Pergamon

Tetrahedron Vol. 50, No. 2, pp. 465-474, 1994

0040-4020/94 $6.00+0.00

0040-4020(93)E0109-S

Electronic Control of Enantioselectivity in the Palladium-Catalyzed Asymmetric Allylic Substitution of *trans* 4-*t*Butyl-1-vinylcyclohexyl Benzoates

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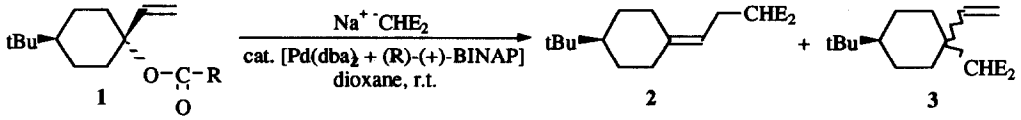
Abstract: *The enantioselectivity in the palladium-catalyzed substitution of allylic benzoates 1 by sodium dimethylmalonate was influenced by polar and steric effects of the substituents in the phenyl ring of the benzoate. Electron-donating p-substituents afforded effective chiral differentiation (up to 90%ee). Electron-withdrawing substituents, t-butyl-p-substituent , N,N-dialkylamino p-substituents or o-substituents were detrimental to steric differentiation (down to 22%ee). Di- and tri-methoxy substituted benzoates gave moderate asymmetric inductions (46-70 %ee).*

Introduction

In enantioselective transition metal-catalyzed reactions, efforts have been made to understand how chirality is transferred from the ligand to the product, in order to determine the parameters which control enantioselectivity and to improve it. For that purpose, an understanding of the overall stereochemical course of such a process requires detailed knowledge of the stereochemistry of each catalytic step and the stereochemical behavior of each intermediate. We have previously contributed to such studies in the palladium-catalyzed allylation reaction[1] by devising stereochemically biased models[2,3] to provide insight into the stereochemical course of the process. Thus, we, and others, showed that the oxidative addition step is under strong stereoelectronic control of the substrate,[2] that it occurs with inversion of configuration,[3,4] and that the stereochemistry of attack of the nucleophile on the η^3-allylpalladium intermediate complex depends on the nature of the nucleophile.[3,5]

Among the parameters which control the asymmetric induction in stoichiometric and catalytic enantioselective reactions, both electronic effects and steric effects have been shown to be significant.[5] In reactions involving aryl-containing substrates and / or reagents, electronic properties of substituents on the benzene ring have been shown to affect enantioselectivity.[7] In homogeneously catalyzed reactions, variations in the electronic character of the substrate[8] or of the catalyst[9] can govern the enantioselectivity.

We have previously reported on the palladium-catalyzed asymmetric substitution of *trans*-4-*t*-butyl-1-vinylcyclohexyl derivatives **1** by sodium dimethylmalonate to afford optically active cyclohexylidene **2** (E = CO_2CH_3).[10] The regioselectivity of this reaction was generally high, regioisomeric *cis*- and *trans*-**3** being produced in only small amounts (< 10% in most cases).



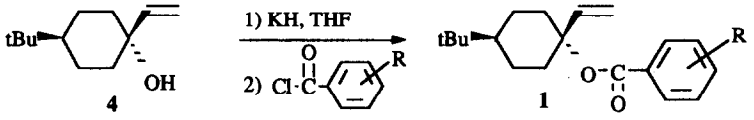
E = CO_2CH_3

Furthermore, we demonstrated that the enantioselectivity was influenced by the nature of the leaving group $RCOO^-$. (*R*)-(-)-**2** was obtained in 90% and 49% ee from 4-methoxybenzoate (**1**, R = 4-MeO-C_6H_4) and acetate (**1**, R = CH_3), respectively.[11] These results, in combination with the analysis of the stereochemical course of the reaction, suggested that oxidative addition is the enantioselective step in the overall substitution reaction.[11] The high enantioselectivities obtained from benzoates prompted us to study in detail the influence of various substituents on the aromatic ring in the substrate.

We report herein new results which show a connection between the steric and electronic properties of the leaving groups and enantioselectivity in the palladium-catalyzed reaction of *trans*-4-*t*butyl-1-vinylcyclohexyl benzoates **1** with dimethyl malonate. Two sets of experiments were conducted, one with *p*-substituted benzoates as leaving groups and the other with mono-, di- and tri-methoxy benzoates. The former were carried out to prove the influence of electronic properties of the leaving group, the latter included both steric and electronic effects.

