64 (s, 3 H), 7.29 (m, 5 H). Methyl 12-(tetrahydropyranyloxy)octadecanoate: IR (neat) 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.22 Hz, 3 H), 1.2–1.9 (m, 34 H), 2.30 (t, J = 7.69 Hz, 2 H), 3.48 (m, 1 H), 3.59 (m, 1 H), 3.66 (s, 3 H), 3.91 (m, 1 H), 4.65 (m, 1 H). Methyl 12-(*tert*-butyldimethylsiloxy)dodecanoate: IR (neat) 1739 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ –0.04 (s, 6 H), 0.80 (s, 9 H), 1.15–1.28 (m, 14 H), 1.37–1.58 (m, 4 H), 2.20 (t, J = 7.69 Hz, 2 H), 3.50 (t, J = 6.60 Hz, 2 H), 3.57 (s, 3 H).

General Procedure for the Preparation of Esters. Reaction of (*S*)-*N*-Acetylphenylalanine with Ethyl Iodide in the Presence of Cesium Fluoride. A mixture of (*S*)-*N*-acetylphenylalanine (207 mg, 1 mmol), CsF (227 mg, 1.5 mmol), EtI (234 mg, 1.5 mmol), and DMF (3 mL) was stirred at 15 °C for 24 h. The reaction mixture was combined with aqueous $NaHCO_3$ (50 mL) and extracted with EtOAc (100 mL). The organic layer was dried (Na_2SO_4) and evaporated. Column chromatography on silica gel (50:50 hexane–EtOAc) gave ethyl (*S*)-*N*-acetylphenylalanine (211 mg, 90%, ≥98% ee determined

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by ^1H NMR in the presence of Eu(hfc)$_3$) having the identical physical data with those of the authentic sample: $[\alpha]^{23}_D$ 87.4° (c 1.0, $CHCl_3$) ($[\alpha]^{23}_D$ (c 1.0, $CHCl_3$) of the authentic sample was 90.9°); mp 91.6–93.3 °C (mp of the authentic sample was 92.0–94.6 °C); ^1H NMR ($CDCl_3$) δ 1.09 (t, J = 7.33 Hz, 3 H), 1.83 (s, 3 H), 2.97 (m, 2 H), 4.02 (q, J = 7.33 Hz, 2 H), 4.73 (q-like, J = 6.59 Hz, 1 H), 6.71 (d, J = 7.69 Hz, 1 H), 7.0–7.2 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 13.6, 22.4, 37.4, 53.0, 60.9, 126.5, 128.0, 128.8, 135.8, 169.6, 171.5.

Large-Scale Preparation of Methyl 7-(Tetrahydropyranyloxy)-5-heptynoate from 7-(Tetrahydropyranyloxy)-5-heptynoic Acid and Methyl Iodide. A mixture of 7-(tetrahydropyranyloxy)-5-heptynoic acid (6.0 g, 26.4 mmol), CsF (8.8 g, 58 mmol), MeI (8.2 g, 58 mmol), and DMF (100 mL) was stirred at 30 °C for 18 h. The reaction mixture was extracted with EtOAc and washed with saturated aqueous $NaHCO_3$ (100 mL × 3). The organic layer was dried (Na_2SO_4) and evaporated to give an oil. Column chromatography on silica gel (95:5 hexane–EtOAc) of this oil provided methyl 7-(tetrahydropyranyloxy)-5-heptynoate (5.0 g, 79%) having spectral data identical with those of the authentic sample.[8]

General Procedure for the Preparation of Esters from Tributyltin Carboxylates and Alkyl Halides in the Presence of Cesium Fluoride. A mixture of hexabutyldistannoxane (656 mg, 1.1 mmol), (*S*)-*N*-acetylphenylalanine (414 mg, 2 mmol), and benzene (30 mL) was heated under refluxed in a Dean-Stark apparatus for 3 h. The benzene was removed under reduced pressure, and DMF (6 mL) was added. To this solution were added CsF (456 mg, 3 mmol) and EtI (468 mg, 3 mmol), and the reaction mixture was stirred at 30 °C for 30 h. Aqueous workup as described for reaction of (*S*)-*N*-acetylphenylalanine with ethyl iodide and column chromatography on silica gel (50:50 benzene–EtOAc) afforded ethyl (*S*)-*N*-acetylphenylalanine (430 mg, 91%, ≥98% ee determined by ^1H NMR in the presence of Eu(hfc)$_3$): $[\alpha]^{23}_D$ 88.0° (c 1.0, $CHCl_3$); mp 92.0–94.0 °C. The product was identical in all respects with the authentic sample.

Reaction of Tributyltin Benzoate with Ethyl Iodide. A. In the Presence of Cesium Fluoride. A mixture of tributyltin benzoate (411 mg, 1 mmol), EtI (234 mg, 1.5 mmol), CsF (228 mg, 1.5 mmol), and DMF (3 mL) was stirred at 30 °C for 2.5 h. Usual workup gave an oil. GLC analysis of this oil revealed the formation of ethyl benzoate in 95% yield.

B. In the Absence of Cesium Fluoride. A mixture of tributyltin benzoate (411 mg, 1 mmol), EtI (234 mg, 1.5 mmol), and DMF (3 mL) was stirred at 30 °C for 19 h. No ethyl benzoate could be detected by GLC analysis.