Results and Discussion

1) Syntheses of the substrates



1a	R = 4-NO_2	**1f**	R = 4-*t*Bu	**1k**	R = 3-OMe
1b	R = 4-CN	**1g**	R = 4-OMe	**1l**	R = 2,6-$(OMe)_2$
1c	R = 4-Br	**1h**	R = 4-NMe_2	**1m**	R = 2,4-$(OMe)_2$
1d	R = H	**1i**	R = 4-NEt_2	**1n**	R = 2,4,6-$(OMe)_3$
1e	R = 4-Me	**1j**	R = 2-OMe	**1o**	R = 3,4,5-$(OMe)_3$

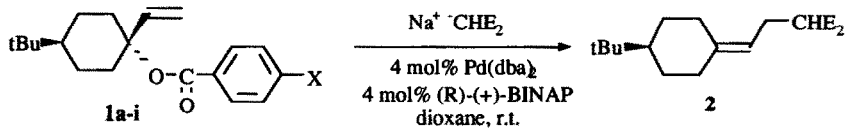
Reaction of benzoyl chlorides (commercial or prepared from the benzoic acid and oxalyl chloride) with the potassium salt of *trans*-4-*t*butyl-1-vinylcyclohexanol **4** gave the corresponding benzoates **1a-o** in moderate to good yields (22-91%).

2) Palladium-catalyzed asymmetric reactions of 4-substituted benzoates

Results on the reaction of *p*-substituted benzoates **1a-i** with $NaCHE_2$ under standard conditions are collected in Table 1. A plot of logarithms of the *R/S* ratios against Hammett's σ values[12] is shown in the Figure. A straight line with a slope of -0.80 was obtained for **1a-1e** and **1g** with a correlation coefficient r = 0.94. The meta-methoxy benzoate **1k** (see below) fits the correlation.

Table 1

Palladium-catalyzed asymmetric reactions of *p*-substituted benzoates



1a-i **2**

	X	σ	yield[a] (%)	regio-selectivity[b]	ee[c] (%)	log[(R)/(S)]
1a	NO_2	0.78	68	88	22	0.19
1b	CN	0.63	72	91	60	0.60
1c	Br	0.23	47	90	68	0.72
1d	H	0	77	95	76	0.87
1e	Me	-0.17	66	93	80	0.95
1f	*t*Bu	-0.20	80	95	73	0.81
1g	OMe	-0.27	63	96	90	1.28
1h	NMe_2	-0.60	90	88	61	0.62
1i	NEt_2	-0.60	73	93	83	1.03

[a]Isolated yield of substitution products **2** + *cis-* + *trans*-**3**. [b]% of product **2** in the mixture **2** + *cis-* + *trans*-**3**, determined by GLC analysis and ^1H NMR spectroscopy. [c]Determined by both polarimetry and ^1H NMR spectroscopy in the presence of $Eu(hfc)_3$.

The parent benzoate **1d** gave **2** in 76% ee. Electron-poor substrates such as nitrobenzoate **1a**, cyanobenzoate **1b** and bromobenzoate **1c** displayed lower enantioselectivities (22, 60 and 68% ee, respectively), whereas electron-rich methyl benzoate **1e** and methoxy benzoate **1g** produced an increase of the ee in product **2** (80 and 90%, respectively). *t*Butyl benzoate **1f** gave the same enantioselectivity as the parent benzoate **1d** within experimental error: the expected benefit of the electron donating alkyl group was not realized, likely for steric reasons. Benzoates **1h** and **1i** were expected to be promising, since the dialkylamino group is strongly electron releasing (σ = -0.60 for NMe_2). However the results obtained with these substrates were disappointing. The dimethylamino group gave a lower ee than the correlation would have predicted. A

possible explanation would be that the nitrogen atom of the substrate **1h** or the leaving group (p-dimethylaminobenzoate) could coordinate the palladium (with or without subsequent decoordination of one phosphorus ligand) to give different complexes from the one ("PdBINAP") involved with other substrates. These complexes could contribute for the catalysis in a lower enantioselective way. Such a defavorable contribution would be diminished for substrate **1i**, where the nitrogen atom is substituted by two ethyl groups thus involving less coordinating species.

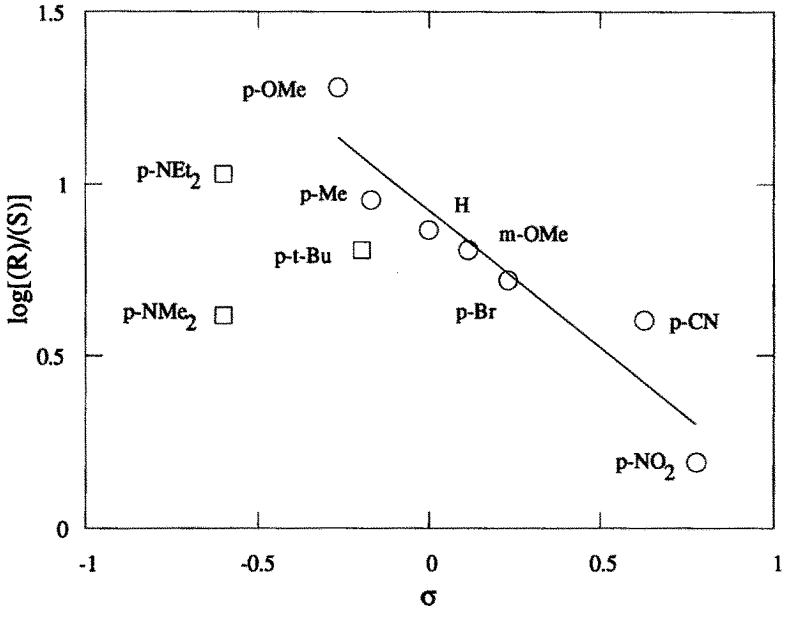


Figure: Hammett plot depicting enantiomeric composition of **2** from the palladium-catalyzed substitution of **1a-i, 1k** with sodium dimethylmalonate (enantiomeric excess range of 22-90%).

3) Palladium-catalyzed asymmetric reactions of mono-, di- and tri-substituted benzoates

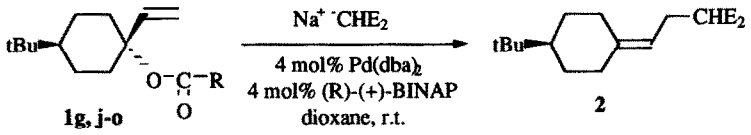
The important beneficial influence of a *p*-methoxy group on the enantioselectivity of this reaction prompted us to study in detail the mono-, di- and tri-substituted benzoates **1j-o** (Table 2). However, none of these substrates afforded **2** with a better ee than *p*-methoxybenzoate **1g**.

The meta-methoxy group, a poor electron-releasing group ($\sigma = 0.12$) in **1k** produced **2** in 73% ee. The ortho-substituted mono methoxy benzoate **1j** was slightly improved (80% versus 76% for the parent benzoate **1d**). It afforded, however, a lower ee than the para-methoxy compound, suggesting that steric hindrance by a 2-substituent is detrimental for asymmetric induction. A strongly unfavorable steric influence was observed with 2,6-disubstituted substrates **1l** and **1n** (46 and 51% ee, respectively). The positive effects of *o*- and *p*-methoxy

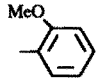
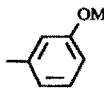
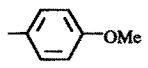
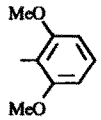
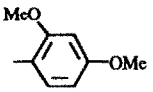
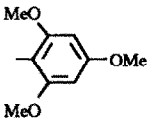
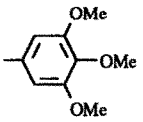
substituents (in **1j** and **1g** respectively) did not cooperate in 2,4-dimethoxybenzoate **1m** which gave **2** in only 70% ee. Electron releasing methoxy substituents in the 3 and 5 positions as in **1o** afforded only fair (61%) enantioselectivity for the reaction.