Registry No. CsF, 13400-13-0; KF, 7789-23-3; benzoic acid, 65-85-0; dodecanoic acid, 143-07-7; cyclohexanecarboxylic acid, 98-89-5; phthalic acid, 88-99-3; triphenylacetic acid, 595-91-5; 2,4,6-trimethylbenzoic acid, 480-63-7; (*E*)-2-hexenoic acid, 13419-69-7; (*E*)-3-hexenoic acid, 1577-18-0; 2-octynoic acid, 5663-96-7; *N*-acetylphenylalanine, 2018-61-3; (*S*)-2-hydroxypropanoic acid, 79-33-4; (*R*)-α-hydroxycyclohexaneacetic acid, 53585-93-6; (*S*)-α-hydroxycyclohexaneacetic acid, 61475-31-8; (*S*)-α-ethylbenzeneacetic acid, 4286-15-1; ethyl benzoate, 93-89-0; allyl benzoate, 583-04-0; benzyl benzoate, 120-51-4; isopropyl benzoate, 939-48-0; *tert*-butyl benzoate, 774-65-2; ethyl dodecanoate, 106-33-2; ethyl cyclohexanecarboxylate, 3289-28-9; butyl phthalate, 84-74-2; ethyl triphenylacetate, 5467-22-1; ethyl 2,4,6-trimethylbenzoate, 1754-55-8; methyl (*E*)-2-hexenoate, 13894-63-8; methyl (*E*)-3-hexenoate, 13898-61-8; methyl 2-octynoate, 111-12-6; ethyl (*S*)-2-hydroxypropanoate, 687-47-8; methyl (*R*)-α-hydroxycyclohexaneacetate, 92587-21-8; methyl (*S*)-α-hydroxycyclohexaneacetate, 121099-13-6; ethyl *N*-acetylphenylalanine, 2361-96-8; methyl 12-(tetrahydropyranyloxy)octadecanoate, 138982-91-9; ethyl cyanoacetate, 105-56-6; methyl 12-(*tert*-butyldimethylsiloxy)dodecanoate, 95841-29-5; ethyl 2-benzoxybenzoate, 604-61-5; methyl 2-acetoxybenzoate, 580-02-9; methyl 4-acetoxybenzoate, 24262-66-6; diethyl phthalate, 84-66-2; 12-(tetrahydroxypyranyloxy)octadecanoic acid, 79967-16-1; cyanoacetic acid, 372-09-8; 12-(*tert*-butyldimethylsiloxy)dodecanoic acid, 77744-42-4; 2-benzoylbenzoic acid, 85-52-9; 2-acetoxybenzoic acid, 50-78-2; 4-acetoxybenzoic acid, 2345-34-8; ethyl iodide, 75-03-6; ethyl methanesulfonate, 62-50-0; ethyl bromide, 74-96-4; allyl bromide, 106-95-6; benzyl bromide, 100-39-0; isopropyl iodide, 75-30-9; *tert*-butyl iodide, 588-17-0; 1-iodo-2,2-dimethylpropane, 15501-33-4; butyl iodide, 542-69-8; methyl iodide, 74-88-4; 12-hydroxydodecanoic acid, 505-95-3; 12-hydroxyoctadecanoic acid, 106-14-9; methyl (*S*)-α-ethylbenzeneacetate, 26164-15-8; 7-(tetrahydropyranyloxy)-5-heptynoic acid, 34506-49-5; methyl 7-(tetrahydropyranyloxy)-5-heptynoate, 50781-90-3; cinnamic acid, 621-82-9; *N*-acetylvaline, 96-81-1; ethyl cinnamate, 103-36-6; ethyl *N*-acetylvaline, 2382-78-7; hexabutyldistannoxane, 56-35-9; tributyltin benzoate, 4342-36-3.

Design, Synthesis, and Characterization of a "Shopping Basket" Bis-porphyrin. The First Examples of Triply Bridged Closely Interspaced Cofacial Porphyrin Dimers

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The biscobalt complexes of quadruply bridged closely interspaced 5,10,15,20-tetraphenylporphyrin dimers have proven to be effective catalysts for the 4e$^-$ reduction of O_2 to water when adsorbed onto the disk of a rotating ring–disk electrode or when dissolved in aqueous acidic medium.[1,2] From electrochemical and NMR data, we find a linear relationship between the interplanar distance in the porphyrin dimer and the percentage of O_2 reduced by the 4e$^-$ reduction pathway.[1]

By use of molecular dynamics, we find that the triply bridged porphyrin dimer **1a**, as compared to a comparable quadruply bridged porphyrin **2** is more flexible and can reach a shorter interplanar distance. Following the CHARM$_m$ modeling design, we have synthesized the first triply bridged porphyrin dimer **1a** and we have chosen to name it a "shopping basket" bis-porphyrin. The R group in **1a** was chosen to be *m*-pyridinesulfonamide because this group proved to effect the smallest possible interplanar distances in the limited family of quadruply bridged dimers that we have studied. In addition, **1a** is a convenient precursor to a water-soluble dimer.

Following Lindsey's method,[3] Lewis acid catalyzed (BF_3·Et_2O) high dilution condensation of 3 equiv of α-bromo-*m*-tolualdehyde[1] and 1 equiv of *m*-tolualdehyde with pyrrole (chloroform, room temperature) followed by in situ tetrachloro-1,4-benzoquinone oxidation of the intermediate porphyrinogen (chloroform, 60 °C) and separation by chromatography on silica gel using ethyl acetate/hexane (1:10) as eluent afforded the parent monom-

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