Table 2

Palladium-catalyzed asymmetric reactions of mono-, di, and tri-methoxybenzoates



1g, j-o **2**

no.	R	yield[a] (%)	regio-selectivity[b]	ee[c] (%)
1j		77	91	80
1k		75	92	73
1g		63	96	90
1l		67	88	46
1m		76	91	70
1n		72	87	51
1o		69	90	61

[a]Isolated yield of substitution products **2** + *cis*- + *trans*-**3**.[b] % of product **2** in the mixture **2** + *cis*- + *trans*-**3**, determined by GLC analysis and ^{1}H NMR spectroscopy. [c]Determined by both polarimetry and ^{1}H NMR spectroscopy in the presence of Eu(hfc)$_3$.

Conclusion

In the palladium-catalyzed substitution of allylic benzoates **1** by sodium dimethylmalonate, it was shown that both polar and steric effects of the substituents in the phenyl ring of the benzoate influenced the enantioselectivity of the reaction. *p*-Methoxy substituent gave the higher ee (90%) in the product. Since the reaction likely proceeds via a reactant-like ee-determining transition state, poor leaving groups (with electron-withdrawing substituents), afforded poorer steric differentiation of diastereomeric transition structures (as low as 22% ee) owing to a great separation between the substrate and catalyst. Di- and tri-methoxy substituted benzoates usually gave lower asymmetric inductions (46-70 %ee). The lower than expected enantioselectivities recorded from the substrates **1h** and **1i** could be due to modification of the catalytic species, owing to the coordinative properties of the dialkylamino groups.

Experimental

General

All reactions involving palladium catalysis were carried out under argon using Schlenk techniques. Tetrahydrofuran (THF) was distilled under argon from sodium benzophenone ketyl immediately before use. Dioxane was dried over CaH_2 and distilled prior to use.

^1H NMR spectra were recorded at 250 or 200 MHz in $CDCl_3$ with tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded at 62.9 MHz in $CDCl_3$. Infrared spectra were recorded on a Perkin-Elmer 883 spectrometer, and are reported in cm^{-1}.

The following materials were obtained from commercial sources: $Pd(dba)_2$ (where dba denotes dibenzylideneacetone);[13] $Eu(hfc)_3$ (where hfc denotes 3-(heptafluoropropylhydroxymethylene)-(+)-camphorato); (R)-(+)-BINAP.

Sodium dimethyl malonate

Sodium hydride (3 g of a 80% dispersion in mineral oil ,100 mmol NaH) was washed with pentane (4 x 10 mL), and then dried under vacuum. THF (100 mL)was added, and then 11.5 mL (100 mmol) of dimethyl malonate over a 2-h period. The turbid mixture was filtered and the solvent was evaporated. The grey solid was stored under argon.

Preparation of *trans*-4-*t*Butyl-1-vinylcyclohexyl Benzoates

The reported procedure for the synthesis of N,N-dimethylcarbamates[14] was adopted as illustrated for the synthesis of **1g**: 2.1 g of a 35% dispersion of potassium hydride in mineral oil was washed with pentane (4 x 10 mL) and dried under vacuum to give 739 mg (18.4 mmol) of dry KH, which was suspended in THF (50 mL). Then *trans*-4-*t*butyl-1-vinylcyclohexanol **4**[15] (2 g, 11.0 mmol) in THF (50 mL) was added dropwise at -10°C.

The mixture was allowed to warm to room temperature, maintained there for 0.5 h, after recooling to -10°C, 4-methoxybenzoyl chloride (2.25 g, 13.2 mmol) in THF (20 mL) was added dropwise. After stirring overnight at room temperature, the reaction mixture was diluted with ether (10 mL), washed with saturated aqueous $NaHCO_3$ (2 x 10 mL). The combined aqueous phase was extracted with ether (3 x 10 mL) and the combined ethereal extracts were dried ($MgSO_4$) and concentrated. The crude product was purified by flash chromatography (silica, hexane/ ethyl acetate: 9/1), and then by Kugelrohr distillation to give *trans*-4-*t*butyl-1-vinylcyclohexyl 4-methoxybenzoate **1g** (2.8 g, 8.9 mmol, 81%).

Non-commercial acyl chlorides (dimethylamino-, diethylamino-, and 2,4,6-trimethoxy-benzoyl chlorides) were prepared by addition of 3 equivalents of oxalyl chloride to the corresponding benzoic acid in hexane solution in the presence of a small amount of DMF. These were used without further purification after evaporation of solvent and excess oxalyl chloride.

4-Nitrobenzoate **1a**, from 4-nitrobenzoyl chloride: 62% yield. ^{1}H NMR δ 0.85 (9H, s), 1.10-1.30 (3H, m), 1.70-1.90 (4H, m), 2.60 (2H, m), 5.37 (1H, dd, *J* = 11 and 1Hz), 5.41 (1H, dd, *J* = 18 and 1Hz), 6.23 (1H, dd, *J* = 18 and 11Hz), 8.12 (2H, d, *J* = 9 Hz), 8.24 (2H, d, *J* = 9 Hz). ^{13}C NMR δ 24.1, 27.5, 32.2, 35.9, 47.4, 84.3, 117.7, 123.3, 130.5, 137.1, 138.5, 150.2, 163.1. IR (KBr disk) 2947, 2868, 1716, 1607, 1524, 1367, 1348, 1300, 1265, 1120, 1104, 1009, 940, 839, 717. Found C, 68.94; H, 7.63; N, 4.25. $C_{19}H_{25}NO_4$ calc: C, 68.86; H, 7.60; N, 4.23.

4-Cyanobenzoate **1b**, from 4-cyanobenzoyl chloride: 71% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.25 (3H, m), 1.65-1.80 (4H, m), 2.55 (2H, m), 5.38 (1H, dd, *J* = 11 and 1Hz), 5.41 (1H, dd, *J* = 18 and 1Hz), 6.23 (1H, dd, *J* = 18 and 11Hz), 7.70 (2H, d, *J* = 9 Hz), 8.07 (2H, d, *J* = 9 Hz). ^{13}C NMR δ 24.1, 27.4, 32.2, 35.9, 47.3, 83.9, 115.8, 117.5, 118.0, 129.9, 132.0, 135.5, 138.5, 163.2. IR (KBr disk) 2965, 2867, 2229, 1712, 1282, 1109, 1019, 946, 861, 768. Found C, 77.17; H, 8.24; N, 4.46. $C_{20}H_{25}NO_2$ calc: C, 77.13; H, 8.09; N, 4.50.

4-Bromobenzoate **1c**, from 4-bromobenzoyl chloride: 55% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.35 (3H, m), 1.60-1.85 (4H, m), 2.60 (2H, m), 5.35 (1H, dd, *J* = 11 and 1Hz), 5.41 (1H, dd, *J* = 18 and 1Hz), 6.23 (1H, dd, *J* = 18 and 11Hz), 7.53 (2H, d, *J* = 8Hz), 7.82 (2H, d, *J* = 8Hz). ^{13}C NMR δ 24.1, 27.5, 32.2, 36.0, 47.4, 83.2, 109.8, 117.2, 127.5, 131.0, 131.4, 138.9, 164.3. IR (KBr disk) 2945, 1713, 1589, 1285, 1263, 1105, 1011, 757.

Benzoate **1d**, from benzoyl chloride: 47% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.65-1.85 (4H, m), 2.55 (2H, m), 5.32 (1H, dd, *J* = 11 and 1Hz), 5.38 (1H, dd, *J* = 18 and 1Hz), 6.25 (1H, dd, *J* = 18 and 11Hz), 7.35-7.55 (3H, m), 7.95-8.00 (2H, m). ^{13}C NMR δ 24.1, 27.5, 32.2, 36.1, 47.4, 82.7, 116.9. 128.1, 129.4, 131.7, 132.4, 139.2, 165.1. IR (liquid film) 2947, 2868, 1717, 1314, 1283, 1263, 1112, 1024, 710. Found C, 79.80; H, 8.90. $C_{19}H_{26}O_2$ calc: C, 79.68; H, 9.15%.

4-Methylbenzoate **1e**, from 4-methylbenzoyl chloride: 72% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.70-1.85 (4H, m), 2.37 (3H, s), 2.60 (2H, m), 5.31 (1H, dd, *J* = 11 and 1Hz), 5.37 (1H, dd, *J* = 18 and 1Hz), 6.25 (1H, dd, *J* = 18 and 11Hz), 7.18 (2H, d, *J* = 8 Hz), 7.85 (2H, d, *J* = 8 Hz). ^{13}C NMR δ 21.6, 24.1, 27.5, 32.2, 36.1, 47.4, 82.4, 116.7, 128.8, 129.0, 129.5, 139.3, 143.0, 165.2. IR (KBr disk) 2952, 1706, 1611, 1283, 1176, 1108, 1018, 902, 754. Found C, 80.12; H, 9.29. $C_{20}H_{28}O_2$ calc: C, 79.95; H, 9.39.

4-*t*Butylbenzoate **1f**, from 4-tert-butylbenzoyl chloride: 91% yield. ^{1}H NMR δ 0.85 (9H, s), 1.10-1.40 (3H, m), 1.35 (9H, s), 1.70-1.90 (4H, m), 2.60 (2H, m), 5.30 (1H, dd, J = 11 and 1Hz), 5.36 (1H, dd, J = 18 and 1Hz), 6.24 (1H, dd, J = 18 and 11Hz), 7.40 (2H, d, J = 9 Hz), 7.89 (2H, d, J = 9 Hz). ^{13}C NMR δ 24.1, 27.5, 31.1, 32.2, 34.9, 36.1, 47.4, 82.4, 116.7, 125.1, 129.0, 129.3, 139.3, 156.0, 165.1. IR (KBr disk) 2963, 2904, 2866, 1713, 1283, 1264, 1248, 1196, 1119, 1016, 934, 854, 778. Found C, 80.95; H, 10.11. $C_{23}H_{34}O_2$ calc: C, 80.65; H, 10.01.

4-Methoxybenzoate **1g**, from 4-methoxybenzoyl chloride: 81% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.65-1.85 (4H, m), 2.55 (2H, m), 3.83 (3H, s), 5.31 (1H, dd, J = 11 and 1Hz), 5.37 (1H, dd, J = 18 and 1Hz), 6.25 (1H, dd, J = 18 and 11Hz), 6.87 (2H, d, J = 9 Hz), 7.92 (2H, d, J = 9 Hz). ^{13}C NMR δ 24.1, 27.5, 32.2, 36.1, 47.4, 55.3, 82.3, 113.3, 116.6, 124.2, 131.4, 139.3, 163.0, 164.9. IR (KBr disk) 2951, 2866, 1709, 1607, 1314, 1280, 1255, 1165, 1112, 1027, 772. Found C, 76.11; H, 8.99. $C_{20}H_{28}O_3$ calc: C, 75.91; H, 8.92.

4-N,N-Dimethylaminobenzoate **1h**, from 4-dimethylaminobenzoic acid: 35% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.65-1.85 (4H, m), 2.55 (2H, m), 3.00 (6H, s), 5.28 (1H, dd, J = 11 and 1Hz), 5.35 (1H, dd, J = 18 and 1Hz), 6.25 (1H, dd, J = 18 and 11Hz), 6.63 (2H, d, J = 9 Hz), 7.84 (2H, d, J = 9 Hz). ^{13}C NMR δ 24.2, 27.6, 32.3, 36.3, 40.1, 47.5, 81.6, 110.6, 116.2, 118.7, 131.1, 139.8, 153.1, 165.7. IR (KBr disk) 2950, 2866, 1694, 1612, 1368, 1286, 1187, 1106, 771. Found C, 76.52; H, 9.51; N, 4.48. $C_{21}H_{31}NO_2$ calc: C, 76.55; H, 9.25; N, 4.25.

4-N,N-Diethylaminobenzoate **1i**, from 4-diethylaminobenzoic acid: 40% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.15 (6H, t, J = 7Hz), 1.60-1.85 (4H, m), 2.55 (2H, m), 3.37 (4H, q, J = 7Hz), 5.27 (1H, dd, J = 11 and 1Hz), 5.34 (1H, dd, J = 18 and 1Hz), 6.25 (1H, dd, J = 18 and 11Hz), 6.58 (2H, d, J = 9 Hz), 7.82 (2H, d, J = 9 Hz). ^{13}C NMR δ 12.4, 24.1, 27.5, 32.2, 36.3, 44.4, 47.4, 81.3, 110.0, 116.1, 117.6, 131.3, 139.7, 150.6, 165.5. IR (KBr disk) 2949, 1694, 1605, 1522, 1405, 1296, 1263, 1185, 1156, 1110, 1025, 768. Found C, 77.36; H, 9.68; N, 3.76. $C_{23}H_{35}NO_2$ calc: C, 77.26; H, 9.87; N, 3.92.

2-Methoxybenzoate **1j**, from 2-methoxybenzoyl chloride: 85% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.65-1.85 (4H, m), 2.60 (2H, m), 3.86 (3H, s), 5.32 (1H, dd, J = 11 and 1Hz), 5.41 (1H, dd, J = 18 and 1Hz), 6.26 (1H, dd, J = 18 and 11Hz), 6.85-7.00 (2H, m), 7,40 (1H, td, J = 8 and 2Hz), 7.71 (1H, dd, J = 8 and 2Hz). ^{13}C NMR δ 24.1, 27.5, 32.2, 36.1, 47.4, 55.9, 82.7, 112.0, 116.8, 119.9, 121.5, 131.4, 132.9, 139.3, 159.1, 164.6. IR (liquid film) 2947, 1727, 1491, 1466, 1310, 1254, 1128, 1076, 1025, 755. Found C, 75.73; H, 9.06. $C_{20}H_{28}O_3$ calc: C, 75.91; H, 8.92.

3-Methoxybenzoate **1k**, from 3-methoxybenzoyl chloride: 59% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.65-1.85 (4H, m), 2.60 (2H, m), 3.85 (3H, s), 5.33 (1H, dd, J = 11 and 1Hz), 5.38 (1H, dd, J = 18 and 1Hz), 6.24 (1H, dd, J = 18 and 11Hz), 7.05 (1H, ddd, J = 8, 3 and 1Hz), 7.29 (1H, t, J = 8Hz), 7.49 (1H, dd, J = 3 and 1Hz), 7.56 (1H, dt, J = 8 and 1Hz). ^{13}C NMR δ 24.1, 27.4, 32.2, 36.0, 47.4, 55.3, 82.8, 113.9, 116.9, 118.8, 121.8, 129.1, 133.0, 139.1, 159.4, 164.9. IR (liquid film) 2952, 2869, 1717, 1586, 1485, 1466, 1284, 1229, 1100, 1044, 755. Found C, 75.93; H, 8.90. $C_{20}H_{28}O_3$ calc: C, 75.91; H, 8.92.

2,6-Dimethoxybenzoate **1l**, from 2,6-dimethoxybenzoyl chloride: 62% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.60-1.85 (4H, m), 2.55 (2H, m), 3.77 (6H, s), 5.36 (1H, dd, J = 11 and 1Hz), 5.48 (1H, dd,

J = 18 and 1Hz), 6.28 (1H, dd, J = 18 and 11Hz), 6.50 (2H, d, J = 9 Hz), 7.21 (1H, t, J = 9 Hz). ^{13}C NMR δ 24.1, 27.5, 32.2, 36.2, 47.3, 55.9, 83.5, 104.0, 114.5, 116.5, 130.3, 139.0, 157.1, 164.9. IR (KBr disk): 2942, 2866, 1732, 1597, 1473, 1432, 1364, 1291, 1255, 1113, 1072, 1019, 925, 902, 789, 736. Found C, 73.01; H, 8.78. $C_{21}H_{30}O_4$ calc: C, 72.80; H, 8.73.

2,4-Dimethoxybenzoate **1m**, from 2,4-dimethoxybenzoyl chloride: 61% yield. ^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.60-1.80 (4H, m), 2.60 (2H, m), 3.80 (3H, s), 3.84 (3H, s), 5.29 (1H, dd, J = 11 and 1Hz), 5.37 (1H, dd, J = 18 and 1Hz), 6.25 (1H, dd, J = 18 and 11Hz), 6.40-6.50 (2H, m), 7.78 (1H, d, J = 9 Hz). ^{13}C NMR δ 24.1, 27.5, 32.2, 36.1, 47.4, 55.4, 55.8, 82.1, 98.9, 104.2, 113.6, 116.5, 133.6, 139.6, 161.4, 163.8, 164.0. IR (liquid film): 2945, 2868, 1721, 1608, 1578, 1465, 1414, 1254, 1211, 1163, 1128, 1077, 1029. Found C, 72.88; H, 8.58. $C_{21}H_{30}O_4$ calc: C, 72.80; H, 8.73.

2,4,6-Trimethoxybenzoate **1n**, from 2,4,6-trimethoxybenzoic acid: 22% yield.^{1}H NMR δ 0.85 (9H, s), 1.10-1.30 (3H, m), 1.60-1.85 (4H, m), 2.55 (2H, m), 3.77 (6H, s), 3.79 (3H, s), 5.33 (1H, dd, J = 11 and 1Hz), 5.45 (1H, dd, J = 18 and 1Hz), 6.05 (2H, s), 6.26 (1H, dd, J = 18 and 11Hz). ^{13}C NMR δ 24.1, 27.5, 32.3, 36.3, 47.4, 55.4, 56.0, 83.2, 90.7, 107.7, 116.4, 139.2, 158.4, 162.0, 164.9. IR (KBr disk): 2954, 1721, 1611, 1591, 1461, 1416, 1274, 1258, 1230, 1207, 1161, 1130, 1098, 1048.

3,4,5-Trimethoxybenzoate **1o**, from 3,4,5-trimethoxybenzoyl chloride: 79% yield.^{1}H NMR δ 0.85 (9H, s), 1.05-1.30 (3H, m), 1.65-1.85 (4H, m), 2.55 (2H, m), 3.87 (6H + 3H, 2 s), 5.34 (1H, dd, J = 11 and 1Hz), 5.39 (1H, dd, J = 18 and 1Hz),.6.24 ppm (1H, dd, J = 18 and 11Hz), 7.23 (2H, s). ^{13}C NMR δ 24.1, 27.5, 32.1, 36.0, 47.4, 56.0, 60.8, 82.8, 106.6, 116.9, 126.7, 139.0, 141.8, 152.7, 164.6. IR (KBr disk): 2949, 1701, 1588, 1463, 1413, 1339, 1229, 1184, 1127, 1024, 951. Found C, 70.02; H, 8.38. $C_{22}H_{32}O_5$ calc: C, 70.18; H, 8.57.

General Procedure for Palladium-Catalyzed Reactions

A typical reaction procedure is as follows: a mixture of $Pd(dba)_2$ (11.5 mg, 0.02 mmol) and (+)-BINAP (12.5 mg, 0.02 mmol) was stirred for 0.25 h in 0.5 mL of dioxane. *trans*-4-*t*Butyl-1-vinylcyclohexyl benzoate **1d** (161 mg, 0.56 mmol) in dioxane (1 mL) was then added by syringe. After stirring for 0.25 h , the solution was added to a stirred suspension of sodium dimethyl malonate (200 mg, 1.30 mmol) in dioxane (0.5 mL). The reaction mixture was stirred at room temperature overnight, then diluted with ether (10 mL) and the organic phase washed with 2 x 10 mL of saturated aqueous NH_4Cl. The combined aqueous phases were extracted with ether (3 x 10 mL) and the combined ethereal extracts were dried ($MgSO_4$) and concentrated. The crude product was purified by flash chromatography (silica, cyclohexane/ ethyl acetate: 9/1), then by Kugelrohr distillation to give a mixture of **2** and *cis*- + *trans*-**3** in a 95 : 4 : 1 ratio (127.5 mg, 77% yield): $[\alpha]_D^{20}$ -11.35°± 0.30° (c 2.89, toluene), corresponding to $[\alpha]_D^{20}$ -11.95°± 0.32° (c 2.89, toluene) for pure **2**: ee 76%± 4%. Examination of the ^{1}H NMR spectrum in the presence of $Eu(hfc)_3$ gave 74%± 5%. **2**: ^{1}H NMR δ 0.85 (9H, s), 0.90-1.20 (3H, m), 1.55-1.75 (1H, m), 1.75-1.95 (2H, m), 2.00 (1H, d), 2.20 (1H, d), 2.45-2.75 (3H, m), 3.4 (1H, t, J = 8Hz), 3.72 (6H, s), 5.00 (1H, t, J = 8Hz). ^{13}C NMR δ 26.8, 27.5, 28.3, 28.4, 29.1, 32.3, 36.9, 48.2, 52.1, 52.3, 52.4, 115.6, 143.1, 169.50, 169.53. IR (liquid film): 2951, 2867, 1755, 1741, 1437, 1365, 1338, 1233, 1149. Found C, 69.08; H, 9.52. $C_{17}H_{28}O_4$ calc: C, 68.88; H, 9.52.

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(*Received* 19 *May* 1993)